Pathogenic Microorganisms, Toxigenic Fungi, Heavy Metal accumulation, and Toxic Materials Contamination in Natural Products

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ABSTRACT

Medicinal Plants still considered as an important part of traditional medicine. They have a long history filled with and use in treatment all through the world. In this way medicinal plants and herbal products must be safe for the patient. This review addresses biological contaminants (microbes and other organisms) and chemical contaminants (mycotoxins, toxic elements such as heavy metals and pesticide residues) regarded as major common contaminants of medicinal herbs and herbal products to prevent contamination and to ensure safety for the infection and to make certain protection and conformity to the quality standard. Herbal products need to be covered in the proper regulatory framework.

INTRODUCTION

Medicinal herbs specifically recognized as being easily and inexpensive available resource for health care. They were an essential part of traditional medicinal practices for thousands of years, 80 % of the world population in most cases is based on traditional medicine, a prime a part of which includes the usage of plant life extracts or their active ingredient. (Akerele, O., 1992) According to the WHO estimates. So because they use in different sectors the commercialization of medicinal plants has been raised with the aid of many folds due to their massive scale such as phytochemicals, pharmaceuticals, nutra-ceutical, herbal remedies, food supplements, perfumes cosmetics and food flavoring other uses furthermore, within agents among the recent beyond, there has been a twofold growth within the cell for medicinal plants in the international market Presently the herbal medicine spread widely, the standardization and quality control of herbal material and the evaluation of their efficacy. According to WHO estimates, the existing demand for medicinal plant life is 14\$ billion every vear. and via the year 2050, it will likely be5\$ trillion. Presently, medicinal herbs are raised in the world because of safetv of using them. The quality of herbal drugs has an immediate impact on their safety and efficacy. One of the primary elements contributing to the bad quality of medicinal herbs is their pollution with pesticides, heavy metals, microbial load, polycyclic aromatic hydrocarbons (PAHs) and other environmental contaminants, such as fumigants (WHO,1998).

Exposure to those contaminants might also have a couple of, cumulative, additive, or synergistic results on human health. Those contaminants can probably intrude with male and female hormones, thereby causing endocrine disruption, infertility, and immune suppressive, carcinogenic, and tetra mutagenic effects. Thus, it is important that herbs and herbal products should be loose from those contaminants or at least managed to prevent their use at a dangerous level (De smet, P.A.G.M., Keller, K, Hansel, R., Chandler, R.F.,1992). With regard to the possible danger that may be caused by the presence of contaminants in herbal materials and medicinal plants, the World Health Organization has published "WHO

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> guidelines for assessing the quality of herbal medicines with reference to contaminants and residues" (WHO, 2007) to promote the quality control of herbal medicines and to ensure the safety and efficacy of the use of traditional medicines.

> (Farnsworth, N.R., Soejarto, D.D,1991.) Suggested that 28% of the world's plant species (flowering plants, gymnosperms, ferns, bryophytes and algae) are used ethnomedically, which accounts for 70,000 - 80,000 species. Thus, the biodiversity of medicinal plants is so huge that it is past the scoped of our review to include all the medicinal plants global extensive as it might shift our awareness to the presence of residues and contaminants in medicinal plant species. Which are commonly used in popular traditional systems, such as Traditional Chinese Medicine (TCM), Indian system of Medicine (ISM), and other Brazilian, Egyptian and south East Asian practices, despite the fact that herbal medicines consist of all raw, processed and formulated products, we've limited our scope to raw medicinal herbs because different food commodities, are normally used the raw shape.

> In this review article, relevant studies were identified by performing an electronic search of CeRA (Consortium of e-Resources in Agriculture, India), PubMed, Google scholar, Research Gate, and other databases. To mine the literature, the main search terms used were "medicinal herbs" combined with the terms "contaminants," "residues," "pesticides," "environmental pollutants," "mvcotoxins," and "heavy metals, among others. The abstracts of all of the articles obtained were initially screened, and if they were found to be appropriate, a fully copy of the article was obtained for further assessment. This review emphasizes the legal limits of the contaminants because of the presence of the contaminants above the critical limits is objectionable in international trade because it can directly be effect on the consumer health and it also discussed the source, occurrence and incidence of common contaminants and the residues in raw medicinal herbs .Crossing the basic limits is unacceptable in global exchange because of its effect on the consumer health .Hence, consistent with our literature survey the most important contaminants in herbal medicines are a widely Classified into toxic elements(mainly heavy metals), mycotoxins pesticide residues, polycyclic aromatic hydrocarbons(P AHs) And

fumigants (Kosalec, ICvek, J, Tomic, S., 2009).

BIOLOGICAL CONTAMINATION

Biological contamination might contain living microbes such as bacteria and their spores, yeasts and molds, viruses, protozoa, insects (their eggs and larvae), and other organisms. Biological contamination refers to impurities in medicinal herbs and their instruction and products. However, products of microbial metabolism such as poisonous, low-molecular-weight metabolites from molds are chemical contaminants. The maximum probably sources of contamination are microbes from the ground and processing facilities ((contaminated air, microbes of human origin). Microbial contamination of herbs and/or products may additionally cease end result from unsuitable dealing within the manufacturing course of and packaging. Move contamination is also possible from external substances which include plastics, glass. and different materials which come in touch with herbs, herbal arrangements or products. medicinal Hypothetically, sources of biological contamination could be human excrement, animal manure and faces used as World Health Organization fertilizers (WHO) contaminant guidelines (World Health Organization (WHO) 2007) propose the necessity to prevent and control the pollution through quality assurance measures such as precision cultivation and collection practices (GACP) for medicinal plants, and good manufacturing practices (GMP) for herbal medicines. Guidelines together with the GACP and GMP are aimed at decreasing the general danger of pollution not only biological. (Directorate for the biological contamination. Quality of Medicines and Health Care of the Council of Europe (EDOM). 2007). Today only small percentage of medicinal plants are collected from the wild and there is too few information to compare biological contamination between wild and cultivated medicinal herbs.

Chemical Contamination

Mycotoxins

European law defines most ranges of mycotoxins (aflatoxinB1and sum of B11,B2,G1andG2) for a variety of foodstuffs and spices such as sweet pepper(Capsicum L.spp) pepper (Pipe L.spp.) nutmeg (Myristica fragrans Houtt.) turmeric (Curcuma long L.) and ginger (Zingiber officinale Roscoe)(Commission Regulation (EC)2002) because а few secondary metabolites produced by molds will be poisonous to human .The European pharmacopeia has introduced testing techniques these days and has set limits for aflatoxin 1(2mg mL-1) and total aflatoxin B1,B2,G1and G2 aflatoxins (4mg mL-1) for some medicinal herbs.

A limit of 20 mg kg -1 for ochratoxin.

A(OTA)has also been adopted for liquor ice root. Over50% of the samples handed the microbial counted limit set through the US Pharmacopoeia according to the study of medicinal herbs that collected from a Brazilian market. The mold burden was highest seen in leaves followed by flowers, rhizomes, roots, barks and seeds. Dominant mold was from Aspergillus gunus, followed by Penicillium gunus. Most aspergillus isolates were potentially Mycotoxin and has aflavus. Aparasiticus, A, ochraceus, Cladosporium spp, Rhizopus spp, Paellomcye spp,.Phoma spp,. and Trichoderma spp,. (Bugnal A, Almodovar IAAB, Pereiral TC, Andreoli Pinto IITI2006). After testing the ability to produce mycotoxin in laborotary 21,97% isolates were found to produce mycotoxin of which 42,9% aflatoxin,22.4 ochratorin and 34.7% citrinin (Bugnol A, Almodovarl AAB, PertrialTC, Andreoli Pinto IIT[2006]. By the study Cvenic and Pepeliniak(Cvenic Z Pepeliniak 1999).The most widespread isolated of molds in medicinal herbs were Aspergillus spp., Penicillium spp., and Mucor spp. Among aspergilla isolates the most common were Aspergillus glaucus, Aflavus and A niger group. Aflatoxigenicity of aspergillus spp., isolates. Was very low {only 1 in 15 isolates from gentian roots (GentianaluteaL.) produced aflatoxinB1}.

Toxic elements

Metals are presented in many foods and they are spread in nature and found freely in soil and water. So it is important to reduce the total population exposure to toxic elements by reducing contamination of herbal products (MazzantiG, Battinelli L, Daniele C, CostantiniS, Ciaralli L, Evandri MG. 2008). However, limit for toxic elements in herbal products are to be set at the global level. Adraft monograph has been issued by the European Pharmacopoeia (. Herbal drugs2008) suggested the following limits for heavy metals in the herbal drug 5mg kg_1for lead,0,5 mg kg_1for cadmium and 0.1 mg kg_1for mercury. The lead, cadmium, and mercury limits in food supplements have been established by the European Commission and been force in since Iulv 2009(Commission Regulation (EC)2008. Table 2 shows national and regional limits for arsenic and toxic metals in different kinds of herbal products suggested by the WHO (3)

The highest number of metals in medicinal plants materials can be given based on temporary acceptable intake (PTI) values that set up by the world Health organization WHO and the Food and Agriculture organization (FAO). At the same time, they've offered ideal ranges of toxic substances that may be ingested on a weekly basis .so called the Provisional Tolerable Weekly Intake (PTWI). PTWI is generally used for contaminants that collect in the body and weekly designation is used to emphasize the importance of reducing intake over period of time such substance (international Program on Chemical Safe (IPCS) 2009. PTWI has been proposed for mercury (5mg kg -1b. w) arsenic (15 mg kg-1b. w) lead (25 mg kg-1b. w) and cadmium (7 mg kg-1b. w) as the major toxic elements. (World Health Organization (WHO).(1978)

Lead and mercury as an example can move the placental boundaries with possibility toxic impact at the fetus while all metals are toxic at some level of exposure (Table1) Many metals considered extremely important. for good health and they have important biological roles for example. zinc. Although zinc is cofactor for more than 100 metallo enzymes but can have numerous negative effects on ordinary growth and development reproduction and immune function.

However, with enough concentration of these important metals can be possibly toxic. (Obi E, Akunyili DN, Ekpo B.Orisakwe OE.2006).

Element	Common Industrial Uses	Principal Toxic Effects
Arsenic	Pesticides, herbicides	Lung cancer, skin diseases
Cadmium	Batteries plastic, pigments, plating	Kidney damage, lung cancer, bone disorder
Chromium	Plating, alloys, dyes, tanning	Respiratory effects, allergic dermatitis
Lead	Batteries, wire and cable alloys	Neurological effects, haematopoietis system
		damage, reproductive effects
Manganese	Pesticides, ceramics, batteries steel	Central nervous system effects
Mercury	Chloroalkali industry, pesticides, thermometers	Neurological effects, kidney damage
	batteries	
Nicked	Coins, jewellery, alloys, plating, batteries	Dematitis
Thallium	Electronics, alloys	Neurological, heart, lung, kidney and liver effects
Zinc	Batteries, alloys, galvanizing, dyes,	Gastrointestinal effects, anemia
	pharmaceuticals	

Table 1. Common uses and principal toxic effects of arsenic and selected metals (ObiE, Akunyili DN, Ekpo B, Orisakwe OE.2006)

Pesticide residues

Pesticide are, grouped as insecticides, fungicides, herbicides, rodenticides and others (e.g. ascaricides, molluscicides). (Britt JK. properties and effects of Pesticide in Williams PL, James RC, Robert SM, editors,2000). According to the chemical structure Pesticides are grouped as organ chlorine pesticides (OCPs) {hexa chlorocyclohexanes (HCH) or benzene hex chlorides (BHC), lindane, dichlorodiphenyl trichloroethane (DDT)}

Organophosphorus pesticides (Ops) (chlorpyrifos and methylchlorpyrifos,coumaphos, dichlorvos, ethion, fenchlorphos (fenclofos), malathion,parathion), nitrogen-containing pesticides (such as atrazine, simazin, or propazin)

Pesticides are chemical compounds used to control eradicate pests based on intended used. (OCPs) were largely used in agricultural and malaria control programmes in the mid-20th century. Their uses cause negative health results therefore they have been completely ended. lipophilicity and gradual degradation cause them to continue within the environment and collected in the food chain. Moreover pesticides (e.g. DDT) potential threat to health because group accumulates in adipose tissue. (Ling YC, Teng, HC,CartwriteC.1999) The over exposure to(OPS) cause negative effect on the nervous system. The symptoms are headache, dizziness, paraesthesia, tremor, discoordination or convulsion(Britt JK .Properties and effect of pesticides In Williams PL, James RC, Rober SM editors 2000). (Ops) are quickly absorbed through ingestion, skin or inhalation because they are lipophilic. They are quickly metabolized, excreted and they have relatively short half-life. They prevent enzyme acetylchlinesterase at its ester site, which in turn leads to the accumulation of neurotransmitter acetylcholine in the nerve tissue and at the effector organ and to continued stimulation of cholinergic synapse. The main continual effect of exposure to (Ops) is caused delayed neuropathy. (Britt JK. Properties and effect of pesticides In Williams PL, James RC, Rober SM editors 2000). Ginger jake paralysis is called for delayed predominantly motor peripheral neuropathy. In 1930 in United States was reported in people drinking ginger liquor infected with tri_ortho_cresl_phosphate (TOCP).

Effect of Herbal Medicines on Clinical Laboratory Testing

The irregular laboratory test results due to the use of herbal medicines can be classified in 3 categories:

1. Because of direct interference of a component of the herbal medicine with the examine. Causes abnormal test

2. Unexpected concentration of a therapeutic drug due to drug-herb Abnormal interactions

3. Because of toxic effects of the herbal product. causes Abnormal test results.

Herbal Medicine and Surgery

Ang-Lee et al (Ling YC, Teng HC, Cartwright C. Supercritical fluid extraction and lean-up of organochlorine pesticides in Chinese herbal medicine. J Chromatogr A1999;). Announced their suggestion for stopping of herbal products before surgery. The patient should stop their herbal products at least 2 weeks before surgery according to the American Society of Anesthesiologists recommended. Ang-Lee et al (Ling YC, Teng HC, Cartwright C. Supercritical fluid extraction and lean-up of organochlorine pesticides in Chinese herbal medicine. J Chromatogr A1999;) because garlic and ginseng herbal have been reported to aggravate bleeding. it suggested that they should be stop at least 7 weeks before surgery. Ginkgo biloba should be stop 3 days before surgery because it prevents platelet aggregation, causing bleeding. Kava should be stop at least 24 hours before surgery because Kava can raise the sedative effect of anesthetics. Ma huang (ephedra) should be stop 24 hours before surgery because ma huang increases the blood pressure and the heart rate. St John's wort should be stop 5 days before surgery.

Misidentification and Adulteration of Herbal Product The identifying of herbal products won't appropriately reflect the content and negative events or interactions referred to specific herbs may relate to wrong identification of the plant. (Ang Lee M J, J Yuan CS.2001) For example a case of neonatal and organization with Siberian ginseng because of unassociated species of Chinese silk vine. (But PP. J Trop Med Hyg.1994). More than 48 cases of nephrotoxicity refer to fang_ji in a weight loss preparation were because of guang fang ji (Aeang DVC.1991).

Toxic Effect of Herbal medicines

Numerous regularly herbal medicines that used are harmful and poisonous. The poisonous effects of common herbal products range from allergic reaction to cardiovascular, renal, neurologic, hepatic and dermatologic toxic effects. The toxic effects of common herbal products are given in (Table2).

Although ginseng is regarded as safe, but the toxicity of ginseng has been reported in the literature.

Herb	Toxic Effect or System Affected	Intended Use (Should Anyone Use)
Comfrey	Hepatotoxic	Repairing of bone & muscle; prevention of kidney
		stone
Ephedra	Cardiovascular	Herbal weight loss
Chan Su	Cardiovascular	Tonic for heart
Borage Oil	Hepatotoxic	Source of essential fatty acid; rheumatoid arthritis,
		hypertension
Calamus	carcinogenic	Psychoactive, not promoted in the united states
Chapanal	hepatotoxic; nephrotoxic;	General cleansing tonic; blood thinner; arthritis
	carcinogenic	remedy; weight loss product
Licorice	pseudoaidosteronism (sodium	Treatment of peptic ulcer; flavoring agent
	and water retention,	
	hypertension, heart failure)	

Table 2: Potentially Toxic Herbs

CONCLUSION

In self-treatment of minor conditions, they use herbal products as the first choice because of safety of herbal products. The use of herbal products continues to extend fast across the world. This makes the safety of herbal products regards as an important public health issue. With this review we argue that the quality of herbal at any production stage directly affect their safety. Medicinal herbs should not be grown or collected in polluted environment. Any chemicals used to boost growth or protect the crop should be kept to a minimum. Recommendation on good agricultural and collection practices in the European and Who guidelines for raw herbal materials provide the basis for suitable quality assurance.

Pollution with toxic elements, microbes, and agrochemical residues after harvesting should be prevented as much as possible. To prevent the spread of animals (insects and rodents) and micro-organisms that brought in with herbal material, effective measures should be taken. And to prevent fermentation of yeast and mold growth mycotoxin production and cross-contamination effective measures should be taken at any treatment to reduce contamination or infestation.

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