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Elemental impurities in Ayurvedic formulation: Guidelines & management

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Abstract

Traditional medicinal herbs, herbs supplement and other medicines are used by the majority of people in the world. Toxicity associated with the use of Ayurvedic product due to their iron content is a public health concern. Some of these preparations are considered to be harmful to health due to the presence of toxic substances, hence it is very important to value the possible risks associated to their consumption. Metal in formulation act by their intrinsic activity, catalytic activity, preservative and nanocarriers. Ayurvedic products due to specific processing like shodhan, maran, satvapatan, do not have metal in toxic form. A significant usage hazard of complementary medicines is the presence of heavy metal(loid)s such as arsenic (As), cadmium (Cd), lead (Pb), and mercury (Hg). Heavy metal in ayurvedic formulation above prescribed limit may be fatal. The permissible limit set by FAO/WHO for herbal medicine are 10µg/g for mercury, 0.3µg/g for cadmium and 50µg/g for zinc. The permissible limit for iron, copper, magnesium and chromium has not established. Plant and animal product may have heavy metal due to high accumulation by their defense mechanism, physiology of environmental variations. Improper manufacturing processes might lead to higher levels of heavy metals remaining in the final product which may be dangerous. They may also be present as impurity rather than being added willfully. Heavy metals possess tendency to accumulate in vital organs and hence, pose a particular health risk. The presence of impurities in drug samples, whether herbal or pharmaceutical, is of great concern, not only because some contaminants are essentially toxic, but also they might have a detrimental effect. The stability of the drug and the lifespan, or they can cause undesirable effects. The quality assurance of herbal formulations is the main concern of current phytomedical era due to the increase in toxicity reports. As a consequence, both organic and inorganic (elemental) impurities must be monitored and controlled in final dosage form starting from the raw materials itself. This article

deals with the various aspects of heavy metals in Ayurvedic medicines such as their sources, methods used for their determination, their therapeutic significance, their toxic effects and also summarizes various guidelines and limits for their regulation.[11,30,41]

Key words : Elemental impurities, Ayurvedic formulations, Regulatory Compliances, Guidelines, Good Manufacturing Practices.

Ayurveda, along with other forms of medicine, is one of the main independent form of medicine that has become popular in western countries in recent years. According to the world health organization 80% of the world's population relies on traditional medicine for their health needs, while 35% to 75% of developed countries rely on traditional medicine[11,30,41].

It uses blend of remedies and lifestyles to treat and cure disease and to maintain health. Ayurvedic bhasma embody heavy metal in primary herbal formulation to magnify potency and therapeutic property[18].

Complementary medicines (CM) are also known as traditional, natural, or alternative medicines, and include herbal medicines, vitamin and dietary health supplements, and traditional Ayurvedic, Chinese, and homoeopathic medicines. Globally, self-prescribed vitamins, herbal medicines, and mineral supplements are the most popular CM products used. Developed nations like the US and the UK have seen a sharp rise in the use of complementary and other medicine in recent years. The phrase "complementary medicine" refers to a broad spectrum of therapies, including diet products, vitamin and mineral supplements, herbal remedies, homeopathy, and conventional medications like Chinese and Ayurvedic remedies. Nevertheless, while many of these treatments are generally safe and may have health advantages, there have been significant concerns raised over the safety of certain supplementary medicine modalities, particularly traditional/herbal medications. There are six primary categories of safety concerns pertaining to herbal and traditional medications.

- The product might expose the patient to components that are intrinsically hazardous (*i.e.*, toxic chemicals or other undisclosed components).
- The product could include impurities from the process of making it (such as pharmaceuticals or heavy metals that are not disclosed due to subpar manufacturing or a lack of quality control);
- Patients who self-administer alternative therapies instead of conventional medications may put off seeking medical advice from a professional or even stop receiving conventional treatment entirely.
- Certain patient groups may be more vulnerable to the negative effects of traditional/herbal treatments than from any conventional medications used concurrently (for example, through drug–herb interactions)
- Patients with specific disease conditions who may be at risk (*e.g.*, those with cardiovascular or neurological sickness that

could be made worse); the elderly, children, and nursing or pregnant women[4,5,6,10,12,13].

Dietary supplements have risen to around 55,000 in the USA, with an estimated 60%, 50%, and 71% of Americans, Europeans, and Canadians using health supplements, respectively[16].

Unlike allopathic medicine, the production and supply of CAMs is not well regulated. In western countries, Ayurvedic medicine is available from national markets, health food store, ayurvedic practitioners, through self importation and over the internet without medical consultation[7,12,34].

While the goal of using complementary medicine items is to improve health, there is insufficient data to support the efficacy of many of these goods. Certain traditional herbal and Ayurvedic formulations may need to be used with caution as they contribute to toxicity caused by pollutants, even if the major part of complementary medicine items are low risk. Heavy metal(loid)s and pesticide residues are among the pollutants that cause the majority of the dangers connected to CM products. Biologically essential elements such as cobalt (Co), copper (Cu), chromium (Cr), manganese (Mn), nickel (Ni), selenium (Se), and zinc (Zn) are examples of heavy metal(loids), as are non-essential elements such as arsenic (As), cadmium (Cd), lead (Pb), and mercury (Hg)Pb, Hg, As, and Cd are the most often found heavy metal(loid)s linked to human toxicity, however beryllium (Be), Mn, and aluminum are also[2,26].

While the majority of CM products might be beneficial to health, there have been reports in recent years of an increase in heavy metal(loid) toxicity after using these items. The majority of nations control the usage and distribution of CM goods. For instance, if CM products are made in Australia, the Australian Therapeutic Goods Administration (TGA) controls them, including herbal, traditional Chinese, and Ayurvedic medications. Herbal medicine imports for commercial use needs to be licensed and evaluated by the TGA. In a similar vein, a number of other nations have established regulations governing the usage and distribution of CM goods as well as the amount of metal(loid)s that may be present. Although they present a challenge to policy makers, effective solutions to reduce or eliminate this risk are essential for maximizing health.

In light of the distribution and bioavailability of metal (loid)s in these products, this review attempts to investigate the effects of heavy metal(loid) contamination on the toxicity and safety of CM products. The origins, concentrations, and distribution of heavy metal (loid)s in different CM products are covered in the review's first section. Next, the bioavailability and bioaccessibility of these heavy metal (loid)s for human health will be compared to their toxicity in CM products. The management recommendations for the safe and advantageous usage of these products are examined in reference to the practical effects of CM-borne heavy metal(loid)s on human health[6,20].

Historical uses of heavy metals :

1. *Lead :*

Since the Roman era, lead's detrimental effects have been known or suspected; in fact, lead has even been suggested to have played a role in the fall of the Roman Empire[23,37].

Although lead has long been used as a cosmetic in Surma, it has no particular medicinal history[17,31].

Mercury :

For many years, mercury has been a crucial component of pharmaceuticals. It is found in diuretics, antibacterial treatments, antiseptic skin ointments, laxatives, hair conditioning products, and dental products (amalgam). In the past, mercury salts, or calomel, were also employed as purgatives. In the past, mercuric salts, like as mercuric chloride, were employed in homicides due to their high solubility and acute toxicity. They were also utilized as disinfectants[19,38].

Arsenic :

In the past, arsenic compounds were frequently prescribed as treatments for a number of illnesses, including anemia, syphilis, acne, and malaria. For more than 150 years, Fowler's solution—which included 1% potassium arsenite—was used to treat a variety of illnesses, such as cholera, psoriasis, cholera, rheumatism, and asthma. syphilis. Less toxic medications have now taken the place of these treatments, while arsenicals are still used to treat uncommon cases of leukemia and African trypanosomiasis, which causes sleeping sickness. Up to the late 19th century, trivalent arsenic compounds—in particular, arsenic oxide (As_2O_3)—was frequently employed in homicides[23,37].

Element classification :

The elements included in this guideline are divided into three group according to their presence and toxicity in medicinal product. The probability of occurrence is determined by factor such as the content found, abundance in nature, and environmental distribution, such as the caps used in chemical processes, and the possibility of segregation with other impurities in material used in medicine. For the purpose of this guidelines, elements with low natural abundance are those with a reported natural abundance of <1atom/106 silicon atom[13]. This classification system is designed to focus on the risk assessment of the most toxic but also potential component in pharmaceutical products. Element impurity groups are.

Class 1 : As, Cd, Hg, and Pb are human toxicants that are restricted or not used in pharmaceutical manufacturing. Their presence in pharmaceutical product is usually due to the most common material (such as mined excipients). Because of their specific properties, these four elements require consideration of all potential sources of impurities and control methods during the risk assessment. The result of the risk assessment will identify equipment that may require additional controls, which may sometimes include testing for class 1component. It is assumed that not all products will require class 1contamination testing and should only be used where the risk assessment indicates that it is an appropriate measure to ensure that PDEs are met.

Class 2 : these elements are generally considered pathway dependent in human chemistry. Class2 substances are divided into subclasses 2A and 2B based on their likelihood of appearing in medicinal products.

Class 2A due to high content of

substances contained in medical devices, the risk assessment must take into account all potential sources of contamination as well as the method of use. Class2A element are Co, Ni and V.

Class 2B these elements are rare in medical products because they are rare and rarely mix with other materials. Therefore they can be excluded from risk assessment unless they are deliberately added during the production of medicines, Excipients or other component of medicinal products. Class2B elemental impurities include: Ag, Au, Ir, Os, Pd, Pt, Rh, Ru, Se and Tl.

Class 3: when taken orally, the toxicity of these elements is relatively low (PDE is high, usually> 500 µg/day), but this should be taken into account when assessing the risk of parenteral and inhalation routes. In terms of management language, these elements do not need to be considered during the risk assessment unless they are intentionally added. For parenteral and inhaled products, the potential for inclusion of these impurities should be assessed during the risk assessment, unless the specific PDE method is higher than 500 µg/day. Elements such as Ba, Cr, Cu, Li, Mo, Sb, and Sn.

Other elements: some impurity elements for which PDEs have not been developed are not addressed in this guideline due to low toxicity and different regional regulations. If impurity elements are present or included in medicinal product, they will be addressed by additional instruction and regional regulation and practice that may apply specifically to the product (*e.g.* lead for renal failure; manganese and zinc for patient with liver dysfunction) or a good decision for final drug products (*e.g.* impurities in protein therapy). Some elements include: Al, B, Ca, Fe, K, Mg, Mn, Na, W and Zn [28,36].

Table-1. High consumption of some heavy metal, their toxic effects and permissible limits.

METAL	Industrial uses	Principal toxic effects	Permissible limits (mg/l)
Arsenic	Pesticides, herbicides	Lung cancer and skin diseases	0.02
Cadmium	Batteries, plastics, pigments, plating	Kidney damage, lung cancer and bone disorder	**0.06**
Chromium	Dyes, alloys, tanning	Respiratory effects, allergic dermatitis, kidney and liver damage	**0.05**
Lead	Batteries, wire and cable, alloys	Neurological effects, hematopoietic system damage and reproductive effects	**0.1**
Mercury	Chloro alkali industry, pesticides, thermometers, Batteries	Neurological effects and kidney damage	**0.01**
Manganese **Zinc**	Pesticides, batteries Pharmaceuticals, dyes, Batteries	Central nervous system effects Gastrointestinal disturbances and anemia	**0.26** **15**

Sources of hazardous chemicals in herbal product :

Heavy metals in the soil, water, and air can readily infect medicinal plants. The most common way that heavy metals contaminate soil is by atmospheric deposition from point sources, such as various industrial processes. Rainfall, air dust, and plant protection agents are additional sources of these components for plants.

Waste water contains toxic substances that can pollute the environment, water supplies, agricultural soils, and ultimately the human food chain. The crops get polluted and end up with undesirable amounts of metals in them. The primary determinants of metal uptake by roots are metal and feature of the soil, types of plants, etc. Therefore, it is crucial to understand plant metal mobility in order to assess how soil pollution affects plant uptake of metals.

The presence of heavy metal(loid)s in Chinese medicine (CM) products arises from various sources, including plant contamination during the cultivation process, processing contamination, and the inclusion of heavy metal(loid)s as a medicinal agent[3].

Heavy metal(loid) uptake by herbal plants:

Uptake of heavy metal(loid)s by herbal plants can occur because of cultivation of these plants in contaminated soils, addition of heavy metal(loid)-enriched organic amendments including manure and compost as a nutrient source, and irrigation of herbal plants with wastewater sources containing heavy metal(loid)s. There has been an high practice to use marginal and contaminated soil for the collection and cultivation of non edible crops like fiber and energy crop and plants for production of plant derived product. Herbal plants sometimes have capacity to accumulate heavy metal when grown in contaminated soils. For example, uptake of metal impurities by plants in a contaminated paddy field and mining affected soils.

Most of the plants used for remedy they are grown organically using phosphate rock composts, animal manures. Some of this source is rich in heavy metal which can be taken up by plants. The use of treated herbal plants to formulate aromatic oil is increasing. Waste water irrigation also increases the uptake of heavy metal in aromatic plant hence low level of toxic element were noticed in volatile oil of these plants like Lal *et al*.[24] study Cd, Cr, Ni, and Pb found to be present in lemon grass oil.

Zheljazkov *et al*.,[42] proved that three essential oil species Marrubium vulgare L. (white horehound), Melissa officinalis L. (lemon balm), and Origanum heracleoticum L. (oregano) did not remove noteworthy amounts of heavy metals and therefore were able to be cultivated in metal polluted smelter soils as high-value crops. Rai *et al*.,[33] observed that Cd concentration in Phyllanthus amarus (gale of the wind) used in the most popular Ayurvedic formulation (Chywanprash) increased with increasing Cd contamination in soil[9,24,33,39,42].

Cross-contamination of heavy metals during processing :

Heavy metal Cross contamination may occur during the processing and manufacturing of plant products. Heavy metal may contaminate

the plant product via bioaccumulation from harvest site and throughout post harvest phase like drying, grinding, and solvent extraction. The increased concentration of Pb of so many Chinese herbal supplements is due to external contamination from drying and manufacturing process and Pb-enriched water used for washing.

The process of production of herbal medicine can effect redistribution of heavy metal like greater amount of metal extracted on boiling the plant in water extracted than immersing in hot water demonstrating heavy metal contamination can be manage by extraction process. Four commonly consumed Chinese herbal medicines in Malaysia such as "Eight Treasure Herbal Tea", "Herbal Tea", "Xiyangshen" (Radix Panacis Quinquefolii), and "Dangshen" (Radix Codonopsis) evaluated by Ting *et al*., (2013) for heavy metal content using boiled and non boiled decoction. They concluded that decoction prepared by boiling reduced the concentration of Cu, even though Cd, Pb, and Zn were not notably different[1,14,27].

Introduction of Heavy metal as a therapeutic ingredient :

In 'Rasayan Shastra' system preparation of Ayurvedic medicine involve addition of heavy metal like As, Hg, and Pb in respective salts form. These heavy metal impart health benefit like As was employed to manage blood count in chronic myeloid leukemia. In similar way in ayurvedic medicine Pb has been used to treat disease like diabetes, spleen swelling, skin disorders.

'Bhasma,' metal based ayurvedic medicine its production require conversion of mrtal into oxides. During preparation metal is treated with plant juice then calcinations at high temperature. 'tamra bhasma' a Cu- based preparation produce using Cu wire. Different spectroscopic technique like scanning electron microscopy is used for conversion of elemental Cu to its oxide form. Bhasma Ayurvedic medicines containing metal(loid)s are used as therapeutic agents. For example Swarna bhasma containing gold (Au) particles is used for its anticancer activity. Similarly,Swarna bhasma used for protein adsorption and blood compatibility.

Naga bhasma, prepared from Pb (100 and 200 mg kg^{-1}), used to evaluate the anti-diabetic activity in alloxan-induced diabetic rats. Naga bhasma showed dose-dependent decrease in glucose levels and brought it to normal on the 14th day of treatment.

Certain Chinese medicine preparatio show remarkable elevated level of Cd, Hg, and Pb, which is correlated to their intentional addition. Xray diffraction analyses performed on some sample demonstrated the presence of As and Hg and mercuric sulphide, respectively. Similarly, XRD data, have shown the presence of a number of crystalline minerals in Ayurvedic medicines, which include arsenic disulphide, mercury sulphide, lead carbonate, lead sulphide, and cadmium carbonate[15,25,29,40].

Effects of toxic chemicals on human health: Heavy metals :

At low concentration, heavy metals are hazardous metallic chemical elements with a relatively high density. Metal can be found easily in soil and water and are widely distributed throughout the natural world. Heavy metal containing herbal preparation might not be the consequence of accidental contamination;

rather they might be added for purported therapeutic benefits. For instance mercury was once used to treat syphilis before penicillin was developed, but compounds derived from arsenic are still used to treat certain types of cancer. Toxic heavy metal that exhibit mutagenesis effects at very low concentration include mercury, lead, arsenic and cadmium. Numerous reports of human sickness, organ failure and deformity have been made as a result of metal toxicity.

Toxic quantities of heavy metals also damage plants and animals. The toxic effect differ depending on the metal for instance, mercury poisoning can result in peripheral neuropathy, psychiatric disorder, and arrhythmias, lead poisoning can induce severe anemia, hemoglobulinuria, vomiting, and dark stool because of lead sulfide, because of its nephrotoxic activity, which result in death, late substantial renal deterioration ensues[21,28,35].

Table-2. Common uses, principal toxic effects and permissible limits of some heavy metals

Toxic metals	Industrial uses	Principal toxic effects	Permissible limits (mg/l)
Arsenic	Pesticides, herbicides	Lung cancer and skin diseases	0.02
Cadmium	Batteries, plastics, pigments, plating	Kidney damage, lung cancer and bone disorder	0.06
Chromium	Dyes, alloys, tanning	Respiratory effects, allergic dermatitis, kidney and liver damage	0.05
Lead	Batteries, wire and cable, alloys	Neurological effects, hematopoietic system damage and reproductive effects	0.1
Mercury	Chloro alkali industry, pesticides, thermometers, Batteries	Neurological effects and kidney damage	0.01
Manganese	Pesticides, batteries	Central nervous system effects	0.26
Zinc	Pharmaceuticals, dyes, Batteries	Gastrointestinal disturbances and anemia	15

Pesticide residues :

Chemical substance called pesticide is used to eliminate or control pests. They fall under the following categories: nematocides, herbicides, fungicides and insecticides. They are categorized as organochlorine pesticides (OCPs), hexachlorocyclohexanes(HCH), dichlorodiphenylethanes (DDT), organophosphorus pesticides dichlorvos, malathion, and parathion] nitrogencontaining pesticides (such as atrazin and propazin); PESTICIDE ORIGINATED FROM PLANT (PYRETHROIDS AND ROTENOIDS), etc based on their chemical structure. Herbal remedies may be contaminated by pesticide residue , their metabolites, and breakdown product that are found in plants or in the soil.

At the moment pyrethroid insecticides have been found in both imported and domestic herbal product , including the root of panax ginseng and notoginseng. Despite being extremely fat soluble, these substances are quickly broken down and eliminated by humans.

The preferred insecticides are gradually being replaced by pyrethroids because to their greater insecticidal efficacy and decreased toxicity to mammals. Long lasting effect are only seen in OCPs like HCH and a small number of Ops (like carbophenothion) (world Health organization) because they act as central nervous system stimulant, organ chlorines can induce tremors, hyperexcitability, and seizures. Despite being less acutely (instantaneously) harmful than organophosphates or carbamates, organochlorine can accumulate in tissue and enter the food chain because they are constantly present in the environment.

They pose a serious risk worldwide, human breast milk contains residues and breakdown product of organochlorinr pesticides. additionally, soil, plant and animal tissue from the centre of the pacific ocean to the arctic circle contain these residue. The primary side effect linked to excessive exposure to Ops is nervous system symptoms, such as headache, vertigo, paresthesia, tremor, incoordination, or convulsion. They prevent acetylcholine from building up in nerve tissue and in the effector organ by inhibiting the enzyme acetyl cholinesterase, which also keep cholinergic synapses stimulated. The primary long term consequences of organophosphorus exposure is delayed neuropathy[8].

Table-3. Permissible Limits According to Who Guidelines

		Arsenic (As)	Lead (Pb) (Cd)	Cadmi-um (Cr)	Chro-mium (Hg)	Merc-ury (Cu)	Cop per	Total toxic metals as lead
For herbal medicines								
Canada	Raw HM	5 ppm	10 ppm	0.3 ppm	2 ppm	0.2 ppm		
	Finished HP	0.01 mg/day	0.02 mg/day	0.006 mg/day	0.02 mg/day	0.02 mg/day		
China	HM	2 ppm	10 ppm	1 ppm		0.5 ppm		20 ppm
Malaysia	Finished HP	5 mg/kg	10 mg/kg			0.5 mg/kg		
Republic of Korea	HM							30 ppm
Singapore	Finished HP	5 ppm	20 ppm			0.5 ppm	150 ppm	
Thailand	HM and Finished HP	4 ppm	10 ppm	0.3 ppm				
WHO recommendations(2)			10 mg/kg	0.3 mg/kg				
For other herbal products								
National Sanitation Foundation draft proposal (Raw DS)a		5 ppm	10 ppm	0.3 ppm	2 ppm			
National Sanitation		0.01	0.02	0.006	0.02	0.02		

HM:Herbal Materials ;HP:Herbal Products; DS:Dietary Supplment

Table-4. Permitted Daily Exposures and Permitted Concentrations for Elemental Impurities [ICH Guidelines[22]

Table-6. Permissible Limits According To ICH Guidelines

Element	Class	Oral Route µg/day		Parenteral Route µg/day		Inhalation Route µg/day	
		PDE	PC	PDE	PC	PDE	PC
As	1	15	1.5	15	1.5	1.9	0.29
Cd	1	5.0	0.50	6.0	0.60	3.4	0.34
Hg	1	40	4.0	4.0	0.40	1.2	0.12
Pb	1	5.0	0.50	5.0	0.50	5.0	0.50
Co	2A	50	5.0	5.0	0.50	2.9	0.29
Mo	2A	180	18	180	18	7.6	0.76
Se	2A	170	17	85	8.5	140	14
V	2A	120	12	12	1.2	1.2	0.12

Acceptable limits for elementa limpurities according to Quality of Natural Health Products Guide, Canada.[32]

Table-5. Permissible Limits According to Quality of Natural Health Products Guide, Canada

Element	Adult Limitper day	Limitperdayperkg body weight	Limit in parts per million (ppm) for Topical Products
Total Arsenic	<10.0µg/day	<0.14µg/kg b.w./day	3 ppm
ORInorganic Arsenic	<2.1µg/day	<0.03µg/kg b.w./day	
Organic Arsenic	<1.4mg/day	<20µg/kg b.w./day	
Cadmium	<6.0µg/day	<0.09µg/kg b.w./day	3 ppm
Lead	<10.0µg/day	<0.14µg/kg b.w./day	10 ppm
Totalmercury	< 20.0 µg/day	<0.29µg/kg b.w./day	1 ppm
Methylmercury	<2.0 µg/daya	<0.029µg/kg b.w./daya	
Antimony	-	-	5 ppm

Table-6. Permissible Limits Accordingto Various Organizations

		Establishedorallimits(µg/day)			
		Arsenic	Cadmium	Lead	Mercury
Limit for finished product: dailydose	AHPA (American Herbal Products Association)	10	4.1	10	2.0
	NSF (National Science Foundation)/ ANSI 173 (American National Standards InstituteANSI 173)	10	6	20	20
	Canada Natural Health Products Directorate	10	6	20	20
	California Prop 65 Reproductive Toxin	Noneset	4.1	0.5	-
	California Prop 65 Carcinogen	10	-	15	-
Limitfortotal daily consumption	US Agency for Toxic Substancesand Disease Registry (ATSDR)	20	14	-	20
	US Environmental Protection Agency (EPA)	20	70	-	7
	USFDA Tolerable Daily Intake	130	55	75	-
	Joint FAO/WHO Expert Committeeon Food Additives (JECFA)	150	70	250	16
	European Union	-	70	250	16

Herbal and ayurvedic medicinal formulation are taken up by a broad range of the world population of which some contain toxic substances such as heavy metals either as a therapeutic agent or as a contaminant. Main source of heavy metals in ayurvedic and herbal formulation is purposeful introduction of metal like As, Hg and Pb as a therapeutic ingredient. Uptake of heavy metal when plant grown in contaminated soil can cause deposition of heavy metal in formulation derived from these plants. Since this metal exist in different solid forms the effect of total concentration of metal are a poor indicator of toxicity. Bioavailability of heavy metal effected by nature and processing of mineral to be used as therapeutic agent. The bioavailability of heavy metal, their biological uptake, and their eco-toxicological effects can be better understood in terms of their chemical speciation. The safety of these formulation can be achieved through by adopting standard operating procedures, medicinal plant must not be grown and collected in contaminated soil which is contaminated by microbes, toxic element and pesticide residue. Spread of animal and microorganism should be avoided to prevent cross contamination. The safety of ayurvedic and herbal formulation can be protected by adopting growing agriculture practice, good manufacturing practices. Hence it can be concluded that estimation of heavy metal and pesticidal residue is highly vital and necessary for the preparation of ayurvdic and herbal formulation.

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