African Herbal Pharmacopoeia: current situation and the need for the standardization of phytomedicines

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41st CONFERENCE OF WASP–SOAP
Phytomedicines

- Herbal medicine is an ancient medical system that provided and still provides the world with safe, effective and affordable medicines

- Most African countries and the West African sub-region are endowed with vast resources of medicinal and aromatic plants
Any disclosure?

• I am not ......
  – a contributor nor a co-editor of the African Herbal Pharmacopoeia or any other herbal monograph
  – not a practicing herbalist and do not have any commercial interest in a herbal product in the market
  – I have no laboratory that consults for regulatory agencies on standardization of herbal products

• I am...
  – a research scientist & and teacher
  – a Pharmacists & a pharmacologist
  – a biomedical researcher
  – have interest in the development and in the safe and effective use of natural products
Herbs

- Crude plant materials such as leaves, flowers, fruit, seed, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered.
Phytomedicines

Finished labeled products that contain active ingredients such as aerial or underground parts of plant or other plant material or combinations thereof, whether in the crude state or as plant preparations.
Outline of presentation

• Current situation
• Challenges
• African Herbal Pharmacopoeia
• The need for standardization of herbal medicines
• Standardization modalities & Standards
Who is a herbalists?
Taking advantage of the huge phytomedicine market

• There is a growing interest, globally, in CAM, natural/organic products and nutraceuticals
• This has created a huge market for phytomedicines
• West African countries could exploit this to their advantage
• Provided this herbal drugs are produced with acceptable quality and safety specifications
• An acceptable official herbal pharmacopoeia will be necessary to document herbal tradition, medicinal plants, their values and standards
Towards modernization

Integrative Medicine combines conventional western medicine with complimentary and alternative therapies.
Our situation

• Some major limitations to the rational and safe use of phytomedicines in the sub-region include:
  • the lack of uniformity
  • active principles are not often well defined
  • equivocal efficacy claims
  • purity, adulteration and contamination
  • unverified and unverifiable (often misleading) claims on these products
  • hawking and unregulated promotion by the road sides
Challenges

- Varying methods of handling, processing and formulation
- Variation in quality is also caused by
  - differences in growth conditions
  - geographical location
  - species
  - time of harvesting
- Less stringent regulatory framework
- Lack of uniform and widely acceptable safety and quality standards
Challenges

• It will help the clamour for Integrative Healthcare System if we could develop and adopt uniform standards for herbal formulations

• This will certainly encourage wide acceptability and confidence

• This engender consensus in approach and serve as a reference tool
Standardization is the way to go

• Quality, safety and efficacy of herbal medicines is achievable with standardization and regulation

• Use of modern techniques, developing and applying suitable standards & Current Good Manufacturing Practices (cGMP) to herbal drugs is advocated
Not entirely gloomy
Herbal Pharmacopoeias: A call to action

• Although the World Health Assembly and Regional Committee for Africa have all adopted resolutions calling upon member states, among others things,
  – to develop herbal pharmacopoeias
  – to apply scientific criteria and methods to prove safety and efficacy of medicinal plant products
• Only few countries have developed national herbal pharmacopoeias
The Need for a AfrHP

- Documentation of medicinal plants in the monographs of a pharmacopoeias would serve
  - as a guide to herbal production
  - Promote commercialization and trade
  - as a guide to ensure quality control and quality assurance
  - assure people who use herbal medicinal plants of their efficacy, safety and standard
African Herbal Pharmacopoeia (AfrHP)
Brief historical perspective

• Previous national attempts in Africa to produce herbal pharmacopoeia have, at best, yielded incomplete plant monographs or an ethnomedical survey/literature on African medicinal plants.

• The first successful attempt was the publication of the 105-plant African Pharmacopoeia (AP) by the OAU's Scientific, Technical and Research Commission (OAU/STRC) in 1985.
Brief historical perspective

• The OAU/STRC also published some national ethno-botanical surveys carried out by experts across West African coast

• Such texts are available for South-west Nigeria, Ghana, Senegal, Cameroon, Benin etc.
National herbal Pharmacopoeia

• The 105-plant African Pharmacopoeia (AP) was followed by the Book of Medicinal Plant Analysis as the volume II in 1986

• The Ghana Herbal Pharmacopoeia (GHP) was published in 1992; 2007 (2nd edition); 2015 (3rd edition)

• Nigerian Herbal Pharmacopoeia (NHP) was published in 2008
Ghana Herbal Pharmacopoeia: 3rd Edition

- Published by the Science and Technology Policy Research Institute (STEPRI) of the Council for Scientific and Industrial Research (CSIR), Ghana
- Technical work and logistics was supported financially by West African Health Organization (WAHO)
Nigeria Herbal Pharmacopoeia

• The first edition of Nigeria Herbal Pharmacopoeia was published in 2008 with the support of the World Health Organization (WHO).

• It contained 42 commonly used medicinal plants in Nigeria.
  – While 22 of the plants were indigenous to Nigeria, 18 were introduced into the country
• Published by the Association of African Medicinal Plants Standards (AAMPS) based currently in Mauritius in 2010

• Edited by Brendler, T., Eloff, J. N., Gurib-Fakim, A., Phillips, L. D.
African Herbal Pharmacopoeia (AfrHP)

- AfrHP is a 288-page book
- Consists of 51 medicinal plants monographs
- Each of the plant was subjected to literature search to provide relevant data under a set of monograph template
The following information are provided in the AfrHP

- Botanical
- Ethnomedical
- Quality control
- Physical information
- Chemical information
- Pharmacological
- Toxicological
- Therapeutic and
- Regulatory standards
Key features of AfrHP

Notably are:

- Great advancement beyond the information in the 1985 African Pharmacopoeia (AP)
- Different types of biomarkers specified for herbal safety monitoring
- Include quality assurance validation for both — the raw materials & finished products
Key features of AfrHP

- Colourful photographs
- Colourful chromatograms
- Clinical data
- Key (proposed) usage & therapeutic indications
- Spectroscopic data
- Bibliography etc.
Some shortcoming of AfrHP

- Non-indication of the “tribe of origin” of the vernacular names used in the monographs
- Lack of information on microscopical data for both the fresh and powdered samples of all the plants

-microscopical information is invaluable standard that could be used for validation and in detecting adulteration especially where pieces of specialized equipment (HPLC, uv/visible, IR) are unaffordable or unavailable
Regulatory Implications of AfrHP

- Ideally, every plant contained in AfrHP has from the time of publication and approval become an official drug raw material which can be formulated into an official herbal product.

- Such products are registrable by the Food and Drugs authorities of various countries provided the overall manufacture complies with the AfrH Pharmacopoeial specifications.
Who needs AfrHP?

- Medical and healthcare-related professionals
- Herbal industrialists
- All categories of plant scientists
- Traditional medicine practitioners
- Integrative healthcare centres
- Food and Drugs authorities
- Relevant national and international agencies promoting the healthcare utilization of medicinal plant resources
STANDARDIZATION MODALITIES & STANDARDS
Standardization of herbal medicines

- Standardization of herbal medicines is the process of prescribing a set of
  - standards or inherent characteristics,
  - constant parameters,
  - definitive qualitative and quantitative values that carry an assurance of quality, efficacy, safety and reproducibility.
- It is the process of developing and agreeing upon technical standards
Standardization

- Standardization of herbal drugs entails
  - confirmation of its identity
  - determination of its quality,
  - determination of purity
  - detection of adulteration and the nature of any adulterant
Why standardize?

• Activities may vary due to:
  • Variation in parts of plant used
  • Variation in species of herb used
  • Seasonal variation in activities
  • Variation due to soil type
  • Variation due to time-of-harvest
  • Variation due to host of epiphytes
  • Variation in harvesting, drying, extraction processes
  • Etc.
Agreeing on uniform standards

• The first important task for us is to evolve such parameters by which the presence of the claimed ingredients in herbal products could be ascertained.
Various chromatographic and spectrophotometric methods, physicochemical properties and unique “fingerprints” are available for the identification of the presence of different ingredients.

Wherever possible these methods can be applied for quantitative estimation of bioactive group of compounds like alkaloids, flavonoids, polyphenolic components or estimation of particular compound.
Fingerprinting shows the unique chromatogram or spectrum of each herbal sample.

Fingerprint analysis should focus on accurate identification (of similar peaks), and not on precise calculations.
Combination of chromatographic fingerprints and quantitative analysis can be readily utilized as a quality consistency method for herbs and herbal products.

1. Quality control of crude raw materials, plant preparations and finished products

2. Stability assessment and shelf life.

3. Safety assessment; documentation of safety based on experience or toxicological studies.

4. Assessment of efficacy by ethnomedical information's and biological activity evaluations.

5. The bioactive extract should be standardized on the basis of active principles or major compounds along with the chromatographic fingerprints (TLC, HPTLC, HPLC, and GC)
Quality Control of Herbal Drugs

• QC of herbal medicine is based on three important pharmacopeial definitions:
  – **Identity**: known ingredient
  – **Purity**: devoid of contamination
  – **Content or assay of ingredients**: the active constituents should be within the defined limits
It is recommended that the variation in component during the proposed shelf-life should not exceed ± 5% of the initial assay value for herbal drug preparations.
Stability

• The **physical, chemical and microbial stability** of the product in the container in which it is to be marketed should be tested under defined storage conditions and the shelf-life should be established.
All procedures should be in accordance with current good manufacturing practices (cGMPs) and should cover:

- Crude plant materials to be used
- Preparation of plant materials
- Finished product
Crude plant materials

- The botanical definition, including
  - genus, species and authority, description, part of the plant, active and characteristics constituents should be specified and, if possible, content limits should be defined

- Foreign matter, impurities and microbial content should be defined or limited.

- Voucher specimens should be authenticated by a qualified botanist and should be stored for at least a 10-year period

- A lot number should be assigned and this should appear on the product label
Plant preparations

- The manufacturing procedure should be described in detail.
- Any the added substance(s) should be mentioned in the manufacturing procedures.
- If identification of an active principle is not possible, it should be sufficient to identify a characteristic substance or mixture of substances to ensure consistent quality of the preparation.
Finished Products

• The manufacturing procedure and formula, including the amount of excipients, should be described in detail
• A finished product specifications should be defined to ensure consistent quality of the product
• The finished products should comply with general requirements for particular dosage forms
Safety assessment

• Phytomedicines are generally regarded as safe based on their long-standing use in various cultures.

• There are several reports of serious adverse events following administration of phytomedicines.

• Toxic effects can be traced to: Toxic herbal plants, Contaminants, Adulteration, Adverse effects drug-herb and drug-food interactions.

• Assessment of the safety of herbal products is the first priority in herbal research.
Investigation of toxicity

- Toxicity investigation will also be required because the analysis alone is unlikely to reveal the contributions to toxicity itself.
- Toxicity assessment involves *in vivo* techniques and *in vitro* techniques, cell line techniques, micro-array and other standard techniques to adequately model toxicity.
Assessment of efficacy

• Herbal medicines are inherently different from conventional treatments, but presently there is no way to assess their efficacy other than by currently used conventional biomedical methodologies, in which efficacy is conventionally assessed by laboratory, clinical, or diagnostic outcomes.
Contaminants of Herbal Ingredients

• Herbal ingredients of high quality should be free from insects, animal matter and excreta.

• It is usually not possible to remove completely all contaminants, hence specifications should be set in order to limit them:
  – Ash values
  – Foreign organic matter
  – Microbial contamination
  – Pesticides
  – Fumigants
  – Heavy metals
  – Radioactive contamination
Labeling of herbal products

- The quality of consumer information about the product is as important as the finished herbal product itself
- Warnings on the packet or label will help to reduce the risk of inappropriate uses and adverse reactions
- Foster confidence and acceptability
- Reduce consumer frustration
Validation

- The validation of herbal products is a major public health concern both in developed and resource-poor countries, where fakers selling adulterated herbal medicines are common.
- It is necessary to ensure scientific validation and periodic monitoring of the quality and efficacy by regulators.
• With standardization, scientific validation and better regulation of herbal products
  – I see a future when only qualified healthcare providers are allowed to prescribe phytomedicines
  – Or herbal practitioners are only allowed to practice within the confines of healthcare facilities in an integrative medicine approach
Steps involved in Standardization & Quality control of Herbal drugs

- Color
- Odor
- Taste
- Texture
- Fracture

Macroscopic
- Shape
- External
- Marking

Microscopic
- Qualitative
- Quantitative
- SEM Studies
- Powder Studies

STANDARDISATION OF HERBAL DRUGS

ORGANOLEPTIC
- Color
- Odor
- Taste
- Texture
- Fracture

BOTANICAL
- Qualitative
- Quantitative
- SEM Studies
- Powder Studies

PHYSICAL
- Moist. Cont.
- Extract. Values
- Ash Values
- Fluores. Analysis

BIOLOGICAL
- Pharmacological
  - Bitterness value
  - Haemolytic activity
  - Foaming index
  - Swelling index
- Toxicological
  - Determination of pesticide residues
  - Determination of heavy metals

CHEMICAL
- Qualitative
- Quantitative
- Chromatography
- Radioactive contamination

Microbial Contamination
A) Total viable aerobic count
B) Determination of pathogens
C) Aflatoxins content

Antagonistic
- Bacterial
- Fungal

HPTLC
- Finger printing
- Sec. Metabolites
- DNA Finger printing

GLC
- Quantitative

HPLC
- Radioactive contamination
Some Chemical Standards

• Most of herbal drugs contain definite chemical constituents to which their pharmacological and biological activity depend
  – Qualitative (Phytochemical studies, HPTLC, DNA fingerprinting, etc.)
  – Quantitative (HPLC, GLC, HPTLC)
  – Other Chromatographic techniques
  – Radioactive contamination
Chromatography & Spectrometry Standards

– Chromatographic Fingerprinting and Marker Compound Analysis (TLC, HPTLC, etc.)

– Hyphenated chromatography and spectroscopy
  • HPLC–DAD
  • GC–MS
  • CE–DAD
  • HPLC–MS
  • HPLC–NMR
Biological Standards

- Pharmacological
- Toxicological
  - Determination of Pesticide Residues
  - Determination of Arsenic and Heavy Metals
- Microbial contamination
Pharmacological Standards

- Determination of Bitterness Value
- Determination of Haemolytic Activity
- Determination of Swelling Index
- Determination of Foaming Index
Toxicological Standards

- Determination of pesticides
- Determination of arsenic and heavy metals
Microbial contamination

- Determination of viable aerobic count
- Determination of pathogenic microbes
- Determination of aflatoxins
Conclusion

• The West African sub-region can play the lead role in the production of standardized, therapeutically effective & safe phytomedicines worldwide

• Assurance of the safety and efficacy of a herbal drugs requires monitoring from collection through processing to the finished packaged product
Conclusion

• Clearly much more work is needed by all to harness the undeniably huge potentials of phytomedicine for the benefit of patients and the healthcare system

• Development and adoption of uniform standards for herbal formulations is paramount
Conclusion

- Documentation of medicinal plants in the monographs of pharmacopoeias would serve as a guide to herbal production, promote commercialization and trade and serve as a guide to quality.

- Publication of African herbal Pharmacopoeia in 2010 by AAMPS is a welcome development and the second edition is long overdue.
• Development of National herbal pharmacopeia should be encouraged and sustained

• A wider consultation and a PAN–African initiative that includes all stakeholders to produce an Africa Herbal Pharmacopeia that will be embraced, recognized and adopted by national regulatory authorities may be the way to go

• We need a deliberate private and government investment, to harness the huge values in herbal drug market
References


Thank You!