

Final Report

Traditional Medicine: Modern Approach For Affordable Global Health

World Health Organization, Geneva

Commission on Intellectual Property, Innovation and Public Health (CIPHI)

Study Nine: Traditional Medicine

Research question: Traditional Medicine: Could more effective use be made of them in providing affordable treatments?

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This study reviews the existing evidence base on the use of Traditional Medicines (TM) in meeting the health needs of populations in developing countries. In doing this, the paper analyzes the benefits in terms of accessibility, availability and affordability, including studies on the health benefit and cost-benefit and considers the scope for using TM systems to deliver modern medicines, and the possibility for conjunctive use. The study also reviews existing evidence on current innovative efforts in TM to combat diseases that disproportionately affect developing countries, and the challenges and difficulties related to: regulatory issues, effectiveness of the patent system, and reliance on renewable natural resources, documenting traditional knowledge about medicine.

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Traditional Medicine: Modern Approach For Affordable Global Health

Executive Summary	4
1. Advances and Inequities - A Paradox in Global Health	10
1.1. Background of Study	
1.2. Science, Technology and Demography	
1.3. Health needs of Developing Countries	
2. A Handy Solution to Impasse - Traditional Medicine	31
2.1. Definitions and Development	
2.2. Diversity and Distinctiveness	
2.3. Healthcare Delivery and Treatments	
2.4. Existing Documentation	
2.5. Current Global Perspective	
3. Merit of the Option	45
3.1. Efficacy and Evidence	
3.2. Safety and Hazards	
3.3. Quality Control and Regulations	
4. A High Priority Need - Public Health Agenda	68
4.1. Availability, Accessibility and Affordability	
4.2. Economics and Financing	
4.3. Policy Issues	
4.4. Relationships and Integration	
5. Global Justice and Ecological Obligation	84
5.1. Intellectual Property	
5.2. Markets, Business and Trade	
5.3. Biodiversity	
6. An Opportunity in Adversity	107
6.1. Innovation and Drug Discovery	
6.2. Research and Development	
6.3. Education and Human Resources	
7. A Win-Win Game and A Reason for Hope	135
7.1. Observations	
7.2. Conclusions	
7.3. Recommendations	
Acknowledgement	159
<u>Annexure:</u>	162
Glossary, Questionnaire, Bibliography and Suggested Readings	

**“Knowledge is proud that she knows so much;
Wisdom is humble that she knows no more”**

William Cowper

Executive Summary:

Last 100 years brought forth the best in science and technology at the service of human kind and yet failed to bring, enlightenment, mechanism and may be luck to make those magnificent advances accessible, available and affordable with decent equity to all. Rather, the world stands more divided and more polarized than ever before and this chasm is widening at an alarming pace. While creativity and talent reinforcement by technological resources seem poised to soar towards unprecedented heights, suddenly we find ourselves confronted and constrained by the old ghouls of wars, pandemics, and poverty that for a brief while we thought we had left behind for good. Moreover, the paradox of the paradox is that this discomfoting reality has afflicted even the rich and the privileged. The richest among the developed countries, the USA has very recently seen the highest number of its citizenry without coverage or access to health care. Leaders, policy makers, and scholars, world over are grappling with solutions to these complex, not just complicated problems - because there is no single magic bullet, no single solution. This report, within the paradigm of health, but against the backdrop of the philosophical underpinnings outlined above, tries to explore the place and utility of Traditional Medicine as a vehicle to affordable health to large un-served or underserved population in the developing countries.

On a closer look we see one more layer to this impasse. Just as, global village is stuck at a bottleneck regarding equity of distribution of modern medicine among the world population the modern science is struck at another stagnation - of bottleneck of innovation. In contrast to availability of humungous data and resources, newer innovative

discoveries are not pouring in at the expected rates or paradigms, tipping the benefit cost ratio to an alarming low. Contemporary conventional drug discovery arena has become devoid or almost empty of players where the old champions are worn out and new are nowhere in sight. The situation seems to demand rejuvenation, not of recruitment efforts but of efforts to shift games to a new arena. The cause behind may seem purely academic and technical but nonetheless, it is inseparably connected with the policy issue delineated above. This must be seen in the light of and against the backdrop of this underpinning.

It is argued that TM runs afoul on validity count. Broadly the deficiencies in TM can be categorized as: Lack of validation, Lack of standardization, Lack of delivery infrastructure, Lack of integration- intra or interdisciplinary. If we analyze undercurrents that fuel these lacunae we see main two - poverty and policy. Poverty, directly connected to the issue of affordability of health care, rampant poverty is the prime cause of use, misuse and abuse of Traditional Medicine. If there were no poverty in the developing countries, modern medicine would have undoubtedly rendered TM extinct through Darwinian processes. Poverty also provoked and provokes abuse of TM by charlatans that in turn fed into skepticism and cynicism about TM in the mind of scholars and policy makers. Admitted that a big component of what is represented by TM might be chaff but it is no wisdom to throw out the baby with the tub. Unless the vicious circle of poverty is broken, neither the stock of majority of population in the developing country as far as the health care is concerned can be raised, nor can what that is good in TM can be salvaged and used to further modern medicine.

The second reason is related to policy and economy that make a feeder loop where both drive each other. To bring affordable health care to the population in the developing world, local governments' and international agencies' involvement is of paramount importance. Prime issues of concern for attention of local government and/or policy makers are: endorsement of TM, validation of efficacy, regulation of safety, standardization of materials and harmonization of practices, professionals' training, construction of delivery infrastructure, protection of intellectual property, enforcement of equitable distribution of TM, guarantee of sustainability of supply of resources, supervision of price structure, IPR inequities and back pressure from pharmaceutical industries (lack of innovations and productive outcomes). This makes new approaches such as Reverse Pharmacology and Systems Biology more attractive that provide innovation opportunities that are based on experiential wisdom and holistic viewpoint of TM. In a utopia, IPR would belong to entire humanity. But we are far from being there. Current policies on Intellectual Property Rights at international level are positive detriments to making health care available and affordable to developing countries and therefore the *sue generis* systems become more important to protect interests of the traditional knowledge from possible exploitations. While new drug discovery slows down, reducing profits from western market, pharmaceuticals are not only in a defensive turf battle posture at home but are applying rules of the game uniformly to uneven playfields. This makes medicines unaffordable to the developing countries while at the same time hurts the corporations by making them lose the partial gain that they could make by flexing to accommodate economic limitations of the developing world. This same aggressive posture on the other hand, turns on a vicious spiral that sends holders -

macro and micro both, into a defensive secretive mode that diminishes innovative original ideas flowing from TM to modern medicine.

This report tried to observe and witness the twilight prior to the dawn of a new age where modern medicine and traditional medicine will blend into a holistic synergy in tune with dynamical complex systems thinking, to provide affordable, available and accessible health to every citizen of global human society and render humanity free from its petty strife to move forward to express the best of its elements. Needless to say, like any twilight vision, what was seen was full of haze, blur, uncertainty, trepidation, insecurity, mistrust and above all confusion. However, the inkling and insinuation of dawn was unmistakable. The observations made broadly were passive (extensive literature review), active-passive (telephonic interviews, questionnaire surveys, private correspondences) and active (visits to Institutes of interest).

Many sections of this report provide flowcharts, tables, logic diagrams, examples, and case studies where the principles discussed put to exemplary real life practice. Lastly, the report provides some key recommendations: need to give basic respect and recognition to TM, more thrust on TM practices, philosophies and basic principles and not just medicines; evidence-based research at all levels of preclinical and clinical stages should be strengthened and supported; increased safety and quality harmonization; global guidelines on policy and regulations, validation mechanisms and TM networking research; innovative and apt methodologies supported by common protocols or guidelines on TM research need to be developed; traditional practices, healers and ecosystem should

not be exploited during bioprospecting, WHO and bodies like CBD should work together to emphasize importance of health related issues at the backdrop of biodiversity; improved financing TM education, research, practice and a road map to strengthen its reach; strengthening existing and create new state-of-the-art- facilities for evidence-based research; human resource development; world class institutions/ colleges should be established in every country where there is strong TM presence; globally trained TM practitioners; develop more WHO Collaborating Centers of TM in countries where it has major presence; undertake or sponsor detailed studies related to TM impact on public health.

Finally, the report returns to the question that CIPIH asked to begin with “Could more effective use be made of Traditional Medicine in providing affordable treatments?” and concludes that at this stage, an assertive answer can indeed be given with sufficient confidence, albeit with numerous caveats. But those cannot be a reason to falter or flinch. After all, what is a problem that is without challenges? The road to affordable health in developing world is rough and full of stumbling blocks en route. Traditional Medicine is one tiny candle (among many) that can illuminate the path in its own limited way, for humanity to achieve an equitable affordable health for each and every citizen of this planet. What if TM is a candle and not a blazing torch? Great Chinese philosopher Con-Fu-Tse said, “It is better to light a candle than to curse the darkness.” In this old wisdom rests our hope and reason to make attempts.

“If the misery of the poor be caused not by the laws of nature, but by our institutions, great is our sin”.

Charles Darwin

Chapter 1

Advances and Inequities: A Paradox in Global Health

1.1. Background of the Study

Disparity in health care delivery, particularly related to affordability issue, and then still more particularly in the developing countries has become a matter of great concern for world polity. While trying to address the above stated challenge The Commission on Intellectual Property, Innovation and Public Health (CIPIH) of the World Health Organization (WHO) Geneva asked, “Could more effective use be made of Traditional Medicine in providing affordable treatments?” This study, among many others, was commissioned to provide CIPIH-WHO a lay of the land of a sort, to navigate the available policy/action space.

Traditional, complementary and/or alternative medicine (generally represented as "Traditional Medicine" or TM in this document) can be used as an input to "modern" pharmaceutical research, but also as a source of effective interventions in its own right. An issue for the Commission is to consider ways in which the potential of traditional medicine for providing affordable treatments could be better realized. Many people in developing countries, particularly those in rural areas, have more access to "traditional" than "modern" medicines and use them more frequently². They often turn to traditional healers to treat sickness. For example, an estimated 90 percent of people in Ethiopia use

² Traditional Medicine – Growing Needs and Potential, WHO Policy Perspectives on Medicine. No.2 May 2002, World Health Organization, Geneva.

traditional medicine to meet their primary health care needs, as do 70 percent of people in Benin, India, Rwanda and Tanzania³. Traditional medicine has been defined by WHO as "diverse health practices, approaches, knowledge and beliefs incorporating plant-, animal- and/or mineral-based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well-being, as well as to treat, diagnose or prevent illness". In some cases, "traditional" medicine may be systematized and written down (e.g. as in the Indian texts such as the Ayurveda); in other cases, it is a body of knowledge, practices and techniques held by communities or individuals and transmitted orally. There might be some wisdom in further classifying TMs as Traditional Medical Systems (TMS) and Traditional Folk Practices (TFP). "Traditional" medicine should not be regarded as a static body of unchanging knowledge - but rather as an evolutionary process as communities and individuals find new uses or techniques, and third parties use such knowledge in the search for better treatments or practices.

The advantages of traditional medicine include its widespread accessibility and relative cheapness, when most people in low-income countries pay for medicines out of their own pockets. The governments of China and India, amongst others, provide governmental support to strengthen training, research and the use of "traditional" medicine in their national healthcare strategies, and a number of African countries are considering how to integrate traditional medicine into "mainstream" healthcare⁴. The possibilities for expanding such initiatives need to be examined. Apart from medical use, the production, sale and export of traditional medicines is an important component in some economies.

3 Eisenberg DM et al. Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. *Journal of the American Medical Association*, 1998, 280(18):1569–1575. .

4 Kimani Chege Kenya to develop traditional medicine action plan, 29 June 2004, SciDev.Net

China, for instance, exports over \$600 million of traditional medicine products annually. Chinese health authorities have recently launched a nationwide program to build up 161 Traditional Chinese medicine (TCM) hospitals, each specializing in the treatment of a particular condition, such as different types of cancers, heart and vascular diseases and hepatitis⁵.

Traditional medicines may have been used for centuries by communities, and found to be efficacious through long experience. But their method of action may not be understood in modern scientific terms, and they often consist of mixtures of different active substances. But this makes it very difficult for them to be subjected to analysis by the methods of "modern" science, or to meet the regulatory and approval mechanisms designed for single molecule modern medicines. This means that the efficacy of traditional approaches has generally not been described in terms of contemporary regulatory standards of the developed world. This has implications for certifying their quality, and for promoting their use outside the communities from which they originate. WHO reports that a growing number of countries are adopting national policies and developing specific regulatory capacity on traditional medicine; moreover, there is strong scientific evidence for some traditional approaches like acupuncture.

Nevertheless, there continue to be considerable challenges, including the varying degree to which traditional approaches are recognized by governments, lack of scientific evidence on efficacy, and difficulties in assuring proper use. A particular feature of traditional medicines is that they are based on natural products. Expanding their use

⁵ Jia Hepeng, China to boost traditional medicine hospitals 2 July 2004, SciDev.Net

therefore may depend on ensuring sustainable supplies of natural raw materials, and consideration of the economics of production and processing, and the implications for the availability and cost of the finished product. Also, as natural products, there may be challenges in ensuring consistency and stability in the product. The study should consider the specific policy and regulatory issues regarding traditional medicine, and their interaction with the systems designed for "modern medicine".

Traditional medicine can provide novel inputs into the drug development process. For instance, a consortium led by the Medical Research Council of South Africa is carrying out a study on traditional medicines used by communities for the self-treatment of fevers, with the aim of discovering active compounds to treat malaria more effectively. Other cases have highlighted the possibility that traditional medicines and natural products may be used as a source of drugs designed principally to meet the needs of developed country markets (e.g. appetite suppressants). At the same time "bioprospecting"-- the search for economically valuable natural resources -- by pharmaceutical companies, or on their behalf, has not been conspicuously successful in recent years. Various institutions, including the Council for Scientific and Industrial Research (CSIR) in India, are taking another tack, exploring alternative paths to modern pharmaceutical research presented by traditional medicine--paths that could be cheaper, faster and more effective. One such strategy involves a process known as "reverse pharmacology" (See Chapter 7 for details), which begins with a useful natural product and works backward, as it were, to identify its active ingredients. CSIR has begun clinical trials on herbal products of medicinal value generated through reverse pharmacology, with several public and private partners. It is

important to consider the relative potential of these approaches to generating cost-effective, safe medical products for poor people.

One important consideration is assuring the preservation of traditional knowledge, particularly oral knowledge, within communities, and for the potential benefit of others. It has been argued that developing mechanisms to document traditional knowledge, such as national inventories, can be beneficial in identifying cases where conservation or cultivation is needed, based on an understanding of existing natural resources used for medicinal purposes. Decisions about access and ownership of information can also be made (including those relating to intellectual property rights, where appropriate) once methods have been found to collect and preserve traditional knowledge. On the other hand, the livelihood of traditional healers may depend on maintaining the secrecy of their healing methods - one argument for consulting with traditional healers as part of the process of planning and executing the collection, storage and testing of traditional medicines.

Extending some form of intellectual property protection to traditional knowledge, of which traditional medical knowledge is a significant part, is being actively debated in WIPO and other international forum. Existing intellectual property regimes can offer protection for purified compounds (produced by scientists and companies) isolated from a natural medicine. But traditional medicines, whose method of action may not be well understood, and which often consist of mixtures of different active substances, may not meet criteria for patentability. The principal impetus for international debate is a desire

to compensate the holders of traditional knowledge appropriately for the use of their knowledge by others, or to prevent so-called "biopiracy" where knowledge or genetic materials are used without the consent of the holder. China and Kenya are examples of countries that have modified their laws in an effort to accommodate traditional medicine. It is not intended that the Commission should enter into this debate, except in so far as aspects of it may be relevant to its terms of reference, in particular stimulating innovation in traditional medicine with the purpose of expanding access to affordable medicines.

This study generally aims to address following important tasks (not necessarily all the tasks will be detailed, discussed and or analyzed in this study purely due to limited time and resources). First, to review the existing evidence base on the use of traditional, complementary, and alternative medicines (TM) in meeting the health needs of populations in developing countries. Analyze the benefits of traditional, complementary and alternative medicines in terms of accessibility, availability and affordability, including studies on the health benefit and cost-benefit. Consider the scope for using TM systems (including healers) to deliver modern medicines, and the possibilities for conjunctive use. Second, to review existing evidence on current innovative efforts in TM to combat diseases that disproportionately affect developing countries. Review and analyze the challenges and difficulties related to performing research on traditional medicine, as well as innovating new conventional medicines from traditionally used medicines. These might include (but not limited to) regulatory issues in establishing safety and efficacy, and practice standards; the effectiveness of the patent system in stimulating innovation in this field, and in promoting sustainable use of TM, and the

possible contribution of new "*sui generis*" IP systems in contributing to these goals; reliance on renewable natural resources as the basis for traditional medicines and constraints on the expansion of use; documenting traditional knowledge about medicine.

Third, assess the actual and or potential importance of traditional medical products to develop new pharmaceuticals and other products. Are there ways in which the greater use of natural compounds could increase the success rate of the modern drug discovery process? Provide examples of traditional medicine furnishing different approaches to drug R&D. How do these approaches compare to conventional R&D, in terms of their cost-effectiveness, and the relevance of their products for developing country consumers?

Fourth, consider specifically possible mechanisms to improve incentives for R&D and innovation in traditional medicine, including governmental support. Such issues are likely to include documentation; regulation; intellectual property; support for training, education and research and development and economic and agro-ecological considerations. Fifth, make proposals for consideration by the Commission as to how better to stimulate innovation in traditional medicine with the purpose of expanding access to affordable medicines.

1.2. Science, Technology and Demography

Last 100 have been perhaps very remarkable and unique years in the entire history of medical sciences. In fundamental sciences, discovery of double helix and completion of human genome project were achievements that had no parallel. In diagnostics,

technologies like MRI and PET scan added brightest feathers ever to our caps. In surgery, bypass, transplants, and prosthetics changed life expectancies upwards dramatically. In therapeutics chemotherapy and SSRI revolutionized longevity and quality of life. The Human Genome Project has opened newer understanding progressing towards personalized medicine.

Developing countries lately have come to be identified and distinguished from the developed world through three key characteristics: disproportionate population growth, disproportionate affliction with a small number of (mainly infectious) diseases and, health care going increasingly out of reach for the most of their inhabitants. The world has reached a population of approximately 6.4 billion⁶ as this report is being written. Out of these about 81.8% lives in the developing countries⁷. An estimated 7.4 million people are living with HIV in China, Indonesia and Viet Nam, 5.1 million in India alone, 1.6 million in Latin America and, 25 million people in sub-Saharan Africa⁸. In contrast an estimated mere 1.6 million people are living with HIV in developed countries all together. There are at least 300 million acute cases of malaria each year globally, resulting in more than a million deaths. Around 90% of these deaths occur in Africa, mostly in young children⁹. Against that, malaria is virtually non-existent in developed world. The number of persons who suffered from Tuberculosis (all forms) in 2002¹⁰ was 532 per 100,000 in Africa and South East Asia put together, out of which 122 died. However, in America and Europe the respective numbers were 97 and 14. Though

6 U.S. Bureau of the Census

7 Based on United Nations, World Population Prospects, The 1998 Revision; and estimates by the Population Reference Bureau.

8 UNAIDS 2004 Report on the Global AIDS Epidemic - Executive Summary

9 Roll Back Malaria (a global partnership initiated by WHO, UNDP, UNICEF and the World Bank) fact sheet

10 WHO fact sheet N °104 revised March 2004

pharmaceuticals account for about 15% of the spending on health, since they make a tangible measure, one can substantiate the argument on affordability of health care needs with the help of their data. In 2000, while average per capita spending on pharmaceuticals in high-income countries was \$400, it was barely over \$4 in low-income countries. At the extremes of the spectrum of the data the difference was 1,000 fold. Moreover, in 2003, while the estimated cost of treatment for HIV/AIDS was \$300 plus per annum, in eight of the 23 countries that make up 80% of the global treatment need, the average spending on the pharmaceutical was \$5 per head in 2000¹¹. A WHO data query engine showed the density of physicians (Modern Medicine) per 100,000 persons in various countries (up to date as of 2004) as: Rwanda 1.87, Ethiopia 2.85, Uganda 4.70, Benin 5.75, India 51.25 and China 164.24, in stark contrast to the numbers for Australia and the USA as 249.13 and 548.91 respectively. The above data show how badly under served the health care needs in developing countries are.

1.3. Health Needs of Developing Countries

The above problem in the developing country though *prima facie* seems to be of their own making needing local fixes, and indeed from a narrow perspective that is so, is a matter of global concern. The health problems of the developing world, if left non reconciled or unresolved can push humanity beyond the tipping point, with dire unprecedented consequences for all humanity, sparing and forgiving none- neither developing nor developed countries. Global wars and terrorism make two glaring examples of the fearful outcomes.

¹¹ World Medicine Situation, 2004, a WHO report

Over one billion people exist on less than one dollar a day, the world population has increased from approximately 2.8 billion to currently in excess of 6.3 billion in the same time period, and today over 2.5 billion people lack sanitation, over 1.5 billion people do not have safe drinking water, and some 3 million people, mostly women and children, die every year from diarrheal diseases directly related to these deficiencies. There is little cause for optimism in these areas: indeed, available evidence suggests that the availability of water in the poor world is likely to diminish rather than increase over the next several decades¹². The importance of a public health infrastructure cannot be overemphasized: the increase in life expectancy during the 20th century was due in significant part to public health services, including sanitation, cleaner water, mass vaccinations, and improved workplace safety^{13, 14, 15}.

Leaders, policy makers, and scholars, world over are grappling with possible solutions to these complex, not just complicated problems- because there is no single magic bullet, or no single solution. Prompted by this concern, at the behest of CIPIH under the auspices of WHO, the following report, within the paradigm of health and against the backdrop of the philosophical underpinnings outlined above, tries to explore one among the possible solutions- the place and utility of TM as an effective and efficient vehicle to affordable health to the large un-served or underserved populations in the developing countries.

12 Aldhous P. 2003. The world's forgotten crisis. *Nature* 422:251–253.

13 Trigg D. Medicines in the 21st Century. *DRUG DEVELOPMENT RESEARCH* 59:269–291 (2003)

14 Longman PJ. 2003. The health of nations. *Wash Monthly* April:16–23.

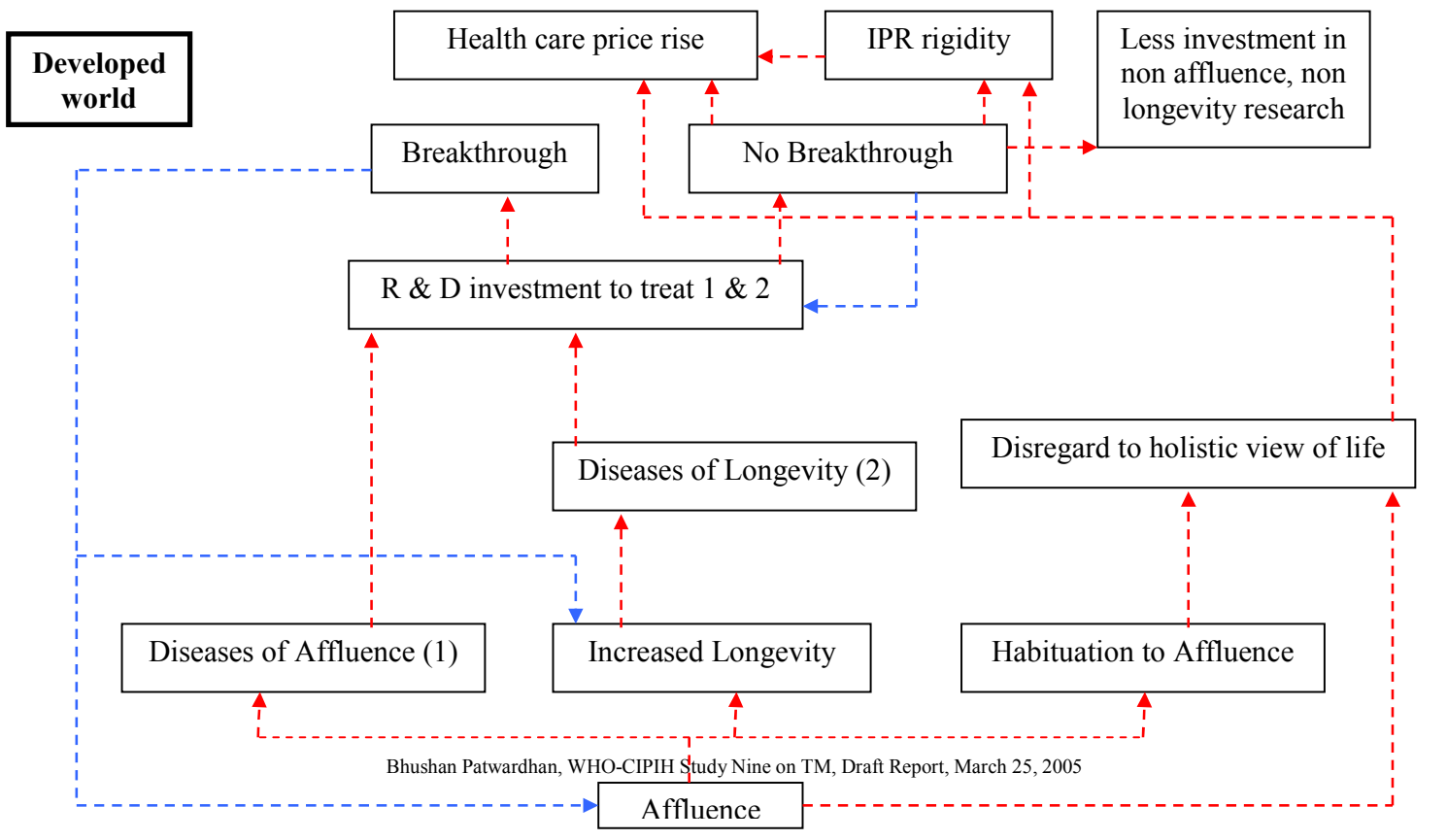
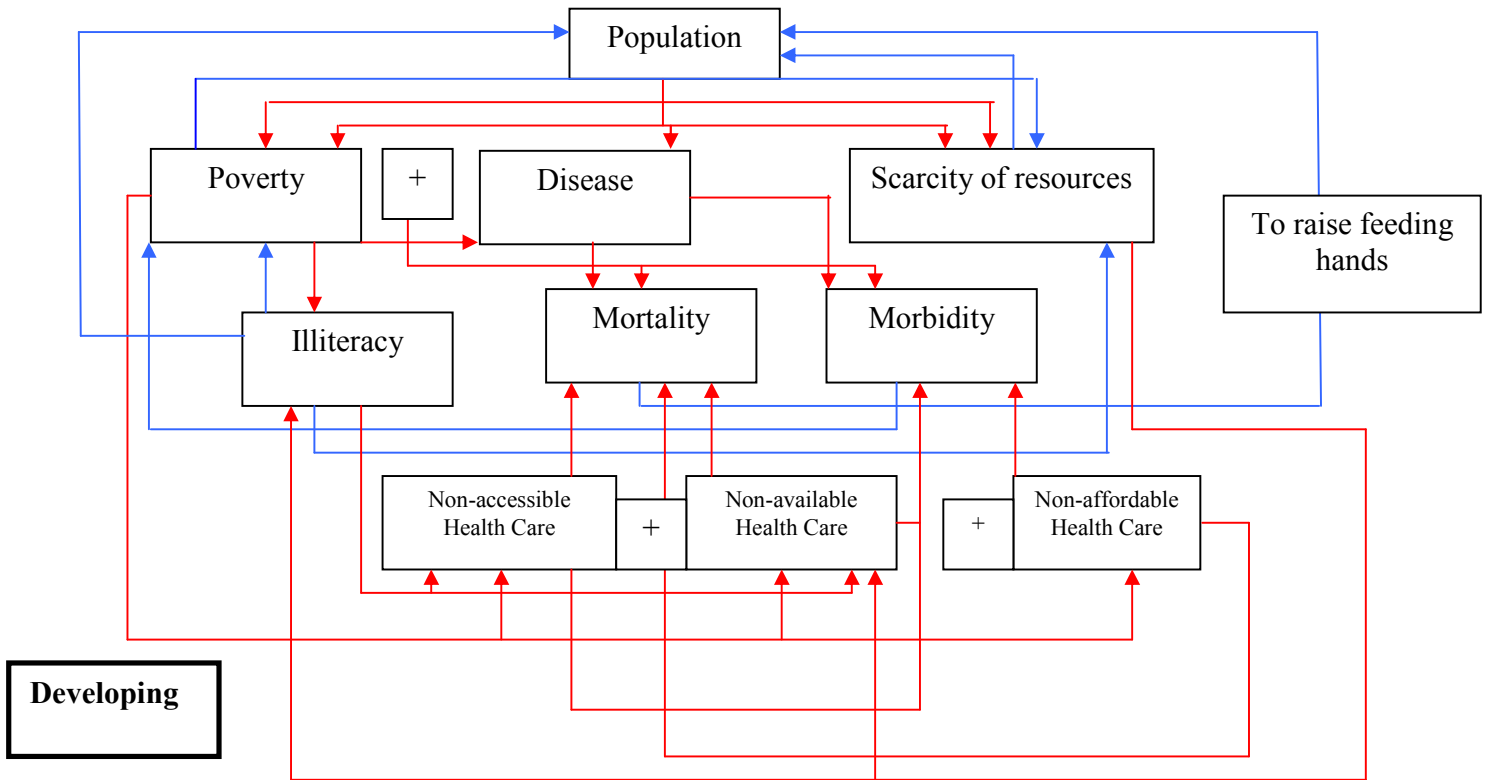
15 Hertzman C. 2001. Health and human society. *Am Scientist* Nov/Dec:538–545.

It is a truism that what you really value is what you miss, not what you have¹⁶. TM has become an extremely valuable commodity for the world today, precisely because it provides what the world misses most. The low-income developing countries miss the modern medicine because they cannot afford it whereas high-income developed world misses the holistic wisdom implicit in TM. The symbiotic mutually interdependent handicap of the two worlds of the world might, it is hoped, through TM, solve the global health crises elucidated at the outset, even while giving a boost to the bottleneck stagnation in modern medicine- a medicine that medicine desperately needs.

Oft times pictures/diagrams deliver a message more lucidly, more convincingly and more forcefully than words. The annexe below are, a series of diagrams based on systems-cybernetics approach to depict the totality of global scenario regarding health care system and connected issues, seen through different lenses, separately and or together. The color-coded arrows/connectors delineate effects, consequences or fallouts and highlight some prominent feed-forward and feedback loops. These diagrams, given consistency of their logic, leave no doubt in a sensible mind regarding inseparability of the world and about how true and tangible globalization is.

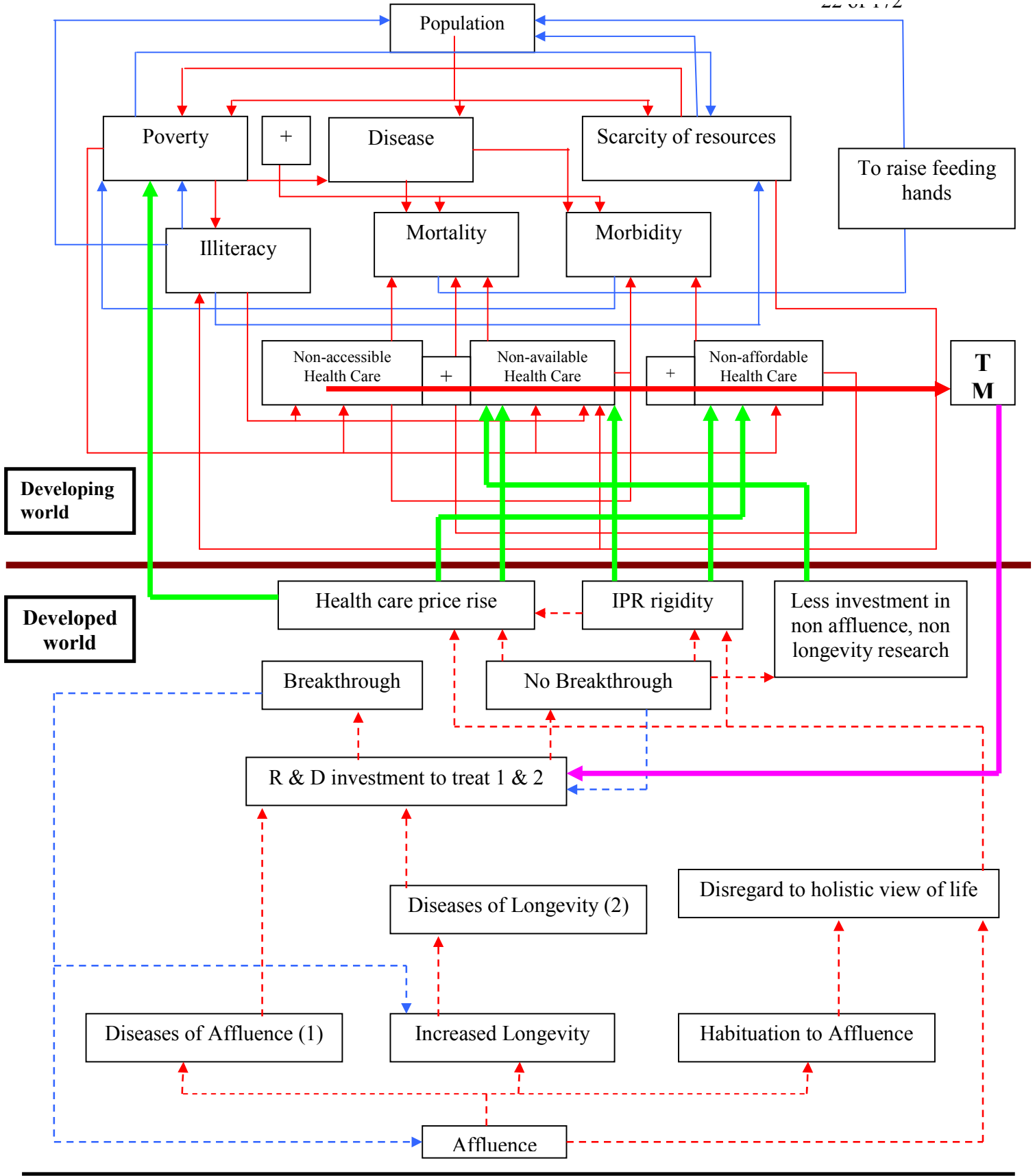
16 Jorge Luis Borges

**Developing and Developed World
Two disconnected demographic-health-socio-economic isolated systems**

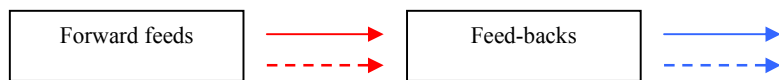
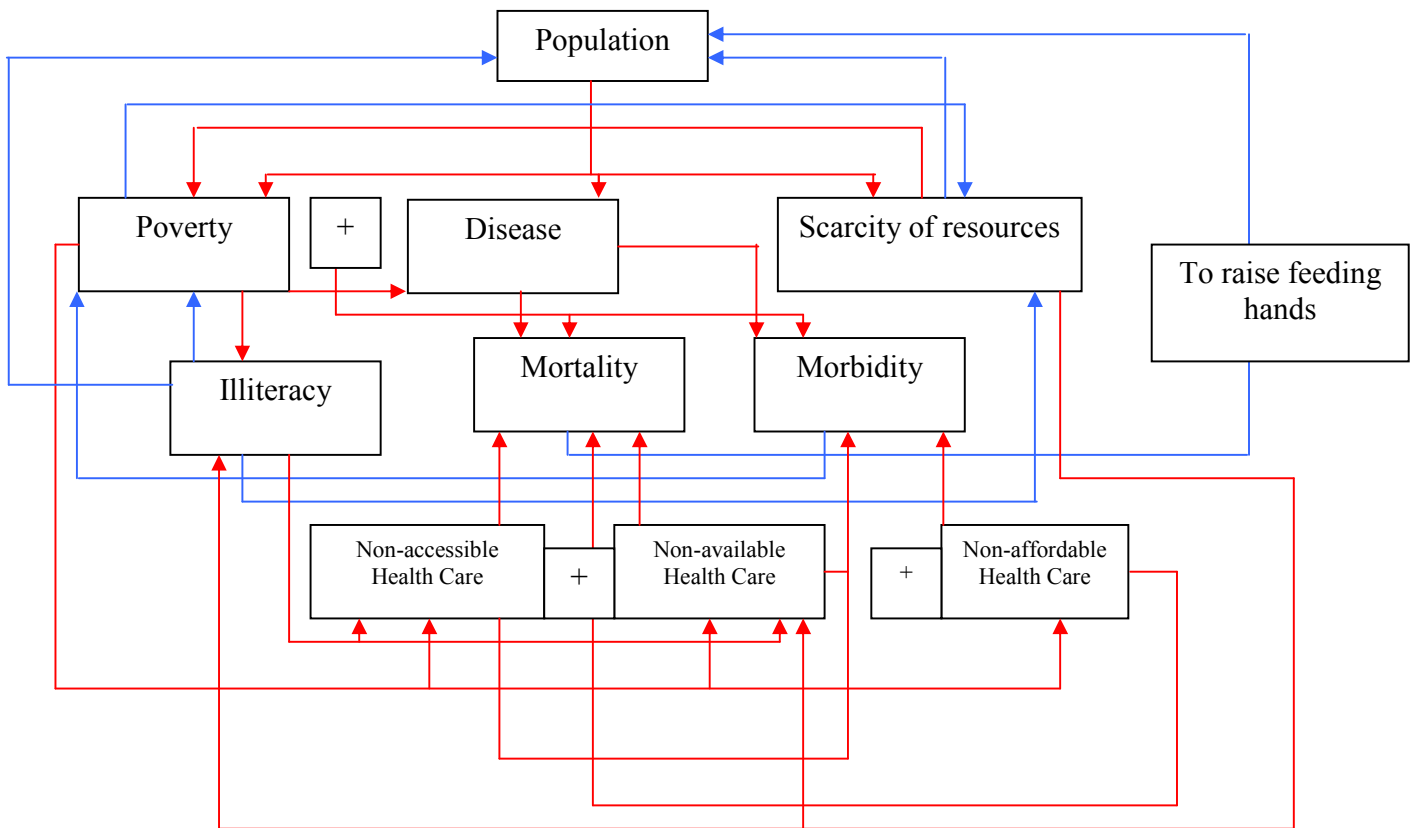


Bhushan Patwardhan, WHO-CIPIH Study Nine on TM, Draft Report, March 25, 2005

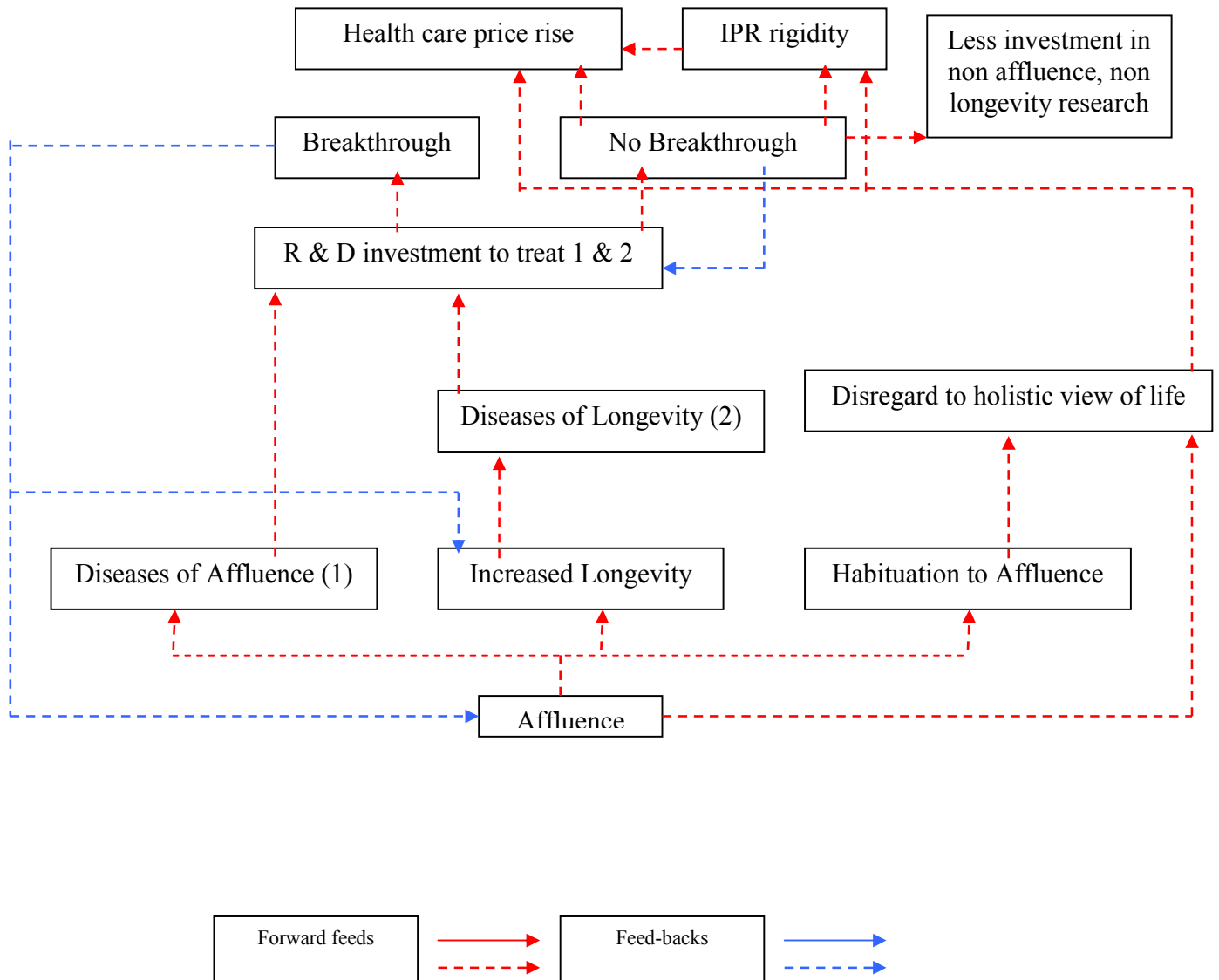
Developing and Developed World
Two connected demographic-health-socio-economic interacting Systems



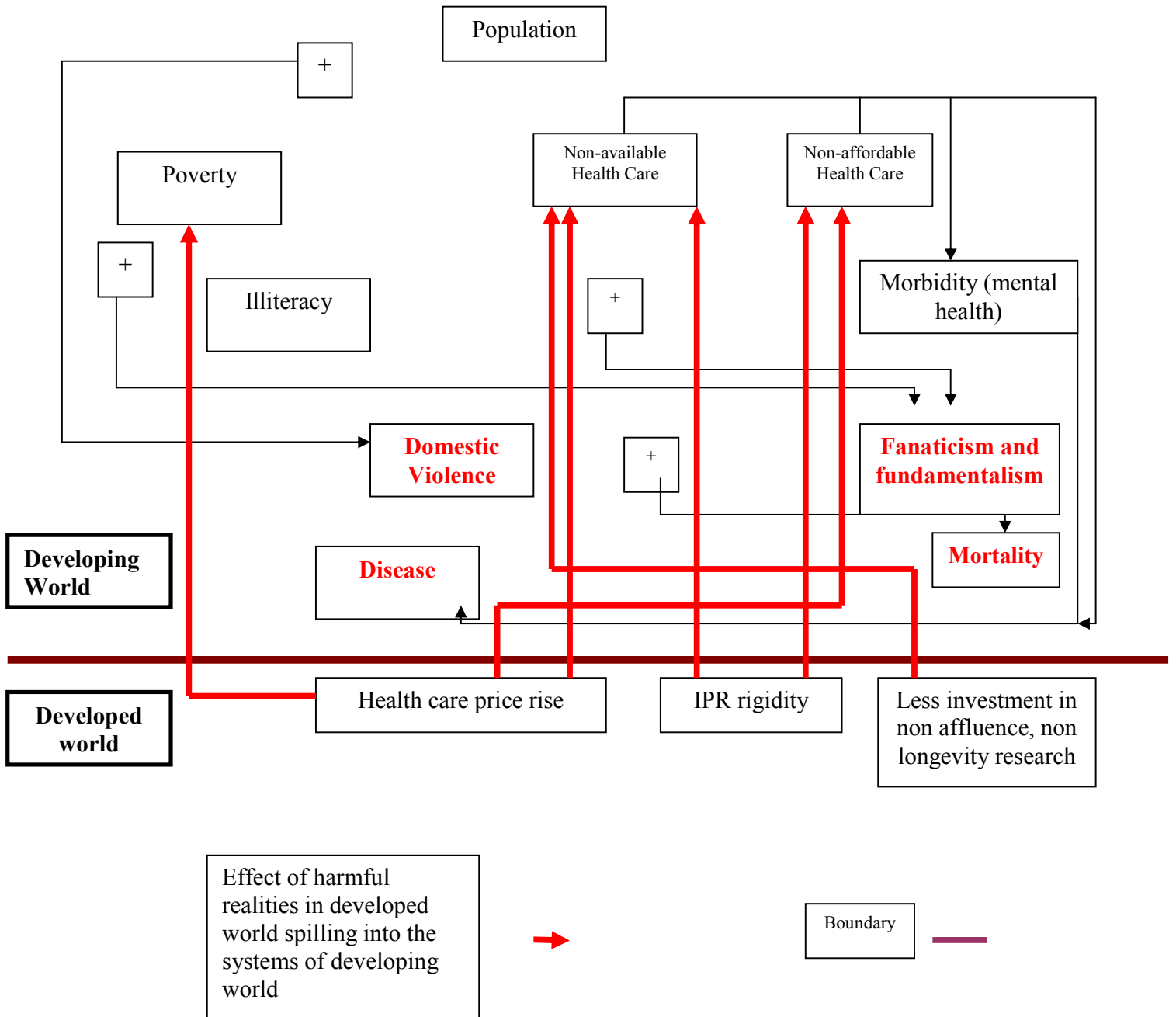
Developing World- Demographic-health-socio-economic system



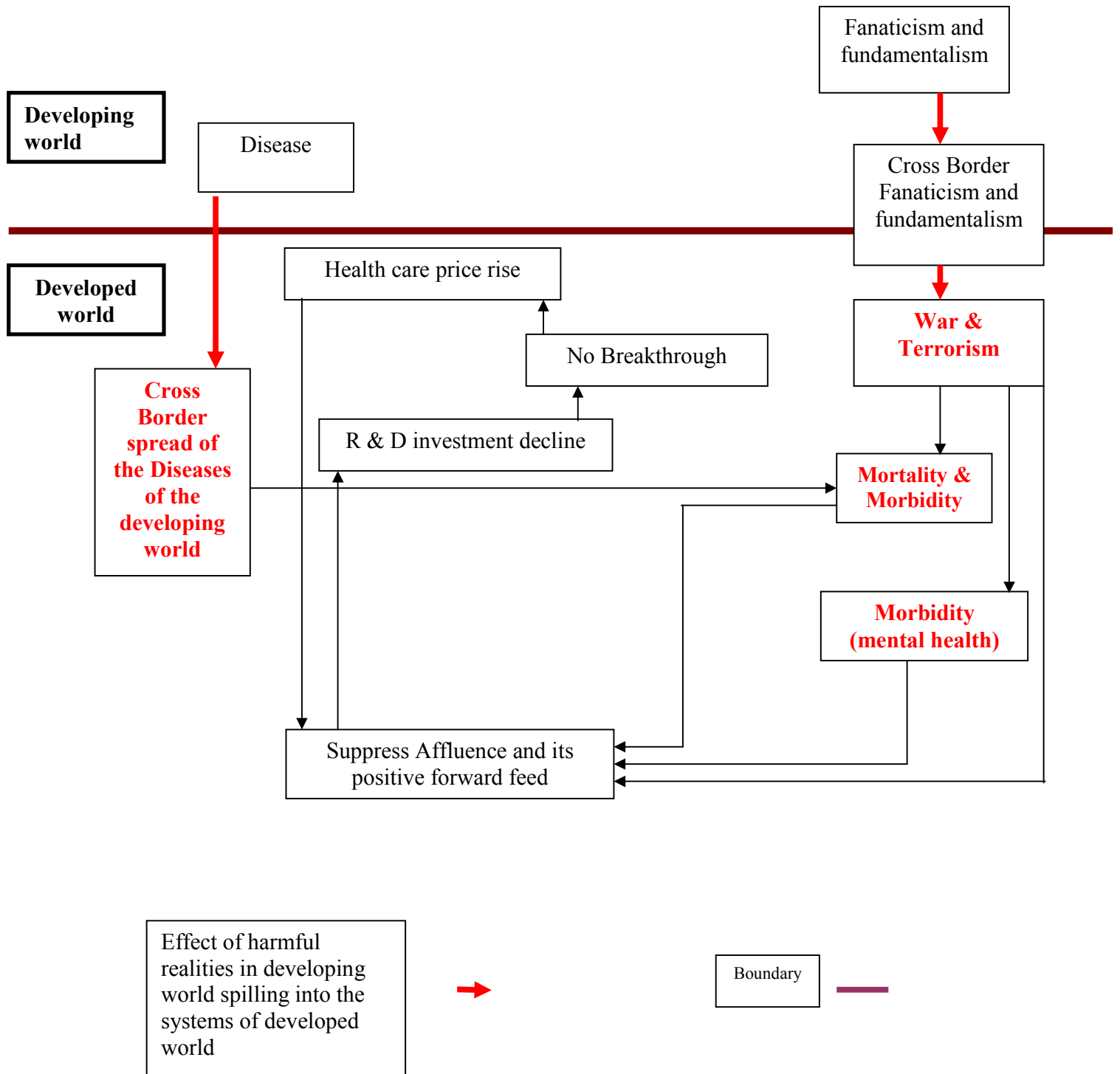
Developed World- Demographic-health-socio-economic system



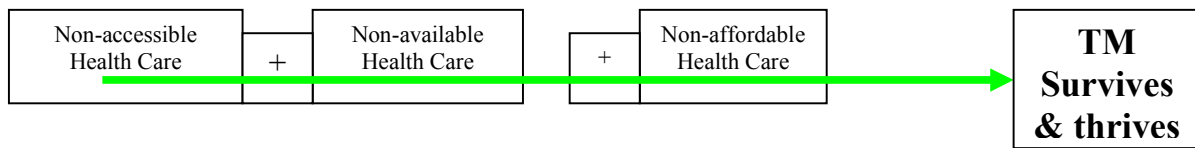
Developing World- Harmful influences from the developed world




Developed World- Harmful influences from the developing world



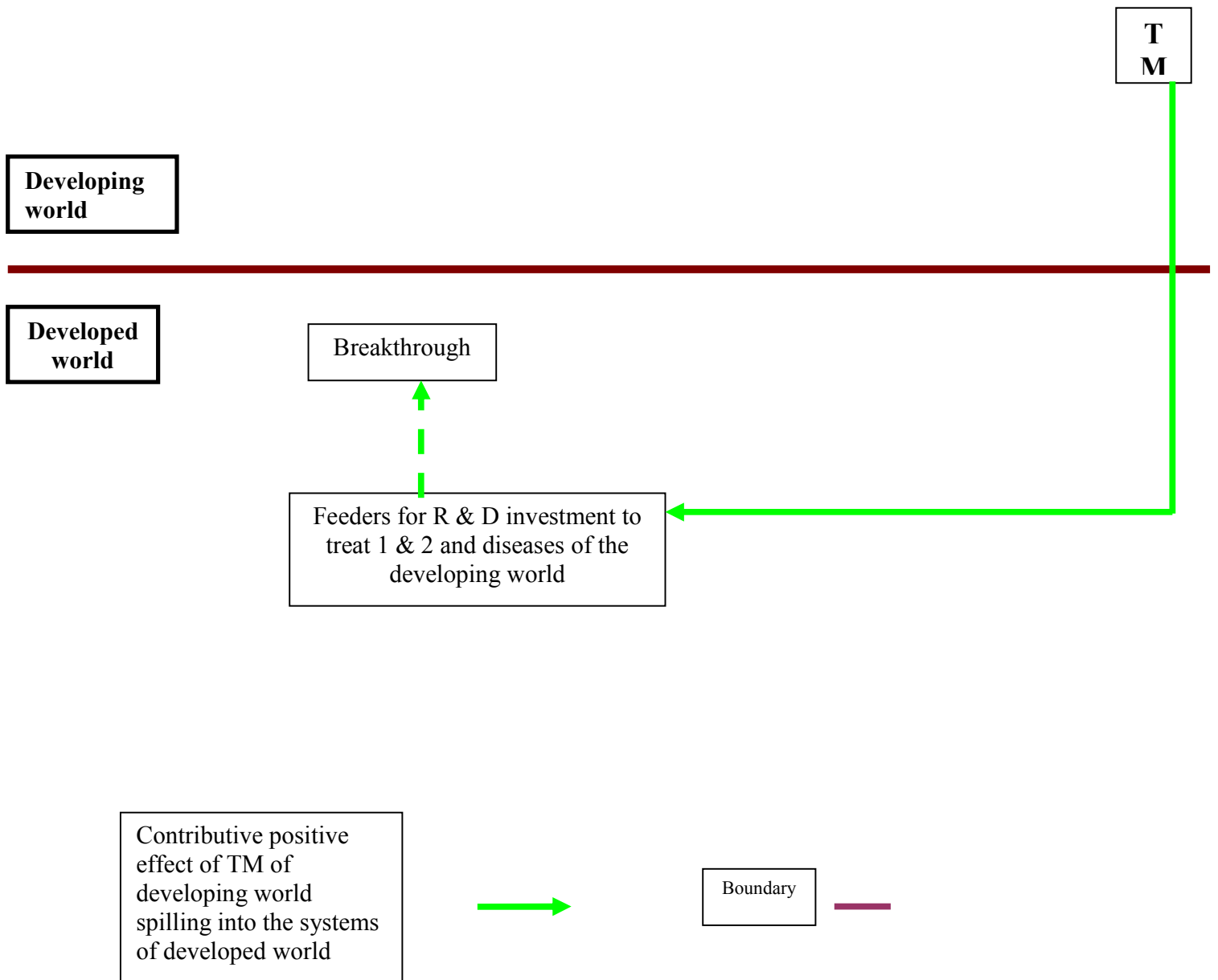
Protective effect of systems dynamics on Traditional Medicine In developing world



Contributive positive effect due to
ABSENCE of INHIBITORY effect of
MM of developed world spares
extinction of TM in developing world



Contributive potential of Traditional Medicine in R & D activities in developed world



Systems symbiosis and a bright future for the entire world

Equitable distribution of health and wealth

For the developing world

- Wealth
 - Decrease in health care price (or at least in its rise)
 - More IPR protection to TM (increase money flow to developing world)
 - Decreased rigidity in IPR in developed world leading to more accessibility of modern health care to developing world
 - Better treatments for developing world diseases (increased investment in developing world diseases R & D as a part compensation to TM IPR barter)
- Health (as wealth rises)
 - Decreased poverty
 - Decreased illiteracy
 - Decrease in population rise
 - Increase in access, availability, affordability towards modern medicine
 - Decrease mortality (disease)
 - Decrease morbidity (disease)

For the developed world

- Decrease in wars and terrorism
- Decrease in the spread of the diseases of the developing world

“We go to war with the army we have, not the army we might want”.

Donald Rumsfeld

Chapter 2

A Handy Solution to Impasse - Traditional Medicine

2.1. Definitions and Development

Historically, terms alternative, complementary or traditional medicine (TM) all referred to a genre of health care practices or services that got bound together as a class through the logic of *reductio-ad-absurdum*, defined by a criteria of “absence from the mainframe of” what has come to be known as Modern Medicine (MM). However, since Stephen Fulder¹⁷, the identities of TM have become more distinct, MM-TM blending more active and, the line separating the two more fuzzy. As of the date, The World Health Organization offers the most comprehensive definition of TM¹⁸.

The report contests the phraseology MM/TM as being syntactically incorrect because it is contended that medicine as such, modern or otherwise, evolves and progresses through traditions. The difference if any, in various traditions of health care practices was that one among those numerous (traditions) rode the crest of the high wave of reductionist-scientific rigor of modernity¹⁹ to reach the shore of global acceptability first and far while the others never crossed the threshold of geographical and cultural locality, remaining untested, neither proved nor disproved. Darwinian principle of survival of the fittest also endorses a truism that survival is a proof of fitness. If that is so, and that is

17 Fulder S. Handbook of Complementary and Alternative Medicine

18 WHO Traditional Medicine strategy 2002-2005, WHO Geneva, 2002

19 Age of Enlightenment, Age of Reason (AD 1600- AD 1900)

indeed so, then it follows that, if not in totality but in some way TM as we know of it today had and have some utility for human health. Moreover, most of the TM across board held human beings and their health in the context of their environment. This criteria, not only defines TM apart from MM but also provides for a reason as to why lately TM is emerging out of long hibernation. Developmentally, MM isolated “human” from its global environmental context as a static, stand-alone, complete, total and delimited system in itself. This reductionist approach though has a very high pay off for the first 90% of human health problems, fails when dynamical non-linear complex systems elements kick in. Mostly ignorantly but also mostly empirically TM covered some parts of those hidden variables and therein lays their utility to modern mankind.

Traditional Medicine (TM) and Complementary and Alternative medicine (CAM) are attracting more and more attention within the context of health care provision and health sector reform. Many factors are contributing to widespread use of TM/CAM. But some important issues must be addressed if their potential is to be developed successfully.

TM is a comprehensive term used to refer both to TM systems such as traditional Chinese medicine, Indian Ayurveda and Arabic Unani medicine, and to various forms of indigenous medicine. TM therapies include medication therapies if they involve use of herbal medicines, animal parts and/or minerals; and non-medication therapies if they are carried out primarily without the use of material medicines, as in the case of acupuncture, manual therapies and spiritual therapies. In countries where the dominant health care system is based on allopathic medicine, or where TM has not been incorporated into the

national health care system, TM is often termed “complementary”, “alternative” or “non-conventional” medicine.

Asian, African, Arabic, Native American, Oceanic, Central and South American and other cultures have also developed a variety of indigenous TM systems throughout history. Influenced by factors such as history, personal attitudes and philosophy, their practice may vary greatly from country to country and from region to region. Needless to say, their theory and application often differ significantly from those of allopathic medicine. Traditional medicine may be codified, regulated, taught openly and practiced widely and systematically, and benefit from thousands of years of experience.

Conversely, it may be highly secretive, mystical and extremely localized, with knowledge of its practices passed on orally. It may be based on salient physical symptoms or perceived supernatural forces. Clearly, at global level, traditional medicine eludes precise definition or description, containing as it does diverse and sometimes conflicting characteristics and viewpoints. But a working definition is nevertheless useful. Such a definition must of necessity be comprehensive and inclusive.

WHO therefore defines traditional medicine as including diverse health practices, approaches, knowledge and beliefs incorporating plant, animal, and/or mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well-being, as well as to treat, diagnose or prevent illness.

TM is a medley. While Gynecology, Dermatology or Pathology are tied up by one empiricism doctrine in MM, there is no similar equivalent for TM, of course, other than that of contextualism. TM are numerous as numerous as the geographical and cultural contexts were that gave birth to respective TM and have become as distinct as those geographical-cultural variables were. Interplay between geography and evolution is only well too known²⁰. Geography, not only shaped human social cultures, it influenced vastly the biosphere and its ecology in any given region. Whether the distinctiveness and diversity of TM is a merit or a demerit depends on the perspective of medical science. While 99+% of the human biology is ditto same all across the planet there is some minor but nonetheless distinct and unique element of variability in human biology. If so, subject to the logic of backward convergence, the diversity and distinctiveness of TM that provide “uniqueness”, so much missed in MM, might come handy for solutions to the dilemmas and challenges of MM.

For instance, Acupuncture is a traditional Chinese medicine therapy. But many European countries define it and traditional Chinese medicine in general as CAM, because they do not form part of their (own) health care traditions. Similarly, since homeopathy and chiropractic systems were developed in Europe in the 18th Century, after the introduction of allopathic medicine, they are not categorized as TM systems nor incorporated into the dominant modes of health care in Europe. Instead, they are regarded as a form of CAM. Accordingly, in this document, “traditional medicine” is used when referring to Africa, Latin America, South-East Asia, and/or the Western Pacific, whereas “complementary and alternative medicine” is used when referring to Europe and/or North America (and

²⁰“Guns, Germs, and Steel: The Fates of Human Societies”: Jared Diamond

Australia). When referring in a general sense to all of these regions, the comprehensive TM/CAM is used.

2.2. Diversity and Distinctiveness

World Health Organization has defined three types of health system to describe the degree to which TM/CAM is an officially recognized element of healthcare. In an integrative system, TM/CAM is officially recognized and incorporated into all areas of health care provision. This means that: TM/CAM is included in the relevant country's national drug policy; providers and products are registered and regulated; TM/CAM therapies are available at hospitals and clinics (both public and private); treatment with TM/CAM is reimbursed under health insurance; relevant research is undertaken; and education in TM/CAM is available. Worldwide, only China, the Democratic People's Republic of Korea, the Republic of Korea and Viet Nam can be considered to have attained an integrative system.

An inclusive system recognizes TM/CAM, but has not yet fully integrated it into all aspects of health care, be this health care delivery, education and training, or regulation. TM/CAM might not be available at all health care levels, health insurance might not cover treatment with TM/CAM, official education in TM/CAM might not be available at university level, and regulation of TM/CAM providers and products might be lacking or only partial. That said, work on policy, regulation, practice, health insurance coverage, research and education will be under way. Countries operating an inclusive system

include developing countries such as India, Equatorial Guinea, Nigeria and Mali which have a national TM/CAM policy, but little or no regulation of TM/CAM products, and developed countries such as Canada and the United Kingdom which do not offer significant University-level education in TM/CAM, but which are making concerted efforts to ensure the quality and safety of TM/CAM. Ultimately, countries operating an inclusive system can be expected to attain an integrative system. In countries with a tolerant system, the national health care system is based entirely on allopathic medicine, but Law recognizes some TM/CAM practices.

Generally a medical system would have a long tradition, organized data base and most of the important components of health care including preventive, promotive, diagnostic, curative and public health; while a medical therapy would be limited to specific therapeutic or interventional functions.

2.3. Healthcare Delivery and Treatments

The health care delivery, its availability, affordability quality and mechanisms differ in various parts of the world as also the choices of treatments vary. Basically, there are different needs and driving forces that make consumers seek for TM based health care delivery and treatments. WHO believes that consumer information and education will help consumers to seek out appropriate types of self-care and as a result, help them to obtain more benefits from TM/ CAM and reduce unnecessary risks. Studies show that many patients use TM/CAM therapies concurrently with conventional medicine, often

without informing their health care provider. Efforts are needed to improve communication between patients and health in the case of self-care treatments, to ensure that consumers are better informed. TM/CAM is unregulated in most countries, communication between patients and health care providers is generally poor, and there is an urgent need to develop consumer information in order to minimize the risks and maximize the benefits of TM/CAM use²¹.

A WHO data query engine shows the density of physicians (Modern Medicine) per 100,000 persons in various countries (up to date as of 2004) as: Rwanda 1.87, Ethiopia 2.85, Uganda 4.70, Benin 5.75, India 51.25 and China 164.24 (in contrast the numbers for Australia and the USA are 249.13 and 548.91 respectively). These data show the under served the health care needs in developing countries.

Against this background, we see that in Tanzania Uganda and Zambia the ratio of TM practitioners²² is between 400 and 500 per 100,000 persons (still less than but comparable to the number of modern medicine physicians available to the USA population) and the number of TM practitioners in Sub Saharan Africa is 100 times that of the modern medicine physicians. It should come as no surprise that 70% Rwandans, 90% Ethiopians, 60% Ugandans, 80% Beninans, 70% Indians and, 40% Chinese among the developing countries²³ use TM as a means to their Health care needs²⁴.

21 Zhang, Xiaorui Department of Essential Drugs and Medicines Policy, WHO Guidelines on Developing Consumer Information on Proper Use of Traditional, Complementary and Alternative Medicine, 2004, World Health Organization, Geneva

22 World Health Organization Traditional Medicine Strategy 2002-2005, WHO Geneva.

23 The explanation to the paradox, why 48% Australians and 42% USA citizens have used TM at least once will be addressed later.

24 WHO TM Strategy 2002-2005

2.4 Existing Documentations:

Very few traditional systems have a fair level of documentations in place. Most of the little traditions, the flow of knowledge is mainly through word of mouth, however, the great traditions such as Ayurveda and Traditional Chinese Medicine do have a good level of documentation. For instance, Ayurveda (Ayur: Life; Veda: Science) means science of life in Sanskrit and aims at holistic management of health and disease. It remains one of the most ancient medical systems widely practiced in Indian subcontinent and has a sound philosophical, experiential and experimental basis²⁵. *Charak samhita* and *Sushrut Samhita* (100-500 B.C.) are main Ayurvedic classics, which describe of over 700 botanicals along with their classification, pharmacological and therapeutic properties^{26, 27}. A classic diagnostic text *Madhav Nidana* includes over 5000 signs and symptoms. During the course of evolution and years actual practice, the interpretation of such documents developed different schools of thoughts and resulted in wide variations in understandings. Similar situation also exists in other systems including TCM. These differences often raise issues related to authenticity and correctness of Traditional Knowledge (TK). Thus systematic documentation, interpretations and harmonization of concepts and practices remain a major challenge in most of the systems of TM. Many governments, professional and community organizations have undertaken such documentation and harmonization exercises. Projects like Traditional Medicine Knowledge Digital Library, AyuSoft, Triskandha Kosha and Medicinal Plants Database

25 Valiathan MS. The Legacy of Caraka, Orient Longman, 2003, Chennai India,

26 Charak Samhita, Translation 1995, Caukhambha Orientalia, Varanasi, India

27 Gogate V.M. Ayurvedic Pharmacology and Therapeutics of Medicinal Plants, 2000, Bharatiya Vidya Bhavan's SPARC, Mumbai

of FRLHT are attempting systematic documentation of Ayurveda in India²⁸. Other databases such as The NAPRALERT (NATURAL PRoducts ALERT) developed by Professor Norman Farnsworth contain bibliographic and factual data on natural products, including information on the pharmacology, biological activity, taxonomic distribution, ethno-medicine and chemistry of plant, microbial, and animal (including marine) extracts. Another project relates to the Global IP, Benefit Sharing and Traditional Medicine Database. It is being developed as a component of the Global Information Hub on Integrated Medicine from the work of the Commonwealth Working Group (CWG) on Traditional and Complementary Health Systems, now directed by the Malaysian Ministry of Health. This Information Hub is planning to create a network of legal centers, scholars and NGOs working together to develop a comprehensive legislative and policy review, information resource and exchange on issues pertaining to IP rights over traditional medical knowledge and the use of medicinal plants²⁹. Other than such efforts, there is limited systematic documentation of TM knowledge and practices.

2.5. Current Global Perspective

To understand general knowledge, attitudes and practices (KAP) about TM, opinions, comments and suggestions on the role of traditional systems of medicine and its potential use in modern drug development; this report invited views from the experts in various systems of medicine and related sciences from several countries. It sent a short Questionnaire (See Annexure) to 120 experts from different parts of the world. It studied

28 TKDL project of CSIR, AyuSoft project of CDAC/MICT Government of India

29 Gerard Bodeker, Traditional (i.e. Indigenous) and Complementary Medicine in the Commonwealth: New Partnerships Planned With the Formal Health Sector, *Journal of Alternative & Complementary Medicine* 1999; 5, 97.

responses from 41 respondents representing India, China, Ghana, South Africa, Ivory Coast, Norway, U.S.A., British Columbia, Canada, Germany, and Switzerland. The experts were selected from different disciplines including Ayurveda, Chinese, Siddha, pharmaceutical sciences, phytochemistry, ethnopharmacology, molecular biology and modern medicine. Broad observations of this survey are as follows: Majority (52%) of the respondents represented academic institutions and were actively involved in research (84%), training (72%) and R & D (44%) activities in collaboration with other institutes, industries, etc. Their keen interest in networking activities and maintaining multifaceted databases was also revealed.

In the opinion of the majority of experts availability and acceptability of TM was more in rural areas as compared to urban centers. However, use of TM in chronic conditions has been rising even at the urban centers. Poor families were likely to use TM more frequently. Effectiveness of TM in all conditions was thought to be equal to that of MM but TM proved more effective in chronic disease conditions. Experts found limited role of TM in management of acute conditions. Use of MM was always preferred in acute conditions. Affordability was undoubtedly accepted by majority of the experts as the biggest asset of TM. All of them unanimously agreed to the lesser side effects of the TM as compared to MM. Health benefits of TM were thought to be more than MM. Equal opportunities exist for market and jobs of TM and MM. With regards to practice of plural therapy, use of modern drugs by Traditional Medicinal practitioners was thought to be limited compared to the traditional medicine use by modern medicine practitioners. However, occasional use of TM by modern medicine practitioners was seen mostly in

chronic conditions. It was also reported that Traditional practitioners referred emergency cases to modern medicine practitioners or made use of modern drugs to save lives. Thus there appeared to be practice of cross therapy and mutual acceptance of the benefits of different systems of medicine. Exclusive use of traditional medicine was seen in more than 75% of the cases in African countries. Nearly 25% of total respondents were directly involved in developing newer drugs with the help of traditional medicine. Majority of their work was in the process of initiating Phase I or II clinical trials on the drugs based on TM. Although no conclusive statement could be made they noted positive and hopeful results in their research on developing new drugs for Type II Diabetes, anti-cancer and combination therapy, metallic preparation for diabetic neuropathy, hypolipidemic, hypoglycemic drugs, treatment for arthritis, immunomodulation for respiratory infections etc. Majority was of the opinion that TM could play major role in preventive and promotive aspect of health such as mother and child health. At the same time they did not rule out the possibility of using TM for combating communicable diseases of public health importance. Respondents expressed faith in the capacity of TM to handle diseases like, respiratory infections, diarrhoeal diseases, malaria, and tuberculosis. TM could manage certain conditions like infertility, injuries, burns etc very well. In a few countries like South Africa, Ghana, TM was effectively used in 80% of the cases of malaria and tuberculosis. In the words of one of the respondents, “ I strongly believe TM has a potential in handling public health problems. It has been doing so in the past. There are many examples to substantiate this view. For example Diarrhoeal disease. Simple combinations of dried pomegranate fruit bark boiled in buttermilk, pinch of turmeric and Cummins seeds stops excess of peristaltic movement and also stops

dehydration. There are numerable simple and combined formulations, which are available locally and can be made simply at home. There are several instances of malaria and respiratory infections treatment by traditional medicines especially in south Karnataka in India". The respondent's institution has a very strong R&D department and is leading in making modern drugs on the basis of TM. It was also expressed that no efforts were made to make low cost medicine using local resources for local needs. Methods described in TM of production of simple formulations can bring down the costs. Majority (60%) unanimously reported that work of protecting (a) the innovations based on TM, (b) process formulation, (c) traditional knowledge per se as well as (d) technology used for innovation should be done on priority basis. Apart from that they also appealed the government to review the licensing system, and also to protect the environment, ecological system from where the raw material of TM is extracted. Six of the experts were not in favor of patenting because they thought, that a) the core principles of medicine should be made available for the usage of all; b) the peripherals of the medicine (not core principles) can be patented and used for wider circulation; c) in African countries, it was feared that most of the traditional practitioners walk in graves without transferring their knowledge to next generation. Younger people were not keen on pursuing traditional medicine associated occupations. Patenting doesn't make any sense in such conditions; d) some were of the opinion that Acupuncture being antique Chinese treasure, those who were not aware about it should be made aware. International collaboration is required for such sciences to grow and wider circulation. The respondents reported eight different types of constraints. 36% of them were more concerned about quality control norms and its implementation in their respective

countries as well as lack of funding for research in TM. Lack of documentation and communication among like-minded was also thought to be major problem in the overall growth of the TM. Safety standards, lack of trained human resource, non-availability of standard research protocol and infrequent supply of raw material were considered as a few more challenges in pursuing research and development work in this area of TM. Government rules and regulation was mentioned as another problem in certain regions, which hampered the progress of TM research. Certain developed countries (e.g. Norway) did not have such government laws, which affected the research process. While some countries (Ghana) lack elaborate and detailing of laws and regulations. It was specifically mentioned by Indian respondents that acquiring coral reef, antlers of deer, musk, and certain plants have been difficult due to government laws. Forest laws and bio-diversity act of 2000 have hampered research because of inadequate supply of fresh material and lack of free exchange of information on traditional knowledge. Many experts stressed need for trained human resource and more research in the system *per se*.

Based on this survey, the report concludes that people in both developing and developed countries have used traditional medicine for centuries. Many have experienced its usefulness and potential in curing various diseases. What is most needed is the awareness in both academia and government that traditional medicine form a major public health asset. Availability of sufficient funds, modern technology for research initiative and wide spread proactive networking activities would see the more rapid progress of TM research and practice³⁰.

³⁰ This survey was conducted in consultation with Professor R.K. Mutatkar (Medical anthropologist) and Aarati Kaulgekar (Social Anthropologist at the Interdisciplinary School of Health Sciences, University of Pune, Pune India, during October-December 2004.

“What would life be if we had no courage to attempt anything?”

Vincent Van Gogh

Chapter 3

Merit of the Option

3.1 Efficacy and Evidence

Efficacy of TM is one of the most debated issues. There are philosophical, cultural, technical, methodological and practical aspects involved in efficacy evaluation. Reports of investigations of their clinical efficacy or otherwise have been published in prestigious international scientific journals. For instance, the efficacy of acupuncture in relieving pain and nausea has been well demonstrated and is now acknowledged worldwide. For herbal medicines, some of the best-known evidence for efficacy of an herbal product includes *Artemisia annua* for the treatment of malaria, St John's wort for the management of mild to moderate depression. Patients usually experience fewer side effects than when treated with antidepressants, such as amitriptyline. Such findings have inspired research worldwide to establish the efficacy of other extensively used TM. Many plant extracts have a variety of pharmacological effects, including anti-inflammatory, vasodilatory, antimicrobial, anticonvulsant, sedative and antipyretic effects. However, very few randomized-controlled studies have been carried out to investigate the practice and treatment delivery of herbal practitioners in their everyday work. Regarding non-medication therapies, the 1999 *British Medical Journal* series on CAM commented that randomized controlled trials have provided good evidence that both hypnosis and relaxation techniques can reduce anxiety, and prevent panic disorders and insomnia.

Randomized trials have also shown hypnosis to be of value in treating asthma and irritable bowel syndrome, yoga to be of benefit in asthma, and tai ji in helping elderly people to reduce their fear of falls. Besides these limitations, there has been enormous research that has been and is underway in many institutions globally. Many of the findings do substantiate the traditional claims. Many of such studies have been published in peer-reviewed journals with good impact factors. This report has tried to take some representative examples of such evidence for efficacy of TM. Due to limited space, many important findings, observations, reports, patents and such other documentation may be missing, however, that does not adversely reflect on their importance. For instance, details of most studied medicinal plant like Ginseng are not covered here. Similarly, many patents, scientific reports and clinical trials of many important diseases such as AIDS are missing here. This will remain one of the limitation of this study and is mainly due to space constrain. Following are few representative examples of recent studies related to evidence of efficacy:

Ginkgo biloba

In a randomized, double blind, placebo controlled comparison of *Ginkgo biloba* and acetazolamide for prevention of acute mountain sickness among Himalayan trekkers for the prevention of high altitude illness could not establish efficacy significantly different from placebo for any outcome; however participants in the acetazolamide group showed significant levels of protection. When compared with placebo, ginkgo was not effective at preventing acute mountain sickness while, Acetazolamide afforded robust protection

against symptoms of acute mountain sickness³¹. A case of persistent postoperative bleeding following total hip arthroplasty was reported to be due to its anticoagulant that inhibits platelet-activating factor, which is contraindicated with aspirin³². In a recent case study, side effects such as bilateral haematoma of chronic treatment with *Ginkgo biloba* following rhytidoplasty and blepharoplasty are reported³³.

Uncaria tomentosa

Also known as cat's claw, is from the highlands of the Peruvian Amazon, and has been used by natives for hundreds of years to treat immunologic and digestive disorders. It was found that two chemo types of *Uncaria tomentosa* with different alkaloid patterns occur in nature. Aqueous extracts and mixtures of oxindole alkaloids have shown positive influence on IL-1, IL-6 and IFN gamma production suggesting immunoregulatory activity. In one of clinical studies, extract exhibited immune adjuvant activity with pneumococcal vaccine resulting in enhanced lymphocyte/neutrophil ratio and persistent antibody titer responses towards different pneumococcal serotypes³⁴. In vitro, in vivo and gene expression studies on extracts of this plant indicated that anti-inflammatory activity is mediated through negation of NF-kappa activation and TNF alpha synthesis suppression³⁵. Randomized clinical studies on a purified extract, rich in pentacyclic

31 Jeffrey H et al BMJ, doi:10.1136/bmj.38043.501690.7C (published 11 March 2004)

32 Bebbington A. Persistent bleeding after total hip arthroplasty caused by herbal self-medication Journal of Arthroplasty 2005; 20(1) 125-126.

33 Destro M. W. B. Bilateral haematoma after rhytidoplasty and blepharoplasty following chronic use of *Ginkgo biloba* British Journal Of Plastic Surgery 2005; 58(1); 100-101.

34 Winkler, C. et al. (2004) In vitro effects of two extracts and two pure alkaloid preparations of *Uncaria tomentosa* on peripheral blood mononuclear cells. Planta Med. 70, 205-10.

35 Sandoval, M. et al. (2000) Cat's claw inhibits TNF alpha production and scavenges free radicals: role in cytoprotection. Free Radic Biol Med. 29, 71-8.

alkaloids, demonstrated safer and moderate benefit in patients with active RA compared with those taking sulfasalazine³⁶.

Echinacea Spp.

The *Echinacea* plant is a member of the *Compositae* family; the three species of medicinal interest include *Echinacea angustifolia*, *Echinacea purpurea*, and *Echinacea pallida*. Most uses of *E. purpurea* are based on its reported immunological properties. There are four types of constituents purported to be pharmacologically active molecules: phenolic caffeic acid derivatives, alkylamides/isobutylamides, polysaccharides and glycoproteins. Several randomized trials have reported health benefits of *Echinacea* extracts in upper respiratory tract infections³⁷.

Withania somnifera

Withania somnifera (WS), known as *ashwagandha*, Indian ginseng, and winter cherry is also classified as Rasayana in Ayurveda. The major biochemical constituents of WS root are steroidal alkaloids and steroidal lactones known as withanolides. Several preclinical studies have examined cytoprotective, immunomodulatory and immunoadjuvant potential of WS³⁸. WS exhibited modulatory effects on cytotoxic lymphocytes production leading to reduced tumor growth. WS treatment in normal and tumor bearing mice resulted positive influence on natural killer cells activity resulting in enhanced cell killing^{39, 40}. In

36 Mur, E. et al. (2002) Randomized double blind trial of an extract from the pentacyclic alkaloid-chemotype of *Uncaria tomentosa* for the treatment of rheumatoid arthritis. *J Rheumatol.* 29, 678-81.

37 Henneicke-von, Z. H. et al. (1999) Efficacy and safety of a fixed combination phytomedicine in the treatment of the common cold (acute viral respiratory tract infection): results of a randomised, double blind, placebo controlled, multicentric study. *Curr Med Res Opin.* 15, 214-227.

38 Gautam, M. et al. (2004) Immune response modulation to DPT vaccine by aqueous extract of *Withania somnifera* in experimental system. *Int Immunopharmacol.* 4, 841-849.

39 Diwanay, S. et al. (2004) Immunoprotection by botanical drugs in cancer chemotherapy. *J Ethnopharmacol.* 90, 49-55.

a comparative pharmacological investigation of WS and Ginseng, WS treated group showed better anabolic and antistress activity than Ginseng with additional anti-inflammatory activity. Clinical studies on WS have shown moderate analgesic, anti-inflammatory and disease modifying activity in arthritis patients⁴¹.

Traditional Spices

A typical oriental traditional diet includes a variety of spices such as black pepper, long pepper, ginger and turmeric. A considerably research has supported antioxidant, immunomodulatory and bioavailability enhancer activity of such spices⁴². For instance, turmeric, which is dietary staple of India, has been used as a home remedy for number of ailments including wound healing. Alzheimer's disease rates are reportedly among the world's lowest in India where turmeric is routinely consumed. Yang and coworkers from University of California Medical School have recently published scientific evidence in support of this. They reported curcumin to block and break up brain plaques that cause the Alzheimer's disease. This spice has also been found to correct the cystic fibrosis defect in mice, prevent the onset of alcoholic liver disease and may slow down the blood cancer multiple myeloma as well as multiple sclerosis⁴³. Anti-invasive gene expression studies and modulation of human multi-drug resistance MDR 1 gene by active ingredient of turmeric (curminoids) has been reported^{44, 45}. Active ingredients of ginger (gingerols)

40 Jayaprakasam, B et al. (2003) Growth inhibition of human tumor cell lines by withanolides from *Withania somnifera* leaves. *Life Sci* 74,125-32.

41 Chopra A, et. Al. (2000) Randomized double blind trial of an Ayurvedic plant derived formulation for treatment of rheumatoid arthritis. *J. Rheum.* 27, 365-72.

42 Regional Research Laboratory Jammu, India Publications and Patents

43 Yang F. et al., 2005. Curcumin inhibits formation of A-beta oligomers and fibrils and binds plaques and reduces amyloid in vivo. *J. Biol. Chem.* 10.1074.

44 Chen H.W. Anti-invasive gene expression profile of curcumin in lung adenocarcinoma based on a high throughput microarray analysis. *Mol Pharmacol.* 2004; 65(1): 99-110.

45 Limtrakul P, Modulation of human multidrug-resistance MDR-1 gene by natural curcuminoids. *BMC Cancer.* 2004 Apr 17; 4(1): 13.

have been reported as a new class of vanilloid receptor agonists^{46, 47}. In short, there is good level of experimental evidence to support various claims and advantages of various spices used in traditional diet and TM.

Malaria⁴⁸:

Traditional medicines have been used to treat malaria for thousands of years and are the source of the two main groups (artemisinin and quinine derivatives) of modern antimalarial drugs. With the problems of increasing levels of drug resistance coupled with affordability and access to effective antimalarial drugs, traditional medicines are considered as an important and sustainable source of treatment. The Research Initiative on Traditional Antimalarial Methods (RITAM) has conducted systematic literature reviews and prepared guidelines aiming to standardize and improve the quality of ethnobotanical, pharmacological, and clinical studies on herbal antimalarials including plant based methods of insect repellence and vector control.

Osteoarthritis

This degenerative disease has high prevalence both in developing and developed countries. Current therapies are mostly symptomatic targeted towards pain management. Glucosamine and Chondrantin sulphate have been in use as nutritional supplements, however, there are mixed efficacy outcomes. NIH has funded one of the large multicentric clinical studies and the current reported data does not support in favor⁴⁹. A

46 Dedov VN. Gingerols: a novel class of vanilloid receptor (VR1) agonists. *Br J Pharmacol*. 2002 Nov; 137(6): 793-8.

47 Ohizumi et al. Stimulation of sarcoplasmic reticulum Ca (2+)-ATPase by gingerol analogues. *Biol Pharm Bull*. 1996 Oct; 19(10): 1377-9.

48 Wilcox Merlin L, Bodeker Gerard, Traditional herbal medicines for malaria, *BMJ* 2004;329:1156-9

49 Cibere J, Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. *Arthritis Rheum*. 2004 Oct 15;51(5):738-45.

moderate efficacy of Indian Ayurvedic formulation has been established in a randomized controlled clinical trial⁵⁰. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee has also been studied in a randomised controlled trial⁵¹. Results of this study on 88 patients demonstrated that Acupuncture plus diclofenac is more effective than placebo acupuncture plus diclofenac for the symptomatic treatment of osteoarthritis of the knee.

Eczema

Efficacy and tolerability of borage oil in adults and children with atopic eczema was studied in randomised, double blind, placebo controlled, parallel group trial. No significant differences occurred between treatment groups in the other assessments. Subset analysis of adults and children did not indicate any difference in response. Although, the treatments were well tolerated, linolenic acid was not found beneficial in atopic dermatitis⁵².

Obesity

Over the 12-week trial, subjects on the active treatment experienced significantly greater weight loss than subjects on placebo, without an increase in blood pressure, pulse, or the rate of adverse events. These benefits were achieved in the absence of any lifestyle

50 Chopra et al, Journal of Rheumatology 2000; J Clin Rheumatology 2004

51 José María León et al BMJ 2004;329:1216.

52 Takwale A et al. BMJ 2003;327:1385-89.

treatment to change dietary or exercise behavior and with lower doses of ephedrine alkaloids and caffeine than those commonly utilized⁵³.

Such mixed responses make a case for TM more difficult to sustain on the evidence-based approaches. There are divided opinions on usefulness of RCTs in evaluating efficacy of TM. The placebo response remains a vital issue⁵⁴. Particularly in case of psychosomatic conditions some of the clinical trials have reported considerable placebo response to the extent of 40% or even more. This makes the independent assessment of efficacy more difficult. There are very few studies where TM has won over placebo. On the other hand, it is argued that TM needs entirely different methodology and the randomized, placebo controlled model is not suitable or apt to evaluate true effects of TM. The typical pyramid of evidence base where there is due consideration to traditional observational and actual use is arguably important. Many a times traditional practitioners and more so the healers, do not maintain clinical records. What weight one should give to traditional or observational experiences and how to bring in consistency and objectivity in clinical studies on TM still remains to be attended satisfactorily. The pharmacoepidemiological studies become important in such situations⁵⁵.

Modern medicine is mostly governed by demands for evidence-based practice and biomedical research increasingly moves towards molecular approaches in the search for new treatments. However, the public preferences are moving in a different direction

53 Coffey C S et al. A randomized double-blind placebo-controlled clinical trial of a product containing ephedrine, caffeine, and other ingredients from herbal sources for treatment of overweight and obesity in the absence of lifestyle treatment *International Journal of Obesity* (2004) 28, 1411-1419.

54 The Science of Placebo, *BMJ* Publication 2003.

55 Vaidya R. et al. *Ayurvedic Pharmacoepidemiology*, J. Asso. Physicians India 2003

where science is not the starting point for decision-making. Concern over side effects of synthetic drugs and a need for more humanistic management of illness have led majority of the population in most industrialized countries in favor of TM/CAM. There is an economic face to this trend. Americans and Australians typically pay out of pocket for CAM services. Americans spend more out of pocket on CAM than on all US hospitalizations. Australians spend more on CAM than on all prescription drugs. Major American medical insurers now routinely cover complementary medical services—a trend which is emerging in Britain as well. At the same time, the majority of people in most developing countries use traditional medicine for their everyday health needs. The economic reality here is that even in the best situations, the medical systems that serve the majority of the population get less than 1% of the national health budget. Thus, through marginalization and policy neglect, traditional medicine research, quality of care and training suffers adversely⁵⁶.

Traditional medicine use in many developing countries is on the increase due to limited availability and accessibility of pharmaceutical drugs that are expensive and often unaffordable. Further, there has been rise in antibiotic resistant strains of bacteria and increasing resistance of the malaria parasite to conventional treatments. On the other hand, traditional health care is familiar, available at the local level and is affordable. Therefore, it will continue to play an important role in national healthcare globally.

56 Bodeker G, Complementary Medicine and Evidence, Editorial, *Annals Academy of Medicine*, January 2000, 29(1).

Need for evidence-based research emphasized by the Commonwealth Health Ministers reflects the wider climate of determining best treatment through a formal approach to gathering and synthesizing research data. Evidence-based medicine (EBM) has become a worldwide movement in clinical medicine. Such high standards are now being called for by established medicine in evaluating the claims of traditional or complementary health practitioners. Possibly, due to the historical marginalization of TM/CAM, very limited research funding has been allocated to evaluating their claims. The relatively limited availability of randomized controlled trial (RCT) data has thus led to charges of there being no evidence in support of the effectiveness of TM/CAM. However, “absence of evidence is not evidence of absence” and there is still debate over what constitutes evidence in TM. For example, how does a scientist measure changes in *qi*—a concept of central importance in traditional Chinese medicine or a concept of *Prakriti* – a way to determine individual constitution as per Ayurvedic system? Should the conventional standards of evidence related to modern medicine be applied to the entirely different theoretical assumptions of traditional health systems and therapies? Such research areas of basic principles have remained ignored so far due to over emphasis on exploiting TM for drug discovery. There are few interesting studies that indicate a proof of concept. An advanced analytical tool (Herboprint[®]) based on three dimensional high pressure liquid chromatography has been developed that correlates the Ayurvedic concepts and helps in primary bioprospecting and quality control by giving additional activity support information⁵⁷. Another interesting study has recently reported genetic correlations

57 Vijay Kumar, US Patent (pending) 2004, Indian Institute of Chemical Technology CSIR, Hyderabad, India

between the various classifications of human beings based on Ayurvedic concept of Prakriti underlines importance of scientific research in these areas^{58, 59}.

In order to address areas not readily studied using RCT methodology, and also to correctly design and interpret RCTs, observational studies are receiving new attention. Observational studies are based on quantitative epidemiological methods and quantitative sociological methods in which data are collected through observation. In traditional medicine, it may be assumed that a natural experiment is already taking place, practitioners are prescribing, patients are using. Observational research of existing practice allows for a first line of data to be collected without the ethical difficulties of assigning subjects to novel treatments. Data are gathered on what is actually happening and what the outcomes are from these interventions. As suggested by Arthur Margolin of Yale University, the validity and ultimate value of RCTs of complementary therapies would be diminished if they were conducted without preliminary foundational studies⁶⁰. Foundational studies should investigate such issues as the reputed efficacy of the active treatment or the reputed non-efficacy of the control treatments.

3.2. Safety and Hazards

Safety is a primary concern regarding traditional and complementary therapies. There are two aspects of safety evaluations. First, to ensure that the right quality of material and apt possesses are used from sourcing to marketing; and second, there is no contamination,

58 Joshi K et al, Genotype-Phenotype correlations based on Ayurvedic concepts. Cold Spring Harbor Symposium on Pharmacogenomics, November 2004.

59 Patwardhan B. et al. Classification of human population based on Ayurvedic concept of Prakriti J Alt Complement Med., 2005 (in press)

60 Margolin A., J Altern Complement Med 1999; 5:103-4.

adulteration or spiking. Few studies have reported adulteration with steroids in some traditional Chinese dermatological preparations. In an analysis of Chinese herbal creams prescribed for dermatological conditions, Keane et al. found that eight of eleven creams analyzed contained steroids⁶¹. Spiking with corticosteroids has been observed in some market preparations claimed to be useful in the treatment of arthritis and asthma⁶².

Recently, Saper et al. from Harvard Medical School have reported heavy metal content of Ayurvedic herbal preparations and have recommended mandatory toxic heavy metal testing⁶³. There have been few reports of heavy metal toxicity following traditional medicine use^{64, 65}. Such studies are important and needed, however they are more related to the quality control failures of the mass manufacturing activities. Often they are wrongly used to limit the use of TM. In reality, such a QC failure should not be considered as a general negative notion to create a bias against TM. We certainly need effective QC and regulation of herbal medicines, without limiting public access to these preparations and ensuring public interest and constituting restrictive trade practice.

Traditionally, Ayurveda uses many metals in therapeutics but it is only after a due purification processes strictly followed in accordance with authentic traditional methods. Such traditional metal preparations (generally called as *Bhasma* and wrongly perceived as oxides are actually organometallic complexes) must qualify three main properties: ultrafine particle size that floats on water and one should not be able to recover metal back from the such preparations. Some of the recent studies have observed presence of

61 Keane FM. Analysis of Chinese herbal creams prescribed for dermatological conditions BMJ 1999;318:563-564.

62 Chopra A. and Doiphode V. Medical Clinics of North America 2002; 86:75-89.

63 Saper R.B. et al. Heavy metal content of Ayurvedic herbal medicinal preparations. JAMA 2004, 292 (23); 2868-2873.

64 Ernst E. Heavy metals in traditional Indian remedies. Eur J Clin Pharmacol. 2002; 57(12): 891-6.

65 Caldas ED, Machado LL. Cadmium, mercury and lead in medicinal herbs in Brazil. Food Chem Toxicol. 2004;42(4):599-603.

nanoparticles in such traditional metallic preparations⁶⁶. Most of the traditional methods for preparation of herbomineral complexes are very tedious and lengthy. Mass scale commercial production often tends to process a compromise that results adversely on its quality. This is the main reason of such heavy metal contaminations. What is more worrying is the fact that traditional preparations such as *mahasudarshan churna and bala guti* where metals are not the part of official formulation have shown high amount of toxic heavy metals. This is certainly a failure of the quality assurance system and a case of bad manufacturing processes. This is equally a failure of the regulatory system particularly the Indian that has not yet been able to evolve and enforce effective quality control and safety assurance of herbal medicines. Government of India has released GMPs herbal medicines that need to be implemented strictly. It will be unfair to convey a general message against Ayurvedic or such traditional herbal medicines. In fact, Ayurveda or TM has nothing to do with it⁶⁷.

Research should consider best evidence for safety, including evidence for adverse effects from treatments and inappropriate applications of traditional therapies. Post-marketing surveillance studies can provide information on adverse effects of botanical herbal preparations. Pharmacognostic and pharmacological research can provide information on the quality, efficacy, safety or toxicity of botanical/herbal medicinal preparations⁶⁸. More broadly, in addressing safety in herbal medicines, a basic question is 'safe with respect to what'? Research has found that in the US, 51% of FDA-approved drugs have serious

66 Ashok Vaidya, 2003, Bhavans SPARC, Juhu Mumbai (unpublished work) and Shastri M., 2004, Nano materials Group, National Chemical Laboratory, Pune India (Unpublished work).

67 Patwardhan et al. 2005. Heavy Metals and Ayurveda, Current Science, 88 (11).

68 Warude D., Patwardhan B., Botanicals: Quality and regulatory issues.. J. of Scientific & Industrial Research, 2005 (In Press)

adverse effects not detected prior to their approval. 1.5 million people are sufficiently injured by prescription drugs annually that they require hospitalization. Once in hospital, the problem may be compounded. The incidence of serious and fatal adverse drug reactions (ADRs) in US hospitals is now ranked as between the fourth and the sixth leading cause of death in the United States, following next after heart disease, cancer, pulmonary disease and accidents⁶⁹. Thus, the safety of and risks associated with medical interventions is an issue across all categories of health care.

Safety must be the starting point in drug development strategies for herbal medicines. While most of the published research on herbal medicine is pharmacological, WHO's 1993 Guidelines on the Evaluation of Herbal Medicines considers that clinical evaluation is ethical where drugs have long been in traditional use. The Council for Scientific and Industrial Research of Government of India along with the Indian Council for Medical Research has offered a model for the clinical evaluation of herbal medicines⁷⁰. This is being followed for the ongoing major herbal drug development program under the New Millennium Indian Technology Initiative has adopted the Reverse Pharmacology Approach (see Innovation and Drug Discovery section for details) and advocates adherence to mandatory requirements for clinical testing of any traditional preparation: Heavy metals, Pesticides, Microbial (pathogenic) load, are within the WHO prescribed limits and basic safety established in experimental animals using OECD guidelines⁷¹.

69 Lazarou J, et al. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. JAMA 1998; 279:1200-5.

70 ICMR Guidelines for Clinical Trials in India, 2003

71 CSIR-NMITLI Government of India, Herbal Drug Development project, Clinical guidelines, 2003

Similarly, the dietary supplements that may come from outside of TM, have also been confronted with adverse events. Palmer et al. have reported in the observational study that Dietary supplements are associated with adverse events that include all levels of severity, organ systems, and age groups. Associations between adverse events and ingredients are difficult to verify if a product has more than one ingredient, and because of incomplete information systems⁷². In Nature Reviews Drug Discovery, Engel & Straus have discussed the regulatory framework for dietary supplements and drugs, outlined the challenges of evaluating dietary supplements for safety and clinical effectiveness, and also describe the evolving drug model for botanicals⁷³.

Global Forum on Safety of Herbal and Traditional Medicine report⁷⁴ has covered the status of regulation of complementary medicine in Australia and comparative examples from Africa and Bangladesh. Safety evaluation, which incorporates quality procedures, was identified as another point of focus. Clear evidence for the non-utilization of plants known to contain certain compounds producing deleterious effects has been exemplified via data and information on the dangers of ingesting pyrrolizidine alkaloids.

The Medicine and Healthcare Products Regulatory Agency of UK (MHRA) has produced a list of frequently asked questions and answers about the safety and quality of traditional Chinese medicines. According to MHRA there are some TCM products on the UK market that may be manufactured to low quality standards and may be deliberately adulterated or accidentally contaminated with toxic or illegal ingredients. These products

72 Palmer M.E. et al., Adverse events associated with dietary supplements: an observational study. *Lancet* 2003; 361: 101–06

73 Engel L. & Straus E., *Nature Reviews Drug Discovery* 2002, 1, 229–237.

74 Noller B.N., *Global Forum on Safety of Herbal and Traditional Medicine*: July 7, 2001, Gold Coast, Australia

do pose a direct risk to public health and it is not currently possible to distinguish between these products and TCMs that are made to acceptable safety and quality standards. The shortfall in quality standards may not be necessarily dangerous (except in cases of heavy metal, pesticide, pathogens or other such contaminations), but there is an element of risk. The risks vary widely, depending on the ingredients and how they are used. The former Medicines Control Agency informed the public in 2001 via the general media of the advice given by the Committee on the Safety of Medicines (CSM) that it was not possible to give the public assurances as to the safety and quality of TCMs on the UK market. Since then the Agency (now the MHRA) has continued to find examples of illegal and dangerous TCMs being supplied in the UK and consumers should be alerted to the continuing problem. Recent samples of TCMs found on the UK, which pose a risk to public health, have contained mercury, heavy metals and toxic herbal ingredients.

The rising use of TM/CAM by the Australian public has also raised the critical issue of safety. Safety is assumed and rarely questioned. There is a general belief (also found in many other communities) that herbal or natural medicines are safe, which is obviously both simplistic and untrue. Yet, an Australian survey of 3027 people in 2000 showed that 90% of users of CAM (especially the elderly) considered the products safe, compared with 65% of non-users. The widespread availability of complementary medicines through health food stores and supermarkets, and the infrequency of litigation against CAM practitioners, has been suggested as evidence of safety. However, these need not be appropriate measures of safety. It is important to realize that any therapy has the potential to cause harm, and that any pharmacologically active product is likely to have adverse

effects. The critical issue in assessing merit of any therapy is its risk to benefit. In modern medicine such therapeutic index outlining the number of individuals experiencing an adverse event versus the number of people achieving a benefit is fairly well studied and documented. The TM/CAM therapies and products need more rigorous assessment, systematic pharmacovigilance and till such time it is achieved satisfactorily, the clinicians should have a definite plan for understanding and valuing safety issues⁷⁵.

Herb-Drug interaction is a growing concern in TM. Single or multiple botanicals are bound to contain several chemical ingredients. Some of these chemicals are directly responsible for therapeutic activity, some are responsible for balancing the toxicity, some are required as carriers and some could be harmful as well. However, if the preparations are the result of traditional practices and continued use, the harmful part of it may be considered as low. However, in the modern world, when there are many other options available, there are many occasions when TM and modern medicine are used together. This opens a new dimension of herb-drug interaction. As such there are very few studies on this subject, however, available data certainly indicates seriousness and importance of herb-drug interactions⁷⁶. Ginkgo: Causes bleeding when used with warfarin; causes raised blood pressure when used with a thiazide diuretic. Ginseng lowers blood concentrations of alcohol and warfarin; induces mania when used with phenelzine. Garlic lowers blood concentration of warfarin; changes the pharmacokinetics of paracetamol; causes hypoglycaemia when used with chlorpropamide. St John's wort⁷⁷ lowers blood concentrations of cyclosporin, amitriptyline, digoxin, indinavir, warfarin,

75 Myers S.P. and Cheras P.A. The other side of the coin. *MJA* 2004; 181: 222-225

76 Izzo A.A. and , Ernst E. Interactions between herbal medicines and prescribed drugs. *Drugs* 2002; 61: 2163-2175.

77 Mills E. et al. Interaction of St John's wort with conventional drugs,. *BMJ* 2004, 329; 27-30.

phenprocoumon and theophylline; causes intermenstrual bleeding when used with oral contraceptives; causes mild serotonin syndrome when used with loperamide or selective serotonin reuptake inhibitors. These are just few studies that underline importance of better understanding of herb-herb or herb-drug interactions where more attention and research is urgently needed to ensure safety.

3.3 Quality Control and Regulations

Traditional Medicine involves extensive use of botanicals and includes various steps starting from a passport data on raw materials, correct identification, pharmacognostic and physico-chemical quality standardization, safety and preclinical pharmacology (acute, sub-acute and chronic toxicity studies), clinical pharmacology (pharmacokinetics and pharmacodynamics) and randomized controlled clinical trials (Phase I to Phase IV). While traditional health systems in developing countries have typically been the primary health service of rural communities and the poorest levels of society, there is now increasing reliance on traditional health care by urban populations as well⁷⁸. In Africa, for instance, the rapid rate of urbanization is changing the face of traditional medicine. Where previously, the village herbalist or healer would provide services and would draw on nearby forests and fields for herbs, urban markets have many herb sellers, each giving advice and many selling both raw plant material and preparations that they have produced themselves. Almost similar situation exists in many parts including India where still main

78 Cunningham, A.B., 1993, African Medicinal Plants: Setting priorities at the interface between conservation and primary health care. People and Plants working paper. UNESCO 1993 Division of Ecological Sciences, Paris.

sources of herbs are coming from nature and not through planned cultivations. Quality control is a challenge under these circumstances.

Addressing quality control and standardization is very vital and needs broader consideration. The dynamic process of evolution could have altered and affected the identity and structure of natural materials. For commercialization, correct identification and supply of raw material to avoid adulteration has become a challenge. Additionally, some botanical species might have been extinct or may have undergone change due to time and environmental factors. Standardization of botanicals and medicines is required differently, although one cannot readily apply the typical modern pharmaceutical pharmacopoeial standards. The concept of active markers in the process of standardization needs a flexible approach in favor of the very complex nature of these materials.

Recently, many international authorities and agencies including the World Health Organization⁷⁹, European Scientific Cooperation of Phytomedicine⁸⁰, US Agency for Health Care Policy and Research⁸¹, European Pharmacopoeia Commission, Department of Health UK⁸², Commonwealth of Australia⁸³, Department of Indian System of Medicine have started creating new mechanisms to induce and regulate quality control and standardization of botanical medicine. European Medicine Evaluation Agency has

79 General Guidelines for Methodologies on research and evaluation of Traditional Medicine In: World Health Organization, Geneva, WHO/EDM/TRM/2000.1. (2000). P 1-73

80 Note for guidance on Quality of Herbal Medicinal Products In: European Agency for the evaluation of Medicinal Products: EMEA/CVMP/814/00, (2001).

81 Draft guidance for Industry on Botanical drug products In: U.S Department of Health and Human services, Food and Drug Administration and Center of drug evaluation and research: August 2000.

82 Department of Health UK, Regulation of herbal medicine and acupuncture, Proposals for statutory regulation, March 2004

83 Expert Committee on Complementary Medicines in the Health System Report to the Parliamentary Secretary to the Minister for Health and Ageing September 2003

prepared proposal for directive from the European Commission for the Traditional Medicinal Products⁸⁴. National Reference Centre for African Traditional Medicines: A South African Model made by Department of Health Medical Research Council, Council for Scientific and Industrial Research presents a good example. While regulation of traditional medicines remains a challenge, progress has been made in South Africa by the National Department of Health to provide for a regulatory framework to register, regulate and control African Health Practitioners. The proposed Traditional Healers Bill will establish a traditional Healers' Council once it becomes law. There is a need for a comprehensive review and development of policy and legislation pertaining to traditional health care, incorporating standards of accreditation, training and research. A botanical drug or a preparation thereof is now regarded as one active substance in its entirety whether or not the constituents with therapeutic activity are known. This will be a major step in development of new generation standardized botanical medicines.

The regulatory and legal situation regarding TM and herbal preparations varies from country to country. In some, herbal medicines are well established, whereas in others they are regarded as food where therapeutic claims are not allowed. Recently, De Smet has discussed many issues related to regulatory standards for herbal medicines in Europe⁸⁵. Developing countries, however, often have a great number of traditionally used herbal medicines and much folk-knowledge about them, but have often inadequate legislative criteria to establish them as part of the drug legislation. For the classification of herbal or traditional medicinal products, factors applied in regulatory systems include: mention in

84 The Draft EC Proposal for a Directive on Traditional Medicines Keller Konstantin Chair of the Herbal Medicinal Products Working Group European Medicines Evaluation Agency, London

85 DeSmet Peter A.G.M., Herbal medicine in Europe – Relaxing regulatory standards. *N. Engl. J. Med.*, March 2005, 352;12:1176-78.

traditional classic books as in case of Ayyurvedic medicines in India⁸⁶. Additionally, description in pharmacopoeia monograph, prescription status, claim of a therapeutic effect, scheduled or regulated ingredients or substances, or periods of use are also considered. Some countries draw a distinction between officially approved products and officially recognized products, by which the latter products can be marketed without scientific assessment by the authority. Dr. Xiaorui Zhang of Traditional Medicine Program of WHO has taken an excellent worldwide overview of regulatory status of TM.

The WHO has published many official and nonofficial documents on TM related subjects including WHO Monographs on selected medicinal plants⁸⁷. Global definitions of botanical products are being developed by international cooperation and a new perspective of standardization, validation, safety and efficacy of botanical medicines is evolving, which is a good sign⁸⁸. Multi-component botanical formulations can be standardized with newer techniques such as DNA fingerprinting⁸⁹, High Pressure Thin Layer Chromatography, hyphenated techniques such as Liquid Chromatography-Mass Spectroscopy. In-house monographs need to be evolved and critically followed. For example, a multi-component botanical formulation (Artrex) designed for the treatment of arthritis contains four botanicals and all ingredients, their respective extracts and the formulation are standardized using HPLC and HPTLC fingerprint profiles with known markers. This formulation has been granted a US Patent⁹⁰ and is commercially available in India and few other countries. Pre-clinical studies on Ayurvedic medicines are more

86 FDA Schedule on Ayurvedic Medicines, Government of India

87 WHO Monographs on selected medicinal plants Volume I and II, 1996, 97.

88 Warude D., Patwardhan B., Botanicals: Quality and regulatory issues.. J. of Scientific & Industrial Research, April 2005 (In Press).

89 Joshi K. et al. Molecular markers in Herbal Drug Technology, Current Science, 2004, 87(2) 159-165.

90 Patwardhan B. A method of treating musculoskeletal disease and a novel composition therefor. United States Patent No. 5,494,668, February 1996.

important for validating drug safety resulting from new procedures or extractions are used during its preparation. The value of animal testing to establish safety and toxicity is not so critical if the botanicals are used in traditional forms. Suitable animal models help in understanding the mechanism of action or pharmacodynamics of medicines, however, no good animal models exist for some human diseases.

The basis of traditional medicine is its use for number of years and therefore its clinical existence comes as a priori assumption. However, for bringing more objectivity and also to confirm traditional claims, systematic clinical trials are necessary. In TM research, clinical experiences, observations or available data becomes a starting point. In conventional drug research it comes at the last. Thus, the drug discovery based on TM follows a ‘Reverse Pharmacology’ path⁹¹. Nevertheless, all the critical Pharmacopoeial tests such as dissolution time, microbial, pesticide and heavy metals contamination etc. must be in accordance with global standards. It is important to ensure that all the TM manufacture is in accordance with Current Good Manufacturing Procedures for herbal products^{92, 93}. There have been many concerns about quality standards and safety issues of herbal medicines⁹⁴. The need for new regulations for TM and natural medicines has been frequently stressed and some such regulations are coming in force in different parts of the world^{95, 96}.

91 Vaidya A.D.B., Vaidya R.A., Nagara S.I. Ayurveda and a different level of evidence: From Lord Macaulay to Lord Walton (1835-2001 AD), Journal of Association of Physicians India (JAPI), 2001; 49:534-537 and Approach Paper, New Millennium Indian Technology Leadership Initiative Herbal Drug Development Program, CSIR New Delhi, 2002.

92 Good manufacturing practices: Supplementary guidelines for manufacture of Herbal Medicinal products In: WHO expert committee on specifications for pharmaceutical preparations. Thirty fourth report. Geneva, World Health Organization, 1996, Annex 8 (WHO technical Series, no 863). P.134-139.

93 Verpoorte R and Mukherjee P. GMP for Botanicals, businesshorizons.com, 2003.

94 Straus S. Herbal Medicines – What’s in the Bottle? NEJM 2002; 347(25):1997-1998.

95 Legal Status of Traditional Medicine- A Worldwide Review, W.H.O. Geneva 2001.

96 Marcus D and Grollman A. Botanical Medicines – The need for new regulations, NEJM 2002; 347(25); 2073-2076.

“Injustice anywhere is a threat to justice everywhere”.

Martin Luther King Jr.

Chapter 4

A High Priority Need – Public Health Agenda

“It has been said that democracy is the worst form of government except all the others that have been tried”, said Winston Churchill. A Public Health perspective to global health issues is to human health and well being what democracy is to their governance. Reconciliation with this fact was until lately a matter of choice, made invariably by a handful of altruist humanitarians. Globalization has converted it into a mandate for mankind. Just as no human is an island, no country or no society can shape its health and well being in isolation. A stifled innovation in some unheard undeveloped country is no more a loss to the local population. The butterfly effect can bring about an unprecedented devastation of epidemic on the other end of the world. To let a struggling pharmaceutical in some remote corner of a developing country crush under the burden of say IPR regulations applicable to mega transnational pharmaceutical corporations can actually announce demise of those very mega corporations that demand compliance with harsh IPR regulations from the former company. A child’s illness or death due to TB in Timbuktu, because its parents could not afford a pack of medicine pills (its one time cost more than the family’s monthly wages) cannot anymore be treated as “not-my-health-problem.” Whether we like it or not, the world population has become too well connected and interlocked.

In uncertain times such as these, TM has much to offer to public Health. While it can fill the missing links for the bottlenecked MM pharmaceutical industries, and provide for supplemental benefit to population in the developed countries that has started to use TM more and more, it can serve as a fast, cheap, beaten path recourse to health care needs of large uncovered developing world population. MM might be the best solution in health to humanity, but in its express absence, TM can play a make-shift substitute in developing world- even if its entirety might be sub-optimal by current MM standards. Since MM has gone a few steps of evolution ahead of TM, it is necessary that MM help TM serve the developing countries for their health care needs.

4.1. Availability, Accessibility and Affordability

According to Peter F Drucker, “The best way to predict the future is to create it”. What future is currently being created for the health of the world’s poorest people? The picture is mixed and confusing. It is encouraging and depressing at once.

Recent years have seen a range of initiatives targeted at improving the prevention and treatment of major diseases, especially tuberculosis, HIV/AIDS, and malaria. The growth of such campaigns, coupled with promises of new funding and high awareness of the health-dominated Millennium Development Goals (MDG), suggests that health in less-developed countries can only improve⁹⁷.

97 Sachs J.D Achieving the Millennium Development Goals - The Case of Malaria, NEJM 2005; 352(2):115-117

On the other hand, John N Lavis et al and others in a series of articles published in *The Lancet*, predicted a very different future and have investigated aspects of health systems—the people, institutions, and resources that must be in place to ensure that disease prevention and treatment can reach those in need—in less-developed countries. The health research must no longer be confined to the drugs, the devices, the vaccines. The Mexico Ministerial Summit was expected to assert boldly and publicly that the traditional biomedical model of health research is wholly inadequate to tackle disease alleviation in the less-developed world⁹⁸. As very critically analyzed by David Triggler of State University Buffalo, this discrepancy in health care parallels the economic disparities that exist between nations and that are in fact increasing rather than decreasing. According to him, the absence of health care is a driving force for the generation and maintenance of poverty and the issue is less of science than it is of public policy but of the will of the rich world to generate the infrastructural environments to enable rewards of science shared equitably. Dr. Triggler discusses the future of biomedical science in terms of the science that will drive advances and the public policy issues that must be implemented to ensure delivery of scientific benefits and endorses that the specialties should also draw on what useful research has already been done in other disciplines, such as the social, behavioral, and organizational sciences as also the TM⁹⁹.

It is worthwhile noting that the use of unconventional therapies for health problems is increasing, but the extent of this use and the costs were not well known until Eisenberg et

98 Editorial, *The Lancet*, , 2004, 364; 1555-56.

99 Triggler D. Medicines in the 21st Century Or Pills, Politics, Potions, and Profits: Where Is Public Policy? *Drug Dev. Res.* 59:269–291, 2003.

al.¹⁰⁰ conducted a national survey in the US to determine the prevalence, costs, and patterns of use of unconventional therapies, such as acupuncture and chiropractic. One in three respondents (34 percent) reported using at least one unconventional therapy in the past year, and a third of these saw providers for unconventional therapy. The latter group had made an average of 19 visits to such providers during the preceding year, with an average charge per visit of \$27.60. The frequency of use of unconventional therapy varied somewhat among socio-demographic groups, with the highest use reported by non-black persons from 25 to 49 years of age who had relatively more education and higher incomes. The majority used unconventional therapy for chronic, as opposed to life-threatening, medical conditions. Among those who used unconventional therapy for serious medical conditions, the vast majority (83 percent) also sought treatment for the same condition from a medical doctor; however, 72 percent of the respondents who used unconventional therapy did not inform their medical doctor that they had done so. Extrapolation to the U.S. population suggests that in 1990 Americans made an estimated 425 million visits to providers of unconventional therapy. This number exceeds the number of visits to all U.S. primary care physicians (388 million). Expenditures associated with use of unconventional therapy in 1990 amounted to approximately \$13.7 billion, three quarters of which (\$10.3 billion) was paid out of pocket. This figure is comparable to the \$12.8 billion spent out of pocket annually for all hospitalizations in the United States. The frequency of use of unconventional therapy in the United States is far higher than previously reported. In light of these facts medical doctors now need to know use of unconventional therapy whenever they obtain a medical history.

100 Eisenberg D.M. et al. Unconventional Medicine in the US: Prevalence, Costs, and Patterns of Use. NEJM 1993, 328:246-252

Many other studies have documented that about half the population of industrialized countries now use TRM/CAM; with numbers ranging widely. However, most research has focused on clinical and experimental medicine (safety, efficacy and mechanism of action), and regulatory issues, to the general neglect of public health dimensions. According to Bodeker et al¹⁰¹ public health researchers must lead the development of a research agenda that considers social, cultural, political and economic contexts, to maximize the potential contribution of TRM/CAM to healthcare systems globally.

Although, there are very limited systematic studies to compare affordability and cost effectiveness of TM, some recent reports have substantiated the general belief that TM is affordable as compared to Modern Medicine^{102, 103}. In a recent randomized controlled study on 401 patients with chronic headache, use of Acupuncture significantly improved health related quality of life at a small additional cost compared with a number of other available interventions in the modern medicine¹⁰⁴. Similarly, interventions through Yoga and meditation especially in cardiovascular, psychosomatic, musculoskeletal and mental disorders have been beneficial at a considerably low cost and risks¹⁰⁵. Saper et. al. reported that an estimated 15.0 million American adults had used yoga at least once in their lifetime and 7.4 million during the previous year. Yoga was used for both wellness and specific health conditions often with perceived helpfulness and without expenditure¹⁰⁶. Thus, some of TM therapies offer a safer, better and cost effective

101 Bodeker G and Kronenberg F, A Public Health Agenda for Complementary, Alternative and Traditional Medicine. *Am. J. Pub. Health.* 2002. 92, 10, 1582-1591.

102 White AR, Ernst E Economic analysis of complementary medicine: a systematic review. *Complement Ther Med* 2000 8;111-8.

103 Evans KW, et al. A. Economic evaluation of oral sumatriptan compared with oral caffeine/ergotamine for migraine. *Pharmacoeconomics* 1997;12:565-77.

104 Wonderling D. et al. Cost effectiveness analysis of a randomised trial of Acupuncture for chronic headache in primary care. *BMJ* 2004;328;747-52.

105 Oz M. Emerging role of integrative medicine in cardiovascular disease. *Cardiol Rev.* 2004; 12(2):120-3.

106 Saper RB et al. Prevalence and patterns of adult yoga use in the United States: results of a national survey. *Altern Ther Health Med.* 2004; 10(2): 44-9.

alternative. More systematic research in these areas is needed to multiply these effects on larger scale.

These data, mainly from the developed countries such as the USA make a case with evidence that TM is indeed a better affordable alternative to MM. In conjunction to the data about costs of TM in developing countries, discussed elsewhere, the world polity therefore, must focus on accessibility and availability issues of TM in the developing countries.

4.2. Economics and Financing

Ignoring or under-funding the traditional healthcare sector generally ensures that the poor and rural communities have much less than critical desired access to services. Learning from best practices, self-regulation, and ongoing training are essential components of policy development in traditional healthcare. Moreover, traditional healthcare providers are not mere cheap resources for conventional primary healthcare program but are viable alternatives to them in their absence. In fact treating them only for the benefit of cost are likely to erode their traditional role and knowledge base to further weakening of the traditional sector. With careful planning and collaboration at different levels of the health sector, a pluralistic healthcare environment based on quality in healthcare could be created which can complement its own subsets like MM and TM¹⁰⁷.

107 Bodeker G. Traditional Health Systems and National Policy. Newsletter 19th November 2003, Research Council for Complementary Medicine London

Developing countries are argued to be abandoning their attributes in their quest to become developed countries. There have been strong opinions and debate related to need to reduce on sophisticated investigations. This could reduce the cost of medical treatments. For example, instead of placing more emphasis on providing social security, a family culture can be a great individual security factor and prevent many psychological problems. Yoga and meditation can be beneficial in preventing obesity and depression, which are becoming the new public health problems in the developed world. Well-conducted clinical examinations with minimal possible investigations can bring down the cost of health care¹⁰⁸.

Traditional healers are a source of health care for which Africans have always paid to healers despite the expansion of modern medicine. It is argued that their success may not come from either supernatural power or gullible clients but rather from the commitment to deliver high quality care. Health economists have long known that the “pay only if cured” contract, or outcome–contingent fees would resolve many market failures in the delivery of health care, however, they have assumed that such contracts could not be implemented. Kennet Leonard argued that not only are traditional healers using this important economic arrangement to deliver care, but also this practice has the predicted impact on patients’ perceptions of quality¹⁰⁹.

108 Pandey K.R. Learning from low income countries: what are the lessons? *BMJ* 2004;329:1185.

109 Leonard K.L. A research note is based on the paper titled “African Traditional Healers and Outcome – Contingent Contracts in Health Care,” February, 2001, work that was funded by NSF grant #94-22768 and a University of California Rocca Fellowship.

The World Bank has facilitated several community-to communities Indigenous/ Traditional Knowledge (IK/TK) learning exchanges within countries, between countries as well as between Africa and South Asia. For example, the Bank has supported national workshops to develop policies and strategies for utilizing IK. In Tanzania this process led to a coalition of NGOs, government institutions and academia that pays attention to traditional healers and recognizes their knowledge as a major subject of research. In Uganda, a similar process has led to a national strategy that incorporates IK into the country's Poverty Eradication Action Program. In Ethiopia and Ghana, the Bank is supporting the development of medicinal plants for the domestic market. In Eritrea, indigenous practices are helping move forward the agenda on early childhood development in the context of a Bank-supported project. In Burkina Faso, the Bank is supporting activities to disseminate indigenous practices to increase agriculture production yields in areas that are subject to drought conditions.

The Bank has already brokered cooperation for the scientific validation of TM practices between other development partners, research organizations and local institutions and civil society. One such effort was aimed at linking the Tanga AIDS Working Group in Tanzania with scientists at the National Institutes of Health (NIH) and The George Washington University in the United States. In another case, in Kenya, the NIH, the Ministry of Health and the traditional healers working together in the fight against HIV/AIDS are exploring the use of medicinal plants. With respect to the challenge of validation, the Bank is exploring scientific centers of excellence in Africa and Asia on the role that South-South collaboration can play in contributing to this issue. For example,

the Center for Scientific and Industrial Research (CSIR) in South Africa and the CSIR in India could bring their scientific expertise to informing the issue of validation. The Global Research Alliance (GRA) that brings together some of the top scientific research institutions in Africa, Asia, Europe, America and Australia is also looking in such aspects. The IK Program of the Bank plans to collaborate with country authorities, other partners, as well as community-based organizations and NGOs in preparation and organization of a forum to help and promote the use of indigenous knowledge for sustainable community-based development and jointly enrich the development process¹¹⁰.

4.3 Policy Issues

In response to the WHO call, several countries have framed TM policies and many are in the making. For instance, Kenya is developing a national policy to promote TM that is intended to regulate a practice on which 80 per cent of its inhabitants depend for medical treatment. The development of the policy is in line with a commitment by the African Union to recognize the period 2001-2010 as a decade of traditional medicine. Kenya is seeking to catch up with Uganda and Tanzania, both of whose policies on TM are significantly more developed. The Nairobi Declaration has formally recognized TM at the Conference on ‘Traditional Medicines and Local Communities in Africa: Challenges and Opportunities of the New Millennium’ by confirming commitment to the collective goal of Health for All through the primary health care approach and the principles of

¹¹⁰ Madavo Callisto Senior Advisor to the President of the World Bank, Speech during the launch of: “Indigenous Knowledge: Local Pathways to Global Development” Dar es Salaam, Tanzania, 20 October, 2004

conservation and sustainable development outlined in the Convention of Biological Diversity.

The Prime Minister of Vietnam recently approved the national policy for traditional medicine through 2010 that defines the inheritance, preservation and development of TM, thereby combining traditional and modern medicines in healthcare. The decision also contains provision for foundation of a national Vietnamese medical system incorporating modern, scientific and popular medicine. The government of India through the Department of AYUSH has framed a policy for Indian Systems of Medicine¹¹¹. The Government of India also has Central Council for Research in Ayurveda and Siddha (CCRAS) that generally oversees intramural and extramural research programs for the department. Similar Councils for Yoga, Homoeopathy and Naturopathy also are functional and are part of this policy. Recently Government of India established a National Commission on Farmers, which in collaboration with Foundation for Revitalization of Local Health Traditions (FRLHT) organized a national consultation to discuss how the benefits of traditional knowledge and sustainable medicinal plants cultivation can help the local, underserved and farmers communities¹¹².

Policy development and infrastructure development needs will have different priorities in different countries. Priorities will necessarily reflect the state of development of existing infrastructure for TM. Increased TM utilization is mainly due to limited availability of modern medical services and pharmaceutical products in most rural areas. Further, it can

111 Government of India ISM Policy 2002

112 Swaminathan M.S. Sustainable Management of Medicinal Plant Resources, National Consultation organised by the National Commission on Farmers in collaboration with FRLHT and University of Agricultural Science, GKVK, Bangalore, May 9 –10, 2005

be expensive, often unaffordable and many drugs are known to be variable in their effect. Macroeconomic factors such as devaluation of currencies, including, as a result of externally imposed structural adjustment programs, can result in a substantial shift from modern to traditional medicine, even in urban populations. There are reports that the introduction of user fees for government health services is resulting in a substantial shift away from modern to traditional medicine¹¹³. In short, the business approaches are also changing in favor of poor, purely for a long-term sustainability reasons and such approaches are likely to benefit the TM future. Improving life's of the billions at the bottom of the economic pyramid is a noble endeavor and the visionary industries are discovering it lucrative too¹¹⁴.

4.4 Relationships and Integration

Many countries have adopted integration models such as China, India, Korea, South Africa, Indonesia, Uganda, Ghana, Nigeria, Cuba and many more. The integrated practice has become a global phenomenon; in some countries it is legal and formalized while it is in process in many others. For instance, Ghanaian health authorities took a major step to resolve a seemingly contentious issue in the fight against HIV/AIDS in the country by seeking to encourage TM practitioners¹¹⁵. The Uganda Law Reform Commission has a law for the recognition, the protection and practice TM. This enables national institutions and international organizations to promote and integrate herbal medicine into their

113 Bodeker G. A framework for cost benefit analysis of traditional medicine & conventional medicine. In Chaudhury, Ranjit Roy. Traditional Medicine. WHO, SEARO, 2001.

114 Pralhad C.K. and Hammond Allen, Serving the words poor profitably. Harvard Business Review, September 2002, RO209C.

115 Afele M. Ghana Seeks Integration of Traditional Medicine Practice. Panafrican News Agency - January 18, 2001

development plans. THETA — Traditional and Modern Health Practitioners Together against Aids and other diseases, is a Ugandan organization where traditional and modern health practitioners are working together¹¹⁶.

The integration of TM into the Nigerian health care delivery system has been studied for legal implications, complications and its relationship to the law of the land explored where the researcher concluded that such integration would be unconstitutional¹¹⁷.

However, things are changing fast in favor of integration all over. The National Center for Complementary and Alternative Medicine of the National Institutes of Health in the US presents a best case where an open minded, science and evidence driven approach is adopted for such integration in practice and research.

Integrated clinics have already been established in response to community demand especially in the west. There is growing evidence base for TM/CAM and its widespread community use compels doctors to understand complementary therapies and to refer patients to TM/CAM practitioners where appropriate. Most general practitioners have patients with chronic illness who could benefit from the services of TM/CAM practitioners, and practically all have patients who require access to mainstream diagnosis and therapy. Collaboration requires shared respect and trust, and education. Dangers of not integrating care include delaying or depriving patients of safe and effective management, and the potential for harmful interactions. Integration is currently being supported in Australia through government and organizations such as the Australian

116 The World Bank, *Traditional Medicine Practice in Contemporary Uganda*. IK Notes No. 54 March 2003

117 Ajai O. The integration of traditional medicine into the Nigerian health care delivery system: legal implications and complications. *Med Law*. 1990;9 (1):685-99.

Medical Association, the Royal Australian College of General Practitioners and the Australasian Integrative Medicine Association¹¹⁸. Similar practices for economic and social reasons are also observed in other parts including EU and the Americas¹¹⁹.

According to Professor Bodeker, integration works best when it is based on self-regulation in relation to standards of practice and training. It needs a central or regional system for drug control and evaluation and maintenance of good manufacturing practice to generate and support a comprehensive program of research. When conventional medicine dominates complementary medicine, loss of essential features of complementary medicine can occur, and professional conflicts can arise. Policy should aim to keep fees for complementary medicine affordable and within reach of all levels of society. Substantial sectoral investment is necessary for the development of effective services for complementary medicine. Under investment contemplates a risk of perpetuating poor standards of practice, services, and products¹²⁰.

In India, the Banaras Hindu University where modern medicine superspecialities and traditional practices such as Ayurveda and Yoga coexist even now adopted the first systematic integration of modern and traditional health care and research. A national center for evidence based Ayurvedic research has been established at the modern medicine medical institution in Mumbai (Dr. Sharadini Dahanukar Center for Ayurvedic Research at KEM Hospital and TN Medical College Mumbai). A separate University for

118 Cohen M. M. CAM practitioners and “regular” doctors: is integration possible? MJA 2004; 180: 645–646.

119 MacLennan A, Wilson D, Taylor A. The escalating cost and prevalence of alternative medicine. Prev Med 2002; 35: 166-173.

120 Bodeker G. Lessons on integration from the developing world's experience. BMJ 2001;322:164–7

Yoga was established at Mungher Bihar and Kaivalyadham Yoga Institute Lonavala for biomedical research has practiced a good integrative model.

China experience is probably the best that began in 1955, when it was proposed that Chinese and Western medicine be combined to boost the health care of the Chinese populace. That same year, the Ministry of Public Health, staffed by both Chinese and Western-trained physicians, was established. Over the next 40 years, China integrated practices from both cultures through a bottom-up approach. Medical students now have to take courses in both Western and traditional medicine, and actively implement their cross-cultural knowledge in hospitals and teaching clinics. As a result, Chinese physicians are now familiar with the strong and weak points of both medical systems and can choose the right combination to maximize the positive effects.

According to Charls Feng of Stanford University¹²¹, the Chinese are firm believers in the efficacy of traditional medicine. They also believe that certain aspects need to be researched and developed further. Many Chinese also believe Western medicine offers alternative approaches and methods, some of which are more effective than their traditional counterparts. Acupuncture has been used to successfully treat heart disease, gallstones, respiratory diseases in infants, and cataracts. According to Pei Wang, author of *Traditional Medicine and Health Care Coverage*, in many respects, the combined Chinese and Western treatment is much better than that of either system applied alone. Research at Chinese and Western universities has also shown that Chinese herbs, when combined with radiation or chemotherapy, worked better in cancer patients, as well as

121 Feng C. Merging Chinese Traditional Medicine into the American Health System. *Journal of Young Investigators*, Issue 5, November 2002

boosted their immune responses. By incorporating aspects of traditional Chinese medicine into the Western health care system and by improving the Chinese understanding of Western medicine, both cultures can improve their skills of medicinal and physical treatments. In the process, this merging of East and West can foster cross-cultural understanding. Such innovative model of integration needs to be suitably modified and adopted by all the countries.

Conglomerations of senior scientists and practitioners from different disciplines are putting efforts in understanding and propagating importance of integration of Body+Mind+Spirit concepts in research and practice. A recently concluded Whole Person Health Summit and Second Qigong Summit has strongly recommended education modules in such areas should become part of conventional medical school curriculum besides a CME program for practicing physicians and surgeons in different countries. Voluntary organizations like The Campaign for Better Health, Friends of Health, The Chopra Foundation, Tai Sophia Institute in the US are making exemplary efforts to create awareness about importance of integrative, holistic or whole person aspects of health¹²².

To sum up, the above discussions show that Public Health agenda to health delivery in general and then for using TM has already taken roots. Yet, as the data show it is sub-optimal to say the least as of the date, and a lot can be and need be done in order to utilize TM, hitherto under used resource, to serve the needs of population and diseases of developing countries.

122 Rustum Roy 2005, Whole Person Health Summit, April 14-17, Bethesda, MD, USA.

“The test of a first-rate intelligence is the ability to hold two opposing ideas in mind at the same time and still retain the ability to function”.

F. Scott Fitzgerald

Chapter 5

Global Justice and Ecological Obligation

In a utopia, IPR would belong to entire humanity. But we are far from being there. Until globalization, that began in a real sense after World War II and gathered unprecedented tempo in last three or so decades, IPR landscape was fairly stable if not utterly calm.

Like any other industry, pharmaceutical goes by the rule that industry must make profit and expand it, or, at its worst maintain it in a status quo. Market and regulatory incentives are two slopes towards which production and its precursors gravitate. Demand backed by affordability (at least true until recently) in the western world drove the pharmaceutical industry to be highly innovative and the IPR protection of market economy in the form of patent monopolies fueled the progress.

Scholars like Dean Baker¹²³ and Aidan Hollis¹²⁴ have argued that monopoly causes, prices of drugs to go 400% to at times 1000% above the fair market prices, excessive money expenditure on marketing, disproportionate increase in production of follow on me-too drugs, decrease in production of non-patentable drugs, and secretiveness about research sharing and at the bottom line pharmaceutical markets are dysfunctional and IPR protection or monopolies do not effectively stimulate drug research and development. On

123 Financial drug research: What are the issues? CEPR September 2004

124 Aidan Hollis October 2004

the other hand, one may argue in concurrence with Kevin Hassett's¹²⁵ eloquent article that to let market forces determine the prices have a better pay off at the bottom line and that price control lowers the revenue, in turn lowers R & D investment, in turn reduces the rate at which new compounds are discovered. To a reader, while both sides and their arguments seem equally convincing, she/he cannot fail to notice that 1. Frame of reference for both schools is western developed countries and 2. Both schools make exclusive economic argument, discounting the purely scientific or technical-technological odds.

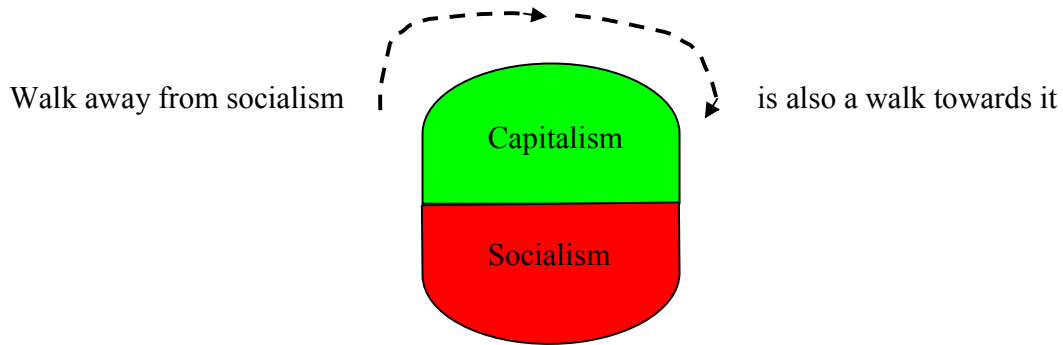
One of the most unsettling facts that modern pharmaceutical industry faces is that lately its pipeline of new drug discovery seems to have almost dried up. It seems that the R & D has reached a point of saturation. On the other hand disease prevalence, general economy, and IPR regulations in the developing countries have deviated so much from their counterparts in the developed world that they have set up a vicious spiral of no win situation for pharmaceutical industry. To make the matters worse, within developed countries themselves, the segment of Price Controlling Countries¹²⁶ is growing larger by the day making the bottleneck tighter still.

Capitalism has its complement in socialism and any one of them can barely survive without the other. Simultaneously co-existing duality is axiomatic in life. However discomfoting it may be, a walk away from one of the above, towards the pinnacle of the

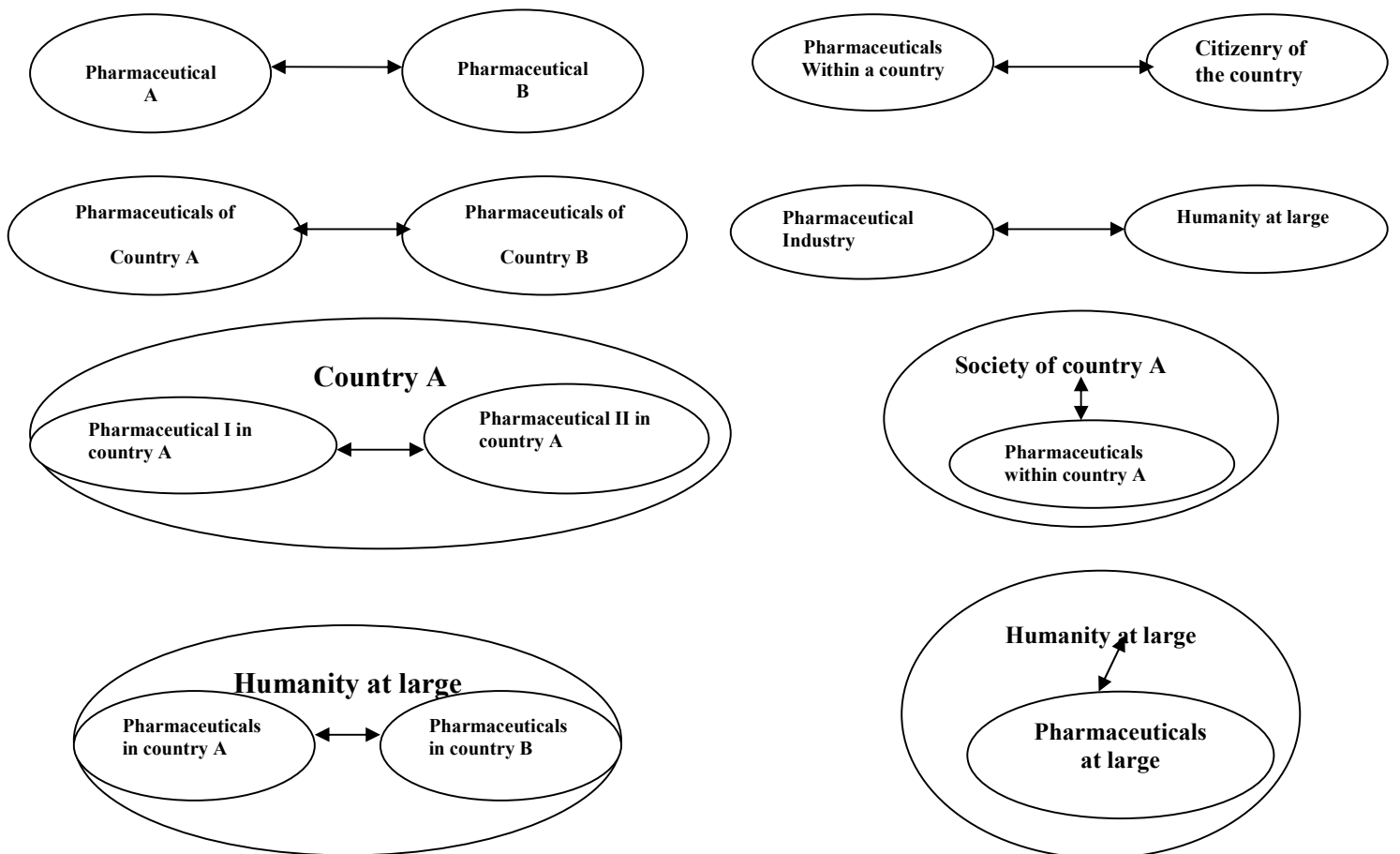
125 Hassett K. Two Trillion in Ten Years, Wall Street Journal, July 27, 2004

126 Patented Medicine Prices Review Board, Canada <<http://www.pmprb-cepmb.gc.ca/english/view.asp?x=132&mid=57>>

other is also a walk towards the first, past pinnacle. To recognize the turning point and to reconcile with it is and had always been painful to humanity.



With respect to the above context one can visualize conflict of interests and systems-cybernetic nesting-relationships diagrammatically as below:



While the globalization has brought world trade issues in general into an unsettling focus, the above metaphor could not be truer for anything in the health care field than with modern pharmaceutical industry. If the arguments by Dean Baker and Kevin Hassett are logically consistent, then the only solution that seems viable in this impasse is that of social-capitalism. Learning from nature its device of selectively permeable membranes/gates/channels¹²⁷, perhaps we need to create a new paradigm for IPR that is holistic in orientation where the entire humanity sacrifices some so that the entire humanity survives, thrives and progresses. The slack given to developing countries, for dealing with diseases rampant in their regions, while investing in R & D in developed world to treat those conditions and then passing the fruits to the needy with minimal IPR barriers will only help the entire humanity. On the more upbeat side TMs need to be given the same IPR latitude that was given to modern pharmaceuticals once (that enabled them to become what they have come to be). TMs, as the countries where they origin, are like a growing baby, just as once MM was.

5.1 Intellectual Property

According to World Intellectual Property Organization (WIPO), the traditional knowledge systems are frameworks for continuing creativity and innovation in most fields of technology, ranging from traditional medicinal plants and agricultural practices, to music^{128, 129}. Traditional medical knowledge remains poorly documented. It is mostly

127 Cellular biology

128 WIPO Report on Fact Finding Missions on Intellectual Property Needs and Expectations of Traditional Knowledge Holders. Geneva, April 2001.

129 Tambutoh D.J. et al. Traditional medicine and intellectual property rights – a move towards protection in developing countries? WIPO Specialization Course on Intellectual Property, Turin, September 3 – November 29, 2001.

transmitted from one generation to the other and is part of the cultural heritage in most developing countries. It has been defined by the WHO Traditional Medicine Program as the sum total of the knowledge, skills and practices based on theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness. The terms complementary/alternative/non-conventional medicine are used interchangeably with traditional medicine in some countries¹³⁰. The importance of Traditional Medicine in developing countries cannot be over-emphasized as indigenous people cannot survive or exercise their fundamental human rights as distinct nations, societies and people without the ability to conserve, revive, develop and teach the wisdom they have inherited from their ancestors¹³¹. The Principle 22 of the Rio Declaration, which states that ‘indigenous people and their communities have a vital role in environmental management and development because of their knowledge and traditional practices’.

The significance of this concern becomes evident in connection with the discussion of article 8(j) of the Convention on Biological Diversity 1992, where it is implied that medicinal plants, blood samples from indigenous people and research conducted by foreigners into indigenous ways of life, supported by indigenous possessors of traditional knowledge, have led to patentable discoveries of benefit solely to those foreign researchers, with no economic return to indigenous people themselves¹³². The traditional medical knowledge of indigenous peoples throughout the world had played an important

130 WIPO Intellectual Property Handbook: Policy, Law, and Use (2001), Geneva, p. 58, § 2.269.

131 Protection of the Heritage of Indigenous People, United Nation, New York & Geneva (1997).

132 UNESCO/WIPO Regional Consultations on the Protection of Traditional and Popular Culture (Folklore), UNESCO Activities, June 1999, p. 38-39.

role in identifying biological resources worthy of commercial exploitation¹³³.

Knowledge about the way in which local people have used plants has always been important to collectors. Unfortunately, no international system has yet successfully designed and implemented a system that provides for an effective legal protection of traditional knowledge holders at the international level.

A discussion paper ‘Traditional Knowledge and Intellectual Property: Issues and options surrounding the protection of traditional knowledge’ written by Carlos M Correa, of the University of Buenos Aires gives an excellent basis to this important debate. The protection under intellectual property rights (IPRs) of traditional and indigenous knowledge (TK) has received growing attention since the adoption of the Convention on Biological Diversity in 1992. Numerous contributions by academics, NGOs and governments have considered the need to provide some form of protection to TK. However, significant divergences exist as to whether IPRs should be applied and which would be the rationale and modalities of protection. It is important to understand the scope of TK, which includes its widespread use in TM and agriculture.

Professor Correa rightly feels that it is premature to promote international IPRs-type standards for TK protection at present and suggests global rules to prevent misappropriation of TK. He also suggests various ways in which Overseas Development Assistance can be used to clarify and improve the present situation¹³⁴.

133 The Protection of Traditional Knowledge under Intellectual Property Law (2000), EIPR, p. 255.

134 Correa C.M. Traditional Knowledge and Intellectual Property: Issues and options surrounding the protection of traditional knowledge - A Discussion Paper commissioned by The Quaker United Nations Office (QUNO), Geneva 2001, with financial assistance from the Rockefeller Foundation.

The field of intellectual property rights is rapidly changing and laws vary from country to country. American Association for the Advancement of Science (AAAS) has published a useful handbook to provide an accurate summary of TK, intellectual property concepts and options. Generally, all options are subject to respective national laws and legislation. AAAS handbook gives a detailed yet simple account of TK and IPR issues starting from the definition, scope, and concerns. It covers all the possible Intellectual Property Protection Options for Traditional Knowledge Holders including: Patents, Petty Patent Models, Plant Patents, Plant Variety Certificates, Traditional Knowledge Registries, Trade Secrets, Trademarks, Geographical Indicators, Prior Art and Defensive Disclosure, Prior Informed Consent, *Sui Generis* Protection Systems, Access and Benefit-Sharing. It also discusses important issues related to documenting TK, locating and identifying TK, Identifying who holds the knowledge, identifying IP options, etc. with lot of examples¹³⁵. Another document of AAAS provides important debate relate to TK and globalized biopiracy¹³⁶.

Currently, some 95% of patents in the world are held in developed countries. International patent law and most national conventional patent law protection requirements of novelty and inventive steps do not seem to be applicable to traditional knowledge and biodiversity. For example, there is no Act under patent law, which could be used to protect the non-medication traditional therapies, such as manual therapies and spiritual therapies. Because of the lack of database and the same medicinal plants growing and being used in various countries and continents, it is very difficult to identify

135 Stephen H. and Justin V. July 2003, Traditional Knowledge and Intellectual Property: A Handbook on Issues and Options for Traditional Knowledge Holders in Protecting their Intellectual Property and Maintaining Biological Diversity American Association for the Advancement of Science (AAAS), Washington, DC

136 Stephen H, Intellectual Property and Traditional Ecological Knowledge: Institutionally Globalized Biopiracy? Professional Ethics Report, 2002; 3(XV), 1-8.

the founder. The great traditions like Ayurveda provide a rich information source. For instance, over 5000 herbo-mineral formulations¹³⁷ with rational are provided by traditional Ayurvedic system of medicine and all would need protection and are truly falling under the prior art. The existing conventional patent law can protect pharmaceutical products. However, herbal medicines and herbal products are quite different from chemical drugs. They are very difficult to be protected by the existing patent law¹³⁸.

Professor Gerry Bodeker has given an extensive review of the whole issue and has suggested new IPR models for the protection of traditional knowledge: Changing IPR law, Certificates of origin; Transforming traditional knowledge into trade secrets; Local innovations databases. Indian example of National TK Database (Traditional Knowledge Digital Library-TKDL) to Establish Prior Art on Indian Medicinal Heritage; International Database to Establish Prior Art on TK Globally are some more examples. He has also suggested some *sue generis* models for an equitable future. While the international focus is on issues surrounding the patenting of TK, it is arguable that a potent threat to the IPR of TK holders comes from the herbal sector. Another effort of FRLHT where women farmers become stakeholders of a public company that undertakes organized cultivation and value addition activities¹³⁹. Thi effort serves many onbjectives, first, it empowers poor rural women farmers by providing newer ways of income generation, secondly it helps in optimal use of traditional medicine knowledge available with the local communities, thirdly, it provides a

137 Paranjape P. Traditional Ayurvedic Formulations, 2003, Chaukhamba Prakashan, Varanasi, India

138 Zhang Xiaorui. Traditional Medicine and Its Knowledge, UNCTAD Expert Meeting on "Systems and National Experiences for Protecting Traditional Knowledge, Innovations and Practices" UNCTAD, United Nations Palais des Nations, Geneva 30 October 2000.

139 Darshan Shankar, Foundation for Revitalization of Local Health Traditions, Bangalore.

quality herbal material to industries and other bulk users and helps in replacing cultivated sources in place of wildy collected herbal materials.

Despite the trend for the herbal sector to develop products based on TK and to rely on market edge and competitive forces as a means of gaining market share and profit, there has been a growing trend of herbal or natural products companies specializing in the medicinal applications of plant extracts to seek patents for application of Traditional Medicine Knowledge (TMK). Some such examples include: an appetite suppressant of the San People of the Kalahari; a traditionally-based AIDS medicine in South Africa; a famous case of Andean Maca and Indian example of Jeevani plant of Kani tribes of Kerala from South India for benefit sharing between the communities and herbal industry¹⁴⁰. Collaborating with traditional healers remains a valid method for the identification of potential lead compounds for novel pharmaceuticals. However, the knowledge of these traditional healers is rapidly being lost. Historic herbal texts provide a unique window to identify plants whose specific uses are no longer known. Buenz et al have identified nine plants in the 17th century, which were documented as having medicinal properties but have not been researched¹⁴¹. Such efforts may help to identify candidate specimens deserving further pharmacological study, yet raise important issues related to IPR.

The international view on this issue is reflected in the June 2002 report in *Science*. The U.S. plans to limit the future patent rights of all foreign recipients of government grants

140 P.Pushpangadan, CSIR India initiative that led to UNDP award 2003.

141 Buenz E.J. Bioprospecting Rumphius's Ambonese Herbal: Volume I. *Journal of Ethnopharmacology* 2005; 96(1-2) 57-70

and contracts to the awardee's own country and to have the U.S. National Institutes of Health retain the rights elsewhere. The *Science* report notes that this impacts immediately on NIH-funded research in Australia which led to discovery of two cytokines that can boost the immune system of cancer patients, and which are now marketed by companies such as Amgen and Schering-Plough and have generated revenues of more than \$1.5 billion a year in U.S. sales. Australian scientists have lodged formal protests. The U.S. view is that such a move is in "the best interests of U.S. citizens" by making sure that they benefit fully from all NIH-funded research. From the perspective of TK, this will call into question the substance of the benefit sharing arrangements in the many inter-country agreements of NIH's National Cancer Institute¹⁴².

IP protection for traditional medicines has multiple and diverse objectives. However, its priorities are often not clear and may confront with strategies and the prioritization of objectives. The differences in stakeholders' concepts on ownership of knowledge add to the problem. The policymakers should address these multiple, multi-layered issues and questions, and try to develop a range of solutions to address and balance the various objectives and interests¹⁴³. One prospective project has been proposed to develop such information is the Global IP, Benefit Sharing and Traditional Medicine Database. It is being developed as a component of the Global Information Hub on Integrated Medicine from the work of the Commonwealth Working Group (CWG) on Traditional and Complementary Health Systems, now directed by the Malaysian Ministry of Health. This Information Hub is planning to create a network of legal centers, scholars and NGOs

142 Jocelyn Kaiser, N.I.H. to Limit Scope of Foreign Patents, *Science*, 2002, 296, 2316

143 Timmermans K. Intellectual property rights and traditional medicine: policy dilemmas at the interface. *Soc Sci Med.* 2003;57(4):745-56.

working together to develop a comprehensive legislative and policy review, information resource and exchange on issues pertaining to IP rights over traditional medical knowledge and the use of medicinal plants¹⁴⁴.

The complexity of the situation outlined above brings us inevitably to consider some *sui generis* options to protect TK and its legitimate owners from exploitation. By very definition such laws do not fit within existing frame of law and such class does not belong to any taxonomic class¹⁴⁵. However, *sui generis* evolved exactly to accommodate such impasse.

Having identified the premise this report discusses one schema proposed and conceived by Advocate Mohan Dewan¹⁴⁶ to elucidate the point. This scheme is based on three important axioms:

Axiom 1: Knowledge by its very nature is all pervading. It influences him that imparts and him that receives. It cannot be segregated into well-defined compartments. An increase in 'knowledge' in one sphere causes an all round increase in 'knowledge' in all other spheres with a multiplier effect.

Axiom 2: The base of any modern knowledge or current knowledge as is known is always traditional knowledge. Without some form of traditional knowledge inputs, it

144 Gerard Bodeker, Traditional (i.e. Indigenous) and Complementary Medicine in the Commonwealth: New Partnerships Planned With the Formal Health Sector, *Journal of Alternative & Complementary Medicine* 1999; 5, 97.

145 http://en.wikipedia.org/wiki/Sui_generis

146 Dewan M. is a senior patent council from India, who is currently engaged in research on IPR and TM at the University of Pune, India under cosupervision of the author of this paper (BP). This scheme is an outcome of Dewan's research, however, since it directly relates to the subject of this report, a summary of the scheme is given here for wider responses and possible refinements before it is formally submitted either for publication or for statutory consideration.

would not have been possible to have current knowledge. Therefore all current knowledge owes its origin to traditional knowledge.

Axiom 3: “Knowledge” is an integral aspect of our humanity as a whole. It cannot be claimed to be the ‘property’ of any particular set of human beings. It cannot be looked upon as a commodity, because it does not have the characteristic of a commodity, in that it does not diminish if it is shared or disseminated. Paradoxically, knowledge increases even in the process of being shared and distributed.

When asked to consider protection of ‘traditional knowledge’ one is faced with three fundamental issues:

- [1] Does the particular traditional knowledge being considered qualify for ownership?
- [2] Once the first question is answered in the affirmative, then who can be considered and therefore designated as the owner of the particular ‘traditional knowledge’?
- [3] After the traditional knowledge and the owner is identified what kind of mechanism should be in place by which the designated owner of the traditional knowledge is compensated by another person making use of the traditional knowledge?

The main problems include identifying steps to qualify ‘traditional knowledge’ and what types of property rights can such a qualified traditional knowledge be entitled to? When dealing with traditional knowledge it becomes quite clear that the existing intellectual property systems, as are known, cannot be used. Two chief pillars on which patent systems are supported are Novelty and Inventive step. Traditional knowledge fails to be supported on either of these pillars. Therefore patent, as a form of protection in the case

of traditional knowledge must immediately be ruled out. However, the substantive examining features of the patent system are worthy of adoption. One must therefore turn to other forms of intellectual property to seek protection for traditional knowledge. The only three possible candidates could be 'trademarks', 'trade secrets' and 'copyright'. Trade secrets fail as because by its very nature traditional knowledge is not in the nature of a 'secret'. Copyrights on the other hand have two fundamental limitations: one, that the art in question must be reproduced in material form, therefore there cannot be any copyright in ideas, and two, copyright has a limited life it exists within the life time of the author and some specified years beyond. In the case of 'traditional knowledge' one cannot define an author and in most cases dealing is with the collective knowledge of a group of persons that has developed possibly through several centuries. Copyright too therefore fails to give a definitive property right for 'traditional knowledge'.

The options left with trademarks and its cousin 'geographical indications' to seek for some property right. Trade Marks or service marks are useful only if they are applied to some goods or services. However, some features of trade marks that seem to be suitable for traditional knowledge is that there is system for registration of the right and the right is a perpetual right subject to periodical renewals.

After examining the current intellectual property rights one finds that traditional knowledge does not fit within the scope and ambit of any known intellectual property schemes.

One can however a *sui generis* schema for ‘traditional knowledge’. The schema should adhere to the following: There shall be a new intellectual property right known as a “registered traditional knowledge right’. Such a right shall be acquired by registration nationally and validated internationally. The right will draw from precedents in the other forms of intellectual property rights. It will have the mechanism of registration as provided by trademark Law. The formal and substantive examination procedures will be drawn from patent law and the principles of universality and revenue disbursement mechanism and licensing procedures and the mechanism of performing right societies from copyright law. In addition it will have innovative features of its own as disclosed herein below:

[1] There shall be an International treaty: suggested name: Universal Traditional Knowledge Protection Convention. Such a convention will acknowledge the base of traditional knowledge for all knowledge and the fact that all knowledge is intimately mixed and adopt the aforesaid axioms.

[2] Under the auspices of the convention every nation subscribing to the convention will set up a “National Traditional Knowledge Protection Registry” for protection of Traditional Knowledge by registration within a Country. Such a registry will be manned by a Registrar, investigators and disbursement officers.

[3] There shall be set up an “International Traditional Knowledge Repository” which shall validate record and make available for view and display the Traditional Knowledge rights registered in the respective national registries.

[4] A Traditional knowledge right can be registered for different works, which are classified in various classes in accordance with a scheme for “International Traditional

Knowledge Classification”. Examples of such classes are: treatment of the human body, food and culinary, dance forms, religious rituals, prayers and symbols, agricultural and horticultural methods, medical application of plants, minerals and animals, handicraft, music, music instruments and musical works, exercise, martial arts and massage, oral traditions, literary works and drama, textiles and weaving folklore, non medical treatments of the body and the mind.

[5] For a work to classify as a traditional knowledge it must comply following: [i] the knowledge must be at least 100 years old; [ii] the knowledge must be reposed in at least one person of a group of indigenous persons in a country called the country of origin; [iii] the knowledge does not require the utilization of any input not available in the country of origin.

[6] An application for registration of a traditional knowledge right shall be made by any person representing the group of indigenous persons in whom the said traditional knowledge reposes. Along with such an application, there shall be included full details of the knowledge and method of utilization of the knowledge, the class in which the knowledge is sought to be protected, the details of indigenous persons who claim that the knowledge is reposed with them, proof that the knowledge is at least 100 years old; and the details of the applicant’s connection with the indigenous people, the ability and competence of the applicant to satisfy the aspirations of a majority of the said people.

[7] On receiving such an application, the national registry shall appoint one investigator to investigate the claim in detail and submit the application to the Registrar for recommendation. After receiving the investigation report the Registrar shall if found

suitable submit, the application and the report together with his recommendations to the International Repository for validation.

[8] The international Repository shall appoint a validator to validate the application and the report and if validated the Traditional knowledge shall be duly registered with the national registry with rights extending to all countries signatory to the convention.

[9] Once a traditional knowledge is registered no person shall publicly use the said knowledge without payment of a license fee. The license fee shall be deposited at the user's national registry, 10 per cent retained for expenses and the remaining shall be transmitted to the International Repository.

[10] Private use means non-commercial use by a person for own benefit any other use is deemed to be Public use. Explanation: If for instance traditional Mantra is registered as Traditional Knowledge a person may chant that Matra but a recording company who makes cassettes of the mantra will be required to obtain a license.

[11] 'Public use' shall include the use of any reference to the said traditional knowledge in a book or article, in a journal, in a patent in a record or a film or for any form of public or private broadcast. Rules shall be framed for determining license fees payable.

[12] At the end of every financial year the license fees received world wide for all traditional knowledge in a particular class will be pooled and divided equally by all live registrations in that class after the international repository has retained 10 per cent of the total fees received for its expenses and transferred 90 percent of the fees amongst all the national registries to be divided in the ratio of the units in each class.

[13] The registered owner of a unit in a class will ensure disbursement of the fees received to all existing members of the group after retaining 10 per cent to defray its own expenses.

This sample *sui generis* model can serve as a platform for a larger debate that can lead to an international consensus on this issue. The axioms and thirteen steps outlined above could provide a general guidance for reaching to such an agreement. A response from like-minded countries consortium that is consistently pushing need for *sue generis* protection from Cancun till now is getting wider support. An Indian case presented by P. Pushpangadan provides a good example (refer Chapter 7).

5.2. Markets, Business and Trade

The IP/TK debate has reached new levels of serious review and new prospects for TK protection since the Doha meeting of November 2001 and the resulting process for the harmonization of TRIPS and Convention on Biological Diversity. The growth of the herbal sector and the constant demand for new and saleable traditional medical products is new in the field of IP and traditional medical knowledge. This trend will clearly grow and should become a primary focus of IPR development. There is a need for the herbal industry to become more proactive and responsive to this dimension. The herbal and traditional medicine industry should voluntarily, develop in house industry standards that are based on ethical practice and are overseen jointly by industry-government-NGO-indigenous monitoring groups. To provide new models for development, information

needs to be gathered on current practice. This in turns needs to be analyzed according to principles of best practice in benefit sharing and IPR. *Sui generis* systems alone may or may not be the way forward although, it offer unique local means of protecting TM that work for the local context. At the same time, it is at risk of being un-enforceable outside of the country or region of origin and hence creating vulnerability to the biopiracy that they are expected to prevent. For *sui generis* systems to work, there is need to be reciprocity among countries to respect one another's local *sui generis* regimes. Although, it would seem somewhat difficult in the current international IP political environment, such developments require backing and enforcement within the context of national and international IPR regimes. This would require WIPO, the CBD and the WTO to coordinate their policies and legal instruments in partnership with TK holders as well as with conventional stakeholders such as governments and industry. If this can be achieved, the health benefits offered to the world through the globalization of traditional medical knowledge also stand to benefit communities and countries in terms of economic development and the growth of national pride in the preservation of culture and its harnessing for human well being in the context of principles of fair trade¹⁴⁷.

At the first Global Knowledge Conference in Toronto in 1997, political leaders and civil society representatives from developing countries endorsed the vision of the World Bank to become a "Knowledge Bank" that intermediates ideas as well as resources. In 2004, the World Bank published a book entitled *Indigenous Knowledge – Local Pathways to Global Development* that was formally launched in October 2004 in Tanzania. The partnership between the World Bank and the GRA in the domain of indigenous

147 Bodeker. G. Traditional Medical Knowledge, Intellectual Property Rights & Benefit Sharing. *Cardozo Journal of Int'l & Comp. Law*, 2003; 11:785-814.

knowledge is expected to contribute in advanced research and development without compromising interest of indigenous communities.

5.3. Biodiversity

Fifth meeting of Global Forum for Bioethics in Research held at Paris in April 2004 dealt in detail issues related to Equity and Intellectual Property. One related presentation by Professor Anil Gupta highlights the inadequacies in the technical competence and infrastructural capabilities of most of the developing countries. An international registry administered electronically by WIPO might provide the most effective tool for meeting the aspirations of grassroots innovators and traditional knowledge holders. This registry should help accomplish a golden triangle of rewarding creativity: link innovation, investment and enterprise around the globe. Without a system of protection of knowledge globally, incentives for disclosure and dissemination cannot be provided to the holders of valuable traditional knowledge about biological and genetic resources as well as other resources. If exploitation of knowledge has to be controlled, we may need on line intellectual property rights administration¹⁴⁸. The symbiotic relation between biodiversity and drug discovery involving natural product drug discovery is well reviewed by Geoffrey A. Cordell, University of Illinois at Chicago¹⁴⁹.

148 Gupta A.K. IP for Traditional knowledge on-line: Recognizing, Respecting and Rewarding Creativity and Innovation at Grassroots. Invited Paper presented at the Second WIPO International Conference on Electronic Commerce and Intellectual Property, Geneva, 19-21 September, 2001.

149 Cordell G.A. Biodiversity and drug discovery - a symbiotic relationship. *Phytochemistry* 2000; 55(6), 463-480

A ‘Banglore Declaration¹⁵⁰ July 2004’ made during a workshop in India deliberated in detail issues related to medicinal plants, biodiversity, cultivation, R&D, IPR, documentation, TM etc. This document provides a good vision statement that stress importance to provide sustainable livelihood opportunities to small and medium farmers and the rural poor in the region through organic cultivation systems and sustainably managed collection; to provide affordable healthcare options in the form of high quality traditional medicines to domestic markets in the region; to progressively build regional brands in the global markets, using this as a means to tap the lucrative and fast growing markets for products and services in the healthcare, nutraceuticals, health foods, fragrances, dyes and cosmetics business segments; aggressive marketing of products while safeguarding the resource base of the raw products.

Many traditional medicines use natural materials including plant and animal origin that may cause serious threat to biodiversity. For instance Tiger bone has been used as a treatment for rheumatism and related ailments for thousands of years in traditional Asian medicine. In the early 1990s, it became evident that medicinal trade in Tiger bone threatened to drive the already endangered Tiger to extinction in the wild. The importance of this threat was documented in the 1994 TRAFFIC report, Killed For A Cure: A Review of the Worldwide Trade in Tiger Bone¹⁵¹. Not just tigers but the whole range of wild animals or their materials are used in TM – Rhino, Deer, Elephants, and many such are under threat. It is same with medicinal plants and marine materials.

Medicinal plants classified as endangered species in the red book such as *Taxus Spp*,

150 Workshop on Medicinal Herbs & Plants: Scope for Diversified and Sustainable Extraction, Funded by Common Fund for Commodities (CFC) Amsterdam in collaboration with Bio Centre and Food & Agriculture Organization, Rome held at Banglore India during July 22 – 26, 2004

151 Michael't Sas-Rolfes, Who Will Save the Wild Tiger?, PERC Policy Series, Issue Number PS-12, February 1998

Swartia Spp. and many others are being prohibited for commercial collection from their habitats. For instance corals, deer horns etc are part of important Ayurvedic medicines and are prohibited for use in medicines. Previously when used for the limited purpose and use for local communities, the increasing market demands are putting pressure on collectors and traders wooing them add to this problem. In India, the Department of Environment and Forest recently raided Ayurvedic manufacturers and filed legal cases for violating the biodiversity conservation regulations. This has created uproar and has resulted in unavailability of such medicine. This issue needs to be properly discussed with indigenous people and has to be resolved with out causing harm to either of the interests. Recently a National Seminar addressing issues related to globalization and herbal products organized at Mumbai gives a very representative Declaration¹⁵² “The Indian subcontinent harbors one of the richest biodiversity of medicinal plants and the therapeutic benefits of these plants have been well documented in various treatise. Though these medicinal plants have documented history of centuries of therapeutic usage, these applications need validation applying the modern scientific approach. These validations need to address issues arising due to modern agricultural practices and mass collection procedures. The issues of safety, efficacy and stability of herbal formulations need to be resolved. Clinical trials need to be initiated keeping in view the traditional methods of diagnosis and prescription with collaborative participation of experts from modern medicine. Well-designed training modules and courses need to be initiated to develop trained human resources for dealing with inter-disciplinary exercises of evaluations and investigations. Special training programs in Good Agricultural and

152 National Seminar On Globalising Ayurvedic And Herbal Products: Challenges And Strategies 4 – 5, February 2005, Renaissance Convention Centre, Powai, Mumbai, India.

Collection Practices for farmers need to be initiated with an aim to ensure consistent raw material quality. Regulatory schedules must be suitably amended to incorporate definition and standards for statistically proven plant based medicinal substances. Standardization programs must involve cultivation of medicinal plants, Raw material sourcing (vendor qualifications), raw material storage and transport, raw material processing, safety, efficacy and stability of formulation, limits of contaminants and adulterants and the patient information dossiers.

“If we all did the things we are capable of doing, we would literally astound ourselves”.

Thomas Edison

Chapter 6

An Opportunity in Adversity

Contrary to “Law of Finite Biology” though the number of genetic codes will exhaust soon in an exponential way (presumably leading to solutions to every known genetic anomaly related health problem), the number of NCE (New Chemical Entity), their number being finite¹⁵³ too, will run out of fuel soon too, despite unraveling of genomic decoding. The bleak scenario in the pharmaceutical field is a testimony to the latter surmise. As many a wise scholar has pointed out, the era of single molecule drug seem to drawing curtains. However, unlike what seems common sense, the era of combinational drug therapies of MM paradigm probably will not foot the bill. Just as very high speed serial computing simulates parallel processing but does not make real time parallel processing, mixtures of prima facie complementary medicinal molecules will perhaps not make combinational recipes. The fundamentals of non-linear dynamical complex systems (NLDCS) paradigm demand so. The odds against success with such efforts are close to odds of success of creating life one bit at a time out of mixing C, H and O molecules in a jar would be. The number of genes might be finite, but data on their combinations (and their corresponding effects) and more so on their permutations (one has to only imagine the vastness of those possibilities) would, as of now or in near future, cause an information overload and comprehension failure¹⁵⁴ (limitation of human biological brain apparatus) pitting researchers and industry against a futility barrier. However, TM provides a silver lining to these bleak analyses. Analytical comprehension of TM recipes,

¹⁵³ Patwardhan Avinash (unpublished work), Refer to explanatory notes below the annexe

¹⁵⁴ Patwardhan Avinash (unpublished work), Refer to explanatory notes below the annexe

regimens or techniques might be unachievable by contemporary science, empirical testing of their efficacy and safety being doable and therefore taken care of, TM can provide an outlet to the drug discovery impasse because the same natural forces that shaped multi-gene interaction into complex and dynamical mode have created some of, if not all, TM solutions.

6.1. Innovation and Drug Discovery

As the logic diagrams provided in the annexe to this chapter suggest, the age of the blockbuster drug seems over, or at least in its last days. The data from a study done by DiMasi and Paquette of Tufts University, suggest that entry barriers have fallen over time for new drug introductions. The increased competitiveness of the pharmaceutical marketplace was likely fueled by changes over time on both the supply and demand sides. The development histories of entrants to new drug classes suggest that development races better characterize new drug development than does a model of *post hoc* imitation. Thus, the usual distinctions drawn between breakthrough and ‘me-too’ drugs may not be very meaningful¹⁵⁵. The pharmaceutical industry has not been as innovative as it claims to be and the regulatory processes are adding more risk and years for the pharmaceutical companies and it is predicated that worst is yet to come¹⁵⁶. Most of the big pharmaceutical manufacturers spend more on marketing than on research and development. Drug companies actively research for new ways to interact with known receptors and seek out new receptors. But the development road is long, stony, and

155 DiMasi J.A. and Paquette C. The Economics of Follow-on Drug Research and Development Trends in Entry Rates and the Timing of Development *Pharmacoeconomics* 2004; 22 (2): 1-14.

156 *The Economist*, Nov 25th 2004, The pharmaceuticals industry From bad to awful.

expensive, as seen in many cases of post approval or marketing withdrawal cases such as a new anticoagulant Ximelagatran of Astra Zeneca¹⁵⁷ or Cox II inhibitor Vioxx of Pfizer¹⁵⁸. Such failures are really becoming nightmares of pharmaceutical companies who are now looking for innovative approaches to drug discovery. There are common approaches to drug discovery including Chemical Biology Approach, Serendipity and Synthetic, Combinatorial, Genomics Approaches. However, the innovative approaches based on TM that are evolving to reduce major bottleneck and to reduce cost and development time, include Ethnopharmacology Approach, Reverse Pharmacology Approach, Systems Biology Approach and Personalized Approach^{159, 160}.

The traditional route to drug discovery, the old pharmacology of testing analogues of active drugs or the slightly newer pharmacology of mass screenings in chemical libraries, is not yet over, but neither has rational drug come up with a blockbuster, although it may do one day. The challenge is set for drug companies to become truly innovative. A good start would be to forget the me-too market and to go and find those receptors, old and new, and the genuinely new compounds to interact with them¹⁶¹. There are clear trends that show the mainstream pharmaceutical research is moving away from single molecule or single target approach in favor of combinations and multiple target approaches¹⁶².

157 Briefing Information, US Food and Drug Administration, Cardiovascular and Renal Drugs Advisory Committee, September 10, 2004

158 Kweder Sandra, Office of New Drugs, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, statement before - Committee on Finance United States Senate, regarding worldwide withdrawal by Merck & Co., Inc. of Vioxx. November 18, 2004

159 Patwardhan B. Symposium on TM, Annual Meeting of Indian Academy of Sciences, Varanasi India, 2004.

160 CSIR-NMITLI Herbal Drug Development Program, Government of India, 2001-2005.

161 Editorial, The Lancet, , 2004, 364; 1100

162 Camille Wermuth, Multitargeted drugs: The end of the 'one-target-one disease philosophy? Drug Discovery Today 19, October 2004

Thus, in the current scenario, TM knowledge database has considerable potential that remains under explored and poorly understood. Developing countries could exploit traditional medicine to kick-start biotech, only if their products measure up to the demands of Western regulators. For example, the traditional Chinese medicine - Kanglaite Injection is ready to enter Phase II clinical trials in the United States for the treatment of several cancers, including breast and prostate cancer¹⁶³. A standardized herbal formulation for treatment of psoriasis developed by Lupin Ltd of India presents a good case where the company has filed several Patents and IND application in India and USA. In short, for several reasons, the modern drug discovery processes have started revisiting TM to reduce the typical innovation deficit faced today that would help reaching to the top in Sciences especially for developing countries like India¹⁶⁴.

6.2. Research and Development

History of medicine dates back practically to the existence of human civilization. The current accepted modern medicine or allopathy has gradually developed over the years by scientific and observational efforts of scientists -- however, the basis of its development remains rooted in traditional medicine and therapies. The history of medicine includes many ludicrous therapies. Nevertheless, the ancient wisdom has been the basis of modern medicine and will remain as one important source of future medicine and therapeutics. The future of natural product drug discovery will be more holistic, personalized and involve wise and innovative use of ancient and modern therapeutic skills in

163 Basu P. Trading on traditional medicines, *Nature Biotechnology* 2004, 22, 263 – 265.

164 Mashelkar R.A., 2005. *Global Voices Of Science: India's R&D: Reaching for the Top*. *Science*, 307 (5714), 1415-1417.

complementary manner so that maximum benefits can be accrued to patients and community¹⁶⁵.

The Greek physician Galen (129-200 AD) devised the first Pharmacopoeia describing the appearance, properties and use of many plants of his time. The foundations of modern pharmaceutical industry were laid when techniques were developed to produce synthetic replacements for many of the medicines that had been derived from the forest. Natural Products Chemistry actually began with the work of Serturmer who first isolated morphine from opium. This, in-turn, was obtained from opium poppy (*Papaver somniferum*) by processes that have been used for over 5000 years. Many such similar developments followed. Quinine from Cinchona tree had its origin in the royal households of the South American Incas. Before the first European explorers arrived, the native people of the Americas had developed complex medical systems replete with diagnosis and treatment of physical as well as spiritual illnesses. Indigenous peoples derived medicines and poisons from thousands of plants. Review of some of the plants that originated from Central and South America indicate that most of them either had potentially toxic or poisonous characters or were from food sources. Following are few examples¹⁶⁶: In the early 1500's, Indian fever bark was one of the first medicinal plants to find appreciative consumers in Europe. Taken from the cinchona tree (*Cinchona officinalis*), the bark was used as an infusion by native people of the Andes and Amazon highlands to treat fevers. Jesuit missionaries brought the bark back to Europe. By the early sixteenth century, this medicine was known as "Jesuit fever bark," quite a

165 Patwardhan Bhushan, Ayurveda and Future Drug Development, International Journal of Alternative and Complementary Medicine 1992, 10(12), 9-11.

166 Steven King, Medicines that changed the world, Pacific Discovery, 1992: 45(1), 23-31.

transformation. The name coca (*Erythroxylum coca*) comes from an Aymara word meaning simply "tree." In Andean cultures, the leaves of the coca tree have been primarily chewed to obtain perceived benefits. From ancient times, indigenous people have added alkaline materials such as crushed seashells or burnt plant ashes to the leaves in order to accentuate the pharmacologically active moiety of coca. In 1860, a German chemist isolated cocaine, the chemical responsible for the biological activity, Carl Koller found cocaine could act as a local anesthetic in eye surgery. As the years passed, scientists observed that cocaine paralyzed nerve endings responsible for transmitting pain. As a local anesthetic, it revolutionized several surgical and dental procedures. Pot curare Arrowhead poison used in the East Amazon is predominately from the species *Strychnos guianensis*. Tube curare in the West Amazon is from *Chondrodendron tomentosum* from which the curare in modern medicine is made from and named as tubocurarine. The jaborandi tree (*Pilocarpus jaborandi*) secretes alkaloid-rich oil. Several substances are extracted from this aromatic oil, including the alkaloid pilocarpine, a weapon against the blinding disease glaucoma. American Indians on the island of Guadeloupe used pineapple (*Ananas comosus*) poultices to reduce inflammation in wounds and other skin injuries, to aid digestion and to cure stomachache. In 1891 an enzyme that broke down proteins (bromelain) was isolated from the fresh juice of pineapple and found to break down blood clots. Other pharmaceuticals that have their origin in botanicals include Atropine, Hyoscine, Digoxin, Cholchicine, Emetine.. Reserpine an anti-hypertensive alkaloid (*Rauwolfia serpentina*) became available as a result of work carried out by Ciba-Geigy in India. It is pertinent to note that most of these

early discoveries are mainly based on traditional medicines; many products could act as poisons in toxic doses.

A major problem with traditional indigenous medicine is discovering a reliable 'living tradition' rather than relying upon second hand accounts of their value and use. In many parts of the world the indigenous systems of medicine have almost completely broken down and disappeared. This includes mostly developed countries and some developing countries where the indigenous population has been marginalized. In others, the system is fragmented with the use of indigenous materials being limited to small tribal and geographical areas as in many parts of Africa. In anthropological terms these are 'little traditions' while the Ayurvedic Indian and traditional Chinese systems are living 'great traditions'. Although, the little traditions are an excellent repository of knowledge about medicinal and poisonous properties of botanicals, the researchers have mainly exploited poisonous sources. This may be primarily because of many reasons. First, it is relatively easy to present and demonstrate poisonous characteristics of botanicals. Second, there may not be a written documentation and by word of mouth poisonous characters get predominance. Third, for an outsider, poisonous characteristics differentiate in between ordinary and extra-ordinary material for pharmaceutical development. Fourth, a considerable time period is required to demonstrate true medicinal activities with proven safety profile. As against, great traditions have relatively organized database, and more exhaustive description of botanical material is available that can be tested using modern scientific methods. Ayurveda and Chinese Medical systems thus have an important role in bioprospecting of new medicines.

Lag phase for botanical medicine is now rapidly changing for a number of reasons. Problems with drug resistant microorganisms, side effects of modern drugs, and emerging diseases where no medicines are available, have stimulated renewed interest in plants as a significant source of new medicines. Pharmaceutical scientists are experiencing difficulty in identifying new lead structures, templates and scaffolds in the finite world of chemical diversity. A number of synthetic drugs have adverse and unacceptable side effects. There have been impressive successes with botanical medicines, most notably, Quinghaosu, Artemisinin from Chinese medicine. Considerable research on pharmacognosy, chemistry, pharmacology and clinical therapeutics has been carried out on Ayurvedic medicinal plants¹⁶⁷. Numerous molecules have come out of Ayurvedic experiential base, examples include Rauwolfia alkaloids for hypertension, Psoralens in Vitiligo, Holarrhena alkaloids in Amoebiasis, Guggulsterons as hypolipidemic agents, Mucuna pruriens for Parkinson's disease, Piperidines as bioavailability enhancers, Baccosides in mental retention, Picrosides in hepatic protection, Phyllanthins as antivirals, Curcumines in inflammation, Withanolides, and many other steroidal lactones and glycosides as immunomodulators¹⁶⁸. A whole range of chronic and difficult to treat diseases such as cancers, cardiovascular disease, diabetes, rheumatism and AIDS all require new effective drugs. Most developing countries have relied and will continue to rely on traditional natural medicines due to the deterrence of high costs and availability of modern allopathic medicines.

167 Dahanukar S.A., Kulkarni R.A., Rege N.N. Pharmacology of medicinal plants and natural products. Indian Journal of Pharmacology 2000; 32: S81-S118.

168 Patwardhan Bhushan. Ayurveda: The Designer Medicine. Indian Drugs 2000; 37(5): 213-227.

TM knowledge and experiential database can provide new functional leads to reduce time, money and toxicity-- the three main hurdles in the drug development. These records are particularly valuable since effectively these medicines have been tested for thousands years on people¹⁶⁹. Efforts are underway to establish pharmacoepidemiological evidence-base to TM, safety and practice¹⁷⁰. Combining the strengths of the knowledge base of traditional systems with the dramatic power of combinatorial sciences and high throughput screening will help in the generation of structure-activity libraries. Development of standardized herbal formulations is underway as an initiative of the Council for Scientific and Industrial Research (CSIR) is playing an important role through public-private profiting partnerships in R&D in a very professional manner and has received due appreciation from the corporate, scientific and governmental sectors¹⁷¹ and its program known as New Millennium Indian Technology Leadership Initiative (NMITLI)¹⁷² and a CORE Network Projects¹⁷³ involving 21 leading national laboratories, Universities and hospitals has claimed several leads in short time. Most of these efforts innovate on existing knowledgebase complemented with cutting edge technologies for drug discovery and developments mainly based on TM. Randomized controlled clinical trials for Rheumatoid and Osteoarthritis, Hepatoprotectives, Diabetes, Hypolipemic agents, Asthma, Parkinson's disease, and many other disorders have reasonably established clinical efficacy. Many CSIR laboratories are active in research and development efforts and innovations related to TM. The regional Research Laboratory (RRL) Jammu, National Chemical Laboratory (NCL), Pune, Central Botanical Research

169 Patwardhan B and Hooper M. Ayurveda and Future Drug Development. *International Journal of Alternative and Complementary Medicine*. 1992, 10(12), 9-11.

170 Vaidya Ashok et al. Ayurvedic pharmacoepidemiology-a new discipline, *Journal of Association of Physicians India (JAPI)*, 2003: 51; 528.

171 Jolly VK. Profiting from R&D, in *World Class India* Ed Ghosal S et. al. Penguin Books India, 2001.

172 Rao Yogeshwar, Technology Network and Business Development Division, CSIR, New Delhi

173 Agarwal O.P. , CORE Network Projects, CSIR, New Delhi

Institute (NBRI) and Central Institute of Medicinal and Aromatic Plants (CIMAP) Lucknow, Institute of Himalian Bioprospecting Technology, Palampur, Indian Institute of Chemical Biology Kolkata, Indian Institute of Chemical Technology, Hyderabad are just few examples. There is growing Industry-Academia partnerships in this field, which is a good indication. For instance, in the NMITLI program of Government of India number of industry partners such as Nicholas Piramal, Lupin, Zandu, Dabur, Dhootpapeshwar, Natural Remedies, are part of the project. A review of some exemplary evidence-based researches and approaches has now resulted in wider acceptance of Ayurvedic medicines^{174, 175, 176}. Research laboratories such as RRL, NBRI and CIMAP have done some innovations through R&D contributions in traditional medicines¹⁷⁷. One of the bioenhancers developed by RRL is Piperine, which has been studied in detail with anti-TB drugs¹⁷⁸. The development of artemisinin and its derivatives, development of superior varieties like Jeevan Raksha and CIM-Arogya producing significantly higher yields of artemisinin, with complete package of agrotechnology. CIMAP has worked on bio-enhancers that could reduce the dosage of antibiotics and subsequently the toxicity. A new antibiotic Oenostacin from the roots of the plant *Oenothera biennis* has been found effective. A new synergistic combination comprising of essential oil of medicinal plant *Foeniculum vulgare* and other plants has been found to be effective as an insecticide against mosquito larvae and has toxic action against larval stages of malarial vector, *Anopheles stephensi*.

174 Chopra A. Lavin P., Patwardhan B, et al. Randomized Double Blind Trial of an Ayurvedic Plant Derived Formulation for Treatment of Rheumatoid Arthritis. The Journal of Rheumatology 200; 27:6:1365-1372.

175 Vaidya A.D.B., Vaidya R.A., Nagaral S.I. Ayurveda and a different level of evidence: From Lord Macaulay to Lord Walton (1835-2001 AD), Journal of Association of Physicians India (JAPI), 2001; 49:534-537.

176 Patwardhan B and Gautam M, 2005. Botanical Immunodrugs: Scope and Opportunities. Drug Discovery Today 10 (7/24), 495-502.

177 Research projects of CIMAP at www.csir.res.in

178 A Process For The Preparation Of Pharmaceutical Composition With Enhanced Activity For The Treatment Of Tuberculosis And Leprosy: Patents- In 172689 ; Us 0650728; Ep 93308653.

Thus the TM knowledge database allows drug researchers to start from a well-tested and safe botanical material. With Ayurveda, the normal drug discovery course of ‘Laboratory to Clinics’ actually becomes from ‘Clinics to Laboratories’— a true Reverse Pharmacology Approach¹⁷⁹. A brief description of Reverse Pharmacology approach and how it could save time, cost and toxicity the tree main bottlenecks in drug discovery is given later in this report as a case study. In this process ‘Safety’ remains the most important starting point and the efficacy becomes a matter of validation¹⁸⁰. Globally, there is a positive trend towards holistic health, integrative sciences, systems biology approaches in drug discovery and therapeutics that has remained one of the unique features of Ayurveda¹⁸¹. A golden triangle¹⁸² consisting of Ayurveda-Modern medicine - Science will converge to form a real discovery engine that can result in newer, safer, cheaper and effective therapies. It will be in the interest of pharmaceutical companies, researchers and ultimately the global community to respect the traditions and build on their knowledge and experiential wisdom¹⁸³.

The R&D thrust, in the pharmaceutical sector is focused on development of new drugs, innovative/indigenous processes for known drugs and development of plant based drugs through investigation of leads from the traditional systems of medicine. This is happening at the drawback of a great innovation deficit that pharmaceutical industry is currently facing. In addition, many nutraceuticals are being consumed in unregulated markets for

179 Ashok Vaidya, Reverse Pharmacology Approach 2002, CSIR-NMITLI Herbal Drug Development Program.

180 Ayurvedic Medicine: Safety and Validation need. Patwardhan B. National Symposium Ayurvedic. Drug Manufactures Association, New Delhi, 1999.

181 Nitya Anand, CSIR Golden Diamond Jubilee Symposium on Rasayana Drugs. August 7-8, 2003, CDRI Luchnow.

182 Mashelkar R.A. Chitrakoot Declaration, National Botanical Research Institute Convention, 2003.

183 Patwardhan B. et al. Ayurveda and Natural Product Drug Discovery. Current Science, 2004: 86(6); 789-799.

perceived benefits in health care and improvement of quality of life. Natural pharmaceuticals (Naturaceuticals), nutraceuticals and cosmeceuticals are of great importance as a reservoir of chemical diversity aimed at new drug discovery and are explored for antimicrobial, cardiovascular, immunosuppressive, and anticancer drugs. Around 80% of all such products are of plant origin; their sales exceeded \$ 65 billion in 2003. Examples of plant products and derivatives used by the pharmaceutical industry include Paclitaxel, Vincristine, Vinblastine, Artemisinin, Camptothecin, Podophyllotoxin, etc. The nutraceutical marketplace in Europe is estimated to be \$ 9 billion, while the US marketplace, estimated to be \$10-12 billion in 2003, is expanding at a compounded rate of more than 20% per year. U. S. Congress has fueled the rapid growth of nutraceuticals with the passage of the Dietary Supplement Health and Education Act (DSHEA) in 1994. Globally, there have been efforts to monitor quality and regulate the growing business of herbal drugs and traditional medicine¹⁸⁴.

Thirty percent of the worldwide sales of drugs are based on natural products. Though recombinant proteins and peptides account for increasing sales rates, the superiority of low-molecular mass compounds in human diseases therapy remains undisputed mainly due to more favorable compliance and bioavailability properties. Approaches to improve and accelerate the joint drug discovery and development process are expected to take place mainly from innovation in drug target elucidation and lead structure discovery. Therefore, need for new concepts to generate large compounds collection with improved structural diversity has been correctly emphasized by Grabley and Thiericke (1999)¹⁸⁵.

184 Prakash P. 2nd Nutraceutical Summit, CFTRI Conference, February 3-5, 2005, New Delhi

185 Grabley S; Thiericke R, Bioactive agents from natural sources: trends in discovery and application. *Adv Biochem Eng Biotechnol* 1999;64:101-54.

There are number of problems connected with the search for new prototype drugs of biological origin. Investigations of plants used in traditional and modern medicine in China serve as a source of inspiration and as models for the synthesis of new drugs with better therapeutic, chemical or physical properties than the original compounds¹⁸⁶. The World Health Organization also has recognized the importance of traditional medicine and has been active in creating strategies, guidelines and standards for botanical medicines¹⁸⁷.

Commercially, these plant-derived medicines are worth about \$14 billion a year in the United States and \$40 billion worldwide. Americans paid an estimated \$21.2 billion for services provided by alternative medicine practitioners.¹⁸⁸ A 1997 survey estimated that over 12% of adults had used herbal medicine during 1996 as compared with 2.5% in 1990 resulting a business of \$5.1 billion¹⁸⁹. Lilly Research Laboratories markets several million dollars worth of Vincristine and Vinblastine -- the periwinkle derivatives used to treat childhood leukemia and Hodgkin's disease. The U.S. National Cancer Institute regularly earmarks large appropriations to screen 50,000 natural substances for activity against cancer cell lines and the AIDS virus. China, Germany, India, and Japan, among others, are also screening wild species for new drugs.

186 Baerheim SA and; Scheffer JJ Natural products in therapy. Prospects, goals and means in modern research., Pharm Weekl [Sci] 1982 Aug 20;4(4):93-103.

187 W.H.O. Traditional Medicine Strategy 2002-2005, W.H.O. Geneva, 2002

188 Eisenberg D.M. et. Al, Trends in alternative medicine use in US, The Journal of the American Medical Association, 1998 November 11.

189 De Smet, Herbal Remedies, The New England Journal of Medicine, 2002: 347: 2046-2056

Proven agro-industrial technologies need to be applied to the cultivation and processing of medicinal plants and the manufacture of herbal medicines¹⁹⁰. The mass screening of plants in the search for new drugs is vastly expensive and inefficient. It would be cheaper and perhaps more productive to re-examine plant remedies described in ancient and mediaeval texts¹⁹¹. Many higher plants produce economically important organic compounds such as oils, resins, tannins, natural rubber, gums, waxes, dyes, flavors, fragrances, pharmaceuticals, and pesticides. Advances in biotechnology, particularly methods for culturing plant cells and tissues, should provide new means for the commercial processing of even rare plants and the chemicals they produce. These new technologies will extend and enhance the usefulness of plants as renewable resources of valuable chemicals. In the future, biologically active plant-derived chemicals can be expected to play an increasingly significant role in the commercial development of new products for regulating plant growth and for insect and weed control¹⁹².

Some of the prominent commercial plant Derived Medicinal Compounds include: Colchicum, Colchicine, betulinic acid, Camptothecin, topotecan (Hycamtin®), CPT-11 (irinotecan, Camptosar®), 9-aminocamptothecin, delta-9-tetrahydrocannabinol (dronabinol, Marinol®), beta lapachone, lapachol, Podophyllotoxin, etoposide, podophyllinic acid, vinblastine (Velban®), vincristine (leurocristine, Oncovin®), vindesine (Eldisine®), Fildesin®, vinorelbine (Navelbine®), docetaxel (Taxotere®),

190 Akerele O. Nature's medicinal bounty: don't throw it away. W.H.O. Geneva, Switzerland. World Health Forum 1993; 14(4): 390-5.

191 Holland BK. Prospecting for drugs in ancient texts. Nature 1994 Jun 30; 369 (6483), Comment in Nature 1994 Sep 1; 371 (6492): 9, Comment in: Nature 1994 Nov 10; 372 (6502): 124; Comment in: Nature 1995 Aug 17; 376 (6541): 546; Cox PA. The ethnobotanical approach to drug discovery. Scientific American 1994 Jun; 270(6): 82.

192 Balandrin MF; Klocke JA; Wurtele ES; Bollinger WH. Natural plant chemicals: sources of industrial and medicinal materials. Science 1985 Jun 7; 228(4704): 1154-60]; Bonati A., Medicinal plants and industry.

J. Ethnopharmacol 1980 Jun; 2(2): 167-71; Wijesekera RO. Is there an industrial future for phytopharmaceutical drugs? An outline of UNIDO programs in the sector. Chemical Industries Branch, United Nations Industrial Development Organization. J Ethnopharmacol 1991 Apr; 32(1-3): 217-24.

paclitaxel (Taxol®), Tubocurarine, Pilocarpine, Scopolamine. The ultimate goal of ethnopharmacology should be to identify drugs to alleviate human illness via a thorough analysis of plants alleged to be useful in human cultures throughout the world¹⁹³.

The number of potential drug targets has already outgrown the number of existing compounds that could serve as drug candidates. Natural products will stay valuable for pharmaceutical companies due to their wide structural diversity and their excellent adaptation to biologically active structures¹⁹⁴. Natural product research continues to explore variety of lead structures, which may be used as templates for the development of new drugs by the pharmaceutical industry. While microbial products have been the mainstay of industrial natural products discovery, in recent years phytochemistry has again become a field of active interest. Drug discovery programs based on microbial products and phytochemicals are discussed and contrasted¹⁹⁵. Glaxo PLC, embarked on a program wherein extracts and fermentation broths were screened in order to detect bioactive principles¹⁹⁶. Many other multinationals and academic institutions have created joint research programs for plant medicine research for example, Virginia Polytechnic Institute, Bedrijf Geneesmiddelen Voorziening Suriname, Conservation International-Suriname, and Bristol-Myers Squibb Pharmaceutical Research Institute. Several such projects were sponsored by the federal agencies of the USA. University of Chicago at Illinois, University of Munich Germany, University of Mississippi, Xeenova, Ayur-Core, Inc and Bio-Ved Pharmaceuticals represent additional examples. Indian pharmaceutical

193 The role of Ethnopharmacology in drug development. Farnsworth NR, Ciba Found Symp 1990;154:2-11; discussion 11-21; Ethnopharmacology and Western medicine. Phillipson JD; Anderson, Journal of Ethnopharmacol 1989;25(1):61-72.

194 Onaga Lisa, EMBO Reports 2001, 2, 4, 263–265.

195 Borris J Natural products research: perspectives from a major pharmaceutical company, Merck Research Laboratories, J Ethnopharmacol 1996;51(1-3):29.

196 Turner D. J Natural product source material use in the pharmaceutical industry: the Glaxo experience. Ethnopharmacol 1996 Apr;51(1-3):39-43.

companies have launched new projects: Dabur, Zandu, Arya Vaidya, Nicholas Piramal, Lupin, Ranbaxy, are few prominent examples. The Pharmaceutical Research and Development Committee (PRDC) Report of Ministry of Chemicals, Government of India also underlines importance of traditional knowledge¹⁹⁷.

Opportunities for multidisciplinary research that joins the forces of natural products chemistry, molecular and cellular biology, synthetic and analytical chemistry, biochemistry, and pharmacology to exploit the vast diversity of chemical structures and biological activities of natural products are best discussed by Clark¹⁹⁸. The exploration of structural chemical databases comprising a wide variety of chemotypes, in conjunction with databases on target genes and proteins, will facilitate the creation of new chemical entities through computational molecular modeling for pharmacological evaluation¹⁹⁹.

In the natural product drug discovery it is important to follow systems-theory and systems biology applications to facilitate the process²⁰⁰. Routine random efforts are not likely to increase the desired success rate of discovery while experience indicates that a modified collection policy offered better chances for the discovery and development of agents for treatment of AIDS and cancer²⁰¹. Numerous drugs have entered the

197 Mashelkar R.A. Transforming India into the Knowledge Power, PDRC Report, Government of India, November 1999.

198 Clark AM Natural products as a resource for new drugs. University of Mississippi, Pharm Res 1996 Aug;13(8):1133-44.

199199 Nisbet LJ; Moore M. Will natural products remain an important source of drug research for the future?. Curr Opin Biotechnol 1997 Dec;8(6):708-12; Biodiversity prospecting and benefit-sharing: perspectives from the field. Soejarto DD, J. Ethnopharmacol 1996 Apr;51(1-3):1-15.

200 Leroy Hood, Principles, Practice and Future of Systems Biology, Drug Discovery Today 2003; 8(10); 436-438.

201 Cragg GM; Boyd MR; Cardellina JH 2nd; Newman DJ; Snader KM; McCloud. Ethnobotany and drug discovery: the experience of the US National Cancer Institute Developmental Therapeutics Program, National Cancer Institute, Bethesda, Ciba Foundation Symposium 1994;185:178-90; 190-96. Kitagawa I, Elucidation of scientific basis for traditional medicines and exploitation of new naturally occurring drugs, Yakugaku Zasshi 1992 Jan 112:1 1-41.

international pharmacopoeia via of ethnobotany and traditional medicine²⁰². There are many similarities in traditional systems of medicine as well as ethnomedicines being connected to each other as 'great traditions and little traditions'. All botanical drugs will have to fulfill the international requirements on quality, safety and efficacy²⁰³.

6.2.2. TM - Non Drug Approaches: Yoga, Meditation and Spirituality

TM does not mean only material medicine. It has many unique features of no drug interventions. Chinese traditional system has acupuncture; Indian Ayurveda has Swasthavrita, Yoga, Panchakarma, and such. A substantial research on scientific basis of acupuncture has been carried out worldwide and is published in good peer reviewed journals. Its economic advantages are reviewed elsewhere in this report. For limitations of space, only Yoga, meditation and spirituality related research is reviewed here, however, similar practices in other cultures and traditions are also important.

Worldwide interest in Yoga and meditation techniques is increasing. In addition to physical and mental benefits, the spiritual and biological effects of these ancient practices remain vital. Yoga--from the Sanskrit root *yuj* "to join"- aims for the perfect union of body, mind, and spirit, through a system of postures, breath control, sounds, meditation, and other practices. Yogis claim that yogic practices can be tailored to help treat specific mental and physical disorders. There are few randomized, controlled trials supporting

202 De Smet PA, The role of plant-derived drugs and herbal medicines in healthcare. *Drugs* 1997 Dec; 54(6): 801-40; King SR; Tempesta MS. From shaman to human clinical trials: the role of industry in ethnobotany, conservation and community reciprocity. *Ciba Found Symp* 1994; 185:197-206; discussion 206-13.

203 Vogel HG. Similarities between various systems of traditional medicine: Considerations for the future of ethnopharmacology. *J. Ethnopharmacol* 1991 Dec 35:2 179-90.

therapeutic benefits. According to Howard Kent, director of the UK charity Yoga for Health Foundation (YHF), the conventional medicine and yoga should complement each other, however, lack of adequate research is a limiting factor. For example, the use of yoga to investigate human neurobiology has been studied by Hans Lou of the John F Kennedy Institute (University of Copenhagen, Denmark) to know how neural networks support different aspects of consciousness. Lou and his team used positron emission tomography (PET) to identify brain regions active in different states of consciousness (eg, active, resting, sleep), "to get an idea of the pivotal regions common to all consciousness. According to Professor David Shannahoff-Khalsa the University of California, San Diego, the study of yoga has led to a new paradigm for understanding physiological states and mind body interactions²⁰⁴. In 1983, Shannahoff-Khalsa with Floyd Bloom of *Science*, and others showed that dominant electroencephalographic activity in one cerebral hemisphere correlated with predominant airflow in the contralateral nostril, in a cycle lasting 25200 minutes when awake²⁰⁵. This pattern of hemispheric activity and nasal airflow has since been linked with rhythmic changes in cardiovascular activity, cognition, autonomic-nervous-system activity, and concentrations of plasma catecholamines, pituitary hormones, and even insulin²⁰⁶. Left-nostril, right-hemisphere dominance indicates a "rest" state whereas right-nostril, left-hemisphere dominance marks the contrary "active" state.

204 Shannahoff-Khalsa DS. An introduction to Kundalini yoga meditation techniques that are specific for the treatment of psychiatric disorders. *J Altern. Complement Med.* 2004 Feb;10(1):91-10

205 Shannahoff-Khalsa, *Human Neurobiol* 1983; 2: 3943.

206 Shannahoff-Khalsa, *Am J Physiol* 1997; 272: R96268.

If stress can cause disease, then peace and calm can cause health, but neuroimmunologist David Jessop (University of Bristol, UK) notes that although there is anecdotal evidence for an association between stress and disease, and although biochemical mechanisms for a causal relation do exist, more rigorous scientific studies are needed. Shannahoff-Khalsa believes that yoga is "a huge and once-secret technology of the mind. People can have difficulty with knowledge from other cultures, yet these techniques are something everyone can experience. 'How they work' is not as important as 'do they work?' Yet despite increasing interest from patients and academia, few efficacy studies of yoga are underway. Trials may not be easy, because a substantial commitment is needed from participants. Robin Monro of UK based biochemist and founder of Yoga Biomedical Research institute has published an excellent bibliography on various research studies in this area. There are some good controlled studies supporting usefulness of Yoga and meditation techniques in diseases like asthma, musculo-skeletal and other psychosomatic and psychological conditions. Yoga is not a quick fix for health, but it may hold surprises for those who are willing to make the effort²⁰⁷. There are studies indicating benefits of long-term regular physical activity, including walking, is associated with significantly better cognitive function and less cognitive decline in older women²⁰⁸. A preliminary study has established benefits of yoga-based regimen in relieving some symptoms and signs of carpal tunnel syndrome²⁰⁹. Bernardi et al. studied effect of yoga mantras and reported them to induce favorable psychological and possibly physiological effects²¹⁰. In a randomized controlled study on lymphoma patients, the participation rates suggested

207 Morris K. Meditating on yogic science. *The Lancet*, 1998; 351 (9108).

208 Weuve J. Physical Activity, Including Walking, and Cognitive Function in Older Women *JAMA*. 2004;292:1454-1461

209 Garfinkel M.S., Yoga-Based Intervention for Carpal Tunnel Syndrome: A Randomized Trial. *JAMA* 1998;280:1601-1603.

210 Bernardi L. Effect of rosary prayer and yoga mantras on autonomic cardiovascular rhythms: comparative study. *BMJ* 2001;323:1446-1449

that a Yoga program is feasible for patients with cancer and that such a program significantly improves sleep-related outcomes²¹¹. A recent prospective, randomized trial compared the efficacy of anti-tuberculosis treatment with two separate programs (yoga and breath awareness), on lung capacities and bacteriological status in pulmonary tuberculosis patients. The improved level of infection, radiographic picture, weight gain and reduced symptoms in the yoga group suggested a complementary role for yoga in the management of pulmonary tuberculosis²¹².

Although, the term spirituality is often misconceived in relation to religion rather than tradition, it has much broader, global and scientific connotations. The mind-body relations are getting better understanding through research on psycho-neuro-endocrinological aspects and the next step appears to be its extension to deeper understanding of concept of soul and spirituality. Already, some studies related to Out-of-Body Experiences have been well documented and studied²¹³ that are reviewed by Frank Tong of Department of Psychology, Princeton University²¹⁴.

6.3. Education and Human Resource

There is a growing consensus that some knowledge of complementary and alternative medicine is essential to both the practitioners and patients for making better and safer healthcare choices. It is becoming all the more important to educate medical students and

211 Cohen L. et al. Psychological adjustment and sleep quality in a randomized trial of the effects of a Tibetan yoga intervention in patients with lymphoma. *Cancer*. 2004 May 15;100(10):2253-60.

212 Visweswaraiyah NK and Telles S. Randomized trial of yoga as a complementary therapy for pulmonary tuberculosis. *Respirology*. 2004 Mar;9(1):96-101.

213 Blanke O. et al. Stimulating illusory own-body perceptions. *Nature*, 2002; 419:269-270.

214 Tong F. Out-of-body experiences: from Penfield to present. *Trends in Cognitive Sciences* 2003, 7:104-106.

registered practitioners about the strengths and weaknesses of TM/CAM therapies and empower them on how to assess their efficacy. There is a huge resource and knowledge base both traditional and modern that relates to experiences, wisdom, scientific investigations, clinical observations and such. For instance, the Cochrane electronic library²¹⁵ currently houses more than 80 TM/CAM-related full-text systematic reviews and about 5000 CAM-related clinical trials that could be used as a teaching resource. Practitioners of today and tomorrow must appreciate that patients may choose to use TM/CAM therapies and that it is important to assist them in making those choices²¹⁶.

Formal collaborations between modern and traditional medical sectors should be encouraged and promoted²¹⁷. Within the Commonwealth, India and Sri Lanka have very developed legislative and policy frameworks for the promotion and development of traditional medicine. Sri Lanka has a ministry of Ayurveda, the classical healthcare system of the sub-Continent. There are now more than 200,000 registered traditional medical practitioners in India and over two hundred degree-granting colleges of Ayurvedic or TM education. In India there is a long tradition of integrated practice. A National Integrated Medical Association has a large membership. Although, for some period, the Indian Ayurvedic graduates were put away from any of the modern exposure, currently, a moderate level of biomedical sciences have become part of their curricula. However, sadly, such practices are not yet observed in the modern medicine school where there is no components related to Ayurveda or such other traditional medicine.

215 Ezzo J, Wright K, Hadhazy Z, et al. Use of the Cochrane electronic library in complementary and alternative medicine courses in medical schools: is the giant lost in cyberspace? *J Altern Complement Med* 2002; 5: 681-686.

216 Peter M Brooks, Undergraduate teaching of complementary medicine. *MJA*, 2004; 181(5), 274-75.

217 Bodeker G. *Traditional Health Systems and National Policy*, Research Council for Complementary Medicine, . 2003 London.

There has been a continuous debate at the Medical Council of India (MCI) and also at Central Council for Indian Medicine (CCIM) to adopt minimum critical components in training. There have been legal cases related to cross-clinical practice and as of now there seems to be a general consensus in favor of such integration, however, according to Michael Cohen of Osher Institute of Harvard Medical School, the way forward involves not only preventing negligence and fraud, but also facilitating therapeutic exchanges between various healthcare providers and their patients²¹⁸.

To integrate and work with globalization, TM needs to reassess and open itself to the requirements of scientific rationality, convert itself in its diagnostic and therapeutic approach methods as well as in its deontology. It will thus ensure its influence, productivity, and progress as well as enhance its therapeutic efficiency and competitiveness²¹⁹. This requires the following: First, the use of modern medicine's diagnostic means and therapeutic control such as laboratory analysis, various diagnostic tests, conventional radiography and tomography, magnetic resonance, and all current and future medical techniques; second, chemical and pharmacological study of medicines to determine their components, active principles, toxicity, and posology and third, introduction of GMP and ICH norms in pharmaceutical industries to ensure quality and safety during the large-scale production. This will help in commercialization internationally.

218 Cohen Michael H. Legal and ethical issues in complementary medicine: a United States perspective. *MJA*, 2004; 181(3): 168-69.

219 World Bank TK Notes No. 68, 2004

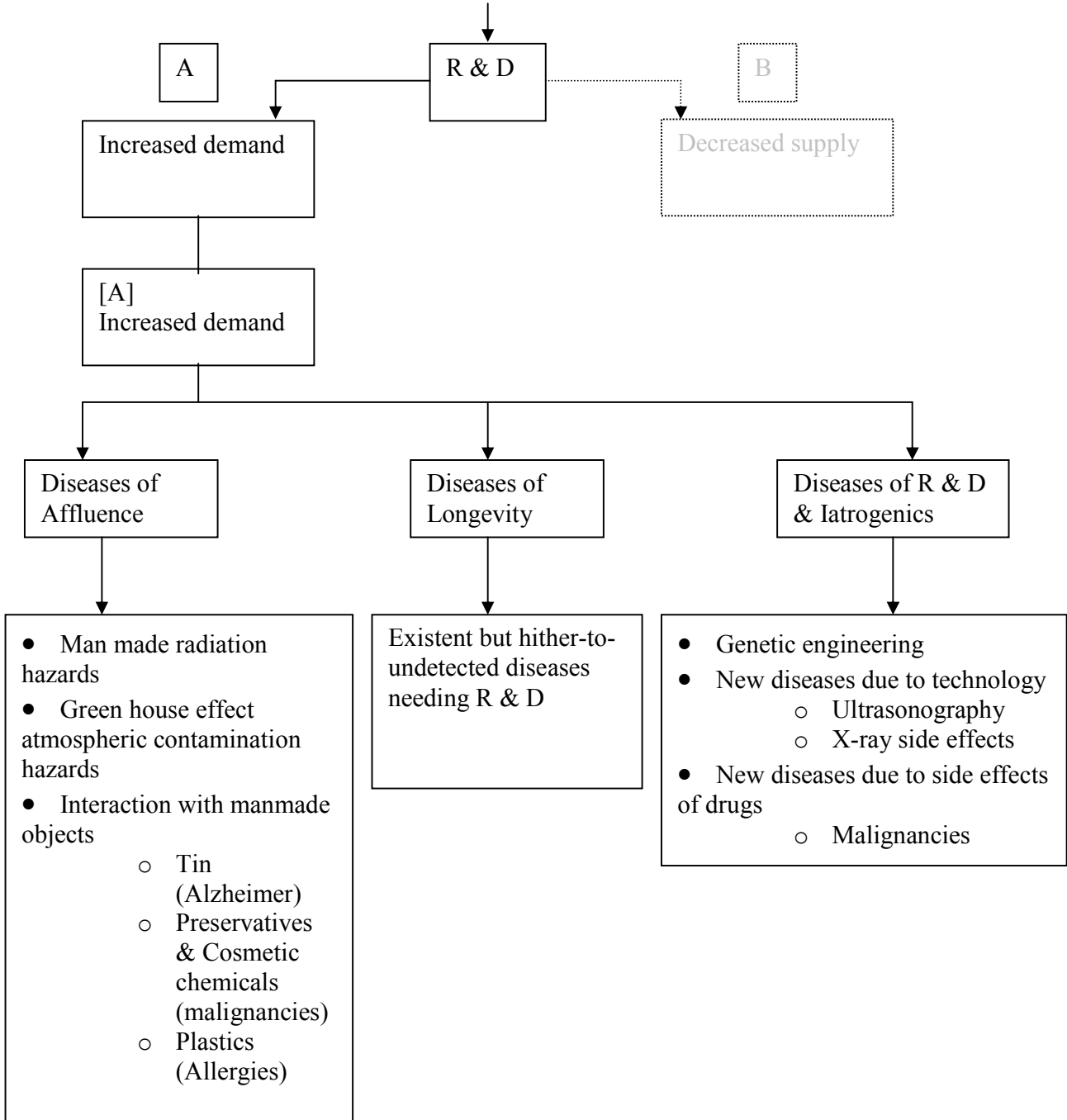
The public authorities should be involved in setting-up traditional medicine and traditional pharmacopoeia institutes for chemical, pharmacopoeia and clinical research; setting-up the national organization of traditional health practitioners; a regular evaluation of the abilities of these organizations through joint (both systems) bodies to ascertain the real impact of their action on people's health; providing legal recognition of this type of medicine; action at the WIPO level to protect traditional knowledge; and the creation and upkeep of protected ethno-botanic gardens to perpetuate vegetal species.

In Korea, the teaching of TM has been institutionalized for more than five decades, and accordingly the formulated educational system has a structure similar to that of MM. It is observed that despite the large differences in philosophy, concepts, and clinical content between the medical disciplines, the professional socializations of TM and MM students were progressing in a similar way²²⁰.

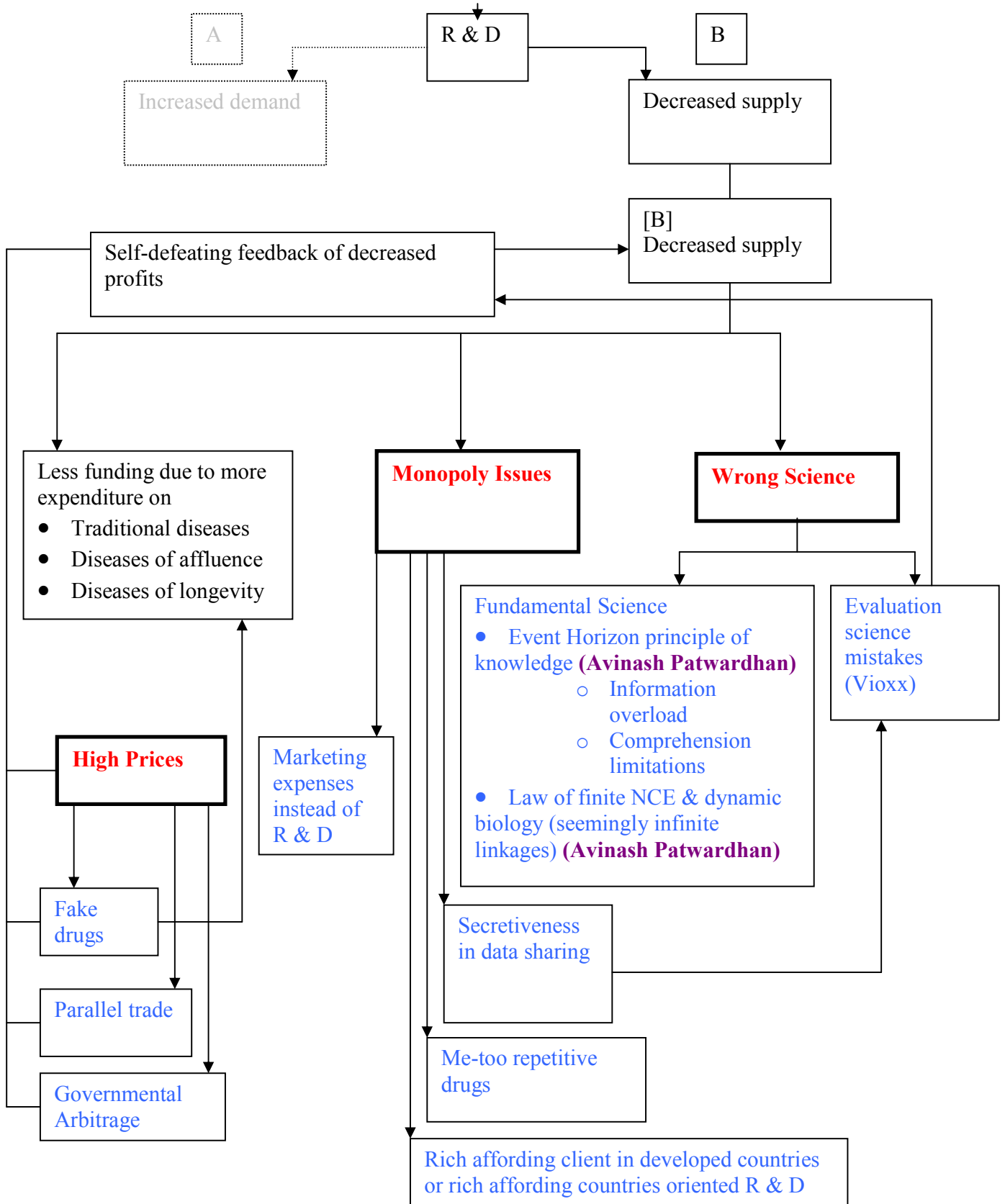
There is an urgent need to create world-class institutions of TM that are based on science and evidence based research where the state of the art technology goes hand in hand with traditional wisdom. TM uses largely herbal medicines and human resource development in this area is a priority. A Masters program in Herbal Drug Technology that is conceived by Interdisciplinary School of Health Sciences with the help of NMITLI team of experts presents a good example of contemporary efforts. University of Pune and University of Madras are in a process of offering this program. One of the important task such institutions should undertake on priority is to create world-class practitioners of TM.

220 Kim CY and Lim B. Modernized education of traditional medicine in Korea: is it contributing to the same type of professionalization seen in Western medicine? Soc Sci Med. 2004; 58(10):1999-2008.

INNOVATION BOTTLENECK



INNOVATION BOTTLENECK



Explanatory notes:

Monopoly issues create four major setbacks to good R & D. 1. Pharmaceuticals spend disproportionately large amount of their profit funds on marketing & advertisement instead of using those funds for innovative R & D. 2. Pharmaceuticals tend to become secretive about sharing of their research finding. This oft times forces the remainder industry to “re-search” the already known facts and reinvent the wheel of progress. This secretiveness also influences evaluation research, leading to false positives (and at times) false negative results. 3. A trend to produce me-too or follow on drugs increases. In a way it is a beneficial practice because it makes drug discovery more and more individual specific but it cuts on the funds for new drug discovery and the industry may not be able to achieve the optimal balancing act between the pros and cons of the trend. 4. R & D starts catering to the affording market rather than being utilitarian (for the good of larger number of human population).

High prices driven by capitalistic drives, making pharmaceuticals seek far larger than marginal profits fuels fake drug industry, inter country arbitrage and, parallel trade that in turn cut on good R & D.

Limitation of science itself is a major shortfall for good R & D. Absence of new drug discovery cuts on profits that in turn cuts on R & D. One limitation is that of faulty and inadequate evaluation methodology (Statistical methods: Linear, simple, static models for evaluation and inadequate sampling before conclusions are drawn). The other is effect of

Event Horizon principle of knowledge (Avinash Patwardhan) and Law of Finite NCE and dynamic Biology (Avinash Patwardhan).

The former principle stipulates that information overload (for scientist community to handle data) and limitation of human mind, individually and as a collective to grasp and comprehend the ecological-global-totality puts a cap on the potentials for new drug discovery. The process of new drug discovery, as in many natural processes would, according to this principle, reach a saturation point beyond which the yield for the investment will fall dramatically.



The Law of finite NCE and dynamic biology stipulates that even as the number of genetic codes are finite and their knowledge grows exponentially for mankind so that soon all the genetic codes will be known to mankind at highly affordable rates (creating potential for ideal customized medicine for every known ailment), the corresponding number of chemical protein or similar molecules is also finite. However, because biology is a dynamic and complex process, the number of permutations or mere combinations of the possible interactions between the finite genetic codes (proteins) arithmetically tends to run into seeming infinity, the possibility of near perfect drug discovery remains and will remain a far away ever elusive dream.

“A human being is a part of the whole called by us universe, a part limited in time and space. He experiences himself, his thoughts and feeling as something separated from the rest, a kind of optical delusion of his consciousness. This delusion is a kind of prison for us, restricting us to our personal desires and to affection for a few persons nearest to us. Our task must be to free ourselves from this prison by widening our circle of compassion to embrace all living creatures and the whole of nature in its beauty”.

Albert Einstein

Chapter 7

A Win Win Game and A Reason for Hope

7.1. Observations

This study was an opportunity par excellence to observe and witness the twilight prior to the dawn of a new age in health care- the age of Post Modern Medicine²²¹, an era, where modern medicine and traditional medicine will blend into a holistic synergy in tune with dynamical complex systems thinking, to provide affordable, available and accessible health to every citizen of global human society and render humanity free from its petty strife to move forward to express the best of its elements. Needless to say, like any twilight vision, what was seen was full of haze, blur, uncertainty, trepidation, insecurity, mistrust and above all confusion. However, the inkling and insinuation of dawn was unmistakable. What did we see? Definition is akin to a picture of an individual while naked. Characterization puts a dress on the body and makes a person out of it. Having already inherited an excellent definition of TM from WHO, we found TM as something theoretically fragmented, affordable, rural, partially explored, IPR unprotected, cohabiting with MM without formal marriage and/or offspring, for chronic conditions, having few side effects and, with a lot of innovative potential.

²²¹ A phrase coined by Avinash Patwardhan

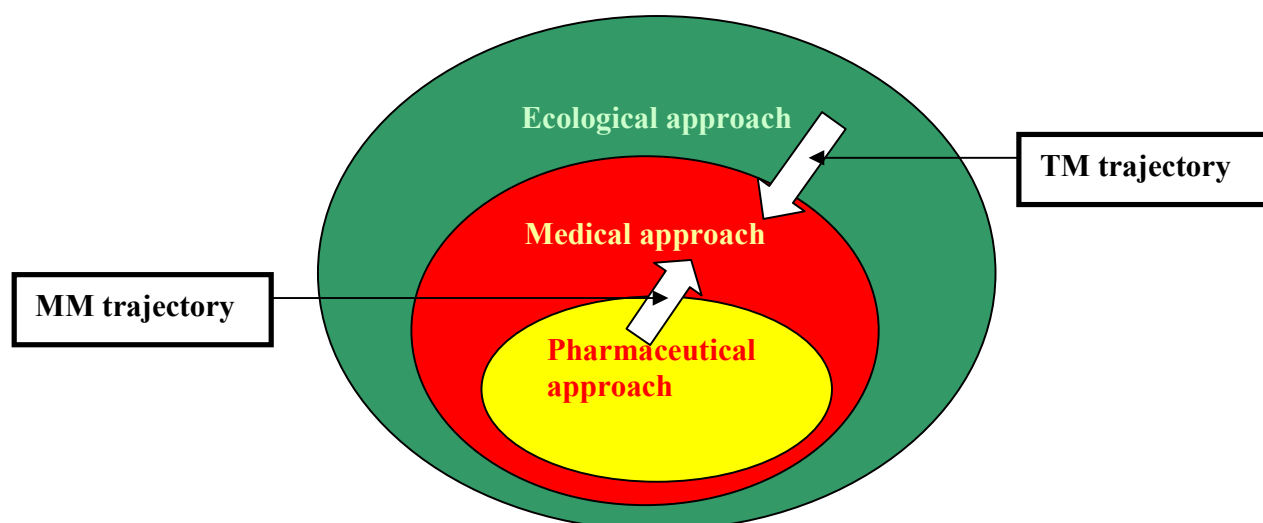
The observations made, broadly were passive (extensive literature review), active-passive (telephonic interviews, questionnaire surveys, private correspondences) and active (visits to Institutes of interest).

While the preceding pages of the report covered most of the observations, some data could not fit in its taxonomy and needed berth. The following section provides, tables, logic diagrams, examples, and case studies where the principles discussed in the report are being put to exemplary real life practice.

7.1.1. Comparison and contrast between modern medicine and traditional medicine in general and in particular context of developing countries

On the issue of	Score of MM is	Score of TM is
Availability	Moderate	High
Accessibility	Moderate	High
Affordability	Low	High
Scientific validity	High	Moderate
Practice standardization	High	Moderate
Delivery infrastructure	Moderate	Moderate
Intra-disciplinarily integration	High	Moderate
Inter disciplinarily integration	Moderate	Low

7.1.2. General approach to human health: Modern versus Traditional



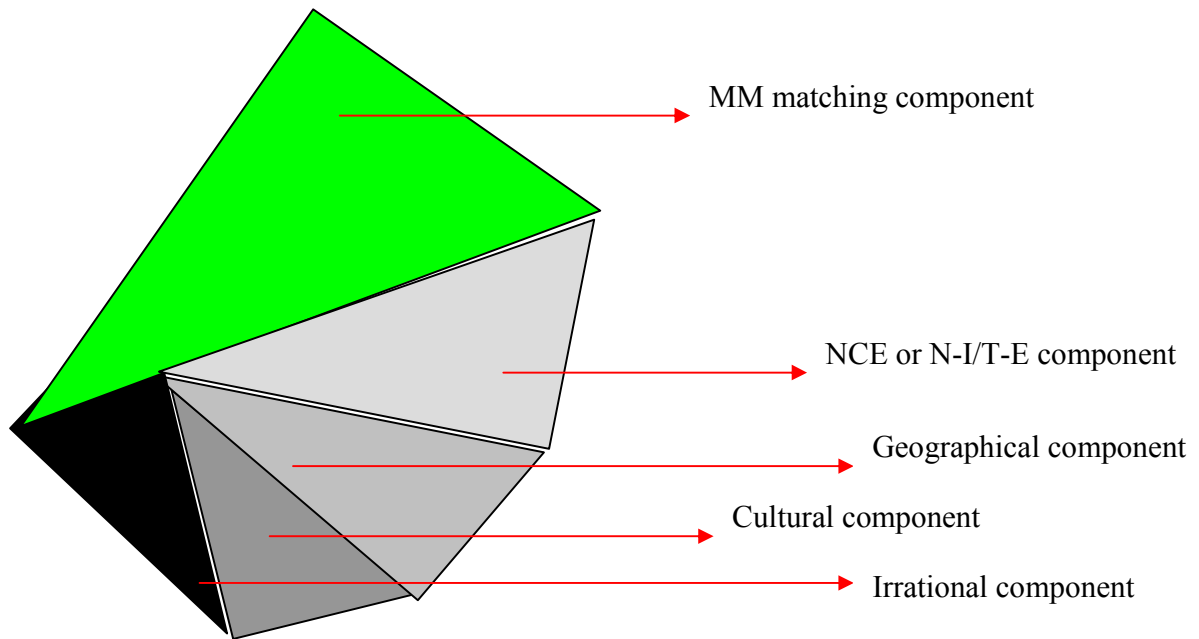
Key to the diagrams

As it is, TM can be deemed as a composite of five components. These are: 1. Irrational: This has stayed with and within TM, as an artifact of its early evolutionary failed experimentations. It is tagging along due to inertial processes. 2. Cultural: This is the component of TM that has evolved and serves the specific cultural needs of the societies for which and in which it arose (for example the utility of cow's urine in Ayurveda carries overtones because cow was considered a sacred animal in the cultural milieu where Ayurveda evolved). 3. Geographical: This is the component of TM that has evolved and serves the specific geographical needs of the societies for which and in which it arose (for example the utility of peyote in Latin American TM is magnified because peyote grew or grow abundantly in that region). Number 2 and 3 may or may not have a large role to play in global human health issues. 4. NCE, N-I/T-E: This is the most valuable and contributive component of TM. Many hither-to-unknown-to-MM new chemical entities might be found in TM (recipes that use natural products like herbs, minerals, animal products etc.). In a similar vein, TM can offer new techniques (Acupuncture for example) that are effective in treatment but are or were not a part of MM. 5. MM Matching: Parallel evolution of good formulations/techniques in not unknown in history. There is a big part of TM that is already incorporated in MM, directly or indirectly. This reinforces the validity of commonality but beyond that has little purpose to serve.

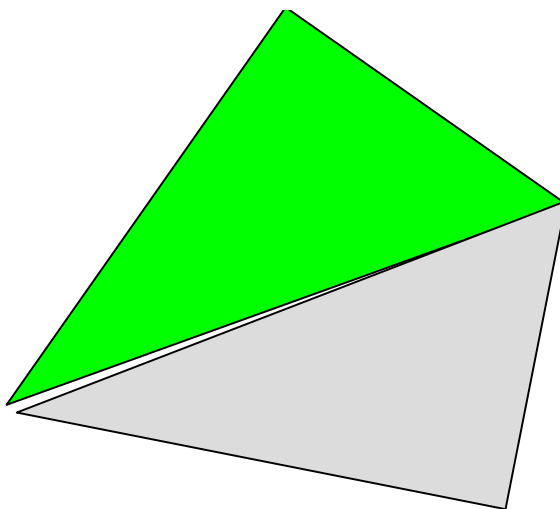
7.1.3. Traditional Medicine in relation to Modern Medicine & Post Modern

Medicine

TM component Hexagon

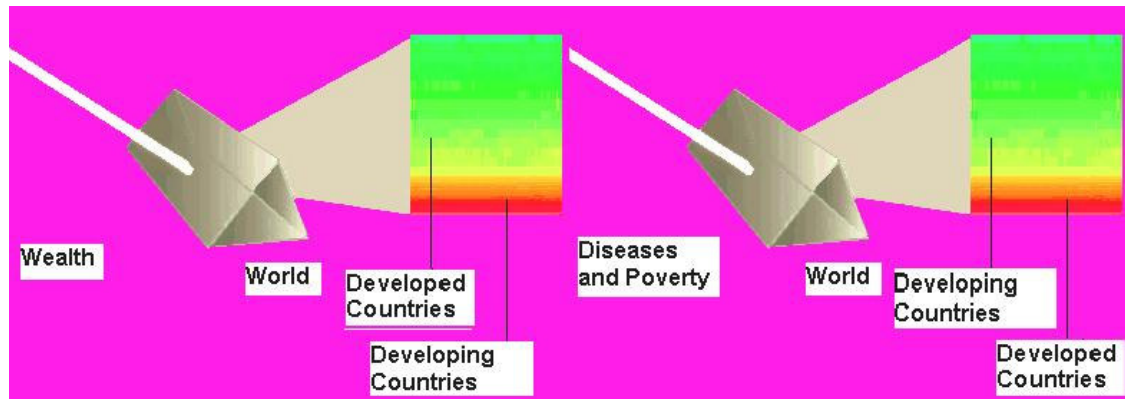


**Post Modern Medicine
From Triangles to Rhombus**

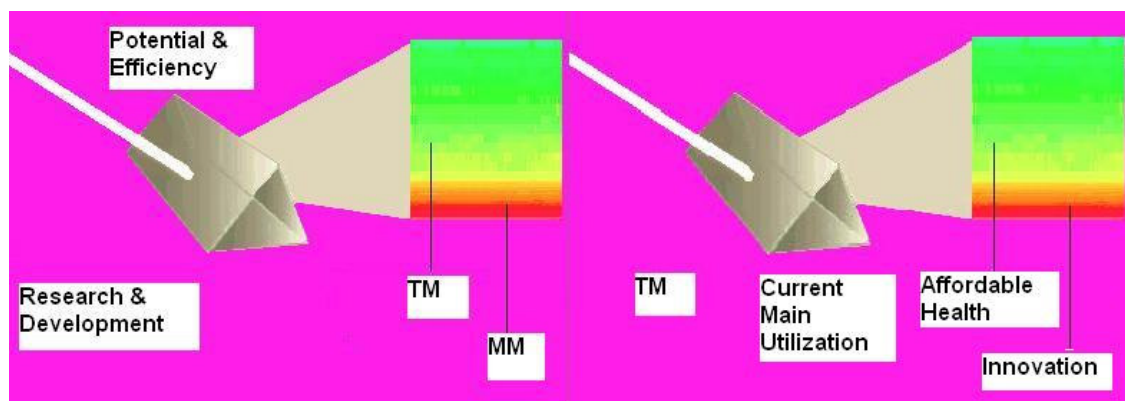


This diagram depicts the futuristic version of what we may call as Post Modern Medicine. It would be a synthesis of all that is good in MM and the NCE, N-I/T-E component of TM

7.1.4. Traditional Medicine in broad social context



This diagram highlights the fact that though the world might have become wealthy in general in last 100 years, it resides mainly in the developed countries and on the other hand, (certain type of contagious) diseases and poverty still find haven in the developing world.



This diagram highlights mainly the up/optimistic side of TM. While it “does not” say that MM has lost steam or R & D in it is inefficient, it points to an observation that given the input and attention, TM carries far more promises than MM as far as future of health care is concerned and gives more return for the dime vis-à-vis MM. The second frame shows

that though TM has excellent potential for innovation its major global utility still is to provide affordable health care in the developing countries in lieu of MM.

7.1.5. Government of India: Integrated Research and Funding

There is a long tradition and practice of Ayurveda and Yoga in this country and there has been a good effort to advance scientific research through various councils. The establishment of AYUSH is considered to be an important step. The Council for Scientific and Industrial Research (CSIR) is currently providing a leadership to innovate on TK. CSIR has been instrumental in creating awareness about IPR and also has put some systems and projects in place (NMITLI, TKDL) for offensive and defensive protection of IPR. The CSIR has many new initiatives and network projects involving national research laboratories, Universities, Medical Colleges and Hospitals along with industries. Issues starting from conservation, cultivation, bioprospecting, passport data, genotyping, chemoprofiling of medicinal plants, preclinical and clinical studies are underway. The Indian Council for Medical Research remains a pioneering body that had undertaken massive effort of pharmacological screening of various medicinal plants. The useful monographs and bibliography of Indian Medicinal Plants remain very important references. The Central Council for Research in Ayurveda and Siddha with its distributed research centers spread across the country has done remarkable work in relation to pharmacognosy, cultivation and conservation of medicinal plants. CCRAS has also contributed in basic research and clinical research related to Ayurveda and Yoga. Recently, the Department of Science and Technology (DST) has Pharmaceutical Research and Development Support Fund (PRDSF) program with the specific objectives to synergies the strengths of publicly funded R&D institutions and Indian Pharmaceutical

Industry in all systems of medicines and to create an enabling infrastructure, mechanisms and linkages to facilitate new drug development. This program also provides soft loan to Pharmaceutical Companies for undertaking R&D where so far 50 industry institutional collaborative R&D projects both in modern and Indian Systems of Medicine have been funded on herbal drugs covering the areas of Ayurveda and Siddha Systems of Medicine for diseases like Rheumatism, Diarrhea, Pancreatitis, Gastritis, Ischaemic Heart Diseases, Skin, Eye, Cardiac disorders, Cancer, AIDS, Malaria, Rheumatoid arthritis, Leucoderma, Respiratory disorder etc. Recently, the Ministry of Information and Communication Technology has supported a major project that aims at harmonizing traditional knowledge and practices and to create a decision support system based on TK of Ayurveda. This will involve systematic algorithm development for intelligent information capturing and retrieval. The Department of Biotechnology and the University Grants Commission also funds education and research projects related to medicinal plants and drug discovery. A masters program in Herbal Drug Technology developed by Interdisciplinary School of Health Sciences with the help of CSIR NMITLI program presents a good example of attempts in contemporary human resource development. Although, this presents a good case where public-private partnership efforts are encouraged with substantial research funding coming from Government of India, there is no interdepartmental coordination, harmonization of practices and common guidelines for such research. This, many times results in a considerable duplication of efforts and resource wastage. Despite these projects and research funding, it is often argued that it is grossly inadequate as the TM sector does not get more than 2% of the total health budget although, the majority of population still relies on these. There is also an issue of due

respectability and visibility to TM vis-à-vis modern medicine. While other developing countries need to follow such efforts, these main limitation needs to be taken into consideration.

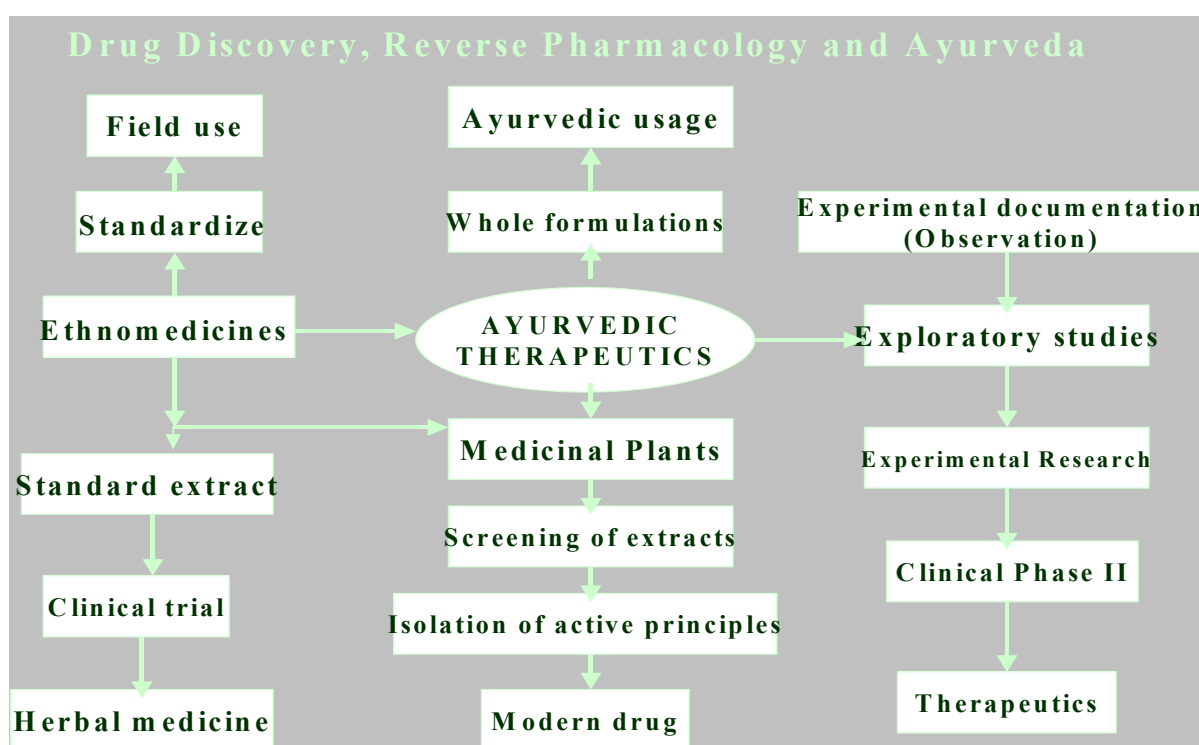
7.1.6. Reverse Pharmacology and Traditional Medicine

Traditional medicine offers immense clinical opportunities for observational Therapeutics and Pharmacoepidemiology. Several major drug groups have emerged due to scientific studies on drugs and poisons, which were traditionally known. The examples are histamine and acetylcholine from ergot, curare derivatives, amine-modulating drugs based on the clinical phenomenology of *Rauwolfia serpentina*, etc. However, such efforts have been sporadic and lead to inordinate delays from the moment of clinical observations to new drug development. There are several paths for research and development for natural products. To institute organized and time-bound scientific endeavor, a new path has been evolved called Reverse Pharmacology²²². Reverse Pharmacology is the science of integrating documented clinical / experiential novel hits into leads by trans-disciplinary exploratory studies (*in vitro* and *in vivo*), at multiple levels of biological organization. Such leads are further developed into drug candidates by relevant science for safety, efficacy and quality by experimental and clinical research. The scope of Reverse Pharmacology is to understand the mechanisms of drug actions, to obtain leads for medicinal chemistry and to introduce safe and effective natural drugs, based on vast experience of traditional medicine²²³.

222 Vaidya Ashok D.B., Sir R.N.Chopra Oration. Reverse Pharmacological Correlates of Ayurvedic Drug Action, 34th Annual Conference Of Indian Pharmacological Society, Nagpur, 2002.

223 Vaidya Ashok D.B., Amonkar AJ, Chandrasekharan S. Reverse Pharmacology & Medicinal Chemistry: Opportunities And Challenges". 9th National Conference On "Bioactive Heterocycles And Drug Discovery Paradigm", Department of Chemistry, Saurashtra University, Rajkot, 2005.

With Reverse Pharmacology, interesting new product development has occurred over the last two decades. *Mucuna pruriens* for Parkinson's disease²²⁴, *Picrorrhiza kurroa* for viral hepatitis²²⁵, *Tinospora cordifolia* for immunopotential²²⁶, *Commiphora wightii* for rheumatoid arthritis and *Curcuma longa* for precancerous mouth lesions²²⁷. The path of Reverse Pharmacology is cost-effective, creative and generative of safe natural drugs from Traditional Medicine. Evidence-based traditional medicine can globally emerge with new natural drugs, with scientific data on safety and efficacy.



224Vaidya A.B., Rajagopalan T.G., Mankodi N.A. et al. Treatment of Parkinson's Disease with the Cowhage Plant –*Mucuna Pruriens* Bak. *Neurology India*, XXVI, No.4: 171 –176:1978.

225Vaidya AB, Antarkar DS, Doshi JC, et al. *Picrorrhiza kurroa* (Kutki) Royle ex Benth as a hepatoprotective agent--experimental & clinical studies. *J Postgrad Med* 1996;42:105-8.

226 Dahanukar SA, Thatte UM and Rege NN. Immunostimulantns in Ayurveda medicine, In *Immunomodulatory Agents from Plants*. Ed. H.Wagner, PP.289-323. Birkhauser VBerlay AG, Basel 1999.

227 Raut AA et al. Anti-rheumatic formulations from Ayurveda. *Ancient Science of Life* 1991;XI: 66-69.

7.1.7. NIH/NCCAM

The National Center for Complementary and Alternative Medicine (NCCAM) is one of the 27 institutes and centers that make up the National Institutes of Health (NIH). The NIH is one of eight agencies under the Public Health Service (PHS) in the Department of Health and Human Services (DHHS). The US Congress established the Office of Alternative Medicine in 1992 and the National Center for Complementary and Alternative Medicine in 1999. The funding started from \$2 million in 1992 has rapidly grown to over \$123 million for 2005. In addition to this budget, NCCAM facilitates use of resources and skills available at other institutes such as NCI, NIAID and such to develop and execute interdisciplinary research projects. NCCAM is setting a priority as Science First and is dedicated to exploring complementary and alternative healing practices in the context of rigorous science, training complementary and alternative medicine (CAM) researchers, and disseminating authoritative information to the public and professionals. Primary focus areas of NCCAM include research, research training, career development, outreach and integration²²⁸. NCCAM gets good support from the Office of Technology Transfer (OTT) and Fogarty International Center of the NIH for intellectual property and policy issues respectively. NCCAM has framed a TM/CAM strategy and has a strong International Health Research program that has developed cooperation with many developing countries including Africa and Asian regions²²⁹. Some of the important clinical studies NCCAM has undertaken include Glucosamine, St Johns wort, *Gingko biloba* and Acupuncture. Although, NCCAM is not directly in human resource development or training of practitioners of TM/CAM, it does gives a good

228 Chesney M.A. and Strause S.E. Complementary and alternative medicine: the convergence of public interest and science in the United States. *MJA*, 2004, 181(6); 335-336.

229 NIH/NCCAM, Strategic Plan 2005-2009, October 2004.

example of a prototype that could be further transformed into World class institutions of higher learning in the field of TM/CAM in different parts of the world.

National Cancer Institute of NIH presents an important case of a massive screening program involving medicinal plants from various parts of the world. In carrying out the collection and extraction of thousands of plant and marine organism samples worldwide, the NCI has established a Natural Products Repository (NPR), which is a unique and valuable resource for the discovery of potential new drugs and other bioactive agents. The rapid progress made in the elucidation of mechanisms underlying human diseases has resulted in a proliferation of molecular targets available for potential drug treatment. The adaptation of these targets to high throughput screening processes has greatly expanded the potential for drug discovery. In recognition of this potential, the NCI has developed policies for the distribution of extracts from the NPR to qualified organizations for testing in screens related to all human diseases, subject to the signing of a legally-binding Material Transfer Agreement (MTA) which protects the rights of all. One of the key terms of the MTA is the requirement that the recipient organization negotiate suitable terms of collaboration and compensation with the source country(ies) of any extract(s) which yield agents which are developed towards clinical trials and possible commercialization. Thus, NCI experience remains very important from drug discovery research and innovation and IPR²³⁰.

230 Gordon C. NIH/NCI parties (see <http://ntp.nci.nih.gov/branches/ntp/repository.html>)

7.1.8. Traditional nutraceuticals: Ayurveda case²³¹

Importance and significance of diet for maintenance of health, prevention of diseases and recovery from illness has been well acknowledged and emphasized in Ayurveda as stated in Charak Samhita²³² “Human body is made up of food we consume, however diet also plays a role in precipitation of diseases. Wholesome diet gives health, while unwholesome diet leads to ill- health.” Food articles on account of their action on body are broadly classified into three categories; substances, which alleviate the disease activity, eg milk in hyperacidity; those, which aggravate disease condition, eg. chilli in hyperacidity; while some substances are considered to be always helpful to maintain health eg rice, green grams, cow’s milk etc. *Viruddashana* is a unique concept of hazards of eating incompatible food items together which are separately wholesome and beneficial, may prove to be other wise if consumed in combination. Ayurveda considers six types of *Rasa* or taste perceptions: sweet, sour, salty, pungent, bitter, astringent. These six tastes have biodynamic effect on human body and its physiological function on Doshas an Ayurvedic concept that determines health of an individual. Excessive use of any of the *rasa* would give rise to diseases and it is important to have balance of all six in diet. Mind is also considered to be influenced by diet. Certain types of diets can stimulate specific responses such as irritability, calmness, sexual desire and such. Ayurveda recommends modification in diet as per the change in season. There are also natural instincts or signals exhibited by body for deficiency/ sufficiency of body constituents are described in classic text Sushruta Samhita as “If there is deficiency of a particular body constituent one develops a strong desire to have similar qualities of food substances.”

231 Raut Ashwinikumar, M.D.(Ayurveda), Deputy Director, Bhavan’s SPARC, Juhu –Mumbai.

232 Sharma H and Clark C. Contemporary Ayurveda, Churchill Livingstone, 1997, Philadelphia USA.

Finally a popular quote from Ayurvedic texts says ‘when wholesome food is consumed, where is the need of medicine? And when wholesome food is not consumed, what is the use of medicine? Many food items and drinks are used in Ayurveda, which can be labeled as Nutraceuticals. It includes medicinal teas made of spices and herbs; medicinal wines (Asavas and Arishtas); health drinks made of herbs such as Amalaki or Kokam; specific dietary regime during pregnancy, lactation and all stages of life from infancy to old age. Such wisdom and rich information source certainly is valuable in health promotion and disease prevention and needs attention, respect and protection.

7.1.9. Access to Benefits Sharing and The Like Minded Countries²³³

The UN Convention on Biological Diversity signed by the countries of the world in June 1992 during the Earth Summit at Rio-de-Janeiro lead to development of the Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization, which were adopted at the Sixth Meeting of the Conference of Parties held in April 2002 in the Hague (COP Decision VI/24). The Bonn Guidelines are voluntary in nature and are a useful first step of an evolutionary process in the implementation of relevant provisions of the CBD related to access to genetic resources and associated traditional knowledge and sharing of benefits arising from the commercial or other utilization of such resources, with the exclusion of human genetic materials.

TRIPS Agreement and Access to Benefits Sharing (ABS) Issues lead to interactive discussions on the relationship between the TRIPS and CBD’s ABS Work Group and also

233 P. Pushpangadan, Director, CSIR National Botanical Research Institute, Lucknow, India and Government of India representative for negotiations January 2005..

about the ways to harmonize intellectual property issues related to biological and genetic resources and associated knowledge. Despite several meetings of the TRIP Council, no consensus has been reached as yet on the prevailing issues of according legal intellectual property protection to genetic resources and associated traditional knowledge. Article 27.3 (b), particularly the clauses of patenting on life forms and developing a *sui generis* system for protection of plant varieties, is the main bone of contention of the ongoing debate between WTO members from the developing countries and those from the industrialized developed countries. The Group of like-minded developing countries has made nine submissions to the TRIPs Council for reviewing the Article 27.3(b) and other relevant provisions of TRIPs and makes them supportive to the CBD objectives. In a recent submission to the Council, the developing country group comprising Bolivia, Brazil, Cuba, Ecuador, India, Peru, Thailand, Venezuela, raised the following three demands for incorporation into the provision mandating applicants for a patent relating to biological resources or traditional knowledge to: (i) disclose the source of origin of biological/ genetic resources, (ii) provide evidence on prior informed consent, and (iii) evidence on benefit sharing agreement (IP/C/W/403 of 4 June 2003; IP/C/W/420 of 12 March 2004; IP/C/W/429 of 20 September 2004, LMMC ‘Delhi Declaration’ dated 21st January 2005). These issues adequately express the concern of the mega-biodiversity countries that are rich in genetic resources and traditional knowledge, but poor in their biotechnologies. However, the debate on TRIPs –CBD harmonization is still continuing without having reached any conscientious decisions. The developed countries’ argument is that integrating intellectual property issues with CBD provisions is unnecessary and unwarranted. An alternate suggestion to the debate by some of the European Countries is

to include, in appropriate cases, declaration of the origin of genetic material in patent applications as a voluntary requirement and include penalty system for failure to comply with the declaration, in which case the patent would be rejected or withdrawn. The Like Minded Mega-diverse Countries (LMMC) in the developing countries and the countries with their economy in transition are pushing ahead with their demands to meet a legally binding solution to the three major issues raised by them.

7.2 Conclusions

A fact that strikes out first and foremost, with glaring obviousness, to an observer of global health care system is that adequate respectable basic health is, not affordable, scantily available and barely accessible to the bulk of humanity- irrespective of whether the medicine is modern or traditional. The second unmistakable phenomenon that comes to notice is that the patterns within health issues strongly correlate with patterns in economy- monetary and/or political. The third trend that seems as important, as impacting and, as immediate as the first two, but not as vivid as the others is that modern medicine is fumbling and faltering, classically in contexts of chronic diseases, side effects of drugs, holistic approach to health and new drug discovery.

The authors of this report believe that taking cognizance of the last observation is of great importance, not only for health and welfare of global humanity but also for that of modern medicine itself, and therefore, and in sync with, and subsequently that of traditional medicine. The problem of measurement in late 19th century brought physics to

an impasse and paved way for the theory of relativity. Similarly, modern medicine having become “the standard” yardstick to measure any issue related to health is posing a distressing challenge- in light of fallibility of this measure.

On the other hand, larger part of humanity, mainly in developing countries, whenever and wherever it has available and accessible health care, pays for it “out of pocket.” A step further, it can be broadly said that almost entire humanity pays “out of pocket” for “traditional medicine health care”- in developing or in developed countries. This leads to a conclusion, particularly the latter part of the previous statement, that traditional medicine is not integrated with modern medicine, and probably, does not enjoy respect from and at par with modern medicine.

Oddly though, the data from the field of economics shows that huge amount of money changes hands annually and globally in connection with some form of traditional medicine. This observation may allow us to conclude two things. One, TM is well recognized by the society at large and that its acceptance is steadily growing, and two, in light of point raised further down this discussion regarding regulatory issues around TM, the field of TM seems still “free for all” arena, vulnerable to opportunistic exploitation, with inadequate regulations.

Data are generated with the help of instituted infrastructures and engines. Data presented in our report notice that while it seems that regarding economic trends, infrastructure and engines are well available and established in developing countries, in stark contrast to the

state of affairs in developed world, equivalent detailed extensive data on use of TM in developing countries seem sketchy, inadequate and vague.

Though it seems a heartening fact that there is a great movement in all quadrants of developing countries about policy issues regarding TM-TK, the absence of substantive concrete exact data about use of TM in developing countries undermine and undercut said efforts. Moreover, while the awakening is commendable at multiple local levels, there seems a total lack of policy at global level where developing and developed worlds participate and agree together.

Sadly though, it was the conflicts arisen out of economic exploits that brought the issues of definition of TM or TK and those of their efficacy and safety to international platform. Nonetheless, it must be deemed as a good sign, because at least this has drawn attention of scientists and government community to explore issues surrounding efficacy and safety with TM. As can be expected, data are equivocal and skewed, at least in part due to unfitting research methodologies and prejudiced biases at underpinnings, if not overtly at technical levels. That once the ball has started to roll, the status of education or absence thereof regarding TM-TK has become apparent. Though admirable progress has been made on the count, processes of documentation, standardization, integration or inclusion have, yet a long way to go. Different locales display divergent stages of evolution of these processes, ranging from comprehensive integration to bare toleration blemished with skepticism.

World community is still new to ecological consciousness. Naturally, regulatory guidelines regarding conservation of natural resources related to TM-TK are yet faint, feeble and tentative.

In the overall precarious and perilous world order of contemporary times, it appears very likely that the domain of Intellectual Property Rights is and will be the battleground on which the fate of all medicine, modern, traditional and post modern, if there would be a one, will be decided. Solid body of research and innovation is emerging on the topic though the lay of the land is far from being clear.

All said and done, at the bottom line of affordability of health, and then good equitable health at that, the picture is still far from being cheerful.

With these data in hands, the report returns to the question that CIPIH asked to begin with, “Could more effective use be made of Traditional Medicine in providing affordable treatments?” Now, at this stage, an assertive answer can indeed be given with sufficient confidence, albeit with numerous caveats. But those cannot be a reason to falter or flinch. After all, what is a problem that is without challenges? The road to affordable health in developing world is rough and full of stumbling blocks en route. There are so many pieces, of different types, shapes and sizes to put together to complete this puzzle, so many issues to resolve and, so many uncharted terrains to cross- still. The magnitude of the challenge is so large that anything that is done is still too little for a while. Traditional Medicine is one tiny candle (among many) that can illuminate the path in its own limited

way, for humanity to achieve an equitable affordable health for each and every citizen of this planet. What if TM is a candle and not a blazing torch? Great Chinese philosopher Con-Fu-Tse said, “It is better to light a candle than to curse the darkness.” In this old wisdom rests our hope and reason to make attempts.

In the next section the report makes a few recommendations that can in turn develop into concrete proposals to help bring aspiration of “WHO-CIPIH” to make adequate respectable basic health available, accessible and equitably affordable to entire humankind true.

Conclusions in a nutshell:

- Three undercurrents of current health care/delivery crisis:
 - Health care affordability receding away from global majority at alarming pace
 - Widening wealth disparity and polarization at global level
 - Failure of modern medicine to deliver panacea despite ultra dazzling advances in its science and technology
- Expenditure on health is still out of pocket for majority
- Expenditure on Traditional medicine is almost exclusively out of pocket in all countries or societies

TM is:

- Getting increasing societal recognition
- Not getting enough recognition or optimum respectability from modern medicine
- Vulnerable to opportunistic health service charlatans

- Concrete substantive data on use of TM comes mainly from developed countries, incompletely and inaccurately from developing countries
- Huge fervor regarding policy issues around TM in developing countries that is driven primarily by heightened awareness and secondarily by data
- Absence of global policy or consensus on TM cutting across barriers between developed and developing countries
- Data about efficacy and safety of TM are equivocal
- Documentation, standardization, education and integration (with modern medicine) wherever it is, is incomplete, inadequate and at times inaccurate and is visible at differential pace at different locales in developing countries
- Regulatory issues such as about natural resources and intellectual property rights are feebly and at times unjustly addressed
- Approach to TM is mostly still reactive than proactive

7.3. Recommendations

Main body of any knowledge has somewhat circular boundaries. What can be called as fringe depends on in what direction we look. Due to peculiar geometry that is circular rather than linear, cutting edge science and quackery both invariably and inevitably run into each other. Long gone are the days when TM was considered as “Fringe Medicine” (with a somewhat derogatory insinuation attached to the word fringe). TM’s contribution to and being a part of mainstream health care and its delivery system is a fact now.

However, mind of the human society tarries in view of acceptance and reconciliation with

such reckonings. Fully aware that there is a huge chasm between recommendation and its gainful fruition, we give a few broad two-tier recommendations, hoping that some of them if not all, would evolve into concrete proposals, leading to fulfillment of task that prompted CIPIH to ask the question that led to this study.

Global recommendations:

1. Post modernism ushered world societies into a new social and political era. The grand theories of last century yielded to juggernaut of data and their meta-analysis of contemporary times. If information is the name and mantra of the age, then, in view of the conclusion noted in the report that there is not enough data on TM from developing countries public health sectors to work on, our first recommendation would be to invite a collaborative mega project, consisting of numerous medium to small sized projects to collect primary data regarding TM in developing countries, first singly and then collectively, from an exclusive perspective of public health, albeit not overlooking relevant purely scientific data.
2. Parallel but optimally following, WHO collaborative centers, fashioned somewhat similar to NCCAM at NIH of the USA, should be developed (to begin with in countries where TM has major presence) to conduct rigorous fundamental and applied research (incorporating novel quantitative and systems approaches) in TM using appropriate methodologies.
3. WHO led global social marketing campaign should be developed and undertaken to disseminate current holistic data on TM (that would educate about not only practices of TM but about philosophies and basic principles underlying respective

- TM practices) to health care sector- particularly in developed countries and among modern medicine service providers at all levels.
4. WHO should develop with help from respective expertise, workable protocols and regimens to treat diseases afflicting developing world population based on TM after weighing in benefit-cost and efficacy-ignorance ratios- in cases where inadequate data tilt towards integral value, and then distribute and disseminate those literature among practitioners in developing countries- traditional or modern.
 5. WHO should fast track, through various world bodies, the issues around IPR protection around TM, to ensure that, while knowledge does not get lost in secrecy and is available to modern medical science to further cause of human health, the major portion of profits from knowledge and technology arising out of TM should be channeled to needs of those populations that historically played custodian to that body of knowledge.

Regional Recommendations

1. Give basic respect and recognition to TM - it needs to be respected and recognized in the main stream of health care delivery.
2. Thrust on TM practices, philosophies and basic principles NOT just Medicines. The real strengths of TM are in its basic philosophical considerations that are based on hundreds or thousands of years of observations and experiences. The modern medicine, science and societies should practice them for furtherance of

- health. TM should not be limited only as an alternative to MM or just a drug discovery engine.
3. Comparative clinical studies of TM and MM options should be undertaken to get best out of various traditional medicines. Evidence-based research at all levels of preclinical and clinical stages should be strengthened and supported. Cost effectiveness and therapeutic benefits of TM should be coupled and weighed with safety, affordability and availability. More Pharmaco-epidemiological studies for scientific assessment of experiential and observational therapeutics.
 4. Safety and Quality Harmonization. Global guidelines on policy and regulations to ensure safety should be given priority.
 5. Global validation mechanisms and TM networking research. Innovative and apt methodologies supported by common protocols or guidelines on TM research need to be developed, preferably in collaborations or advice from ICH or GRA like initiatives.
 6. Traditional practices, Traditional healers and Ecosystem should not be exploited during bioprospecting. Biodiversity issues should be given predominance. Collection from wild or natural resources for commercial purposes should be controlled and gradually tapered. WHO and bodies like CBD should work together to sensitize importance of health related issues at the backdrop of biodiversity. Encourage use of Good Agricultural Practices, promote organic farming of medicinal plants and ensure quality and safety of raw material to be used in TM.

7. Financing TM: Education, Research, Practice. All the Governments should revisit the actual financing to TM related education, research and practice and should make a road map to strengthen it to reach to equal to that of MM. New state-of-the-art- facilities should be created for evidence-based research. Major budgets to existing TM institutions for modernization. Avoid duplicative efforts and financing by developing inter and intra national networks of research institutions and funding agencies. Include TM exposure to MM educational institutions and vice versa
8. Human resource development: TM practice, Research, ToT. World class institutions/ colleges should be established in every country where there is strong TM presence. Globally trained TM practitioners.
9. Develop WHO Collaborating Centers of TM in countries where it has major presence.
10. Undertake or sponsor detailed studies related to TM impact on public health

We are aware that above recommendations are far from being exhaustive, but we feel that they cover up major gaps in existing landscape. With these, we conclude that we have done our little turn, a coarse job of a sort, of putting the stakes on this road less traveled by. We hope and are confident that abler, wiser and finer artists will take over from here so that in rhythm with Robert Frost's famous lines, ages and ages from the hence, future healthy generations might reflect and say, "...and those initial baby steps have made all the difference."

Acknowledgements

Acknowledgement and expression of gratitude is no easy task, particularly when genuine. Those who know, know, that one just cannot escape a persistent apprehension while writing this section that enough may not have been done- and to all. In the same spirit of what Newton rightly said, "If I have seen farther than others, it is because I was standing on the shoulders of giants."

At the outset I would like to thank Dr R.A. Mashelkar, for recommending my name to the Commission. All throughout this work, he was not only a continuous support and guide, but also a mentor.

I also thank all the members of the Commission for giving me an opportunity to present my views during its visit to India. I wish to thank Dr. Charles Clift, Secretary, Müge Olcay, Technical Officer, and other staff at the Secretariat of the CIPIH/WHO for their timely advice and help. Although, the present study was expected to be a critical review of the current status of TM with respect to IP, Innovation and Public Health, I thought of addressing this task in a broad participative manner and to involve directly or indirectly larger number of experts' viewpoints. Secondly, I also thought of providing a broad philosophical basis to this entire exercise. As a first step, I shared my thoughts with the Commission secretariat and with encouraging consent, started planning for collecting some primary data. I consulted of R.K. Mutatkar and Dr. Aarati Kaulgekar, two renowned local scientists to develop a questionnaire for my specific needs based on

typical Knowledge, Attitude and Practices (KAP) study. I involved my own research students and associates for initial feedback. Before finalization, the draft questionnaire was graciously (internally) peer reviewed by Dr S.D. Gokhale and Ms. Girija Sapre. Subsequently an exhaustive list of experts (220) was prepared based on recent publications in peer reviewed Journals with known impact factor (IF 1 and above). The questionnaire was sent to these experts by email along with a covering letter explaining the outline of the study and expectations from the survey. A subsequent reminder was sent. We received important responses from different countries that gave a good cross section of various regions (list of names of all the respondents is annexed).

Separately, I started contacting some of the eminent institutes and experts in the field for detailed interviews and visits. Through the US Embassy in India (Dr Altaf Lal), I contacted NIH/NCCAM for a visit. I wish to thank all, Dr. Ashok Vaidya of SAPRC, Mumbai; Dr. David Triggler of SUNY Buffalo, Dr. Gerry Bodeker of University of Oxford, Subhash Mehta of FAO, and Dr. Jack Killen and his colleagues of NIH/NCCAM for detailed responses and useful information.

Parallel, I contacted one of my good friends and a former professional associate Dr. Avinash Patwardhan who has formal training in Modern Medicine (General Practice and OB & GYN), a strong background in research (former Research Scientist at The George Washington University, Washington D.C. U.S.A.) and also has a very good understanding of traditional medicine. Dr Avinash kindly agreed to become a consultant to this project and also graciously accepted to be my host during my visit to

NIH/NCCAM. During my visit to the USA, he and I worked together to conceptualize the whole report. His main contributions came in for visualizing, creating and organizing the overarching basic philosophical and logical framework for the entire project, although he contributed his bits at every stage and phase of creation of this report.

Following the three weeks of absence (thanks to VC UoP for special leave), I was mostly involved in report for two more weeks when my colleagues (Aneeta, Aarati, Shilpa, Anjali, Angelin, and Kalpana) and research students (Girish, Manish, Dyaneshwar, Preeti, Yogita, Kamalesh) provided all the support I needed and sought and I thank them all. I was sitting in a special cell at the Science and Technology Park that also provided all the logistics, administrative and coordination support (Thanks to Dr. Rajendra Jagdale Director, Dr Subhash Mali, coordinator and other staff of STP). After the first draft took a reasonable shape, I requested a few senior scholars/researchers from different fields to critique it as a part of internal peer review (Professors Gerry Bodeker, Gautam Sen, R.K. Mutatkar, Aneeta Benninger, Madhav Deo, Ashok Vaidya, Arvind Chopra, Mohan Dewan). These experts provided valuable comments that helped me in further shaping the report and I profoundly thank them all. I thank Madhav Khanwelkar for good suggestions and Vijay Thombare of Market Missionaries India for cover design concepts. Finally, I wish to thank my research colleagues Dr. P. Pushpangadan, Dr. G.A. Qazi, and others at NMITLI Herbal Drug Project for valuable information, and discussions.

Last but not the least, thanks to all respondents, listed and unlisted both who took time from their busy schedule and returned the completed questionnaire in time.

Annexures: Glossary, List of Respondents, Internal Peer Reviewers Profile

Abbreviations and Glossary

AAAS: American Association for the Advancement of Science (AAAS). In addition to publishing *Science* and other science-related publications, hosting scientific conferences and meetings, and helping scientists advance their careers, AAAS undertakes numerous programs and activities that promote science to the public and monitor issues which affect the scientific community.

ADR: Adverse Drug Reactions. Medicines can treat or prevent illness and disease. However, sometimes medicines can cause problems. These problems are called adverse drug reactions.

AIDS: Acquired Immuno - Deficiency Syndrome is caused by infection with the human immunodeficiency virus HIV-1. The HIV virus infects cells in the body that fight infection.

AYUSH: Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy. Formerly known as Department of Indian System of Medicine and Homeopathy (ISM&H). Ministry of Health and Family Welfare, Govt. of India, established AYUSH to promote ISM & H.

CAM: Complementary and Alternative medicine is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.

CBD: Convention on Biological Diversity. The three goals of the CBD are to promote the conservation of biodiversity, the sustainable use of its components, and the fair and equitable sharing of benefits arising out of the utilization of genetic resources. This Convention on Biological Diversity was negotiated under the auspices of the United Nations Environment Program (UNEP).

CCRAS: Central Council for Research in Ayurveda and Siddha (CCRAS) is an apex body for the formulation, coordination and development of research in Ayurveda & Siddha on scientific lines. It was established in March 1978 after reorganization of CCRIM&H. The Minister of Health & Family Welfare, Govt. of India, is the President of the Governing Body of the Council.

CIPIH: Commission on Intellectual Property, Innovation and Public Health was established by the World Health Assembly in 2003 to collect data and proposals from the different actors involved and produce an analysis of intellectual property rights, innovation, and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries.

CSM: Committee on the Safety of Medicines (CSM) is one of the independent advisory committees established under the Medicines Act which advises the UK Licensing Authority on the quality, efficacy and safety of medicines in order to ensure that appropriate public health standards are met and maintained.

CSIR: Council for Scientific and Industrial Research (CSIR), India, is an autonomous body registered under the Societies Registration Act, 1860 with a wide-ranging charter for promotion and development of science and technology India. Established in 1942, by Govt. of India, CSIR has a network of 40 laboratories and 80 Field Extension Centers spread all over India.

CGMP: Current Good Manufacturing Procedures are set of current scientifically sound methods, practices or principles that are implemented and documented during product development and production to ensure consistent manufacture of safe, pure and potent products.

CWG: Commonwealth Working Group is an association of 53 countries. It's 1.8 billion citizens; about 30 percent of the world's population are drawn from the broadest range of faiths, races, cultures and traditions. Members range from vast countries like Canada to small island states like Malta.

DBT: Department of Biotechnology is established by Govt. of India as a separate Department under the Ministry of Science and Technology in 1986 for providing new impetus to the development of the field of modern biology and biotechnology in India.

DSHEA: The Dietary Supplement Health and Education Act of 1994 was enacted by Congress following public debate concerning the importance of dietary supplements in promoting health, the need for consumers to have access to current and accurate information about supplements, and controversy over the Food and Drug Administration's regulatory approach to this product category.

DST: Department of Science and Technology was established in May 1971 by Govt. of India with the objective of promoting new areas of Science & Technology and to play the role of a nodal department for organizing, coordinating and promoting S&T activities in the country.

EBM: Evidence-Based Medicine/Healthcare is looked upon as a new paradigm, replacing the traditional medical paradigm, which is based on authority. It is dependent on the use of randomized controlled trials, as well as systematic reviews (of a series of trials) and meta-analysis, although it is not restricted to these. There is also an emphasis on the dissemination of information, as well as its collection, so that the evidence can reach clinical practice.

EMA: European Medicines Agency is a decentralized body of the European Union with headquarters in London. EMA is an agency to contribute to the protection and

promotion of public and animal health by mobilizing scientific resources from throughout the European Union to provide high quality evaluation of medicinal products, to advise on research and development programs and to provide useful and clear information to users and health professionals.

EU: European Union is a union of twenty-five independent states based on the European Communities and founded to enhance political, economic and social co-operation. Formerly known as European Community (EC) or European Economic Community (EEC).

FDA: Food and Drug Administration of US is a federal science-based law enforcement agency mandated to protect public health and safety. FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

GCP: Good Clinical Practices is a standard for design, conduct, performance, monitoring, audit, recording, analyses and reporting of clinical trials that the data and reported results are credible and accurate, and that the rights, and confidentiality of trial subjects are protected.

GRA: Global Research Alliance represents the combined knowledge and experience of nine of the world's leading knowledge-intensive technology organizations. The alliance will explore ways of exploiting the resources of the participatory members to the benefits of the society at large.

FRLHT: Foundation for Revitalization of Local Health Traditions is a non-government organization situated at Bangalore, India, and working towards conservation of India's traditional medicinal heritage.

HIV: Human Immunodeficiency Virus (refer to AIDS).

HPLC: High Performance Liquid Chromatography is a popular method of analysis. Modern HPLC has many applications including separation, identification, purification, and quantification of various compounds.

HPTLC: High Performance Thin Layer Chromatography is a sophisticated and automated form of TLC. The main difference between HPTLC and TLC is particle and pore size of sorbents.

ICH: The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use; is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.

ICMR: The Indian Council of Medical Research is a apex body in India for the formulation, coordination and promotion of biomedical research, is one of the oldest medical research bodies in the world.

IK: Indigenous Knowledge can refer to the knowledge belonging to a specific ethnic group, for example: ‘Indigenous knowledge is the local knowledge that is unique to a given culture or society. It is the basis for local-level decision-making in agriculture, health care, food preparation, education, natural resource management, and a host of other activities in rural communities.’

IP: Intellectual Property is a property that enjoys legal protection and stems from the exercise of the mind. Includes patents, trademarks, copyright, design protection and some minor rights.

IPR: Intellectual Property Rights are Creative ideas and expressions of the human mind that possess commercial value and receive the legal protection of a property right. The major legal mechanisms for protecting intellectual property rights are copyrights, patents, and trademarks. Intellectual property rights enable owners to select who may access and use their property, and to protect it from unauthorized use.

KAP: Knowledge, Attitudes and Practices, is a method, developed from family planning research has been widely used in HIV/AIDS studies and programs especially media exercises. Usually using a questionnaire to a small target sample the KAP has the advantage of rapidly revealing more accurately than vague impressions what people are thinking and doing about the pandemic and later to evaluate how well a campaign is going.

MDG: The Millennium Development Goals commit the international community to an expanded vision of development, one that vigorously promotes human development as the key to sustaining social and economic progress in all countries, and recognizes the importance of creating a global partnership for development. The goals have been commonly accepted as a framework for measuring development progress.

MHRA: Medicines and Healthcare-products Regulatory Agency, UK is the executive agency of the Department of Health for protecting and promoting public health and patient safety by ensuring that medicines, healthcare products and medical equipment meet appropriate standards of safety, quality, performance and effectiveness, and are used safely.

MRI: Magnetic resonance Imaging (MRI) is an imaging technique used primarily in medical settings to produce high quality images of the inside of the human body.

MM: Modern Medicine

NCCAM: The National Center for Complementary and Alternative Medicine is center of National Institutes of Health dedicated to exploring complementary and alternative

healing practices in the context of rigorous science, training complementary and alternative medicine researchers, and disseminating authoritative information to the public and professionals.

NCI: The National Cancer Institute of NIH is established under the National Cancer Act of 1937, is the Federal Government's principal agency for cancer research and training.

NAPRALERT: The NATural PRoducts ALERT contains bibliographic and factual data on natural products, including information on the pharmacology, biological activity, taxonomic distribution, ethno-medicine and chemistry of plant, microbial, and animal (including marine) extracts.

NCE: A New Chemical Entity is a compound not previously described in the literature.

NIH: National Institutes of Health founded in 1887, is one of the world's foremost medical research centers, and the Federal focal point for medical research in the United States. The NIH, comprising 27 separate Institutes and Centers, is one of eight health agencies of the Public Health Service, which, in turn, is part of the U.S. Department of Health and Human Services.

NGOs: Non-Government Organizations.

NMITLI: New Millennium India Technology Initiatives initiated by The Department of Scientific & Industrial Research (DSIR) as initiatives of Council of Scientific and Industrial Research (CSIR) India, and aimed at Technological Self Reliance.

OECD: Organization for Economic Co-operation and Development groups has 30 member countries sharing a commitment to democratic government and the market economy. With active relationships with some 70 other countries, NGOs and civil society, it has a global reach. Best known for its publications and its statistics, its work covers economic and social issues from macroeconomics, to trade, education, development and science and innovation.

PCT: Patent Cooperation Treaty, allows an inventor to get wider coverage and priority protection in member countries.

PET: Positron Emission Tomography, is a procedure that allows a physician to examine the heart, brain, and other organs. PET images show the chemical functioning of an organ or tissue, unlike X-ray, CT, or MRI, which show only body structure.

QA: Quality Assurance. All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with good clinical practice and applicable regulatory requirements.

QC: Quality Control: The operational technique and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

RCT: A Randomized Controlled Trial is a study design used to evaluate the effectiveness of health care interventions. RCTs are not only used to evaluate pharmacological treatments, but also physical and psychological therapies, diagnostic tests, or preventive and public health measures.

RITAM: The purpose of Research Initiative on Traditional Antimalarial Methods is to facilitate exchange and collaboration among those studying and using plants in the control of malaria with a view to developing a coordinated strategy for more effective, evidence-based use of traditional antimalarial methods. RITAM was established during 1999 as a network of researchers and others active or interested in the study and use of traditional, plant-based anti-malarials.

RP: Reverse pharmacology (RP) is a drug discovery approach that draws strengths from traditional and experiential wisdom to facilitate new drug discovery process and reduces time, cost and toxicity the three main bottlenecks in discovery pipeline.

SSRI: Selective Serotonin Reuptake Inhibitors (SSRIs) are commonly prescribed psychotherapeutic agents.

TM: Traditional Medicine refers to health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses or maintain well-being.

TCM: Traditional Chinese Medicine is defined as a medical science governing the theory and practice of traditional Chinese medicine. It includes Chinese medication, acupuncture, massage and Qigong.

TFP: Traditional Folk Practices. Since different usage of a folk medicine may reflect cultural or regional differences, a detailed collation of the folk knowledge of traditional medicine can help to identify common applications derived from different empirical knowledge as well as variations in appreciation of the value of the same source in different cultural settings.

THETA: Traditional and Modern Health Practitioners Together Against AIDS and Other Disease, was originally established as a collaborative research program of The AIDS Support Organization and Médecins Sans Frontières that demonstrated the effectiveness of local herbal medicines used by traditional healers for AIDS-related illnesses.

TK: Traditional knowledge' refers to tradition-based literary, artistic or scientific works; performances; inventions; scientific discoveries; designs; marks, names and symbols;

undisclosed information; and all other tradition-based innovations and creations resulting from intellectual activity in the industrial, scientific, literary or artistic fields.

TKDL: Traditional Knowledge Digital Library India is based on fifteen well known Ayurvedic books and knowledge of well known to Ayurvedic practitioners. TKDL, besides ensuring prevention of the grant of wrong patents for non-original inventions in our traditional knowledge system at international level, shall also ensure enhancement of modern research in Ayurveda and provide immense benefit to MD and PhD students, researchers and manufacturers.

TMK: Traditional Medicine Knowledge

TMS: Traditional Medical Systems are the curative practices of a society, which constitute a cultural system involving lay beliefs and practices, indigenous folk medicine and codified systems of medicine but do not constitute the Modern medicine.

TRIPS: Trade-Related Aspects of Intellectual Property Rights is a WTO Agreement on an international agreement on the subject of "intellectual property". It covers copyright, patents, trademarks, trade secrets, industrial designs, geographical indicia and integrated circuit layouts.

WHO: The World Health Organization is the United Nations specialized agency for health established on 7 April 1948.

WIPO: The World Intellectual Property Organization is an international organization dedicated to promoting the use and protection of works of the human spirit. WIPO plays an important role in enhancing the quality and enjoyment of life, as well as creating real wealth for nations.

WTO: The World Trade Organization is the only global international organization dealing with the rules of trade between nations. WTO agreements are negotiated and signed by the bulk of the world's trading nations and ratified in their parliaments. The goal is to help producers of goods and services, exporters, and importers conduct their business.

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Final Report

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Traditional Medicine: Modern Approach For Affordable Global Health

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**“Upakramopasauharo abhyasopurvata phalam
aarthavadoopapatti cha lingam tatparya nirnaye”**

This ancient Mantra is from Vedic tradition that goes back sometime 5000 BC.....

Key:

”*Upkram*: Introduction; *Upsaumhar*: Summary; *Abhyas*: Referencing (studiedness) *apurvata*: Novelty; *Phalam*: (Practical) utility/solutions; *aarthavada*: Lateral thinking (metaphor, analogy, parable); *Uppatti*: Logicalness of construction; These Seven, the wise say are the criteria, that must be used to evaluate a thesis/text/doctrine/scripture”

Lokmanya Bal Gangadhar Tilak, a great scholar, thinker and freedom fighter of India probably used this ancient Mantra for his *Geeta Rahasya*²³⁴ – an excellent critique on *Geeta*.

We have followed it to test our writing against this philosopher's touchstone.

The Seven Chapters of Report thematically depict this philosophy and are dedicated to innumerable unknown creators of such traditional wisdom...

234: Tilak B G, Geeta Rahasya Edition 9, 1968, page 20, Publisher JS Tilak, Pune, India