Challenges of expediting the conduct of ethically approved phase II and III clinical trials on herbal medications in Africa

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Overview

- Background
- Highlight factors driving the demand for the use of herbal remedies
- Response to the demand
- To highlight some ethical and regulatory, methodological issues in the conduct of large scale clinical trials with herbal medication for such as HIV/AIDS, malaria etc in modern health care facilities.
- To identify preconditions for determining suitable herbal medication for clinical testing.
- To identify possible solutions and avenues for expediting trials on herbal medication.
- Conclusions
- Future perspectives or speculations

Deciphering the Code of the topic

- **The Challenges = problems of expediting = speeding up the conduct, of ethically approved = with ethical issues fully addressed, phase II and III clinical trials in relatively large numbers of patients**
- **on herbal medications using medicinal plant materials in Africa = Africans**

Background

- In many African countries there is an increasing demand to explore the possibility of integrating **TM** into the conventional health system (CHS).
- In some countries there is mounting **pressure** for R&D institutions to explore the possibility of testing herbal medication in **humans**.
- The urgency of the matter is dividing opinion as to the understanding of TM and the best ways of evaluation it and to make it widely accessible.
- *We should make a clear distinction between TM and herbal medication* (Phytotherapy).

- **What is the way forward??.**

Introduction

- Humans have always looked to biodiversity to meet their health needs from time immemorial.
- This activity transcends all cultures across the globe.
- It is argued that the biodiversity of Africa (plants and fungi) constitutes a major resource that remains to be exploited fully for the socio-economic benefit of the peoples.
- This rich resource may provide the necessary leads to effective therapies for menacing health problems including HIV/AIDS, tuberculosis, malaria and other medical conditions.
- To quote Dr Prakashi statement, '*Herbal medication is undoubtedly the mother of most conventional medicines*'.
- **To date the only sources of drugs remain: <u>Natural, Semisynthetic and Synthetic</u>.**

The traditional herbal medication is on revival?

- Probably not on, but it is being given attention/noticed
- In some Africa countries, 80% of patients attending formal health facilities would have previously received TM. This may be in the home or at established traditional healers.
- In South Asia e.g. China, Vietnam, the Koreas, TM has been developed and is integrated in the formal health system
- In developed countries TM is termed as alternative or complementary medicine (CM) it is increasing in popularity and expenditure on CM is staggering (WHO 2006). Being run parallel to the CHS
- In Africa, despite the demand there is unequalled policy response to embrace TM into the CHS. In the recent past TM* was illegal esp. in colonial settings

- ** its association with other behaviours*

Approaches

- Review of literature on national and international guidelines for ethical conduct of trials on herbal remedies.
- Review available legislation governing the use of herbal medication ethical for clinical trials.
- Review of guidelines concerning identification of suitable herbal preparations for clinical trials.
- Review reports of ethical issues of conducting trials on herbal preparations.
- Review methodological issues and guidelines for conducting trials on HM.
- Discuss with medical practitioners and herbalist their perception concerning the conduct of trials on HM.

What drives people to consult traditional healers for common health problems?

- Difficulty in accessing conventional health care because of prohibitive costs, easy accessibility of TM, distance to CHS, privacy, stigma, personal and cultural beliefs, (body mind and spirit) or nature of the health problem or a combination of factors.
- Trust in the traditional healers: they may be in a position to meet spiritual or mental needs of their clients.
- The situation may even differ from community to community across the continent.

What is driving the demand for use of traditional medication by governments?

- The realization of the high usage of TM by a large number of the population.
- The difficulty in controlling of emerging or re-emerging diseases with limited therapeutics options.
- The prohibitive cost of drugs for common public health problems beyond national health budgets.
- Reducing dependence on conventional medications and reducing the cost of health care
- Advanced technological platform and improved research methodologies have created confidence for better understanding and harnessing Indigenous Knowledge.
- Need to document and verify claims by TH before some of the dwindling plant species become extinct.

What is the International response to the increasing demand for traditional herbal medication usage in Africa?

- It has been recognized that TM is an important component of health care.
- Regional and International organizations such as the WHO, SADC, AU (thru NEPAD)** are responding to this demand and have or are developing guidelines and tools to support evidence-based usage of TM.
- There are guidelines to integrate TM into the national health system
- At country level there is little evidence of tangible integration of TM in the CHS
- **** Proceedings of the first NEPAD/SANBio workshop on scientific validation of traditional medicines for affordable treatments of HIV/AIDS and opportunistic infections 15-16 March 2007, Lusaka, Zambia.**

Specific Responses from Regional and international bodies

- Set a framework for integration of TM into the health system
- Mechanisms to protect Intellectual property rights
- Advocacy to promote for TM with key stakeholders at all levels. Funding agencies – community support)
- Provide Guidelines and technical support to implement or strengthen national policies on TM.
- Promote collaboration and consultation among parties and partners
- Specific guidelines on methodologies of clinical trials are being developed

Definition of Traditional Medication

- **The WHO defines traditional medicines (TM) as "*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 the prevention, diagnosis, improvement or treatment of physical and mental illness*".**
- ***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***
- ***For the purpose of this discusion I will try to stick to with herbal medication (Phytotherapy).***

http://www.who.int/mediacentre/factsheets/fs134/en

Regulatory issues

- Registration of Herbal medication is mentioned in legal and regulatory guidelines, but it is scanty and not enforced
- 74% of countries do no have pharmacopeia on HM. In some countries it is not even legally binding**
- 78% countries not have herbs on the Essential Drug list
- Pharmacovigilance systems exist on paper but they are not applied

**** (Regulatory situation of herbal medicines, Anonymous, 2000)**

Methodological issues

- **The crux of the matter is to take herbal materials for testing in humans through the fastest route. There is no clear answer to this question, but much depends of the strength of evidence available to support the claims.**

- Where do we begin from and do we follow the classical step in drug development through all the drug development phases? **Yes and NO**

- How do we prove the claims that a herb(s) are doing what they are supposed to be doing. Do we go Back to the bench??

- The WHO has issues guidelines** and developed countries have procedure for doing this in complementary medicine

** (WHO/EDM/TRM/2000.1)

Methodological issues (2)

- Study design:
  - Observational??, Comparative or Equivalency
  - Choosing a study population and subjects
  - Choosing a representative numbers
  - Patient allocation or treatment allocation
  - Blinding or use of placebo
  - Choosing Endpoints or indicators
  - Stopping rules
  - Follow up and scheduling AE monitoring
  - Analytical methods etc etc
- **And many other issues…should we have separate GCP, GMP, Ethics for herbal medication??**

Ethical issues

- Distinguishing between Ethics of treatment and research
- Providing adequate information about the herbal product to be used. Preliminary information about efficacy, safety, formulation
- Information about available alternate medicines in CHS.
- Is the Ethical review process adequately prepared to handle trials on HM
- Investigators vs healers responsibilities
- What are the Responsibilities of the sponsors

Other important issues

- Research infrastructure not geared to handle TM.
- Where should the trial be conducted
- Maintenances of surveillance or pharmacovigilance
- Reporting systems
- Funding to support trials and identifying partners in R&D
- Educational and training needs – who provides that training.

Summary (1)

- Demand for clinical trials on herbal medications especially for HIV/AIDS and infections such a malaria is on the increase.
- Clinical testing of herbs is highly developed in countries e.g. China, although regarded as alternative medicine in the West, there is an increase in the use of herbs in cancer research.
- However, there is a paucity of clear guidelines on the ethical conduct of trials on herbal remedies jn many settings in Africa.
- There is a lot of debate about suitable guidelines for identification of suitable herbal materials for clinical testing.

Summary (2)

- There is suspicions by some Herbalists with regard to the motive behind the validation of healing properties of existing herbs and on issues concerning IPR.
- In some cases there is dichotomy in understanding what TM means to different people.
- There is a serious ethical dilemma concerning the use of unproven herbal medication to patients in the presence of proven therapies.
- Even in developed countries where Herbal medications are considered alternative medicines, hence not fully accepted in conventional medical practice.

Conclusions

- Human rights and socio-economic and political pressure has also given impetus demand for clinical trials in herbal medication.
- Appropriate Guidelines on GMP, GCP and ethics concerning clinical trial on herbal medication are needed to address the increasing demand.
- Appropriate regulatory and legal framework is needed to support and guide this component of research. In some countries this is conspicuously absent or vague.
- Inadequate or no investment and resources to enhance capacities to facilitate evidence-based herbal medication application

Future perspectives

- There is need to bridge the gap that exists between convention and traditional medicine. This requires concerted effort from all stakeholders in R&D and health care systems.
- Relevant and standardised GMP, GCP and ethical guidelines should be formulated or strengthened and made widely available.
- Guidelines for selecting suitable herbs extracts for trials are required to guarantee reliable measurement of efficacy and safety HM.
- Standardised methodologies of determining efficacy and safety of herbal preparations are to be developed.
- Adaptive legal and regulatory framework is needed to protect, IPR proprietors, sponsors, trialists,and subjects.

Question

- Are we ready to conduct reliable clinical trials on HIV/AIDS, malaria or TB using herbal medication in large numbers of subjects?

Thank you for your Attention