MEDWIN PUBLISHERS
Committed to create value for Researchers

International Journal of Pharmacognosy and Chinese Medicine
ISSN: 2576-4772

A Review of Trends in Herbal Drugs Standardization, Regulation and Integration to the National Healthcare Systems in Kenya and the Globe

Onyambu MO[1]*, Gikonyo NK[1], Nyambaka HN[2] and Thoithi GN[3]

[1]Department of Pharmacognosy, Pharmaceutical chemistry & Pharmaceutics and Industrial Pharmacy, School of Pharmacy, Kenyatta University, Kenya

[2]Department of Chemistry, School of Pure and Applied Sciences, Kenyatta University, Kenya

[3]Department of Pharmaceutical Chemistry, School of Pharmacy, University of Nairobi, Kenya

***Corresponding author**: Meshack O Onyambu, Department of Pharmacognosy, Pharmaceutical chemistry & Pharmaceutics and Industrial Pharmacy, School of Pharmacy, Kenyatta University, Nairobi, Kenya, Tel:+254726099487; Email: onyambu.meshack@ku.ac.ke

Review Article

Volume 3 Issue 3

Received Date: June 20, 2019

Published Date: July 09, 2019

DOI: 10.23880/ipcm-16000168

Abstract

Herbal medicines contribute to the provision of primary healthcare to millions of people in the world today. With increasing disease burden, there is proportionate increase in demand for those medicines with ethnobotanical evidence of efficacy against communicable and noncommunicable diseases. Because of availability, acceptability and affordability, herbs along with other forms of complementary and alternative medicines have the potential to fulfill the need for universal health coverage as envisaged by world health organization. In this paper, we review the status of herbal medicine use in Kenya and selected countries with a view to highlighting the reasons why some countries have been able to integrate while others have not. There is a general observation that those countries that have been able to define measures for quality assurance and standardization have integrated herbal medicines to their mainstream healthcare systems and have well defined regulatory systems. We conclude that quality remains a challenge and suggest possible approaches for quality control as recommended by WHO. There is a further urgent need to formulate quality assurance mechanisms for highly utilized medicinal products especially for African countries who heavily rely on these forms of medicines for their primary healthcare.

Keywords: Regulation; Standardization; Integration; Herbal Medicines; Kenya

Introduction

Many governments in the world today continue responding to the Beijing declaration of 8th November, 2008. In this call, the World Health Organization assembly advised governments to take responsibility for the health of their people by formulating national policies, regulations and standards that will ensure appropriate,

safe and effective use of traditional medicine [1]. It is common knowledge that traditional medicine has shown the potential of fulfilling the WHO requirement for universal healthcare because of its contribution to the provision of affordable care to millions of people in the world [2]. This has been confirmed by studies which show that patients attended by a general practitioner with additional training in complementary medicine have lower healthcare costs and mortality rates than those who do not [3]. Cost reduction was attributed to fewer hospital stays and fewer prescription drugs. Therefore, the global importance of complementary and alternative medicine (CAM) which majorly uses plant products as drugs is now a subject that every government in the world has prioritized. These medicines are used as home remedies, dispensed over the counter, and as raw materials for the pharmaceutical industry. They form a substantial proportion of the global drug market contributing to the provision of primary healthcare to millions of people in the world.

Trends in the use Regulation, Integration and Quality Control of Herbal Medicines

Global Trends: In Europe for example over 100 million people are using traditional medicine products and practices with one fifth using it as an alternative medicine and the same number using it as complementary to conventional medicine (www.eiccam.eu/home.php). This kind of integration is reported in the United Kingdom with 40% of the physicians said to make referrals to alternative practitioners. Populations in France, Canada and Australia use Complementary and Alternative Medicine (CAM) in 49, 76 and 46 percent respectively.

In Asia, China's estimated output of Chinese herbal medicine was US dollar 83.1 billion in 2012 while the republic of Korea's annual expenditure for Traditional medicinal products rose from US dollars 4.4 billion in 2004 to 7.4 billion in 2009 (www.sdpa.govt.cn/gyfz/gyfz/t2013 0248 530336.htm).

On regulation, traditional Chinese medicines are regulated by government authorities and fully integrated into the mainstream healthcare system. There is a well-established Chinese Pharmacopoeia to ensure quality for Chinese material medica with over 1146 species having been recorded by 2005. Among these species, 45 have TLC methods of analysis developed, over 479 can be analyzed by HPLC and 47 by GC [4,5]. In Japan over 148 formulations from different manufacturers have been standardized and approved by ministry of standardization and methodology [6]. In addition, over 210 formulas are used in medical facilities and sold over the counter.

In Hongkong about 60% of the population consults traditional healers. In Singapore for example, local researchers use computer software to analyze multi-herb preparations [7]. There is legislation governing use of simple preparations (cut and dried) and those in different dosage forms (Statues of Peoples Republic of Singapore). Regarding safety and quality, only those products which meet required standards can be listed and allowed to be manufactured, imported, supplied or sold.

In the United States, the estimated out of pocket spending for natural products was US dollars 14.8 billion in 2008. Further estimates from South America indicate that 71% and 48% of populations in Chile and Colombia respectively use traditional medicines. Some institutions in these countries teach traditional medicines in medical schools.

On regulation, the United States of America's FDA recommends a combination of tests to ensure the identity, quality, purity, potency and consistency of herbal drugs. The multiple tests for drug substances and products use chromatographic fingerprints, chemical assays and characteristic markers. Process controls for raw materials and validation for drug substances are also done. Microscopy has also played a crucial role towards preparations of herbal monographs in the US [8].

In Africa, many countries are yet to integrate these forms of medicines into their mainstream healthcare systems. According to Ghana, South Africa and Nigeria have integrated traditional medicine to their mainstream healthcare system [9]. While others including, Tanzania, Ethiopia and Rwanda have partially integrated it. More other countries including Uganda, Chad and Gabon are developing policies to integrate.

The World Health Organization estimates that 70-90 % of Africa's rural population relies on traditional medicines to meet their health needs [10]. The World Health Organization confirmed the continuous reliance of herbal medicine by majority of African populations in a decade long survey [11]. A review by Chatora, et al. [12] paints a picture of an African continent still heavily relying on traditional medicinal products and services for primary health care (Table 1). Table 1 compares the traditional medicine (mostly herbalists) practitioners to the ratio of conventional doctors and the population in nine African countries.

Country	Traditional practitioner ratio to population	Conventional doctor ratio to the population
Kenya (National average)	1:833	1:4761*
Zimbabwe	1:600	1:6250
Swaziland	1:100	1:10,000
Nigeria (Benin city)	1:110	1:16,400
National average	No data	1:15,740
S. Africa (Ventra area)	1:700-1200	1:17,400
Ghana	1:1200	1:20,000
Uganda	1:700	1:25,000
Tanzania	1:400	1:33,000
Mozambique	1:200	1:50,000

Table 1: Traditional practitioners and conventional doctors compared to population in some African countries.
Source: Chatora, et al. [12], *Economic survey [13]

Abdullahi [14] alludes to the growing use of traditional medicines in Africa amid the challenges facing it thereby supporting Chatora's study report of 2003. This means that in spite of the changing times, the increasing populations have shown increased demands for herbal medicines over the years.

The global increase in the use of traditional medicine especially herbal drugs has been attributed to the rise in chronic and non-communicable diseases, their accessibility and affordability [2,15]. In Africa for example, inaccessibility to modern drugs in the middle and low-income countries is a factor contributing to the widespread use. A study by Cameron, et al. [16] in 36 low and middle-income countries reported conventional drugs being way beyond reach for huge sections of the populations. This can be corroborated with data from nine African countries in Table 1.

In order to enhance integration of herbal medicines to mainstream healthcare system of member states, the World Health Organization has developed a traditional medicine strategy 2014-2023. The strategy's major aims are; evaluating, regulating, integrating and harnessing the potential of traditional medicine for the benefit and health of people [17]. The strategy has outlined some of the issues affecting traditional medicines and ways of addressing them with respective member states and other stakeholders by 2023. The issues include its continued uptake, growing economic importance globally, advances in research and development, intellectual property rights and integration to health care systems [17].

Trends in Kenya: In Kenya, estimates indicate that more than 1200 species of medicinal plants are used from a flora of approximately 10,000 members [18]. Between 2009 and 2012, over 120 herbalists from across Kenya had reported using at least 3 herbs in their practice with good success rates in therapeutic claims against various diseases including malaria, typhoid, pneumonia, diarrhea, arthritis, sexually transmitted infections, toothaches and helminthiasis among others. Table 2 shows a list of 10 most widely used plants, disease manage d and frequency of use by herbalists between 2009 and 2012.

No.	Plant species	Disease treated	Frequency
1	*Prunus Africana*	Sickle cell, prostate hyperplasia, allergies	41
2	*Aloe secundiflora*	Skin blisters, malaria, diabetes	39
3	*Warbugia ugandensis*	Malaria, pneumonia, arthritis, bronchitis	29
4	*Azadirachta indica*	Rheumatism, malaria, diabetes	21
5	*Moringa oleifera*	Typhoid, anaemia, immune booster	18
6	*Withania somniferum*	Typhoid, ulcers, dyspepsia	4
7	*Caesalpinia volkensis*	Malaria, ulcers, diabetes	14
8	*Urtica masaica*	Diuretic, kidney, anaemia prostate gland	13
9	*Erythrina abbysinica*	Typhoid, ulcers	12
10	*Senna occidentalis*	Ulcers, skin disease, blood pressure	10

Table 2: Widely used medicinal plants by herbalists in Kenya (2009-2012).
Source: Department of Pharmacy and Complementary/Alternative Medicine, Kenyatta University.

With malaria and diarrheal diseases still ranking as major causes of mortality rates for all ages in the developing world, the contribution of herbal medicines is of much significance considering also that many households in Kenya can more easily access the herbalist than the conventional practitioner [19]. Mwangi alludes to the major role of herbal medicines in the treatment of allergy, duodenal ulcer, poor venous return, hemorrhoids, both insulin dependent and independent diabetes, cancers of breast, liver, cervix and prostate among other disease in Kenya. However, only few plants in the list such as Prunus *africana*, and aloes (Table 2) have had their quality control parameters standardized [20]. This has impacted heavily on the quality of these products and difficulty in regulations thereby showing the need for urgent formulation of quality control parameters.

Regarding regulation policies, there have been efforts to fully regulate traditional and complementary medicines for some time in Kenya. For example, in 2007, a draft Policy on traditional medicine and medicinal plants was developed with key subjects of priority being safety and efficacy, conservation, production and domestication and commercialization. This document however remained at the draft level which has been a subject of debate over the years. In the year 2008, Traditional medicines were included in the Kenya National Pharmaceutical Policy (KNPP) with the aims of having appropriate, safe, quality and efficacious traditional medicines [21]. Among the proposals in the policy was the, establishment of a unit within the Ministry of Health to coordinate traditional medicine activities and promotion of local production of useful and commercially viable traditional medicines for human and veterinary use [21]. The implementation of this policy has started hence a major step in the route towards integration.

In 2012, the Kenya Health Bill 2012 on traditional medicine was proposed. The bill advocated for the formulation of policies to guide the practice of traditional medicines in Kenya. Part viii of the proposed bill addresses traditional and complementary medicines. Key proposals in the bill are the promotion and regulation of the practice, documentation and mapping and standardization [22]. This bill was recently signed into law thereby a major step toward quality control and integration of complementary and alternative medicine to the national healthcare system which is currently conventional medicine based. Inspite of the bill coming into law, the regulation efforts are still slow.

Currently the Ministry of Health has a coordination department for traditional and complementary medicine as earlier proposed but the regulation of the practice remains with the Ministry of Sports Culture and Social Services which issues certificates of recognition to herbalists. However, according to Legal Notice 192 of 2010 and Gazette No. 1879 of 21st march 2014, the powers of regulating herbal medicines, products and dietary supplements are with the Pharmacy and Poisons Board of Kenya [23]. The Board has guidelines for registration of herbal and complementary products along with the application process [24]. In the guidelines, specifications on quality control of raw materials include botanical identification, description of living plant, microscopic and macroscopic identification, geographical source of the plant, harvesting and collection methods, drying, storage and preservation mechanisms. The guidelines also give specifications on quality control of the finished product with recommendation that an analysis certificate report from an independent recognized quality control laboratory be attached during application for registration of herbal medicinal products. This is in compliance with World Health Organization requirements [25,26].

National Quality Control Laboratory (NQCL) analyses medicinal products and devices majority of which are conventional products with specifications in pharmacopoeias. However, in order to analyze non-pharmacopoeal samples, they must be accompanied by in house manufacturer's method of analysis and chemical reference substances according to the guideline for submitting samples [27]. The NQCL therefore have the ability to analyze herbal medicines though many of those utilized locally are not manufactured under good manufacturing practices (GMP) and therefore lack in house methods of analysis and chemical references that may be declared. This therefore makes it impossible to register products with the regulatory bodies as they cannot meet the requirements.

More efforts for continued development and research in quality herbal medicines do exist in Kenya today. In 2013, Kenya Medical Research Institute (KEMRI) Center for Traditional and Complementary Medicine came up with Traditional Medicine and Drug Development Program (TMDDP). The objective was to partner with other relevant institutions in identifying and developing effective traditional and alternative medicines for use against human diseases. In addition, the program was intended to provide information on quality of selected drugs in the Kenyan market [28]. Under this program research on many local products is being done and outcomes published [29]. Most data from the studies however focus on establishment of activity and/or efficacy. There is therefore need to start focusing on other quality

parameters for many plants whose efficacy has been established.

Among institutions of higher learning, the University of Nairobi has the Mitishamba Drug Research Centre (MDRC). The center carries out phytochemical, pharmacological, toxicological and microbiological studies of traditional herbal remedies for human and veterinary use. The facility also offers consulting services and reports on traditional medicines and other complementary medicines, formulation and presentation of herbal remedies, information on essential oils, their formulations and uses, consultation and dispensing of selected evidence-based herbal medicines. Herbalists who come to the Mitishamba Drug Research Center are issued with a certificate of recognition which enables them to register with the ministry. For promotion of more research and practice in traditional medicine, the University of Nairobi offers a Master of Science degree in Pharmacognosy and Complementary Medicine, the only one in the region.

More efforts to promote quality control and commercialization of traditional medicine have been ongoing in Kenyatta University for over 12 years now. The University has well over 20 hectares of farmland dedicated for medicinal plants and managed by the Department of Pharmacy and Complementary/Alternative medicine (PCAM). The medicinal plant populations are maintained by good agricultural practices (GAP) as recommended by WHO [30]. Among the major medicinal plants in the garden is *Warbugia ugandensis*, others include *Moringa oleifera, Artemisia annua, Aloe secundiflora, Prunus africana* and over one hundred other species**.** The populations of these species are determined by physical count and their taxonomy, distribution, reproductive biology and ethno botanical information records are available. More species are being introduced based on their ethnomedical history to enable research and development of quality control methods and product development.

Challenges Associated with Herbal Medicines use: Despite their popularity and global nature, CAM products, practitioners and self-care have not been exempted from many risks. Pretorius, (1999) cites fake healers and poor-quality products in Africa due to economic and regulatory challenges. Moreover, the alludes to the use of poor quality, adulterated and counterfeit products as a major risk affecting the use of herbal medicines in member states [30]. Other risks include unqualified practitioners, misdiagnosis, and exposure to misleading information, herb-drug interactions and sometimes failure to seek conventional treatments in time.

A global survey of WHO member states cited lack of mechanisms to monitor the safety, control and regulate the quality of CAM products among 60-78 countries [31]. In the same survey, over 65-member states reported their greatest need as technical guidance and support on research and evaluation of CAM safety, quality and efficacy. In this regard, the WHO strategy 2014-2023 advocates for setting up and adopting standards for CAM products as a strategic action by member states. According to the strategy, the key outcome should be the development of methodology for evaluating the safety, efficacy and quality of the products which will also be a key performance indicator to measure the success of CAM advancements in member states [30].

Many other factors have been identified as key to influencing the quality of herbal drugs. For example, herbal drugs being mixtures of many constituents, the specific active principles are in most cases unknown. Moreover, the selective analytical methods or reference compounds may not be available commercially. Variation in chemical and nature of plant materials has also been established to occur due to differences in geographical origins, genetic resources and quality of raw materials [32].

Harvesting, drying storage, transportation and processing methods also affect the quality of herbal medicines. Other factors associated with difficulty in controlling the quality of herbal medicines include adulteration with other herbs and synthetic drugs, microbial contamination, heavy metal contamination, misidentification and limited information about active components [33].

Herbalists decry the requirements to submit analytical methods and chemical information by regulatory bodies in order for their products to be considered for registration. This is difficult because majority of herbal practitioners have no knowledge of chemical information for the herbs they use. Moreover, there is huge amount of investments required to study the chemical composition and technical knowhow of analytical methods. This means that the evaluation of quality, safety and efficacy of traditional medicines has not been fully achieved in Kenya hence integrating herbal medicine to the national healthcare system might still take time.

Information acquisition, exchange and dissemination on traditional medicines and medicinal plants has been inadequate or not well documented and not properly packaged to enable effective utilization in the fields of conservation, production, safety and efficacy and commercialization. This has also contributed to an

increasing loss of information from one generation to the next as the few remaining practitioners die without sharing their knowledge.

In conservation, the phenomenal international growth in demand for plant based or phytotherapeutic treatments has led to the decline of many medicinal plant populations. This has been largely due to intensive harvesting that is not scientifically monitored and the use of unsustainable harvesting techniques for plants such as *Prunus africana.* A study by Kairu, et al. [34] reported the intensity of destruction for *Warbugia ugandensis* in Mount Kenya forest. The study established that debarking and uprooting accounted for 32 and 7 percent of threats and loss of this species respectively. For a plant ranked among the ten most utilized herbal medicines in East Africa, there is need for concerted effort to avert its extinction that of many endangered more.

Because regulation is still minimal, the authenticity of many herbal drugs used is not assessed. This is a major threat to safety because many drugs are not produced under controlled cultivations but originate from wild collections and varied climatic zones. Harvesting is also done under altered conditions and therefore botanical authenticity and homogeneity within a defined plant species is not guaranteed. Accidental consumption and mistaken identity of some medicinal plants is on the rise.

Approaches to Quality Control of Herbal Medicines

The World Health Organization has set parameters which guide evaluation of herbal medicine quality. They include botanical, physico-chemical, pharmacological and toxicological parameters [25,26]. Using these parameters, the World Health Organization documented about 58 plants with all their quality control information in WHO monograph Vol. 1 and 2 [26]. Some of the herbal materials whose quality control has been standardized include Bulbus allii cepa which is the dried or fresh bulbs of *Allium cepa*, family Liliaceae indigenous to western Asia [35]. Aloe the dried juice of *Aloe vera* leaf from the family Liliacea is also standardized [36]. Others are Radix astragali a dried root of *Astralagas membranosus* family Fabaceae and Radix gingseng the dried root of *Panax gingseng* family Araliaceae (Chinese Pharmacopeia, 1992). Rhizoma curcumae longa, the dried rhizome of *Carcuma longa* family zingiberaceae is also standardized. Herba echinaceae purpurea consisting of fresh or dried aerial parts of *Echinaceae purpurea* family asteraceae is standardized. Folium ginkgo consisting of dried leaves of *Ginkgo biloba* family Ginkgoacea among others.

Globally, though few plant species that provide medicinal herbs have been scientifically evaluated for their possible medical applications, documentation on safety and efficacy has not been done on many and this is a major hinderance in attainment of quality drugs thus derailing integration efforts for these forms of medicines to the national health care systems of many countries. There is therefore concern that quality, safety and efficacy data available on herbal forms of medicine does not sufficiently meet the criteria to support their use. This is partly attributed to lack of adequate or accepted research methodology for evaluating herbal materials.

Botanical Techniques

These parameters include organoleptic and sensory (macroscopy) evaluation and microscopy. Organoleptic and sensory evaluation serves as the simplest and quickest means of establishing the identity and purity of a particular sample thereby ensuring quality [25]. This evaluation is important before any tests are carried out. They include evaluation of color, odour, size, shape, taste and special features which include touch and texture. Availability of authentic specimen is recommended to serve as a reference material. The fractured surfaces are important in characterising cinchona, quillia and cascara barks. Evaluation using shape of the drug is widely used such as cylindrical in sarsapilla, subcylindrical in podophyllum and conical for aconite. Size represents length, breadth, thickness and diameter while color is mostly for external evaluation and varies from white to brownish black. Taste is a specific type of sensation felt by epithelial layer of tongue. It may be acidic (sour), saline (salt like), saccharic (sweetish), bitter or tasteless (possessing no taste) [25].

Microscopy involves a detailed examination of the drug with the help of a microscope. It is mostly used for qualitative evaluation of entire and powdered forms of organized crude drugs by their known histological characters. It can be relied on to determine the correct species and confirm the presence of the part of species specified. It is also useful when different parts of the same plant are used for different treatments [37]. Cellular tissues such as trichomes, stomata, starch granules, calcium oxalate crystals and aleurone grains play a role in identification of crude drugs [38,39]. Other microscopic identification techniques of crude drugs include cutting the thin transverse sections (TS) and longitudinal section (LS). In addition, microscopic evaluation of plant constituents

can be done by staining with proper reagents such as iodine for identifying starch and hemicelluloses give blue color, all lignified tissue gives pink stain with phloroglucinol and HCl. Mucilage stains pink with ruthenium red and can also be used to distinguish cellular structure.

Histological characters of fundamental importance in identifying crude drugs include type of stomata such as paracytic or rubiaceous or parallel- celled stomata. This is the type of stomata common to cocca and senna leaves. Diacytic or caryophyllaceous or cross-celled stomata is common with peppermint while anisocytic or cruciferous or unequal celled stomata is found in *Belladona* and *Datura* species. The other type of stomata is anomocytic or ranunculaceous or irregular celled common to *Digitalis* and *Lobelia* species [26].

Trichomes are elongated tubular outgrowths of epidermal cells which serve as protective, secretion of essential oil and absorption of water. They form important diagnostic features. Major types include non-glandular or covering trichomes, lignified trichomes such those found in *Strophanthusm, Nux- vomica, Lobelia and Cannabis* species. Covering trichomes are multi cellular T-shaped trichomes such as in *Artemisia* and *Pyrethrum* species. Others are, covering unbranched trichomes such as in *Datura Stramonium* and *Belladonna* species and Glandular unicellular such as in *Digitalis purpurea*, *Digitalis thapsi* and *Cannabis sativ* [30]. Calcium oxalate crystals occur in different types and shapes including Microphenoidal- *Belladonna*, Prism -*Hyoscymus*, *Senna*, Raphides -*Squill, Rauwolfia, Cinnamon***,** Rosetts -*Senna, Rhubarb* and acicular crystals- *Squill, Ipecacauanha*. Stomatal number and index, palisade ratio, vein-islet number is important aspects of quantitative microscopy which play an important role in the identification of crude drugs. Other aspects include size of starch grains and length of fibers [39].

The American Herbal Pharmacopoeia outlines a five-point criterion for authoritative microscopic characterization [38]. Firstly, prepared sections of whole or powdered plant material cellular structures and contents are compared with Pharmacopoeial or Botanical reference material (BRM). Secondly, in the event that there is no Pharmacopoeal reference material the sample should be well determined by a certified botanist and a voucher specimen deposited in recognized herbarium. Thirdly, the plant material should be of determined quality and its purity being well established. The fourth aspect of authoritative characterization is that multiple samples of the herb being characterized be examined thereby ruling out any intra-species variation. The fifth and final consideration on authoritative microscopy requires the examination of whole un-milled samples of the plant part being characterized. According to the AHP any characterization that meets the above criteria can be considered authoritative and appropriate to use as an identity standard [38].

Phytochemical and Physico-Chemical Techniques: Phytochemical and physico-chemical parameters are important in quality control of medicinal plants. They include foreign matter, ash value, moisture content, bitterness value, swelling and forming indexes and phytochemical tests such as presence of saponins, alkaloids, tannins, glycosides among others [39].

Foreign matter consists of parts of a medicinal plant material or materials other than that named in the specifications and descriptions of the plant material concerned, mineral admixtures not adhering to the medicinal plant material, such as soils, stones, sand and dust. Herbal drugs should be devoid of other parts of the same plant or other parts apart from the stated ones and other contaminants [25]. Macroscopic examination is used to determine foreign matter.

The ash remaining following ignition of medicinal plant materials is determined by three different methods. The total ash method measures total amount of material remaining after ignition. The acid-insoluble ash is the residue obtained after boiling the total ash with dilute hydrochloric acid, and igniting the remaining insoluble matter while water-soluble ash is the difference in weight between the total ash and the residue after treatment of the total ash with water.

Extractable matter is the number of active constituents extracted with solvents from a given amount of medicinal plant material and should be determined for materials which no suitable chemical or biological assay exists [25].

Determination of moisture content or loss on drying is important because excess water in medicinal plant materials is likely to encourage microbial growth, thereby attracting fungi, bacteria and insects. This can lead to deterioration due to hydrolysis. Limits for water content are therefore set for every plant material especially those materials that absorb moisture easily or deteriorate quickly in the presence of water. Tests for loss on drying determine both water and volatile matter.

Bitterness value is an important parameter to be tested for medicinal plant materials that have a strong bitter taste. Though bitter substances can be determined

chemically, it is first necessary to measure total bitterness by taste since they are mostly composed of two or more constituents with various degrees of bitterness [39].

Determination of swelling index is important for gums and plants containing appreciable amounts of mucilage, pectin or hemicellulose. Foaming index is significant for medicinal plants containing saponins and measures ability of aqueous decoctions to form when persistently shaken.

Tannins are substances with ability to turn animal hides into leather by binding proteins to form water-insoluble substances resistant to proteolytic enzymes. It is an important parameter for quality determination especially for medicinal plants suspected to have tannins.

Pesticide residues and arsenic heavy metals accumulate due to practices such as spraying, treatment of soils during cultivation and administration of fumigants during storage of medicinal plants. It is therefore recommended that determination is done for medicinal plant materials grown naturally or cultivated. The amount of arsenic in the medicinal plant material is estimated by matching the depth of color with that of a standard stain [25].

Microbiological Techniques: A majority of medicinal plants are associated with a broad variety of microbial contaminants represented by bacteria, fungus and virus. Microbial contaminants majorly depend on environmental factors and impact heavily on the overall quality of herbal products and preparations. Poor harvesting methods, cleaning, drying handling and storage cause additional contamination especially with *Escherichia coli* and *salmonella spp* [37]. The WHO specifies limits for specific microorganisms. The limits of bacterial and fungal contamination given in the British Pharmacopoeia [40] are: Total aerobic microbial count (TAMC) not more than 10^7 bacteria and total yeast and mould count (TYMC) not more than 10^5 fungi for herbal products to which boiling water is added before use. For herbal products to which boiling water is not added before use the TAMC should not be more than 10^5 bacteria while TYMC should not be more than 10^4 fungi. For all, *Escherichia coli* and *Salmonella* spp should not be present [33]. Cases of microbial contamination for herbal medicines have been reported before in Kenya [40].

Chemical Techniques

The chemical techniques observe chemical composition and or constituents of the plant material. Chromatographic examination has been recommended as the most appropriate investigative tool in assuring herbal chemical quality [41-45]. In chromatography the separation of molecules based on differences in structure and composition is considered. Preparation of the materials to be separated move over a stationary support thus molecules in the test preparation will have different interactions with the stationary support leading to separation of similar molecules. Test molecules which display tighter interactions with the support will tend to move more slowly through the support than those molecules with weaker interactions. In this way different kinds of molecules can be separated from each other as they move over the support material. Chromatographic separation can be carried out using a variety of supports including immobilized silica on glass plates (TLC), very sensitive high-performance thin layer chromatography (HPTLC), volatile gases (gas chromatography) paper chromatography and liquids which may incorporate hydrophilic insoluble molecules (liquid chromatography).

Thin Layer Chromatography: Thin layer chromatography is a simple versatile method used in pharmaceutical analysis for both qualitative and quantitative evaluation of chemical constituents. Compared to other chromatographic methods, TLC has been associated with many advantages including use of simple equipments, short development time of 15 min to 1 h, wide choice of stationary phases and quick recovery of separated constituents. Moreover, easy visualization of separated components by UV light makes TLC a method of choice for simple quick and easy analysis [46]. Further, detection can be achieved visually for colored substances. However, some specific classes of compounds can be detected using specific reagents. For example, sesquiterpenoids can be detected by spraying 0.5% anisaldehyde in sulphuric acid, glacial acetic acid and methanol in ratios, 5:10:85 respectively and heating at 105°C for 5 minutes before observing in daylight. Appearance of purple, blue or red color shows presence of terpenoids. Peter, et al. [47] further suggests use of 50% sulphuric acid for visualization of organic compounds which appear as yellow, brown or black zones when heated at 105°C for 10 minutes and observed in daylight.

Thin layer chromatography has been utilized in standardization and quality control of many plant drugs including *Aloe babadensis, Centella asiatica, Commiphora mukul* and *Glycyrrhiza glabra*. The evaluation of chromatogram or fingerprints can be achieved quantitatively or qualitatively. Qualitative evaluation can determine the R_f (retention factor) values of the separated solutes. The R_f values represent differences in rate of movement of the components in the extract caused by

their solubility in the mobile and stationery phases. The R_f value is determined by dividing the distance of centre of spot from the starting point by distance of solvent front from starting point and it is constant for each component only under identical experimental conditions. This concept was therefore applied in the current study to determine TLC fingerprints for controlling the quality of W. *ugandensis*.

High Performance Liquid Chromatography: High performance liquid chromatography is one of the modern-day applications highly utilized in separation and isolation of natural pharmaceutically active compounds including alkaloids and glycosides whose role in modern conventional medicine is undisputable. It is the most preferred method for quantitative analysis of complex mixtures. This technique with accompanying chromatogram is desirable with the goal of providing methods that can be validated and used to quantify compounds most correlated with pharmacological activity or qualitative markers [48]. Among its application in quality control of herbal medicines is the estimation of total gymnemasaponins in Gymnema sylvestre and other constituents in Hypericum perforatum and Passiflora incanata.

Resolution and peak symmetry can be used to determine a good separation during HPLC method development [49]. Resolution (R_s) is described as a measure of the methods ability to separate two consecutive analytes (A and B) and peak symmetry (A_s) as a measure of peak symmetry. Resolution is mathematically expressed as, $R_s = 1.18(t_{RB}-t_{RA}/ (W_{0.5A}+W_{0.5B})$, where t_{RA} and t_{RB} are the retention times of analytes A and B respectively, and $W_{0.5A}$ and $W_{0.5B}$ are the peak widths at half peak height of analyte A and B respectively with A as the earlier eluting peak. Peak symmetry (A_s) is mathematically expressed, as= $W_{0.05}/2_A$, Where $W_{0.05}$ is the peak width at 0.05 peak height and A is the distance between a perpendicular dropped from the peak maximum and the leading edge at 0.05 peak height. Peak symmetry (A_s) is unity for a totally symmetrical peak. An R_s value of more than 2.0 is recommended for routine methods while an as value of 0.9 to 1.2 is also desirable [49]. Resolution and peak symmetry formed the basis of determining a good separation during HPLC method development for *W. ugandensis* quality evaluation.

Gas Chromatography and Mass Spectrometry: Many biologically active chemical compounds are volatile thereby making gas chromatography an important tool in quality control of herbal medicine. It has high sensitivity of detecting almost all the volatile and thermostable chemical compounds. A review by Ali et al. [50] shows numerous applications of gas chromatography in separation, identification and quantification of phenolic compounds in plants including condensed tannins and flavonoids. It has been further demonstrated that gas chromatography produces more sensitivity when combined with mass spectrometry [51]. The combination of a chromatographic separation system online with a spectroscopic detector gives structural information on the analytes present in sample. The technique also helps in identification and confirmation of the identity of target and unknown chemical compounds.

When chromatography is combined with mass spectrometry, there is the advantage of both separation and identification hence the use of GC-MS as powerful tools for standardization and quality control of both the raw material and finished product. The results from these techniques provide a chemical fingerprint as to the nature of chemicals or impurities present in the plant extract [43]. Scientific experts have advocated for this method as the best, presently available, non-sophisticated and feasible for quality proof of herbal drugs [45].

Chromatographic Fingerprinting: A fingerprint is a specific profile or pattern which chemically represents a sample based on the detected compounds [52,53]. Chromatographic fingerprints are therefore chromatograms which represent the chemical characteristics of a herbal product. In addition, samples with similar chromatographic fingerprints are likely to have similar chemical and pharmacological properties [52,54]. The importance of using this technique to consider multiple constituents in the herbal drug extract as opposed to individually considering one or two markers for evaluating the quality of herbal extracts has been emphasized [55,56]. This is because the efficacy of herbal products is dependent on the concentration of many bioactive compounds [53].

Fingerprinting concept is ideal for evaluation of identity, authenticity and consistency of herbal products. Identity, authenticity and consistency are important aspects in quality control thereby making fingerprinting an integral method that must be explored for standardization of quality control especially in commercialized herbal products. Moreover, a chromatographic fingerprint could demonstrate both sameness and differences between various samples successfully.

Chromatographic fingerprinting technique has been applied for quality evaluation of many herbal products [57-59]. Data from chromatographic fingerprints can be

visually inspected or statistically compared. However, the use of either method to examine data may need pretreatment because of the chemical information and random variation associated with raw data from instrumental analysis [52]. Variation may include peak retention time shifts, background noise and slope inconsistencies. Hendriks, et al. [60] used normalization pretreatment technique in analyzing chromatographic data for determination of geographical origin of salir species. In normalization, each signal value for each sample is divided by the sum of all the signal values for that specific sample [61,62].

In similarity analysis the entire fingerprint can be used or not [63,64]. However, when the entire fingerprint is not used, similarity analysis is based on individual compounds including their relative retention time and relative peak areas [65,66]. In addition, reference samples should be included for quality evaluation purposes during similarity analysis. If authentic standards are not available, it is recommended that a mean or median fingerprint or signal is compiled and the similarity of individual chromatograms determined against the compiled chromatogram for quality control [67].

Conclusion

In spite of the challenges, the consumer and healthcare professionals' need of up-to-date authoritative information on the safety and efficacy of medicinal plants is growing by day. There is need for Macroscopic, microscopic, microbiological, physico-chemical, phytochemical and chromatographic fingerprinting mechanisms of quality assurance for widely used herbal medicines. The mechanisms will guarantee safety of commercialized products, restore confidence to the consumer and make regulation of products easier. The correct knowledge of specific parts used is an important aspect in preparation, safety and efficacy of the herbal products. Determination of macroscopic and microscopic characteristics will play a significant role for quick authenticity of the whole drug and powders while in the market and during post-market surveillance by the regulatory bodies. Similarly, determination of phytochemical constituents will contribute to knowledge of activity. Physico-chemical parameters such as extractable matter will add knowledge on the amount of soluble constituents in a given amount of medicinal plants thereby useful in quality and purity determination. In addition, microbiological studies will add to the knowledge of purity, for products, and its relationship with preparation mechanisms. Determination of chromatographic fingerprints (TLC and GC) will contribute to knowledge of chemical patterns that may be involved in synergistic therapeutic activity and enhance effective quality control. Further information on chemo-varieties from different geographical zones will contribute to knowledge on how geographical location of a herbal material can affect its quality hence creation of standards for each herb from a particular location.

The therapeutic activity of herbal formulations depends on their phytochemical constituents and quality. With the gaps identified in this review, there is urgent need for analytical methods and parameters that can be reliably used to authenticate herbal formulations, assure the quality and profile the phytochemical composition of the products. This is a long overdue challenge that African countries must overcome for meaningful realization of full integration for herbal, complementary and alternative forms of medicine to the mainstream national healthcare systems of respective countries.

References

1. WHO (2009) Traditional medicine in 62nd world health assembly 18-22nd May 2009, resolutions and decisions (WHA 62/2009/REC/1).

2. Chan (2013) Speech by WHO director general Dr. Margaret Chan at the international conference on traditional medicine for South East Asian countries. New Delhi India, pp: 12-15.

3. Koreeman P, Baars EW (2012) Patients whose general practitioner (GP) knows complementary medicine tend to have lower costs and live longer. Europ J Health Econ 13(6): 769-776.

4. Chinese Pharmacopeia (1992) The State Pharmacopoeia Commission of People's Republic of China, Beijing, China.

5. Chinese Pharmacopeia (2005) Pharmacopoeia of the People's Republic of China, Beijing: Chemical Industry Press, pp: 7-117.

6. Haruki Y, Kampo Y (2004) Medicine and chemotherapy. (Published in Japanese) Nippon Kagaku Ryoho Gakkai Zasshi 52: 547-555.

7. Wang JF, Cai CZ, Kong CY, Cao ZW, Chen YZ (2005) A Computer Method for Validating Traditional Chinese Medicine Herbal Prescriptions. Am J Chin Med 33(2): 281-297.

8. American herbal Pharmacopoeia AHP (2011) Botanical Pharmacognosy Microscopic Characterization of Botanical Medicines. CRC press, New York.

9. WHO (2001) Legal status of traditional medicine and complementary/alternative medicine. A worldwide review, WHO, Geneva.

10. WHO (2002) Regulatory situation of herbal medicines; a worldwide review. World health organization, Geneva.

11. WHO (2011) Progress report on decade of traditional medicine in the African region, Brazzaville, WHO, Africa region (AFRO) AFR/RC61/PR/2.

12. Chatora R (2003) An overview of the traditional medicine situation in the African region. African health monitors 4: 4-7.

13. Economic Survey (2015) Kenya National Bureu of statistics.

14. Abdullahi AA (2011) Trends and challenges of traditional medicine in Africa. Afri J Trad Comp Altern Med 8(5): 115-123.

15. Lewal OA, Banjo AD (2007) A survey of usage of arthropods in traditional medicine in south west Nigeria. Jour of Entomol 4(2): 104-112.

16. Cameron A, Even M, Ross Degnan D, Bail D, Laing R (2008) Medicine prices availability and affordability in 36 developing middle income countries. A secondary analysis. Geneva WHO.

17. WHO (2013) World Health organization, Traditional medicine strategy 2014-2023.

18. Kokwaro JO (2009) Medicinial plants of East Africa. 3rd (Edn.), University of Nairobi Press.

19. Jamison DT, Feachem RG, Makgoba MW (2006) Disease and mortality in Sub-Saharan Africa. 2nd (Edn.), Worldbank, Washington DC.

20. Mwangi JW (2012) Herbal medicines; Do they really work? Inaugural lecture at University of Nairobi, University of Nairobi press.

21. Kenya National Pharmaceutical Policy (2008) Ministry of medical services.

22. Health bill (2014) Ministry of health, Kenya.

23. Pharmacy and Poisons Board (2010) Registration of herbal and complementary products; guidelines to submission of applications by PPB.

24. Pharmacy and Poisons Board (2014) Herbal medicines in Kenya: Review of efficacy, safety and regulation. PPB Newsletter.

25. WHO (1998c) Quality control guidelines for medicinal plant materials, World Health Organization Geneva, pp: 1-111.

26. WHO (1999) World Health Organization monographs on selected medicinal plants. World Health Organization, Geneva.

27. National Quality Control Laboratory, NQCL (2013) Guidelines for submitting samples to the national quality control laboratory.

28. KEMRI, Traditional Medicine Drug Development Program (2013) The TMDDP Strategies and Objectives; TMDDP Newsletter 1.

29. KEMRI, Traditional Medicine Drug Development Program (TMDDP) (2014) Publications on Traditional Medicine by KEMRI staff/ITROMID students in 2013; Natural Products Newsletter 2.

30. WHO (2003) WHO guidelines on good agricultural practices (GACP) for medicinal plants. World health organization, Geneva.

31. WHO (2012) Interim data from 2nd WHO TRM global survey as of June 2012. World Health Organization.

32. WHO (2007) World Health Organization guidelines for assessing quality of herbal medicines with reference to contaminants and residues, Geneva.

33. Gao WY, Duan HQ, Xiao PG (2002) Quality control of Traditional Chinese Medicine. Frontiers of Biotechnology and Pharmaceuticals 3: 359-376.

34. Kairu A, Gichuki N, Kanya J, Kindt R (2013) Disappearing medicinal plants in Mount Kenya forests. A case study of East African greenheart (Warbugia ugandensis sparague). Topclass Journal of Herbal Medicine 2(7): 159-165.

35. Breu W, Dorsch W (1994) Allium cepa L (Onion): Chemistry analysis and pharmacology. In: Wagner H, Farnsworth NR, (Eds.), Economic and medicinal plants research London. Academic Press 6: 115-147.

36. (1996) The United States Pharmacopeia *XXIII, USP* Rockville, MD, US Pharmacopeial Convention.

37. Surekha D (2011) A review on role of quality control and quality assurance systems in regulation of herbal drugs. Int J Rea life Scie 1: 97-105.

38. Trease Evans (2009) Pharmacognosy. 16th (Edn.), Saunders Elsevier Ltd, New York.

39. Onyambu MO, Chepkwony HK, Thoithi GN, Ouya GO, Osanjo GO (2013) Microbial quality of unregulated herbal medicinal products in Kenya. African Journal Pharmacology and Therapeutics 2(3): 70-75.

40. (2007) British Pharmacopoeia 2: 184-192.

41. WHO (1998a) Quality control methods for medicinal plant materials. World Health Organization, Geneva.

42. WHO (1998b) Guidelines for the appropriate use of herbal medicines. WHO regional publications, western pacific series, Manilla 31.

43. WHO (2002c) General guidelines for methodologies on research and evaluation of traditional medicine. World health organization, Geneva.

44. Zafar R, Panwar R, Sagar Bhanu PS (2005) Herbal drug standardization. The Indian Pharmacist 4: 21-25.

45. Jian G, Rui T, Sheng M (2010) Comprehensive principle of HPLC fingerprint in the construction and evaluation of Chinese herbal medicines. N Am J M and Scie 3(2): 120-127.

46. Ashutosh K (2005) Pharmaceutical drug analysis (methodology, theory, instrumentation, pharmaceutical assays-cognate assays, 2nd (Edn.), New age international publishers New Delhi, pp: 409-430.

47. Peter JH, Amala R (1998) Laboratory handbook for the fractionation of natural extracts. London Chapman and Hall, pp: 91-102.

48. Wani MS (2007) Herbal medicine standardization. Pharmainfor, pp: 1-6.

49. Snyder LR, Glajch JL, Kirkland JJ (1988) Practical HPLC Method development. John Wiley and Sons, New York, pp: 68-69.

50. Ali K, Meredith AW, Thomas HR (2013) Techniques for Analysis of Plant Phenolic Compounds. Molecules 18(2): 2328-2375.

51. Shellie RA, Marriott PJ, Huie CW (2003) Comprehensive two-dimensional gas chromatography (GC×GC) and GC×GC-quadrupole MS analysis of Asian and American ginseng. J Sep Sci 26: 1185-1192.

52. Alaerts G, Dejaegher B, Smeyers BJ, Vander HY (2010) Recent developments in chromatographic fingerprints from herbal products: Set-up and data analysis. Combinatorial Chemistry and High Throughput Screening 13(10): 900-922.

53. Tistaert C, Dejaegher B, Vander HY (2011) Chromatographic separation techniques and data handling methods for herbal fingerprints: A review. Analytica Chimica Acta 690(2): 148-161.

54. Fan X, Cheng Y, Ye Z, Lin R, Qian Z (2006) Multiple chromatographic fingerprinting and its application to the quality control of herbal medicines. Analytica Chimica Acta 555(2): 217-224.

55. Fan G, Yi Zeng L, Reishan X (2003) Information theory applied to chromatographic fingerprint of herbal medicines for quality control. J Chromatogr A 1002: 25-40.

56. Liang YZ, Xie P, Chan K (2004) Quality control of herbal medicines. J Chromatogr B 812: 53-70.

57. Alaerts G, Matthijs N, Smeyers VJ, Vander HY (2007) Chromatographic fingerprint method development of herbal extracts. A screening and optimization methodology on monolithic columns. J Chromatogr A 1172(1): 1-8.

58. Ji B, Xu QS, Hu YZ, Heyden Y (2005) Development, optimization and Validation of a fingerprint of Ginkgo biloba extracts by High-performance liquid chromatography. J Chromatogr A 1066(1-2): 97-104.

59. Lekhooa M, Walubo A, Du Plessis JJ, Matsabisa MC, Molefe D (2012) Evaluation of traditional medicine; identification of phela using different chromatographic techniques. Afri J Trad Comp Alt Med 9: 27-39.

60. Hendriks MMWB, Cruz Juarez L, De Bont D, Hall RD (2005) Preprocessing and exploratory analysis of chromatographic profiles of plant extracts. Analytica Chimica Acta 545(1): 53-64.

61. Alaerts G, Van EJ, Pieters S, Dumarey M, Van NAM, et al. (2012) Similarity analysis of chromatographic fingerprints as tools for identification and quality control of green tea. J Chromatogr B 910: 61-70.

62. EMEA (2005) Guidelines on quality of herbal medicinal products/Traditional medicinal products. EMEA/CV Mp81400, Review European agency for medicinal products, EMEA London.

63. Pretorius R (1999) South African health review. 5th (Edn.), Durban health systems trust, traditional healers, pp: 249-256.

64. Statutes of the Republic of Singapore, Medicines Act (2005) Chapter 176, Singapore: The Government Printer, Ministry of Health.

65. Xie PS, Chen SB, Liang YZ, Wang XH, Tian RT, et al. (2006) Chromatographic fingerprint analysis, a rational approach for quality assessment of traditional Chinese herbal medicine. Journal of Chromatography A 1112: 171-180.

66. Liang YZ, Xie P, Chan K (2004) Quality control of herbal medicines. J Chromatogr B 812: 53-70.

67. Zhao YL, Fan RH, Yuan HX, Yu M, Bi KS, et al. (2011) Development of fingerprints for quality evaluation of Viscum coloratum by High-performance liquid chromatography. J Pharm Anal 1(2): 113-118.