Safety Monitoring Of Traditional Medicines

Pharmacovigilance Training Course, Lusaka, Zambia
26th March 2003
Overview

- Traditional medicine - definition(s)
- Use and misuse of traditional medicines
- Herbal antimalarials
- Safety monitoring of traditional medicines
- UMC and traditional medicines
- Examples of ADRs involving herbals
- Conclusions
Traditional Medicines - definitions

Traditional Medicine is the sum total of the knowledge, skills, and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in prevention, diagnosis, improvement or treatment of physical and mental illness - WHO
Traditional Medicines - definitions

- Practices based on beliefs and ideas recognised by the community to provide health care by using herbs and other naturally occurring substances” (Ghana, Traditional Medicine Practice Act, 2000 Act 575).

- Herbal medicine = “any finished labelled medicinal products that contain as active ingredients aerial or underground parts of plants or other plant materials or the combination of them, whether in crude state or plant preparation. Plant materials include juices, gums, fatty oils and any other substance of this nature”.

Use (misuse) of herbal medicines

- Up to 70% of population in high income countries use TM
- Up to 80% of population in low income countries rely on TM
  - WHO Strategy for Traditional Medicine 2002-2005
- Morphine, Cocaine, Cannabis
- Digitalis, Atropine, Hamamelis, Senna,
- Hypericum, Kava
Use (misuse) of herbal medicines

- Herbal medicines widely used
  - Role of TM Practitioner in Communities can be powerful (not always for profit)
- Single ingredient products
- Multiple ingredient products
- Properly registered herbal medicines
- Unregistered herbal medicines - home-grown or bought from “mobile pharmacies”
Potential Problems

- Drug Interactions (ADME) e.g. *Hypericum* with HIV-protease inhibitors;
- Product related - different plant parts (different constituents); different plants looking nearly identical; effects of geography on products
- Adulterated products - with orthodox medicines including steroids
- Fake products - imitations of popular brands
- Products with toxic principles e.g. *kava*,
- Chronic illnesses - TM in favour of allopathic
Herbal Anti-Malarials

- Artemisinin derivatives (?)
- Products containing root extracts of *Cryptolepine sanguinolenta*
- Products containing leaf/root extracts of *Azadzirata indica* (neem)
- Others - ???
- Efficacy?
- Recrudescence - does resistance to a herbal product confer cross-resistance to other antimalarials?
Safety Monitoring Of Herbal Medicines

★ Why monitor?
   – For signals?
   – To protect the public?

★ Challenges
   – Regulation and Quality Control of Herbals
   – Scientific challenges especially with unregistered products
   – Political - integration of TM products and practices into allopathic care
Safety Monitoring Of Herbal Medicines

- Widespread usage
- Attitudes of health professionals and general public to “natural products”
  - Lack of training/understanding of TM
  - Lack of patient medication (TM) records
- Attitude of patients
  - “It is natural so it must be safe”
  - Herbals and allopathic work through different mechanisms to augment effects
Safety Monitoring Of Herbal Medicines

- Traditional Medicine Products must be monitored
- Same system should be used for herbal and allopathic products
- Nomenclature and terminology important
- Synonyms can be dangerous in TM!
UMC and Herbals

- UMC leading in developing tools for recording ADRs due to herbals
- UMC database already contains ADR due to herbal medicines
- Standards for case recording, retrieval, comparison etc.

<table>
<thead>
<tr>
<th>Valid scientific name</th>
<th>Author</th>
<th>Synonym name</th>
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<tbody>
<tr>
<td>Senna alexandrina</td>
<td>Garsault</td>
<td>Cassia acutifolia Delile</td>
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<td>(Brenan)</td>
<td>Cassia senna var. obtusata Brenan</td>
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<td>Common Name</td>
<td>Chemical relation</td>
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<tr>
<td>Panax ginseng Meyer</td>
<td>Chinese, Asiatic Ginseng</td>
<td>Standard</td>
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<td>Panax quinquefolius L.</td>
<td>American Ginseng</td>
<td>Similar</td>
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<tr>
<td>Panax pseudoginseng Wall.</td>
<td>Tienchi Ginseng</td>
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<tr>
<td>Eleutherococcus senticosus Maxim.</td>
<td>Siberian Ginseng</td>
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<tr>
<td>Acanthopanax senticosus Harms.</td>
<td>Russian Ginseng</td>
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<td>Rumex hymenosepalus Torr.</td>
<td>Brazilian Ginseng</td>
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<td>Pfaffia paniculata (Mart.) Kunze</td>
<td>Wild Red Am. Ginseng</td>
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<td>Echinopanax horridum (Sm.)Dcne.</td>
<td>Alaskan Ginseng</td>
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<td>Withania somnifera (L.)Dunal</td>
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<tr>
<td>Lepidium meyenii Walpers</td>
<td>Ginseng of the Anders’</td>
<td>Different</td>
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Data model for HSNs

- Valid Latin binomial name
- Scientific and Common name synonyms
- Herbal substance
- Part_lx
- Extract_lx
<table>
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<tr>
<th>New substance name</th>
<th>Old CASnr</th>
<th>New HSNnr</th>
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Reports related to herbals - Case 1

- F, 20 year old
- Class Malacure for malaria
- Stevens Johnson’s Syndrome
- Admitted
- Outcome - recovered
Reports related to herbals - 2

- Male 64 years
- Artesunate – 200 mg bd then 200 mg od for 5 days
- Vivid and frightening dreams.
- Patient on no other medication
- Reactions ceased immediately tablets were withdrawn
Reports related to herbals - Case 3

- Male 69 years
- Artesunate 200mg bd then 200 od for five days
- Confusion, Excitability lasting 13 days from time of first administration of artesunate
- Other drugs – Long term tenoretic, chlorthalidone for hypertension
Reports related to herbals - Case 4

- Male – age not stated (medical practitioner)
- Artesunate – 2 tablets bd
- General weakness, dizziness of sudden onset, shock
- Recovered after a “short time”
Reports related to herbals - Case 5

- M, 20 years old
- Herbal bitters containing *Cyperus esculentus* (said to be aphrodisiac)
- Pre-dosing with tablets to prevent hang-over
- SJS/TEN?
- Died
Who/What To Report

- Varies from country to country -
  Doctors, Pharmacists, Nurses [yes]
- Patients [yes]
- Only “Registered” Products? [NO]
- All herbal products [yes]
- Problem of noise with unknown/unlabelled products [create special category e.g. UHP]
Conclusions

- Herbal medicines are medicines
- Need to monitor herbal medicines
- New tools required - some being developed by UMC
- Who to report and what to report should be defined
- Consumers should be educated and encouraged to report (to NC or Dr.)
Reference Sources

- www.who-umc.org
- www.fda.gov
- www.mca.gov.uk
- SPCs, Martindale, Index Nominum
- Napralet
- Kew Gardens