Consultation and Interaction at CSIR New Delhi with
WHO-CIPIH
Traditional Medicine Approach

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Innovation Deficit

- Just 26 NCEs in 2003
- Average innovation deficit: 1.3 NCE/ year
- Increased Development time
- Safety and Efficacy remain challenging
- Failure at the end of pipeline
- Substantially increased development costs

Figure 6. Drug Development Time Stays Steady Despite Gains in Approval Time

Bioprospecting challenge

• Symptomatic therapeutics now aims at cause of disease.
• Earlier therapeutics: indirect, conjectural and coincidental, is now, direct and definitive based on intent.
• CombiChem of Nature
• Major Discovery Engines are based on knowledge of little traditions.
• Great traditions are the true resources
Drug Discovery Approaches

- Ethnopharmacology Approach
- Serendipity and Synthetic Approach
- Chemical Biology Approach
- Genomics Approach
- Reverse Pharmacology Approach
- Systems Biology Approach
- Personalized Approach
Reverse Pharmacology: From Clinic to Laboratory

- Clinical wisdom
- National Consultations
- Team India
- Pharmacoepidemiology
- Bioprospecting
- Quality control methods
- Chemoprofile
- Herboprint

- Disease focus
- Pharmaceutics
- Pre-clinical
- Protocol development
- Stage I RCT
- Data consolidation
- Phase II and Phase III
- Pharmacodynamics
NMITLI Herbal Drug Development
3 Years Outcome

• Rheumatic and Musculoskeletal Disorders
  – Osteoarthritis, Rheumatoid arthritis
  – Stage I RCT indicated one formulation significantly better than Glucosamine

• Hepatic Disorders
  – Pre-clinical suggest better activity than sylimarine

• Diabetes
  – Pre-clinical suggest better insulin sensitizing activity
Leads from Ayurveda

Curcumin, Gingerol, Gugullosterones, Eugenol, catechins, Anethol, Piperine, Apocynin, Genestein, polysaccharides from TC, biflavonoids from Semecarpus, Gallates, Bacosides, Boswellic acid, Glycerrhizin, Allicin...
Curcuma longa

- Ayurvedic description
- Lead molecule: Curcumin

- Biological targets: Aryl hydrocarbon receptor, Cytochrome P450 enzymes, Glutathione S-transferase, kinases, COX, iNOS, MMP
- Therapeutic class: Cancer, Inflammation, Diabetes and Chemo prevention


Zingiber officinale

- Ayurvedic description
- Lead molecule: Gingerols

- Biological targets: Vanilloid receptors
- Therapeutic class: Antipyretic, analgesic, antitussive, cardiotonic, and sedative


Multiple Targets Need A Combo

Activity Matrix: Systems-Biology Approach

- Pain, Cartilage
- Inflammation
- Oxidative stress
- Osteoporosis
- Anabolic
- CNS
- Immunomodulato
- Antistress
- Bioavailability
- Lubricant

Bhallataka
Guggulu
Ginger
Ashwagandha
Nirgundi
Guduchi
Pipali
Erand
Combinatorial, Holistic and Systems Approach: The Most Modern View

• The preparation of dual- or multiple-ligands on an almost rational basis is now conceivable and it can be expected that many of these molecules will yield drugs of superior clinical value compared with monotarget formulations.

Multitargeted drugs: The end of the ‘one-target-one-disease philosophy?
Camille Wermuth, DDT 19, October 2004
Ayurveda: Systems Advantage

- Standardized traditional formulations for in-house use
- Science base Evidence to understand mechanisms
- Drug Discovery engine to reduce Target to Lead bottleneck
- Chemical biology approach for new Leads
- Natural product extract libraries
- Holistic and Personalized Concepts
Traditions and Modernity: Future Medical Science

Golden Triangle approach promotes effective integration of traditional wisdom, power of contemporary science & technology and the evidence base of modern medicine where the holistic strategies reflect from the systems biology principles. Golden Triangle approach provides holistic or whole person healing viewpoint besides a new platform for drug discovery.

Mashelkar R.A., Chitrakoot Declaration, 2003
Thank You!

With

Dr. Ashok Vaidya and the CSIR NMITLI Team
Backup slides
Arthritis: Commonly used plants

- Bhallataka: Pain, Multi-targets?
- Erand: Cartilage? Lubricant
- Guggulu: Inflammation
- Ginger: Oxidative stress, Osteoporosis
- Ashwagandha: Anabolic, Adaptogen, CNS
- Nirgundi: Pain, Inflammation
- Guduchi: Antistress
- Pipali: Bioavailability
A comprehensive, interactive and intelligent software to assist Medical Practitioners and Researchers in Application of Basic Principles of Ayurveda
AyuSoft: Decision Support System
Prakruti assessment, Disease Diagnostics, Diet & Lifestyle advice

PIMS

Encyclopedia

Knowledge Database

Drug Database

Diet, Lifestyle Database

Treatment Principles

Disease Database

Shaarir: Dosha, Dhatu, Mala
Classification of human population based on Ayurvedic concept of Prakruti: (n=76)

Distribution of HLA alleles in Prakruti

Cold Spring Harbor November 2004: Pharmacogenomics
Drug Discovery and Development Process

Expensive, time consuming, numerous bottlenecks

- TARGET IDENTIFICATION
- LEAD IDENTIFICATION
- LEAD OPTIMIZATION
- PRECLINICAL STUDIES
- CLINICAL TRIALS

DRUG TO MARKET

Economical, time sparing, least bottlenecks

Reverse Pharmacology

- LARGE SCALE TRIALS
- RELEVANT SCIENCE
- DRUG DEVELOPMENT
- PRECLINICAL STUDIES
- CLINICAL TRIALS PHASE II & I

DRUG TO MARKET
Other Efforts

- CSIR-TKDL, NMITLI Efforts
- Not just materials BUT the Systems
  - Traditional wisdom has a message, logic and capturing intelligence from traditional information is important knowledge that needs protection AyuSoft project of MICT

Thank you!