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Evaluation of microbiological criteria and quality of packaged herbal medicinal products

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Abstract

The broad use of packaged herbal medicinal products has highlighted many issues associated with the quality, safety, and efficacy (QSE) of these products. Regardless of extensive applications of herbal medicines, this fact cannot be denied that the plant materials are exposed to various contaminants like toxic elements, pesticide residues, insects etc. But the main contaminants responsible for the deterioration of the herbal medicinal products (HMPs) are the microbes. They exert a bad impact on the overall quality and shelf life of the herbal products. The qualities of these products not only revealed changes in the physical appearance but could also pose a risk of acquisition of pathogenic microbial agents such as bacteria spores and mycotoxins to those taking these products. Exposure to these microbial agents can cause adverse health effect and toxicity. The integrity of composition depends upon the harvesting, handling, packaging, distribution, and storage conditions. In absence of good manufacturing practice, however, the nutritional richness of HMPs makes the product good medium for microbial growth, vehicle of microbial pathogens and associated complications. In Nigeria the issues of non-standardization, improper regulation and registration of these herbal products has raised a lot of questions about the inherent health risk associated with the consumption of these products, especially now there is increasing popularity of the use of herbal medicines. This paper addresses microorganisms and their agents as the major contaminants of herbal medicinal products. It reviews precise sources of microbial contamination and harmful effects of contaminated herbal medicinal products, when consumed by the consumers. It also reviews the methodological aspects regarding the influence of different commonly used pharmaceutical preparation techniques on the microbiological criteria of the products. And finally discussed the way forward to ascertain these quality, safety, and efficacy (QSE), of herbal medicinal products, quality standards which could be considered for guidelines and or possible inclusion in herbal pharmacopeia.

Keywords: Herbal medicinal products [HMPs]; Microbial contaminants; Microbiological criteria; Quality, Safety, and efficacy (QSE)

1. Introduction

Microbial contamination is the undesired introduction of impurities (chemical or microbiological or foreign matter) onto a starting material, intermediate product or finished herbal medicinal products during cultivation, harvesting, process/production, packaging, transport, or storage of this products [65]. Microbial contamination may involve living microbes such as bacteria and (their endospores), yeasts and moulds (their spores), viruses, protozoa, insects (their eggs and larvae), and other organisms. However, products of microbial metabolism such as toxic, low-molecular-weight metabolites from moulds are microbial agents. Microbial contamination originates from primary and secondary contamination. Primary contamination is the naturally occurring microbial flora of the plant to be harvested. Secondary contamination is caused by handling of the plant material (human intervention, equipment, buildings, air ventilation

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systems, and contamination during transportation). Generally, the presence of coliforms in herbal medicinal products (HMPs) implies the possibility of recent faecal contaminations and inadequate sanitation measures in the cascade of HMPs production process, which can lead to impaired performance of the herbal medicinal product due to disruption of the stability of the formulation, modification of physical characteristics and appearance and lead to inactivation of the active ingredients and excipients in the formulation. Minimizing HMPs contamination with micro-organisms and microbial toxins should be ensured ideally by monitoring and limiting both primary and secondary contamination, i.e., by prevention rather than by use of decontamination methods. According to European Union (EU) legislation herbal substances are produced in compliance with good agricultural and collection practice (GACP) and, from the starting material onwards, herbal preparations are manufactured in compliance with good manufacturing practice (GMP), Herbal medicine essentially represents a natural form of health care which has been used through generations to generations. Nigerians have a deep belief and reliance on the services of herbal medicine practitioners for their health care needs. An estimated 75% of the population still prefers to solve their health problems by consulting herbalists [3]. Herbal medicines present safety concerns as they carry a relatively high risk of contamination by pathogenic microbes, organic and inorganic residues including toxic metals and nonmetals, organic pollutants, mycotoxins, endotoxins, and agrochemical residues [58,1, 26]. World Health Organization survey indicated that about 70-80% of the world population particularly in the developing countries rely on non-conventional medicines mainly of herbal sources, so there is need to put in place an effective quality assurance system such as microbiological analysis of herbal medicine to ascertain the quality and safety of herbal preparations [65]. The increase in the consumption and popularity of natural drugs made their use a public health problem due to the lack of effective surveillance of the use, efficacy, toxicity, and quality of these natural products, [70]. The general perception that herbal remedies or drugs are very safe and devoid of adverse effects is untrue and misleading. Herbal medicinal products have been shown to be capable of producing a wide range of undesirable or adverse reactions when contaminated, which can be a potential source of infections which in turn can result into a wide range of complications from gastroenteritis, sepsis, blindness and even death [10,28,69]. The therapeutic efficacy of plants depends on their active constituents which are effective against the specific ailments. In the case of high microbial load in plants it may be possible that active constituents of the plants may deteriorate. Substances derived from plants remain the basis for a large proportion of the commercial medications used today for the treatment of asthma, premenstrual syndrome, eczema, rheumatoid arthritis, migraine, menopause symptoms, chronic fatigue, and irritable bowel syndrome. Herbal medicines had been and still used in the treatment of typhoid fever, malaria, infertility, fever, waist pain, chest pains, pile insomnia, ulcer, carbuncle, dizziness, blood prostration etc. have independently reported on the in vitro applications of plants extracts in the treatment of diseases associated with *Mycobacterium tuberculosis, Staphylococcus aureus* and several other gram-positive bacteria and fungi [19,7,17]. It has been claimed that the active components in some plants act by inhibiting bacterial DNA dependent RNA polymerase inhibition of cell wall synthesis, damage to the cytoplasm membrane, inhibition of nucleic acid and protein synthesis and inhibition of specific enzyme system of microorganisms [12]. During preparation, handling, and storage of herbs by local herbalist, the chances of the final products being contaminated is very high. The roots, stems, barks, and leaves of plants harbour a lot of microorganisms [2,15]. In most cases the water used for washing and preparation of the HMPs may not be sterile. During drying, soil and air microorganisms may contaminate final products. In Nigeria, herbal medicines and related products are introduced into the market without any mandatory safety or toxicological evaluation and lack effective machinery to regulate good manufacturing practices and quality standards. These herbal products are continuously made available to consumers without prescription in most cases [28]. Plant materials used in herbal medicine preparations are organic in nature, providing nutrition and support microbial growth which could lead to contamination when proliferated [44] The packed herbal medicines play an important role in fulfilling natural requirements of consumers at affordable prices. The composition of these herbal medicines is based on standard requirements of the consumers; the integrity of composition depends upon the processing and storage conditions. The consumption of herbal medicines could have both positive and negative effect on the part of consumers. Herbal medicinal products processed under hygienic condition could play important role in enhancing consumers' health e.g., inhibition of breast cancer, congestive heart failure (CHF), and urinary tract infection. In absence of good manufacturing practice, however, makes herbal medicinal product good medium for microbial growth, vehicle of pathogenic organisms and associated complications. Recently, herbal medicinal products have been acknowledged as "emerging vehicles" for illnesses due to bacterial pathogens, protozoa and fungal. In Nigeria herbal practitioners have capitalized on the poor health conditions of the masses and high cost of synthetic orthodox medicine by organizing herbal trade fare indiscriminately. The probability of a patient on herbal remedies contracting more deadly diseases cannot be totally ruled out considering the unhygienic and crude method of production and storage. However, this paper attempted to addresses the microorganisms and their agents as the major contaminants of herbal medicinal products by considering the microbial source and their harmful effects on the consumers when taken contaminated herbal medicinal products, it also reviews the influence of different preparation techniques on the microbiological quality and finally discussed the way forward for assurance of quality, safety, and efficacy of herbal medicinal products in Nigeria.

2. Common microbial contaminants and illness associated with the consumption of contaminated and adulterated herbal medicinal products

The microbial contaminants are easily transferred by air and soil borne vectors as well as by irrigating water. The bacterial endospores and fungal spores are the two dominant groups of contaminants associated with herbs/ herbal medicinal products. It is well known that (HMP) is a good source of all nutrients required for growth and survival of micro-organisms and can contain a diverse and complex population of micro-organisms including food-borne bacterial pathogens. Consequently, (HMP) are considered as "high-risk medicines" of plants origin, and some HMP are also considered as riskiest of all medicines that can pose a similar risk to humans [4]. The prevalence of pathogens in (HMP) is important since they are prepared exclusively from raw plant and are not heat-treated for the inactivation of these pathogens before consumption. Therefore, it is highly likely that the pathogens present in raw plants will naturally be present in such products.

Since various medicinally important components are being utilized by heterogenous groups of adherent microbial flora during storage, the phytochemicals of the raw and powdered herbal drugs are drastically changed both quantitatively and qualitatively during that period. Hence significance of phytochemical analysis of the specific plants and their parts becomes insignificant unless storage conditions are being optimized to keep the level of the phytochemical's constants. Doses prescribed in indigenous medicine system in herbal medicine are affected due to loss of ingredients and therefore both loading and symptomatic relief may be varied.

The bacterial pathogens are the main hazards which pose one of the greatest threats to medicines safety presenting various disease risks and causing severe health consequences in humans. The most microbial contaminants presenting serious health hazards in human health have been reported to be *Bacillus*. *Staphylococcus aureus*, *Salmonella spp*., *Shigella spp*., *E. coli*, *P. aeruginosa and Aspergillus spp* [60, 43, 41, 63, 82]. Most of the isolates are resident in the soil, water, air and vegetations, and their public health implications had been reported. *Bacillus cereus- Bacillus cereus* is a spore-forming bacterium ubiquitous in the environment. It is readily isolated from soil, cereal crops, and vegetables etc. It has been reported that soil can contain approximately 1,000 to 100,000 spores per gram [27]. Hence, it is not uncommon to find this bacterium in products, especially in raw agricultural products such as raw fruit and vegetables, raw herbs. These foods usually contain less than 100 spores per gram, but higher amount may be found in some herbs and spices [27]. *B. cereus* can form spores which are able to resist heat and survive the cooking temperature. It can either grow in the presence or absence of oxygen. The optimal growth temperature for B. cereus is around 30°C to 37°C. At temperature below 10°C, *B. cereus* is unable to grow and produce toxin that causes vomiting [27]. Therefore, controlling storage temperature of any products is important to prevent disease caused by this bacterium. There are two types of poisoning caused by different toxins produced by B. cereus. Emetic (cause vomiting) intoxication is caused by a heat-stable toxin (which can resist 126°C for 90 minutes) preformed in food. Symptoms including nausea and vomiting occur in the first few hours after ingestion of incriminated food, followed by diarrhea in some cases. Another type of poisoning is diarrheal, which is characterized by watery diarrhea associated with abdominal pain. This type resembles the illness caused by Clostridium perfringens in which the toxins are produced in the intestine by ingested spores or vegetative cells. The illnesses of these two types of poisoning are generally mild and persist no longer than 24 hours. [80,8].

Escherichia coli is consisting facultative anaerobic Gram-negative bacilli, belonging to the family, *Enterobacteriaceae. E. coli* has most commonly been reported in (HMP) in many countries in Africa including Nigeria, Ghana, and Zimbabwe. It has also been reported at 33 % prevalence in the top 10 most common bacteria present in (HMP) in Nigeria. *E. coli* is naturally found in the intestinal tract of humans and other warm-blooded animals and its presence in food indicates a direct or an indirect faecal contamination, is widely distributed anaerobe, inhabiting the large intestine of humans and warm-blooded animals. Even though, most *E. coli* strains live harmlessly in the colon and do not always cause disease in healthy persons; several pathogenic strains can cause intestinal and extra-intestinal diseases, both in healthy as well as immunologically weak individuals [36]. *Escherichia coli* O157 and another Shiga toxin-producing *E. coli* (STEC). Shiga toxin-producing. When *E. coli* strains attain certain genetic material, they can become pathogenic. Gastroenteritis, urinary tract infections and neonatal meningitis can be caused by virulent strains of *E. coli. E. coli* is a group of *E. coli* that produces one or more verocytotoxins (VT), also known as Shiga-like toxins. This group of bacteria is also called Verocytotoxin-producing *E. coli* (VTEC) [81]. STEC is transmitted to humans' primarily through consumption of contaminated herbal medicinal products, such as raw or uncooked products, contaminated herbs and vegetables and direct contact their environment. Direct person-to-person transmission through the oral-faecal route can also occur. *E. coli* O157:H7 is the predominant serotype in a pathogenic subset of STEC, designated enterohaemorrhagic *E. coli* (EHEC). The designation is based on their capacity to cause attaching and effacing lesions in epithelial cells of intestine, and their ability to cause hemorrhagic colitis (bloody diarrhea) and a life-threatening complication hemolytic uraemic syndrome (HUS) in humans. Other non-O157 serogroups, including O26, O91, O103, O104, O111, O113, O117, O118,

O121, O128 and O145, have been associated with occasional outbreaks of human disease, and others may be associated with sporadic cases [67]. The illness caused by STEC infection usually present with diarrhea, often bloody diarrhea, abdominal cramps, and vomiting. In serious cases, the infection may lead to HUS which is a type of kidney failure. Symptoms of HUS vary, depending on the patient's health and the extent of the infection. People of any age can become infected. Very young children and the elderly are more likely to develop severe illness, but even healthy older children and young adults can become seriously ill. In general, the non-O157 serogroup is less likely to cause severe illness than *E. coli* O157:H7; however, some non-O157 STEC serogroups can cause the most severe manifestations of STEC illness [81].

Salmonella spp. *Salmonellae* are bacteria found in the intestinal tract of man and animals. More than 2,500 serotypes of *salmonellae* have been identified and *Salmonella Enteritidis*, followed by *Salmonella Typhimurium*, are the most isolated serotypes in Hong Kong. Food may be contaminated by *salmonellae* in animal faeces and cross-contamination may occur during further processing and preparation. *Salmonellae* may survive in the environment and equipment of food-processing facilities. *Salmonellae* reside in the intestinal tract and are shed in the faeces of infected animals and humans as well. Many foods, particularly those of animal origin and those subject to sewage pollution, have been identified as vehicles for transmitting these pathogens [7]. Poultry and poultry products are commonly linked to *Salmonella* and the bacterium can also be found in eggs. Eggs may be contaminated via two different routes: vertical transmission through the ovary or transovarian or horizontal transmission through the shell or trans-shell [7]. Through vertical transmission, bacteria are introduced from infected reproductive tissues to eggs prior to shell formation. Horizontal transmission usually occurs from faecal contamination on the eggshell as the eggs are released via the cloaca, where the excretion of faeces also takes place. It also includes contamination through environmental vectors, such as farmers, pets and rodents. Under appropriate conditions, bacteria on the shell can move across shell into the egg content [30]. Enteric fever (also known as typhoid fever) is an illness caused by *S. typhi* and *S. paratyphi* type A, B and C [62]. Symptoms of typhoid fever include high fever, diarrhea or constipation, headache and sometimes a rash [80]. It can be complicated by intestinal bleeding and perforation, impaired consciousness and even death if untreated. On the other hand, symptoms of non-typhoidal salmonellosis, which is caused by serotypes other than *S. typhi* and *S. paratyphi*, include nausea, vomiting, abdominal cramps, diarrhea, fever, headache [80].

Shigella spp. Shigella bacteria are found naturally in the intestinal tracts of humans and other primates. People who eat food or drink water contaminated by *Shigella* can become ill with bacillary dysentery (shigellosis). In addition, the bacteria may spread from person to person by physical contact. Contamination through food handler is one of the major sources, and food can also become contaminated by flies carrying sewage or faeces [56] Severity of illnesses varies with the host and the type of *Shigella.* The illness is characterized by sudden onset of fever, diarrhea with abdominal cramps and nausea or vomiting. The stool may contain blood and mucus (dysentery). Mild and asymptomatic illness can occur. Complications include toxic dilation of large intestine and acute kidney disease. *Shigella dysenteriae* type 1 is of particular concern in developing countries, where it spreads in epidemics and is often associated with serious disease and complications. The case–fatality rates have been as high as 20% among hospitalized cases [8]. Locally, the most common species isolated from patients is *S. sonnei* [23]. *Staphylococcus aureus. Staphylococcus aureus* is a bacterium which is commonly present in human nasal passage, throat, hair, and skin without causing any discomfort. It can produce several enterotoxins that are responsible for food poisoning. *Staphylococcus aureus* produce potent enterotoxins associated with food borne intoxication, toxic shock syndrome and diseases from localized skin and soft-tissue infections to life-threatening septicaemia, which can also cause blood stream infections [71]. The temperature range for the bacterium to form toxin is from 10 to 45°C and optimal at around 35 to 40°C. Hence, normal refrigeration temperature can restrict the formation of toxin. On the other hand, *S. aureus* is a salt-tolerant microorganism and grows at a water activity as low as 0.85 which corresponds to a salt content around 25% w/w. Hence, it may grow better than the other bacteria in salt-containing products or products with low water activities [56]. Even though most cases of infection are caused by *S. aureus*, other coagulase-positive Staphylococcus species, such as *S. intermedius* can also produce enterotoxins that cause food poisoning [9] The bacterium can be destroyed by normal cooking procedures or pasteurization, while the toxins produced are more resistant to heat; they may survive in food causing food poisoning [56]. The most common way of contamination of food is by contact with food handlers' hands, especially in the cases where the food is handled after cooking. Prolonged storage without refrigeration allows the bacteria to grow and form toxins. Since the toxins are heat stable, the incriminated food may also cause food poisoning even if it is further heat treated. The main symptoms of *Staphylococcus aureus* poisoning are nausea, vomiting, retching, abdominal cramping, and prostration, often accompanied by diarrhea and sometimes fever. In severe cases, patients may present with headache, muscle cramping, severe fluid and electrolytes loss with weakness and low blood pressure or shock. Patients usually recover within two days but can take longer in severe cases that may require hospitalization [8].

Coliform bacteria can originate from faecal contamination or from the environment. Coliform bacteria are normally not present in natural mineral water sources. They are considered as an indicator of contamination of the water at source

or during the packaging process [80]. In addition, coliform bacteria should be absent immediately after disinfection, and the presence of these organisms in water or (HMPs) indicates inadequate treatment. *Enterococci* are a sub-group of faecal streptococci. Compared to *E. coli* and coliforms, they tend to survive longer in the water environment and are therefore used as an additional indicator of faecal contamination [80]. The spores of spore-forming sulphite-reducing anaerobes are very resistant towards various kinds of environmental stresses. These bacteria can originate from faecal contamination and due to the length of their survival in unfavourable environments, they are usually used as an indicator of faecal contamination [80]. *Pseudomonas aeruginosa* is a common environmental microorganism and can be found in faeces, soil, water, and sewage. *P. aeruginosa* which is primarily a soil bacterium and the cause of various infections, e.g., of burns, urinary tract infections, respiratory tract infections, bacteraemia, dermatitis, bone and joint infections, soft tissue infections, GI infections etc [40]. It can multiply in water environments and on the surface of suitable organic materials in contact with water. *Pseudomonas aeruginosa* is not a normal component of the natural flora of natural mineral waters. Its presence is considered as an indicator of contamination of the water at source or during the packaging process [80]. *Enterobacter sakazakii (Cronobacter spp*.) is a pathogen that generally causes disease only in people with weakened immune systems. The bacterium can cause invasive infections (e.g., sepsis or meningitis) in infant. Neonates (≤ 28 days old) and infants less than 2 months of age, those that are pre-term, low-birthweight (<2.5 kg) and immunocompromised, are at greatest risk. Powdered infant formulae were established as the source of *E. sakazakii (Cronobacter spp*.) [8].

Several complications and disorders in certain humans may occur due to ingestion of adherent fungal flora with herbal medicinal products. It is indicated that initially in the lower gut of human body there are about 4 -8 lbs of friendly bacteria. This comprises about 85% of all organisms in the bowels, and remaining proportion (15%) are mainly fungi and are excessively toxic in nature and more powerful than bacteria.

High counts of some fungi species like *Aspergillus, Penicillium and Rhizopus* may endanger the health of consumers as they have been implicated in human pathogenicity. Most *aspergilla* isolate like *A. flavus*, *A. parasiticus, A. ochraceus*, *A. niger* and *A. fumigatu*are have no antibodies to protect itself but are a risk because of the possibility to produce deadly mycotoxins, such as flatoxin, that may result in failure of digestion and assimilation of all the nutrients. Organs and glands are deprived of its building blocks and systems begin to fail. Aflatoxin is also a carcinogen toxin and other mycotoxicoses as well as mycotic infections of the liver, kidney, and skin. The WHO also recommends a test to detect the possible presence of aflatoxins, which are highly dangerous contaminants in any material of plant origin. To lower down the risk with adherent microflora of herbal medicine, precaution should be taken that herbal medicine should be properly sterilized before their intake.

3. Sources of microbial contamination in herbal medicinal products

Nature has blessed us with a very prosperous botanical asset and a huge number of varied types of plants are growing in different parts of the world. These medicinal plants are further processed for various formulations of cosmetics, food supplements etc. They are also used as spices and herbs in day-to-day life. These plants are utilized for their extensive applications, due to their antimicrobial, nutritional, antioxidant and other medicinal properties. Although, the medicinal plants with their chemical constituents carry huge applications in the treatment or prevention of various diseases, this fact cannot be denied that the plant materials are exposed to various contaminants like toxic elements, pesticide residues, insects etc. But the chief contaminants mainly responsible for the deterioration of the herbal products are the microbes. Due to the exposure of plant materials to the microbial contaminants during their cultivation, harvest, collection, processing, storage, distribution, and sale exert a bad impact on the overall quality and shelf life of the herbal products[75,35].Contamination of herbal medicinal products is defined as, "the undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a starting material, intermediate product or finished flavourer product throughout production, sampling, packaging or repackaging, storage or transport"[61]. Introduction of microorganisms in the herbal medicinal products can alter the physicochemical characteristics of the product, which may lead to harmful effects to the quality of the herbal medicinal products [32]. Hypothetically, the most likely sources of contamination are microbes from the ground and processing facilities (contaminated air, microbes of human origin) World Health Organization contaminant guidelines [65]. Insanitary utilization of herbal medicinal products by the patients. The manufacturing procedures when the ready-made herbal medicinal products are prepared [13]. Cross contamination is also possible from extraneous materials such as plastics, glass, and other materials that are in contact with medicinal herbs, herbal preparations, or herbal medicinal products.

4. Influence of preparatory procedures on the microbiological quality

The production of an herbal medicine generally involves the steps in which a vegetable is subjected to unfavorable conditions to survival of microorganisms. For these reasons, some of these processes and their influence on the microbial load was introduced.

4.1. Cultivation of plants

For cultivated plants, the growing conditions should be chosen to avoid unnecessary microbial contamination. For instance, if manure is used as a fertilizer, the manure may be carefully composted before use. Because many micro-organisms are host specific human faeces must not be used as fertilizer and direct use of sewage must also be avoided.

Where justified, fungicides can be used during cultivation of the plant to reduce fungal growth. Growing the plants in green houses provides some opportunity to control airborne and animal contamination.

4.2. Harvesting /collection of excipients

For both cultivated and wild plants, the time of harvest should be chosen so that the presence of external water on the plants is limited, i.e., by avoiding harvesting during or immediately after rainfall or heavy morning/evening dew. After harvest, unless frozen, herbal substances intended for fresh use, should be processed immediately. If the herbal substance is cleaned by washing with water, the quality of the water should be considered as a possible risk for microbial contamination.

4.3. Drying process

Drying is basically defined as the decreasing of plant moisture content, aimed at preventing enzymatic and microbial activity, and consequently preserving the product for extend shelf life [74] Drying is the most common and fundamental method for post-harvest preservation of medicinal plants because it allows for the quick conservation of the medicinal qualities of the plant material in an uncomplicated manner. This process may also contribute to facilitate the marketing of plants, because drying results in reduction of the weight and volume of the plant with positive consequences for transport and storage [74, 55].

The optimization of the drying process contributes to physical, chemical, and microbiological stability of the medicinal herbs. The choice of drying conditions depends on the moisture content of tissue at harvest, the plant parts used, and the temperature best suited for preservation of the requested ingredients. For this reason, adequate dryers are needed, using temperature, velocity and humidity values for drying air that provides a rapid reduction in the moisture content without affecting the quality of the active ingredients of medicinal plants [74]. Medicinal plants can be dried in several ways: in the open air (shaded from direct sunlight); placed in thin layers on drying frames, wire-screened rooms, or buildings; by direct sunlight, if appropriate; in drying ovens/rooms and solar dryers; by indirect fire; baking; lyophilization; microwave; or infrared devices. When possible, temperature and humidity should be controlled to avoid damage to the active chemical constituents. In the case of natural drying in the open air, efforts should be made to achieve uniform drying of medicinal plant materials and so avoid mould formation [64]. Spray drying technique has been widely used to obtain dried extracts presenting better technological characteristics and greater concentration of biological active constituents. This method is widely used in the pharmaceutical industry, despite the high temperature drying (100°C to 200°C), the contact time between the material to be dry and hot air is extremely fast, less than 1 minute, theoretically is not enough to remove the microorganisms [59]. Comparative microbiological analysis of drug pulverized, extraction in liquid phase and the spray drying extraction, using *Phyllanthus niruri* L., revealed that there is a significant reduction in microbial load, caused by the extraction in liquid process, while the spray dryer, despite the high temperature, did not affect the microbial load [77]. Drying at high temperature decreases the total aerobic microbial count in herbs. Water is a significant component of biological materials. Drying methods can lower the water activity to the level required for preventing growth of *Aspergillus species* and to ensure quality of medicinal herbs which may get destroyed upon over drying [47]. Exposure of herbs to microwaves and warm-air ovens can be efficient to reduce the microbial load, but they are not recommending to medicinal herbs containing volatile oils. The reference evaluated both method of drying of plant, and reduction the microbial load present on the plants was observed but the effect on the volatile oil profile was profound by microwave drying, and warm drying air revealed that at temperatures >60°C, most of the volatile constituents were lost [24]. Other methods such as freeze-drying, oven drying and tray drying have been previously used to preserve medicinal herbs but to date there is little information in the literature on the effect of these drying conditions on the decrease of microbial loads [39]. Once drying is complete, plants are packaged in preparation for shipping or other further processing.

4.4. Extraction methods

Water is almost universally the solvent used to extract activity. At home, dried plants can be ingested as teas (plants steeped in hot water) or, rarely, tinctures (plants in alcoholic solutions) or inhaled via steam from boiling suspensions of the parts. Dried plant parts can be added to oils or petroleum jelly and applied externally. Poultices can also be made from concentrated teas or tinctures [20]. These kinds of preparations are usually called medicinal teas and are prepared using natural plants collected, dried, and packaged without an effective hygienic and sanitary control. In addition, there can be microbiological contamination and controlling microbial contamination can be difficult in aqueous extracts [53].

Environmental dust settled on different parts of the plant and other contaminations can carry very significant amounts of bacterial and moulds spores [53]. However, those drugs which are subjected to cold water extraction (herbal maceration) may host a considerable number of microbes, and the extraction procedure carried out at ambient temperature usually enables microbial multiplication [46]. The application of hot water extraction usually compensates for microbiological contaminations, since it can be expected that boiling water markedly reduces the viable counts by several log units and inactivates possible pathogens [46]. However, bacterial spores of the Bacillaceae family are resistant to thermal treatment usually applied in infusion preparation, and this thermal shock may stimulate spore germination. Some of these bacteria like *B. cereus* and *C. perfringens* are recognized as having potential pathogenicity and have been incriminated in food poisoning [49]. Thus, in extractions using only water, hot or cold, as extractor liquid, the stability of the extract becomes compromised, and the risk of microbiological contamination increases significantly. This contamination can compromise the quality and integrity of the plant material itself, as well as products arising from its use [54,5]. In addition to extraction temperature, the choice of extraction solvent is another important factor to prevent microbial contamination. The aim of an extraction process should be, of course, to provide for the maximum yield of substances and of the highest quality (concentration of target compounds and pharmacological power of the extracts). For extraction of active phytochemicals, the most used solvents are methanol, ethanol, hexane, chloroform, and diethyl ether [18]. Herbal extraction which made by ethanol or methanol extraction should, in general, provide good hygiene conditions, but the result depends on the alcoholic concentration applied [46]

4.5. pH influence

The pH value is one of the main factors influencing the quality of medicine. It always controls many chemical and microbiological reactions [51]. When the pH value is low (presence of acidic substances), the bacterial count could be low, but at neutral or higher pH the level of contamination of the herbal preparations could observed to be higher. This suggests that a neutral or alkaline pH favoured high contamination levels of the herbal preparations. This agrees with the observation that bacterial growth is optimal at neutral pH, around pH 5-8.5 [1].

4.6. Transportation temperature

The transportation temperature for (HMB) determines the type of pathogens that will survive and grow since all micro-organisms including the pathogens require an optimum, maximum, and minimum temperature for their growth. Micro-organisms are grouped according to the temperatures at which they grow. Most of the pathogens are either psychrotrophic or mesophilic. During the transportation of (HMP), pathogens may also grow if the temperature required is not maintained.

4.7. Storage temperature

Most pre-storage processing of plant material, such as that involving drying, heat, cooling, and packaging, can prevent the degradation of plant material during storage [34]. Storage of medicinal herbs is an important part in the process production. During storage, due to the factors in the outside world and their own physical and chemical properties of the interaction, gradually occurring physical, chemical, and biological changes. Prolonged storage in poorly ventilated storehouse usually increases sample moisture content in the bulk due to heat exchange capacity, rendering herbs more susceptible to molds growth and toxin production. Fungi are the predominant contaminants of herbs, but most such microbial populations are probably regarded as commensal residents on the plant that survived drying and storage. Most fungi are present on plants, which develop after harvest if relative humidity is not controlled during storage [11,52]. Moulds are responsible for biodeterioration of several substrates including raw materials of some medicinal plants. These moulds reduce raw herbal drugs shelf life and market value. The fungal deterioration adversely affects the chemical composition of the raw materials and thereby decreases the medicinal potency of herbal drugs [48]. Samples of herbal parts stored for sale in markets located in Ibadan, Nigeria were analyzed for microflora associated with their storage and twenty-eight fungal species were isolated, showing that herbal drug plant pieces are hazardous for human health [29]. Some samples of herbal raw materials have been reported to contain aflatoxin. The reference determined the incidence of toxigenic fungi and their mycotoxins on 152 dried medicinal and aromatic herbs from Argentina, which are used as raw material for drugs [72]. *A. flavus* and *A. parasiticus* were the predominant species isolated, and high

aflatoxin concentrations were detected. There is a potential risk for mycotoxins contamination, especially during prolonged storage in poorly conditions without temperature and moisture control that usually render medicinal plants more susceptible to moulds growth and mycotoxins production [16, 47, 48]. The reduction of plant enzyme activity and inactivation of microorganisms is achieved by drying. Dried plant materials tend to be hygroscopic (readily absorbing moisture) and must be stored under controlled humidity. Rehydration can lead to the decomposition of the bioactive metabolites by enzymes from microorganisms or the plant itself. Significant contamination by bacteria and fungi suggests inadequate storage facilities and poor hygienic practice during preparation of these medicinal plants. The storage processes of such products are stages during which it is important to avoid even further contamination [37]. Studies on long-term stability of dried herbal teas and preparations are rare. A study examined the deterioration of herbal drug samples which were stored for 6-9 months by traders after collection [48]. Some of the contaminated materials were found to be deteriorated by toxigenic strains of A. flavus and contain aflatoxin B1 which was above the permissible limit. In a study of dried P. lanceolata leaves were exposed to atmospheres of different relative humidity (75, 45 and 0%) for 24 weeks and was evaluated the chemical changes of the compounds of interest [37]. It was shown that exposure to water results in loss of bioactive molecules of P. lanceolata dried leaves, and that colonizing fungi are the key contributors to this loss. The fungal deterioration adversely affects the chemical composition of the raw materials and thereby decreases the medicinal potency of herbal drugs. Biodeterioration of herbal products samples by associated fungi during storage has drawn attention regarding quality maintenance of these products [52, 37, 75]. It is common practice for herbalists to prepare herbal medicines and store them in a refrigerator. However, in previous study the effect of microbial contaminants on active compounds of African plant extracts was assessed and indicated that after 25 days of storage in low temperature there may be little or no active compounds due to spontaneous biodegradation by naturally occurring microbes [2]. Similarly, if (HMP) is stored at favourable temperatures for bacterial growth, pathogens are likely to grow. The World Health Organization (WHO) recommends that whenever required and when possible, fresh medicinal plant materials should be stored at appropriate low temperatures, ideally at 2-8°C; frozen products should be stored at less than -20°C. Processed medicinal plant materials should be packaged as quickly as possible to prevent deterioration of the product and to protect against unnecessary exposure to potential pest attacks and other sources of contamination.

5. Absence of quality

There are many ways in which medicines can be of poor-quality e.g: Low medicinal content, Poor formulation and Containing impurities, intermediary compounds, or isomers.

The World Health Organization (WHO) addresses the issue through The Medicines Quality Assurance Programme. The program develops norms, guidelines and provides country support. WHO has also set up a Member State Mechanism for substandard and falsified medical products to cover the issue comprehensively? The terminology regarding absence of quality problems with medicinal products has been difficult to comprehend; the terms have partially overlapped and have been used differently in different countries or settings. In the international debate, this has caused confusion and hindered progress as it also often addressed counterfeit medicinal products that infringe on intellectual property in parallel to the quality issues. As a result, the following terminology has adopted by WHO for quality related problems with medicinal products.

A. Substandard Medical Products. Any authorized medical products that do not meet quality standards or specifications or both also called “out of specification”

B. Unregistered/Unlicensed Medical Products. Any products that have not been evaluated and/ or approved by the regulatory authorities for the market in which they are marketed, distributed, or used.

C. Falsified Medical Products. Any product that are deliberately or fraudulently misrepresent their identity, composition, or source. Additionally, a category of degraded medical products defines medicines of poor quality because of exposure of good-quality medicines to light, heat, and humidity, as described in the WHO good distribution practices guidelines. It can be difficult to distinguish degraded medicines from those that left the factory as substandard, but the distinction is important as the causes and countermeasures are different. We use the term poor quality antibiotics to encompass all quality-related problems and strictly refrain from involving intellectual property considerations when discussing quality of antibiotic products.

It is often difficult to prove causal relationships between poor quality antibiotics and immediate health outcomes in countries without functional surveillance systems. The effects often do not manifest immediately, and confounding factors make it difficult to identify causality correctly. However, the predictable consequences of poor-quality antibiotics are treatment failure, prolonged illness, greater risk of complications and adverse drug reactions, and

increased rates of morbidity and mortality. For end users, therapeutic failure is often the only indication of poor-quality medicines.

Fragmented health services and lack of access to quality-assured medicines at an affordable price often led patients to take incomplete courses of treatment and may also increase exposure to medicines with illicit origin. All these not only endanger patient safety, but consequently also risk loss of patients' trust in the health care system.

Poor quality antibiotics can lead to resistance. In addition, poor quality antibiotics may lead to lower, sub inhibitory concentrations of the active pharmaceutical ingredient. Too low antibiotic concentrations can in turn lead to treatment failure and may also fuel resistance development. If the antibiotic concentration is lower than what is needed to kill or inhibit growth of bacteria, there may be room for resistance to develop and be selected, as has been observed in *Mycobacterium tuberculosis* as well as in other bacteria.

5.1. Problems

Many countries have weak or no quality assurance systems for medicines due to limited resources of Medicines Regulatory Authorities and lack of qualified personnel. Also, despite a significant proportion of countries' health expenditures going towards medicines procurement, there are usually no harmonized quality assurance systems for the procurement organizations involved. But substandard and falsified medicines are not only a problem for low- and middle-income countries, they are found also in high-income countries with developed regulatory systems. It is also not only a problem in human medicine: Veterinary medicine suffers from the problem in the same way as humans, and the consequences are the same.

According to the WHO Global Surveillance and Monitoring System, 17% of the reports to the system were on antibiotics and 20% on antimalarials, making antimicrobial drugs the largest category of falsified and substandard drugs. However, the numbers in the report are expected to be underestimates: many countries have not reported to the system, and even more countries do not have the capacity to find all poor-quality drugs. This is serious, not only due to the concerns of resistance, but also because these drugs are in fact lifesaving.

According to a simultaneously released review of 100 scientific articles, approximately 10% of all medicines sold in low- and middle-income countries are substandard or falsified. A model presented in the article estimating the effect of poor-quality antibiotics on childhood pneumonia states that up to 72000 deaths are attributable to poor quality. In a worst-case scenario, where the antibiotics are assumed to contain no active ingredient at all, the death toll would increase to up to 170000 deaths.

6. Herbal medicinal products research today

The goal of herbal medicinal products research and development program is to discover single entity and multicomponent bioactive natural products that may serve as leads for the development of new pharmaceuticals which address unmet therapeutic needs. Traditional knowledge-driven drug discovery will serve as a powerful search engine and most importantly, will greatly facilitate the focused and safe natural products research to rediscover the drug quality process. There are over 750,000 herbal medicines on earth. Relatively speaking, only a very few of the healing herbs have been studied scientifically. Of these, from the research findings so far, a study reported the presence of *Salmonella species* from drug samples and dietary products [50].

[33] studied 138 medicinal herbal drugs and reported association of several microbial pathogens including *Escherichia. coli, Staphylococcus haureus, Campylobacteria* and *Candida albicans*. They also found several fungi from these samples, which were potent mycotoxins producers. There are several related to production of mycotoxins by various fungal species from different countries.

Another study collected 10 solid and 10 liquid preparations from the markets of South-East Nigeria and evaluated their microbiological quality. The results showed that, the herbal preparations were heavily contaminated with bacteria and fungi at levels far above the limits for oral pharmaceutical preparations. A total of 45 bacterial (including *E. coli, Klebsiella, Citrobacter*, *Proteus, Eubacterium* and *Staphylococcus*) and 20 flora (including fungus, *Microsporium* and *Curvularia*) strains were isolated from the preparations [31].

A study of microbial contamination in herbal medicines: a serious health hazard to elderly consumers. The microorganisms are mostly isolated from the herbal medicines were *S. aureus* (49.2%), followed by *Salmonella spp.*

(34.8%), E. coli (25.8%), and *P. aeruginosa* (14.4%). Of water samples analyzed, 77.8% were positive for total coliforms (1ml) and in 66.7% water samples *E. coli* was detected (1ml), making them unfit for consumption [77].

Another research study assessed the microbial contamination in some herbal solid dosage forms in the city of Meerut, India. 20 herbal products as tablet, capsule and powder were assessed for the microbial contamination as per USP. After the study, the results showed that, the total aerobic count for all the products had more than 1100 microbes per gram. All the samples were contaminated with *Salmonella spp*. and no sample was contaminated with *S. aureus, E. coli, P. aeruginosa* and *Candida albicans* [38]

Evaluated the microbial contamination in the herbal medicines in Bangladesh by comparing the pathogenic load with microbiological standards mentioned in the British Pharmacopoeia. Out of 85 oral-liquid samples, 2 were detected with high contamination of total aerobic bacterial count of 1.24×10^5 CFU/ml. Fungi was detected in 10 samples (1.2×10^4, 6.3×10^4 CFU/ml) [57]. Contamination by coliforms was shown by one sample. *Salmonella spp.* and *Shigella spp.* were absent in all the samples. Out of 40 semi-solid samples, one sample indicated contamination with bacteria (1.93×105 CFU/gm) and 5 samples were detected for fungi ranging from 1.5×104-2.2×104 CFU/gm [58]. It studied the evaluation of Pharmaceutical and Microbial Qualities of Some Herbal Medicinal Products in Southwestern Nigeria. The microbial load of the products varied considerably. Ten (47.6%) of the samples were contaminated by *E. coli,* seven (33%) were contaminated by *Salmonella*, fifteen (71.4%) were contaminated by *Staphylococcus aureus* and twelve (57.1%) were contaminated by fungi.

A study has showed the prevalence of antibiotic resistant bacteria in twenty-nine herbal supplements purchased from local stores in the USA [14]. They isolated the following resistant species: *Bacillus spp., Erwinia spp., Ewingella americana, Staphylococcus spp., Enterobacter cloacae,* and *Stenotrophomonas maltophilia*. The prevalence of antibiotic resistance was high to ampicillin, nalidixic acid, trimethoprim, ceftriaxone, and streptomycin. Opportunistic microbial species (bacteria and moulds) in teas can cause infection and pose a threat to immunosuppressed patients, especially those with AIDS.

Microbial contamination of herbal medicinal products may result from improper handling during production and packaging, which can lead to impaired performance of the products due to disruption of the stability of the formulation, modification of physical characteristics and appearance and lead to inactivation of the active ingredients and excipients in the formulation and cause loss of confidence in the company.

The active ingredients of HMPs are herbal substances and/or herbal preparations derived from herbal substances. Being of natural origin, the active ingredients in HMPs tend to have higher microbial contamination than chemically defined active substances and the microbial population present may differ qualitatively and quantitatively. Therefore, particular attention should be paid to the microbiological quality of HMPs. The European Pharmacopoeia (Ph. Eur.) recognizes the need to allow wider acceptance criteria for the microbial quality of HMPs depending on the nature of the product and method of preparation e.g., herbal teas. propose that contamination should be avoided and controlled through quality assurance measures such as good agricultural and collection practices (GACP) for medicinal plants, and good manufacturing practices (GMP) for herbal medicines. Today, only a small percentage of medicinal plants are collected from the wild, and there are too few data to compare microbial contamination between wild and cultivated medicinal herbs. Guidelines such as the GACP and GMP aim at reducing the overall risk of contamination, not only biological. Aligned Pharmacopoeia chapters have been published on microbial limits or absence of specified microorganisms in herbal medicines [32].

Total aerobic microbial count and total yeast and mould count (presented as colony-forming units per gram or milliliter (cfu g-1 or cfu ml-1) of herbal medicinal products or dosage forms), WHO procedures have drawn the following specifications for products for oral use: 10^4 aerobic bacteria/g or ml, 10^2 fungi/g and absence of *Salmonella spp*, *Shigella spp*, *E. coli* and *S. aureus.* (Or limited count) and Gram-negative bacteria species tolerant to bile have been used as indicators of microbiological quality [32]. Table 1 shows the limits for different categories of microbiological quality of herbal medicinal products. Category A herbal medicinal products, which contain herbal drugs with or without excipients and are intended for preparation of infusions or decoctions with boiling water. This category includes traditionally brewed tea. Category B includes extracts and/or herbal drugs pre-treated to reduce microbial contamination. If pre-treatment (processing or extraction with low strength alcohol or non-boiling water) does not meet Category B criteria of decontamination, the products fall in Category C (see Table1).

Table 1 Recommended microbial contamination limits for finished herbal medicinal products (values in CFU/g)

Contaminants	USA	EU	WHO	Brazilian
Aerobic bacteria	105/104/102	107/105	*/107/105	107/105/104
Mould and yeast	103/102/10	105/104	105/104/103	104/103/102
Enterobacteria and other Gram-negative bacteria	103/*/*	*/103	*/104/103	104/103/102
E. coli	Absent	103/absent	104/102/10	Absent
Salmonella sp.	Absent	*/absent	*/absent/absent	Absent

Key: * - Limits are not specified, Category A/B/C or value respectively

Microbial count is just one of medicinal herb quality indicators. All products must be clear of true bacterial pathogens such as *Salmonella spp.* and *Shigella spp*. Microbial Contamination of medicinal herbs and herbal products with bacterial strains resistant to known antibiotics poses a particular health risk of inducing infectious diseases or other unwanted effects in patients taking the HMP. Such micro-organisms should not be present in the HMP.

7. The way forward for assurance of quality, safety, and efficacy of herbal medicinal products

The way forward to achieve these quality, safety and efficacy of herbal medicinal products is very necessary because, In Nigeria, herbal practitioners have capitalized on the poor health conditions of the masses and high cost of synthetic orthodox medicine by organizing herbal trade fare indiscriminately. The probability of a patient on herbal remedies contracting more deadly diseases cannot be totally ruled out considering the unhygienic and crude method of production and storage.

7.1. Herbal education

Herbal education should be introduced into the curricular of medical students in the inventory, so that the students will learn the two (Orthodox and Herbal medicine) to make it more acceptable to the society both locally and internationally, also that people should be told about local herbal medicinal remedies by helping them to identify the various herbs and plants that are used for the treatment of common diseases. Due to inherent variations of microbial contaminants in the concentrations of active constituents, which sometimes make it difficult to establish how effective herbal medicines are, a lot of skeptics have been associated with the use of herbal medicine. These observations, and others, bring therefore the need for standardization of herbal medicines. Without standardization, herbal medicines, as they are now prepared in Nigeria, are likely to contain high levels of contaminants. Standardization should begin with cultivation of medicinal plants, and herbal medicine manufacturers should encourage using cultivated medicinal plant raw materials in the production of their medicines. Quality needs to be maintained for betterment of the consumers. This can be done by improving preprocessing and post processing techniques. Government should set a strict quality control unit so that the local herbal medicine practitioners can be continual training and inspection of plant harvesting/ collection, simple hygiene, general health concept, health education, elementary healthcare, referrals and record keeping; so that they can contribute their quota towards the attainment of the goal of health at all levels in order to control microbiological hazards that may be influenced by current and changing aquaculture, agronomic, processing, distribution and storage practices. One of the important measures in this regard is to create awareness among the public regarding how to check the quality of packed herbal medicinal products before consumption. The excessive microbial contamination of the drugs might increase health hazard to consumers rather than curing illnesses. Finally, the government should enforce the policy on local content patronage and consumption in the herbal medicine industry in the country, as this will go a long way in protecting local herbal medicine industry from the fierce competition presented by the advanced herbal systems, which are currently holdings way in the country.

7.2. Research future based on herbal medicinal products

Government should encourage and finance research into our local herbs to find cure to diseases that have developed resistance to orthodox medicine, and this may also eliminate doubts and establish confidence in the minds of people about the efficacy of local herbal medicine and the role it plays in the society.

The research on the medicinal plants should be extended with the identification of the active principles in the plants. Scientific examination of the remedies could lead to standardization and quality control of the products to ensure their

safety. It is after such evaluations that they can be approved for use in the primary health care. Such research activities could also lead to the development of new drugs.

Basic research programmers on herbal medicinal products should be focused on the contaminants and efficacy relationship for those potent poisonous herbal substances according to the principles as practiced in Chinese medicine with doses applied for composite formulae.

To overcome those environmental factors that are related to contaminations from contaminated air, microbes of human origin there should be control measures to implement necessary standard operating procedures (SOP) for good application practice (GAP) and (GMP) good manufacturing practice are also needed to produce good quality medicinal products from herbs or natural source.

Due to the particular concern of contaminants, poor quality and adulteration of ready-made herbal medicinal products in the market the priority of research on product-related treatment in particular herbal products, is to ensure QSE of the end products used by consumers. Herbal preparations in the developing countries are produced through unhygienic conditions. Many contaminants or residues that may cause harm to have been reported, many are natural such as naturally occurring radioxides, toxic metals, bacteria, and fungi. The growing, harvesting and manipulating methods usually applied cannot avoid microbial contamination of the plant material which therefore reflects the environmental conditions as well as the specific hygiene during the diverse treatments [46]. For most cases, the biological contamination refers to impurities in medicinal herbs their preparations and products and may involve living microbes such as bacteria their spores, yeasts and moulds, viruses, protozoa, insects which is either too harmful or with no therapeutic activities. Most herbal medicines are used in the form of an aqueous decoction. Therefore, research projects should be centered on development of analytical and biological procedures for the use, to give the quality assurance and control, and clinical assessment of efficacy and safety of these products. Government should introduce harsher penalties for manufacturers who make misleading or false claims

7.3. Regulatory aspect

In Nigeria or other ethnic herbal medicinal products when supplied, as medications, should be regulated for quality, safety and for appropriate evidence of efficacy. It advocates the establishment of a new category of licensed herbal medicines, prepared in accordance with current Good Manufacturing Practices (cGMPs), which meet standards of quality and safety, and which are regulated by local government health department that should have reciprocating arrangements with organization such as the Medicines Control Agency in the UK, Food and Drug Administration in the USA and those in the European Union.

The licensing requirements in this new category (i.e., herbal medicines) may not be as demanding as those currently apply to licensed medicines. Specifically, "the level of proof'' of activity may not need to be as high as for allopathic medicines. Efficacy may be accepted based on documentation of traditional use over a long period, as suggested by WHO.

Safety may deem to have been demonstrated by virtue of traditional use. However, these products ought to be required to substantiate a history of safe use, preferably in the European Union (EU) for dosage and indications for treatment to be approved, and the license should clearly indicate the inappropriate conditions of use (contraindications). It would be dangerous to agree product safety as the basic, default position. In addition, the "test of time'' criterion detects common acute adverse events, but not rare adverse events or those with a long latency. Also, today's users of herbal medicines may differ from those in earlier eras.

The governmental departments in Nigeria, such as National Agency for Food and Drugs Administration Control (NAFDAC), should issue regulations and registration guidelines and procedures for Nigeria herbal medicinal products. Consultation with these guidelines will help to set up regulations in Nigeria for herbal medicinal products. Consultation of the commission European structure from Germany will also help to formulate Regulation Guidelines for herbal products as medicines. Appropriate regulations may help to sort out problems on the quality assurance and control issues.

8. Conclusion

Since the long history of use of herbal medicinal products cross-culturally demonstrates their importance to consumers. Satisfactory quality of HMPs with respect to microbiological and mycotoxin contamination cannot merely be controlled by final testing; it should be built-in the entire process, from starting material to finished product. Minimizing and

testing/monitoring of microbial contamination and mycotoxins in herbal substances, herbal preparations and herbal medicinal products must be based on a case-by case risk assessment. The Therapeutic Good Administration (TGA) should require independent testing of herbal medicines before placing them on market, and legal action should be considered when products did not comply with regulations. The products should also be closely monitored once on the market. To gain public trust and to bring herbal product in Nigeria into mainstream of today's health care system, the researchers, the manufacturers, and the regulatory agencies must apply rigorous scientific methodologies to ensure these HMPs standard.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they share no conflict of interest.

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