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### An Outlook Towards the Microbial Quality of Marketed Herbal Medicinal Formulations

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#### ABSTRACT

According to World Health Organization, 70-80% of the world's population depends on the herbal medicines for their primary health care. 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 chiefly responsible for the deterioration of the herbal products are the microbes. They exert a bad impact on the overall quality and shelf life of the herbal products. Thus, evaluation techniques for contamination should be pointed out at every manufacturing step to assess the microbial contamination level on crude drug.

**Keywords:** Contamination, Evaluation techniques, Herbal medicines, Microbes, Plant materials.

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## INTRODUCTION

The occurrence of infectious and non-infectious diseases among human population across the world is increasing day by day since many decades. The data available regarding these diseases suggests that the infectious diseases are transmitted from person to person by direct or indirect contact. Certain types of viruses, bacteria, parasites and fungi can cause various infectious diseases. Malaria, measles and respiratory infections are the examples of infectious diseases. Non-infectious diseases are not caused by the infectious agents and these diseases last for longer periods of time and develop slowly. Diabetes, Alzheimer's, cancer, osteoporosis, cardiovascular diseases are the examples of non-infectious diseases. Non-infectious diseases are the chief cause of deaths, worldwide. The increase in the incidences of infectious and non-infectious diseases is also due to the lifestyle changes, human behaviour etc.

With the advancement in the medical field, many treatment options like Allopathy, Ayurveda, Siddha, Unani, Amchi and folk medicine are available to cure these diseases by various means or routes of administration.

### **Allopathy System of Medicine:**

Allopathic System of Medicine is the most commonly adopted treatment option to cure these diseases, due to its symptomatic relief. An allopathic treatment aims to fight these diseases by using remedies, such as drugs or surgery to defeat the effects of diseases. But, allopathic treatment carries various drawbacks such as-

- i) Synthetic drugs can cause various adverse drug reactions (ADRs),
- ii) Higher costs,
- iii) Compatibility issues of synthetic drugs with human body,
- iv) Drug resistance,
- v) Drug dependence etc. [1]

### **Ayurvedic System of Medicine:**

Ayurvedic System of Medicine is indigenous to India. The term 'Ayurveda' comprises of two Sanskrit words, 'Ayu' means 'life' and 'veda' means 'knowledge'. [2] It is defined as the science, through which one can obtain knowledge about useful and harmful ways of life, happy and miserable types of life, as well as, the very nature of life. [3] Since many years, Ayurveda has been helping the people to cure the diseases, in which the allopathic treatment has failed to show the desired results.

### **Siddha System of Medicine:**

Siddha System of Medicine is one of the oldest systems of medicine in India, which is originated in South India. Siddha medicine represents the fundamental nature of Ayurveda (plant extracts), Unani, Acupressure (sensitive points), Reiki (energy field), etc. in the theories of Siddha medicine. Chanting of *mantra* during the preparation of medicines and utilization of plant extracts and metal oxides are involved in the Siddha System of Medicine. [4]

#### **Unani System of Medicine:**

Unani System of Medicine is the mixture of current traditional medicinal system in Egypt, Syria, Iran, Iraq, China, India and various other East countries. According to Unani System of Medicine, management of any disease depends upon diagnosis of disease. [5]

#### **Amchi System of Medicine:**

Amchi or Sowa-Rigpa System of Medicine is an earliest well-renowned traditional medicinal system, which was accepted in Tibet, Mongolia, Nepal, Bhutan, Himalayan region of India, some parts of China and former Soviet Union. The practice of Amchi System of Medicine is somewhat similar to Ayurvedic System of Medicine. [6]

#### **Folk Medicine:**

Folk drugs may well be outlined because the entire processes and practices adopted by the general public so as to spot and cure varied diseases with their own efforts. Folk medicine plays significant role in the maintenance of health and curing diseases in large number of people residing in rural or tribal communities. Folk medicine uses herbs and other remedies based on traditional beliefs. Near about, 8,000 plant species are employed in folk medicines and around 25,000 efficient plant-based formulations are utilized by rural and tribal communities of India. [7] Although, there is an availability of treatments like Allopathy, Siddha, Unani, Amchi and folk medicine, Indian population is much attracted towards Ayurveda due to following reasons-

- a. Minimum possibility of adverse effects,
- b. Lower costs,
- c. Easy availability,
- d. Well-acceptability by human body,
- e. Helpful in patients with chronic or incurable diseases like arthritis, diabetes, cancer or AIDS. [2]

Ayurvedic medicines involve the use of herbs for the treatment of various diseases. These herbs are further employed in the formulation of various herbal products.

With restricted oversight and robust advertising, several seasoning merchandise have created their approach into pharmacies and health retailers and into patients' self-prescribed medical care. Most

patients receive their data concerning herbs and supplements from sources aside from their attention supplier. Being natural merchandise, patients incorrectly believe they're continually safe, others worry that attention professionals could have negative attitudes towards their use and don't report mistreatment of such remedies to avoid confrontations. All healthful agents have doubtless sudden effects together with toxicity, and herbs aren't any totally different. As with other drugs, the risk of unexpected effects may be influenced by a user's age, genetics, nutrition status, gender, and concurrent disease states and treatments. In clinical observe, recognizing adverse effects of seasoning drugs isn't routine and their news is even less frequent. [8]

According to World Health Organization (WHO), Herbal Medicinal Products (HMPs) are defined as, medicinal products containing as active substances exclusively herbal drugs or herbal drug preparations. They may contain seasoning preparations made of one or a lot of herbs. If over one herb is employed, the term 'mixed seasoning product' may also be used. They'll contain excipients additionally to the active ingredients. In some countries, seasoning medicines might contain by tradition, natural organic or inorganic active ingredients, that don't seem to be of plant origin (e.g. animal materials and mineral materials). typically but, finished product or mixed product to that with chemicals outlined active substances are further, as well as artificial compounds and/or isolated constituents from seasoning materials, don't seem to be thought-about to be herbal. [9]

#### NEED TO LOOKOUT TOWARDS THE MICROBIAL QUALITY OF HERBAL MEDICINAL PRODUCTS:

Although, flavoring merchandise became progressively standard throughout the globe, one in every of the impediments in its acceptance is that the lack of normal internal control profile. The quality of flavoring medication, that is, the profile of the constituents within the final product has implications in effectualness and safety. However, owing to the complex nature and inherent variability of the constituents of plant-based drugs, it is difficult to establish quality control parameters. The methods of harvesting, drying, storage, transportation, and processing (e.g. mode of extraction and polarity of the extracting solvent and instability of constituents) also affect herbal quality. [10] In almost all the Traditional System of Medicine, the quality control aspect has been considered from its inspection of its *Rishis*, *Vaidyas* and *Hakims*. Unlike in ancient times, where traditional practitioners prepared and tested the qualities of herbal medicines, the problems faced today are of economics of industrial scale production, shelf life and distribution to long distances. These have necessitated development of contemporary and objective standards for evaluating the security, quality and efficacy of these medicines. People also are turning into awake to the

efficiency and aspect result. To gain public trust and to bring herbal product into mainstream of today's health care system, the researchers, the manufacturers and the regulatory agencies must apply rigorous scientific methodologies to ensure the standard and lot-to-lot consistency of the normal flavoring merchandise. [11]

#### INTERNATIONAL MARKET SCENARIO OF HERBAL MEDICINAL PRODUCTS:

According to World Health Organization (WHO), about 80% population of developing countries like Africa, Asia, and Latin America etc. still depends on the traditional herbal medicines for their primary health care. Revenue of herbal medicines in developed countries like United States of America (USA), Canada, Europe and Australia was approximately US\$ 30 million in the year 2000, which was increased by 5-15% for the last decade. The annual retail sale of botanical products in USA had been increased from US\$ 200 million in 1988 to US\$ 5.1 billion in 1997. The botanical sale in USA was US\$ 14 billion in 2009 and by 2050; it had been estimated to increase by US\$ 5 trillion. It was predicted that herbal use had been increased by 380% between 1990 and 1997, in the United States alone. Likewise, industry demand for herbal products was also increased due to emergence of new products like hygiene products, health foods and natural cosmetics. Overall, international trade in medicinal plants and their products was US\$ 60 billion in 2000, with average annual growth rate of 7% and is expected to increase to US\$ 5 trillion by 2050. Current value sales within the US herbal products market grew by 3% through 2012, reaching a value of US\$ 4.4 billion in 2012. [12]

Medicinal plants contain a wide range of micro-organisms and thus, they put forward a major impact on the overall quality of the herbal products. Many herbal products are failing to compete in the International market due to high microbial load, as plant materials are extremely prone to microbial contamination. [13]

#### INDIAN MARKET SCENARIO OF HERBAL MEDICINAL PRODUCTS:

Kamboj VP, in the year 2000, studied that, the revenue of herbal products in India as over-the-counter (OTC) products, ethical and traditional formulations and home remedies of Ayurveda, Siddha and Unani Systems of Medicine is about \$1 billion with an inadequate export of \$80 million. [14]

Sharma A, in the year 2008, studied that, the consumption of herbal products is increasing day by day and the market is on the rise step by step. The turnover of Indian herbal medicinal industry is about Rs. 2,300 crores as against the turnover of pharmaceutical industry of Rs. 14,500 crores with a growth rate of 15% per annum. [15]

Aneesh TP, in the year 2009, studied that, India ranks third in the category of herbal medicine with less than 2% of the worldwide market share and thus, India lags behind as compared to other countries. The chief reason for this lesser market share may be the poor quality of herbal materials or due to the differences in the quality control procedures, methods of production and evaluation of herbal products. [16]

#### 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. [13]

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”. [17] Introduction of micro organisms 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. [18]

The sources of contamination in the herbal medicinal products are as follows-

- i) Environmental conditions in which the medicinal plants are grown or collected.
- ii) Drying and processing conditions of the herbal medicinal products.
- iii) The conditions under which the herbal medicinal products are stored and transported.
- iv) Insanitary utilization of herbal medicinal products by the patients.
- v) The manufacturing procedures, when the ready-made herbal medicinal products are prepared. [19]

#### HARMFUL EFFECTS OF MICROBIAL CONTAMINATION OF HERBAL MEDICINAL PRODUCTS:

The demand for the herbal products, due to their extensive applications is increasing day by day, not only in the developing countries, but also in the developed countries. Besides, the contaminated herbal products, which are commonly used by the people, have become the public health issue. Various contaminants like pesticides, toxic metals, micro-organisms etc. may be associated with the herbal products. The micro-organisms mainly present in the herbal products are *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*), *Salmonella typhi* (*S. typhi*), *Pseudomonas aeruginosa* (*P. aeruginosa*) etc. When herbal products contaminated with these micro-organisms are consumed by the people, they can cause serious health issues.

The genus, *Escherichia* was named after the German paediatrician, Theodor Escherich, consisting facultative anaerobic Gram-negative bacilli, belonging to the family, Enterobacteriaceae. *E. coli* 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, a number of pathogenic strains can cause intestinal and extra-intestinal diseases, both in healthy as well as immunologically-weak individuals. [20] 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*. In some cases, peritonitis, mastitis, Gram-negative pneumonia, septicaemia and haemolytic-uremic syndrome is also caused by virulent strains of *E. coli*.

The first description of “micrococci” isolated from furuncles and abscesses was provided by Sir Alexander Ogston and Louis Pasteur in 1880. *Staphylococcus aureus* is originated from the Greek words, ‘Staphyle’ means ‘bunch of grapes’, ‘coccus’ means ‘round-shaped’ and ‘aureus’ means ‘golden’, as most of the colonies on the agar plates show characteristic orange-yellow colour, indicating the presence of *S. aureus*. *S. aureus* have the capability of growing in the temperatures ranging between 7°-48.5°C with an optimum growth temperature of 30°-37°C. Thus, alteration in the temperatures during storage of the herbal medicinal products may result in the production of *S. aureus* in them. *S. aureus* can also develop in a wide range of pH ranging 4.2-9.3 with an optimum pH of 7-7.5. Hence, alteration in the pH during manufacturing of the herbal medicinal products may lead to the growth of *S. aureus* in them. *S. aureus* is an adaptable pathogen, causing a large number of diseases from localised skin and soft-tissue infections to life-threatening septicaemia. *S. aureus* can also cause blood stream infections. [21]

*Salmonella* infection may be a common microorganism malady that affects the enteric tract. *Salmonella* normally exists in the animal and human intestines. Usually, *Salmonella* infection is not life-threatening but, if the *Salmonella* infection spreads beyond the intestines, the life-

threatening complications may develop. The development of complications can be more dangerous, especially in infants, older people, young children, pregnant women, transplant recipients and immunologically-weak people. [22]

*Pseudomonas* is a tremendously versatile Gram-negative bacterium with an ability of flourishing in the broad spectrum of environments. *Pseudomonas aeruginosa* can cause urinary tract infections, respiratory tract infections, bacteraemia, dermatitis, bone and joint infections, soft tissue infections, GI infections etc. [23]

#### REGULATORY GUIDELINES TO CONTROL MICROBIAL CONTAMINATION OF HERBAL MEDICINAL PRODUCTS:

The number of patients pursuing the herbal therapy is increasing very rapidly. But, the fact of negligibility of the regulatory guidelines for the herbal products cannot be denied, as the recent observations indicate that, the herbal products produce severe health issues, when consumed by the people. Most of the herbal products in the market today had not gone through the drug approval process. According to several case reports, corticosteroids, lead, mercury, arsenic, poisonous organic substances and micro-organisms were found in unsafe amounts in the herbal medicinal products. Most of the commercially available herbal products do not even comply with the preliminary regulations of the ancient Ayurvedic texts. Many of the herbal products do not even hold an expiry date and the possible adverse effects on their label.

There is no assurance that, the container carrying the herbal formulation is the same as what is mentioned on the label, due to the lack of quality control procedures. The name of many reputed and important herbal formulations is at stake, due to the prevalent negligibility and conscious carelessness towards quality control process in the manufacturing industries of the herbal products. Hence, it is high time to set up the internationally distinguished and stringent guidelines for assessing the microbial quality of the herbal products. The World Health Assembly (WHA, a forum of WHO), the world's highest health policy setting agency comprised of health ministers from 194 member nations- in its resolutions WHA 31.33 (1978), WHA 40.33 (1987) and WHA 42.43 (1989) has stressed the necessity to confirm the standard of the seasoner merchandise by using fashionable management techniques and applying appropriate International standards. [24]

In India, traditional medicines are ruled by Drugs and Cosmetics Act, 1940 and Drugs and Cosmetics Act rules of 1945. They govern the import, manufacturing, distribution and sale of drugs and cosmetics. The Indian Government recognized the traditional systems of medicine and revised the Drugs and Cosmetics Act to include drugs which are obtained from traditional Indian

medicine. No products obtained from traditional systems may be manufactured without a license from the State Drug Control Authorities. Patent and proprietary medicines obtained from traditional systems must comprise ingredients, mentioned in the recognized books of the above systems, as stated in the Drugs and Cosmetics Act. [25]

Herbal products represent a serious share of all the formally recognized systems of health in India, namely, Ayurveda, Yoga, Unani, Siddha, homoeopathy and treatment, except medical aid. The herbal medicines in India are regulated by IMCC (Central Council of Indian Medicine) Act, Research Councils (ICMR and CSIR), Department of AYUSH (Ayurveda, Yoga, Unani, Siddha, Homeopathy and Naturopathy) and Drugs and Cosmetics Act (Amendment). Herbal remedies and medicinal plants to be incorporated in the modern system (allopathic) must follow the regulations of Drug Controller General of India (DCGI). [26]

Several case reports suggested that, the only way to maintain the quality, efficacy and safety of the herbal medicinal products is to follow the Good Manufacturing Practices and suitable preclinical tests. [24]

**Table 1: WHO limits for microbial contamination in finished herbal products**

Sr. No.	Micro-organisms	WHO limits for finished product
1.	<i>E. coli</i>	10 <sup>1</sup> CFU/gm
2.	<i>S. aureus</i>	10 <sup>5</sup> CFU/gm
3.	<i>P. aeruginosa</i>	10 <sup>3</sup> CFU/gm
4.	<i>Salmonella</i> spp.	Nil

#### RESEARCH WORK DONE SO FAR FOR MICROBIAL QUALITY ASPECTS OF HERBAL MEDICINAL PRODUCTS:

Due to several case reports of the microbial contamination in the herbal medicinal products, tremendous researches of the same are being performed throughout the world. Few of them are discussed below-

1. Esimone CO (2001) collected 10 solid and 10 liquid preparations from the markets of South-East Nigeria to evaluate 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*, bacteria genus, *Proteus*, *eubacterium* and *Staphylococcus*) and 20 flora (including fungus, *Microsporium* and *Curvularia*) strains were isolated from the preparations. [28]
2. Chomnawang MT (2003) with an aim of evaluating microbiological quality of herbal products in Thailand collected 57 non-registered herbal products from all over the country and examined the microbial contents in the herbal products as suggested in the Thai Pharmacopoeia.

Out of which, 50 samples did not comply with Thai Pharmacopoeial standards, due to unacceptable amount of Total aerobic bacteria (6 samples), yeasts and molds (10 samples), *E. coli* (11 samples), *S. aureus* (45 samples), *Salmonella* spp. (12 samples) and *Clostridium* spp. (18 samples). This data suggested that, the herbal products available in Thai markets need an urgent and serious action in the improvement of the quality of the herbal products. [29]

3. Abba D (2009) evaluated the contamination of herbal medicinal products marketed in Kaduna metropolis with selected pathogenic bacteria. After the study, the results showed that, out of 150 samples, 70 (46.67%), of the herbal products were contaminated with *S. typhi*, 29 (19.33%) with *Shigella* spp. 88 (58.67%) with *E. coli* and 98 (65.33%) with *S. aureus*. The results of total aerobic plate count showed that, the highest average count of  $5 \times 10^7$  Colony Forming Units per gram (CFU/gm) was found in 89 (59.33%) of the products, while, average plate count of  $\leq 5 \times 10^7$  CFU/gm was found in 42 (28%) and no bacterial count was found in 19 (12.67%) of the products. [30]

4. Enayatifard R (2010) scrutinized the microbial quality of some herbal solid dosage forms marketed in the city of Sari, Iran. All the products had more than 1100 micro-organisms per gram was indicated by total aerobic count. *S. aureus*, *P. aeruginosa*, *E. coli* and *Candida albicans* were not found in any samples, but all the samples were contaminated with *Salmonella* spp. [31]

5. Kalaiselvan V (2010) evaluated five different brands of Dasamoolaristam available in the market as per WHO and Indian Pharmacopoeial specifications. The preparations were found to contain unacceptable limits of microbial load, although all showed the absence of *Escherichia coli*, *Salmonella* species, and *Staphylococcus aureus*. [32]

6. Odonkor ST (2011) evaluated the microbiological quality of some herbal medicinal products sold in Accra, Ghana by collecting 10 different herbal medicinal products and performing the microbial count on the products. Isolation and identification of various micro-organisms from the herbal medicinal products were also carried out. After the study, the results showed that, the lowest microbial count was  $2.2 \times 10^3$  CFU/ml and the highest microbial count was  $6.2 \times 10^3$  CFU/ml. No bacterial growth was observed in two (20%) of the products. The predominant organism isolated was *Staphylococcus aureus* and *Bacillus* spp. Fungi was isolated from only one sample. However, *E. coli*, *Klebsiella* spp. and *Salmonella* spp. were absent in all the 10 samples. [33]

7. Bais SK (2012) with an aim of evaluating the microbiological quality of Antidiabetic Churna of various brands marketed in India and examining the microbial contents as per WHO, collected 10 herbal products, out of which 3 samples did not confirm to WHO guidelines. The

- results showed the presence of *E. coli*, in 5 samples, *S. aureus* in 3 samples and *P. aeruginosa* in 4 samples. [27]
8. Gupta DK (2012) 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*. [34]
9. Noor R (2013) 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  $1.24 \times 10^5$  CFU/ml. Fungi was detected in 10 samples ( $1.2 \times 10^4$ - $6.3 \times 10^4$  CFU/ml). 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 ( $1.93 \times 10^5$  CFU/gm) and 5 samples were detected for fungi ranging from  $1.5 \times 10^4$ - $2.2 \times 10^4$  CFU/gm. [35]
10. Onyambu MO (2013) evaluated the microbial quality of unregulated herbal medicinal products in Kenya and thus, collected 30 samples of registered and unregistered herbal medicinal products. The study indicated that, all registered products carried microbial load below 100 CFU/ml, complying with BP and United States Pharmacopoeia (USP). Besides, the unregistered samples carried microbial load ranging from  $3 \times 10^6$ - $1.56 \times 10^{10}$  CFU/ml, not complying BP or USP requirements. 15 different bacterial genera and 7 fungal genera were isolated from the samples. *E. coli* was detected in 75% of unregistered products, *Klebsiella pneumoniae* in 70%, *Enterobacter aerogenes* in 60% and *S. aureus* in 45% of the samples were found. 40% of the samples were detected with *Salmonella* spp. and 20% of the samples were detected with *Shigella* spp. [36]
11. Osei-Adjei G (2013) with an aim of assessing the quality of aqueous herbal/medicinal products sold on the Ghanaian market, collected decoctions from the Ghanaian market and investigated for their microbial quality. The results showed that, 3 samples were detected with highest microbial counts greater than  $1 \times 10^9$  CFU/ml and 1 sample was contaminated with lowest aerobic bacterial count of  $1 \times 10^2$  CFU/ml. 13 samples were contaminated with fungal contaminations (81.3%). 1 sample was detected with highest fungal contamination of  $3.2 \times 10^5$  CFU/ml. The characterization of isolates revealed 6 bacterial genera and 8 fungal genera with *Bacillus subtilis* (50%) and *Cladosporium herbarum* (34.5%) being predominant bacterial and

fungal isolates, respectively. After 3 months storage, the samples showed the microbial load within acceptable limits and isolates also showed a reduction for *B. subtilis* (23.8%) and *C. herbarum* (14.3%). [37]

12. Bais SK (2014) with an aim of evaluating the microbiological quality of hepatoprotective herbal formulations of various brands marketed in Yavatmal, India and examining the microbial contents as per WHO, collected 10 herbal products, out of which, 3 samples did not confirm to WHO guidelines. The results showed the presence of *E. coli* in 4 samples, *S. aureus* in 3 samples and *P. aeruginosa* in 4 samples. [38]

13. Mahmudul Islam AFM (2014) with an aim of evaluating microbiological profile of some herbal preparations manufactured by pharmaceutical and herbal manufacturers in Bangladesh, collected 30 different herbal medicinal products of various dosage forms. Total viable aerobic bacterial counts in the samples tested, ranged between  $3.8 \times 10^4$ - $3.2 \times 10^8$  CFU/ml or CFU/gm and 36.67% were within British Pharmacopoeial (BP) standard limits. *S. aureus* was found in 53.33% (16) of the samples ranged between as estimated  $3 \times 10^2$ - $9.2 \times 10^6$  CFU/ml or CFU/gm which was above USP standards. *E. coli* was found in 40% (12) of the samples, ranged between  $1 \times 10^2$ - $4.8 \times 10^4$  CFU/ml or CFU/gm that were above USP standards. The fungi counts were ranging between  $3.4 \times 10^3$ - $3.1 \times 10^6$  CFU/ml or CFU/gm and 46.67% of which were within BP standards. [39]

14. Bais SK (2015) with an aim of determining the presence of microbial content in the Ashwagandha formulation of various brands marketed in Yavatmal, India selected the formulations randomly and tested for microbial contamination as per WHO. The data obtained after the study indicated the presence of *E. coli* in 3 samples, *S. aureus* in 4 samples and *P. aeruginosa* in 4 samples. [40]

15. Igbeneghu OA (2016) with an aim of assessing the microbial quality of some oral-liquid herbal medicines marketed in Ile-Ife, South-Western Nigeria collected 50 herbal medicinal samples from selected markets of Ile-Ife. They determined the microbial load of each sample and identified the contaminants associated with each sample. The results after the study indicated that, 90% of the samples carried microbial loads beyond officially permissible limits with presence of *E. coli* and *Salmonella* spp. in 2% and 6% of samples, respectively. The results of this study suggest that, the herbal oral-liquid products available in the markets of Ile-Ife are of unacceptable quality. [41]

16. Keter L (2016) with an aim of evaluating microbial quality of herbal products marketed in Eldoret and Mombasa, Kenya collected the herbal products in the form of powders, liquids, tablets,

oils and capsules. After the study, 90% of the total samples showed the bacterial contamination and those with  $>1000 \times 10^4$  CFU/gm or ml was 20% Eldoret and 46% for Mombasa samples. Only 16% of the herbal product samples met the standards for microbial limits as specified in the Pharmacopoeias. [42]

17. Archibong EJ (2017) assessed the microbiological quality of 60 (20 The National Agency for Food and Drug Administration and Control (NAFDAC) registered and 40 unregistered) liquid herbal medications sold in Awka metropolis, Anambra state, Nigeria. NAFDAC registered samples were detected with total bacterial count of  $1.0 \times 10^3$ - $2.1 \times 10^6$  CFU/ml, total coliform count of  $1 \times 10^3$ - $7.8 \times 10^4$  CFU/ml; *E. coli* count of  $1.0 \times 10^2$ - $2.0 \times 10^2$  CFU/ml and total fungal count of  $1.0 \times 10^2$ - $1.4 \times 10^5$  CFU/ml, while the unregistered samples were detected with total bacterial count of  $3.6 \times 10^3$ - $1.11 \times 10^7$  CFU/ml; total coliform count of  $2.0 \times 10^2$ - $4.4 \times 10^5$  CFU/ml; *E. coli* count of  $2.0 \times 10^2$ - $2.0 \times 10^6$  CFU/ml. According to the results obtained, 70% of the registered samples met the WHO standards, while 28% of the unregistered samples met the WHO standards. Isolates obtained from both registered and unregistered samples includes *E. coli* (21.6%), *Enterobacter asburiae* (25%), *Providencia rettgeri* (13.3%), *Acinetobacter baumannii* (11.6%), *Staphylococcus* spp. (16.6%), *Bacillus* spp. (10%), *Scedosporium aurantiacum* (5%), *Candida albicans* (28.3%) and *Candida krusei* (13.3%). [43]

## CONCLUSION:

Herbal medicinal products are achieving great interest worldwide because of their enormous applications in the treatment of various diseases and disorders. But, it has also been reported that some products are not of standard quality, which has brought up solemn apprehensions about safety and efficacy. Countries including India and International agencies have taken rigorous measures by modifying laws to certify quality, safety and efficacy of herbal medicines. Additional efforts are being made across the world to frame necessitated legislation, develop monographs, publish pharmacopoeias, and improve existing monographs and so on. But, disappointingly the majority of countries do not have their own legislation, monographs, or pharmacopoeia. Some initiatives have already been taken in this arena by quite a few countries and agencies together with WHO, IRCH (International Regulatory Cooperation for Herbal Medicines), EU, and so on. Regardless of such isolated initiatives, it is very important to consider the problems or contaminations related with the cultivation, collection, processing, harvesting, post-harvesting etc. of the medicinal plants, so as to produce a stable herbal medicinal product (i.e. free from contaminants like micro-organisms, toxic metals etc). According to several studied case reports,

applying Good Manufacturing Practices (GMPs) to all the manufacturing processes of herbal medicinal products is very important to produce a product of quality, safety and efficacy and thus, a proverb, "Prevention is better than cure" can be proved true.

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