

# Safety Aspects of Ayurveda

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## Introduction

Ayurveda forms an important component of health care in India. This is based upon centuries old observation, rich in traditional wisdom and with its own strong basic principles and philosophy as its skeleton and body. As per ayurvedic concepts, every material of earth is made up of 5 basic elements, which are *prithvi* (earth), *jal* (water), *tej* (fire), *vayu* (air), *aakash* (space). This is true for both plants as well as human beings providing their interface.

Aims and objectives of Ayurveda are:

1. To preserve and promote the health of a healthy person
2. To alleviate the disease in a patient.

Ayurveda, therefore, followed a holistic approach to tackle any day-to-day health promotive, protective and disease related issues.

The traditional usage and wide ranging concurrent usage through out India by millions of people on daily basis there is a perfect case of providing Ayurvedic medicines a status of GRAS. This is especially applicable to the pure herbal formulations. Strict compliance of GMP should be able to take care the safety of metallic, mineral or their combination products by monitoring stringently for application of textual methods for manufacturing these medicines. In certain cases, however, there is a scope of more stringent regulatory guidelines to conduct toxicity studies of Ayurvedic products, though such instances may be few. Lack of such data, however, should not be used as non-tariff barrier in trade by any country.

Following Acts and Rules passed by Indian Parliament govern Ayurvedic medicines in India:

- (i) Drug & Cosmetic Act, Chapter IV A, Rule 161, Schedule T
- (ii) Drugs & Magic Remedies Objectionable Advertisement Act
- (iii) Biodiversity Bill
- (iv) Environment & Forest Act (Director General Foreign Trade)
- (v) Indian Patents Act
- (vi) Central & State Excise Act

**Ayurvedic formulations**

To meet the above objectives, Ayurveda recommends using behavioural dietary and medicinal modalities comprising of

- Food items
- Used as both food and drug e.g. Spices
- As drugs

**Evidence for safety****1. Traditional use**

Ayurvedic medicines have been traditionally used for thousands of years in India. In 1998 as per statistics of Govt. of India, there were 609,400 Physicians of Indian Systems of Medicine and Homeopathy in India<sup>1</sup>. Out of which, more than half belong to Ayurveda stream. Global resurgence of Ayurveda specially its herbal component has led to the need of its scientific validation both in terms of efficacy and safety. Few recent events published in international journals have refocused the attention on safety aspects of Ayurvedic products.

About 80% of the population in India depends on traditional medicine. Out of which almost 70-75% depend on Ayurvedic medicines in one form or the other. That means if approx. 2,50,000 Ayurvedic physicians see on an average 10 patients per day it converts to 2.5 m patients per day. Almost equal number of people does not go to physician and use these medicines on their own. That means, almost 5 m people use Ayurvedic medicines on daily basis in India. Forth estate enjoys full freedom in India and even then media reported incidents of side effects are almost nil. This is the best evidence of safety of Ayurvedic medicine going by their traditional usage pattern.

**2. Regulatory**

Drugs and Cosmetic Act of India control Ayurvedic medicines<sup>2</sup>. This Act has recognized the use of toxic substances in preparation of Ayurvedic medicines and has given a separate Schedule E1 for listing of such substances. During preparing the formulation of such ingredients need to undertake detoxication called *shodhan* has mentioned in the ancient textbooks. All the Ayurvedic formulations containing such substances need to carry a warning on their labels 'to be taken under medical supervision only'.

Ayurvedic formulations do contain poisonous substances, metals, etc. which if not used following Ayurvedic principles, may show symptoms of toxicity (Table 1).

### **3. Generally Recognized As safe (GRAS) list**

As mentioned earlier, Ayurveda use holistic approach of treatment where food, medicine and non-therapeutic measure like exercise and behaviour go together. Ayurvedic formulations contain food ingredients, as well as therapeutic food ingredients. Therefore, it is presumed that all other ingredients except published in Schedule E1 do fall under the list of GRAS i.e. Generally Recognized and Safe though it has not been notified separately.

### **4. Adverse Drug Reaction Monitoring**

There is no formal system of ADR monitoring of Ayurvedic medicines in India. However, India has a free press and very active print and electronic media. So far case of adverse drug reaction of Ayurvedic medicine have not been reported.

### **5. Toxicity studies**

Drugs and Cosmetic Act of India control manufacturing of Ayurvedic medicine. However, there are certain conditions, which a manufacturer is to meet before granting manufacturing permission. Toxicity studies and clinical trials are not mandatory for grant of such licenses. As such there are no guidelines to conduct toxicity studies on Ayurvedic medicines in India. However ICMR has recently issued preliminary guidelines<sup>3</sup> for the same and which are reproduced below:

“It is important that plants and herbal remedies currently in use or mentioned in literature of recognized Traditional System of Medicine is prepared strictly in the same way as described in the literature while incorporating GMP norms for standardization. It may not be necessary to undertake phase I studies. However, it needs be emphasized that since the substance to be tested is already in use in Indian Systems of Medicine or has been described in their texts, the need for testing its toxicity in animals has been considerably reduced. Neither would any toxicity study be needed for phase II trial unless there are reports suggesting toxicity or when the herbal preparation is to be used for more than 3 months. It should be necessary to undertake 4 - 6 weeks toxicity study in 2 species of animals in the circumstances pointed out in the preceding sentence or when a larger multicentric phase III trial is subsequently planned based on results of phase II study.”

Several Ayurvedic products have undergone toxicity studies at both academic institutions as well as industries in India. Due to want of clear-cut guidelines most of these studies have covered the following:

- Acute toxicity – LD50 in two species
- Sub chronic toxicity – 28 day-6 months by oral route in single species
- Ames test in certain cases

**Table 1—Commonly used metals and precious stones with indications, adverse events and dosage as per Ayurvedic texts**

<b>Metal</b>	<b>Indication</b>	<b>Adverse events</b>	<b>Max recommended daily dose (mg) as per Ayurvedic texts</b>
Gold	As a cardiac and nerve tonic, memory enhancer, psychiatric disorders, poisoning, rejuvenation, chronic cough	Weakness, urticarial rash, death	15-30
Silver	Diabetes, anti-aging, nerve tonic	Weakness, urticarial rash, major diseases	30-60
Copper	Non-healing wounds, anaemia, haemorrhoids, bronchitis, chronic rhinitis, acid-peptic disease, worms, inflammatory conditions, hepatic dysfunction	Burning, excessive perspiration, anorexia, giddiness, fainting, diarrhoea, vomiting, death, hepatitis, cirrhosis, tremors, haemolytic, anaemia, renal dysfunction	8-30
Iron	Anaemia, eye tonic, poisoning, haemorrhoides, splenomegaly, hyperlipidaemia, anthelminthic	Erectile dysfunction, cardiac disease, calculi, hiccups, death lethargy, coma, shock, liver injury, renal failure	30-240
Lead	Diabetes, as an aphrodisiac, worms	Dermatological conditions, prunitus, fistula-in-ano, anaemia, renal diseases, peripheral neuropathy with demyelination of long neurons, ataxia, convulsions, coma, death	30-125
Diamond	Cardiac tonic, chronic/recurrent infection, ascites, eye disorders, erectile dysfunction	Anaemia, dermatological conditions, paraplegia	12.5

## Factors responsible for toxicity of Ayurvedic medicine

### 1. Improper manufacturing process

Certain products contain metallic ingredients which have to be prepared strictly as per the classical Ayurvedic text books which include methods to render them non toxic. Sometimes unscrupulous manufactures may use shortcuts and safety problems may arise. However, if Ayurvedic drugs are prepared properly this problem do not arise. To give an example, one of the most commonly used Ayurvedic products is *Swarna Vasant Malti*, which contains gold-based mercury and sulphur.

A study was conducted on these formulations on 20 volunteers subject to blood chemistry profile of these volunteers<sup>4</sup>. Before and after 3 months of therapy of this drug is reproduced in Table 2.

**Table 2—Blood chemistry before and after gold therapy**

S.No.	Parameter	Pre-drug value	Post-drug value
1.	Urea (mg/dl)	21.0 ± 4.6	21.8 ± 4.2
2.	Creatinine (mg/dl)	0.84 ± 0.12	0.89 ± 0.14
3.	Bilirubin (mg/dl)	0.60 ± 0.12	0.65 ± 0.11
4.	GOT (U/L)	29.9 ± 10.7	29.2 ± 11.1
5.	CPK (U/L)	90.9 ± 31.5	78.8 ± 28.1
6.	LDH (U/L)	319.3 ± 76.1	291.8 ± 71.7
7.	Hemoglobin (g/dl)	11.2 ± 1.1	11.4 ± 1.1

Government of India has issued Good Manufacturing Practice, which are already in vogue. This regulatory measure is quite effective to tackle the improper procedure of manufacturing.

### 2. Contaminants

Recently 17 out of 70 Ayurvedic products tested were reported to contain heavy metals<sup>5</sup>. An analysis of the products referred is given in Table 3.

The above table reveals that though in certain cases heavy metals were containment, in certain other cases they are intentionally added to provide therapeutic efficacy as per the Ayurvedic textbooks labeling them as toxic. The following points need intense scientific debate on this issue.

- a. Various methods used to test heavy metals involved process of digestion, which converts, bound metal into free metals, which are then tested using various techniques. Do these products undergo the same process inside the human body and actually release metals from bound to free form?

Table 3—Ayurvedic herbal medicinal products containing Lead, Mercury, and / or Arsenic

S. No.	Ayurvedic HMP	Manufacturer	Herbal/Herbomineral	Metals added intentionally (Lead, Arsenic, Mercury, Tin, Silver, Gold, Cadmium)	Heavy metals Detected
1.	Bal Chamcha	Jalaram	Composition not known	?	Lead (10 mg/g)
2.	Bala Gutti	Zandu	Composition not known	?	Lead (5 mg/g)
3.	Bala Sogathi	Navjeevan	Composition not known	?	Lead (43 mg/g); Mercury (28 mg/g)
4.	Balguti Kesaria	Kesari Ayurvedic Pharmacy	Composition not known	?	Lead (7 mg/g); Mercury (17,600 mg/g); Arsenic (37 mg/g)
5.	Gesari	Harinarayan Pharmacy	Composition not known	?	Lead (7 mg/g)
6.	Karela	Himalaya	Herbal	Nil	Lead (7 mg/g)
7.	Mahasudarshan Churna	Dabur	Herbomineral (Herbs + Sphatika -alum)	Nil	Lead (17 mg/g)
8.	Mahasudarshan Churna	Zandu	Herbomineral (Herbs + Sphatika -alum)	Nil	Lead (40 mg/g)
9.	Mahalakshmi Vilas Rasa with gold	Baidyanath	Herbomineral (Herbs + Loha -Iron, Abhraka-Mica, Tamra- Copper, Suvarna Makshika- Iron pyrite)	Suvarna (Gold), Parada (Mercury), Vanga (Tin), Rajata (Silver)	Lead (300 mg/g); Mercury (72,100 mg/g); Arsenic (2800 mg/g)

(Contd.)

<b>Table 3—Ayurvedic herbal medicinal products containing Lead, Mercury, and / or Arsenic</b>					
<b>S. No.</b>	<b>Ayurvedic HMP</b>	<b>Manufacturer</b>	<b>Herbal/Herbomineral</b>	<b>Metals added intentionally (Lead, Arsenic, Mercury, Tin, Silver, Gold, Cadmium)</b>	<b>Heavy metals Detected</b>
10.	MahaYogaraja Guggulu with silver & Makardhwaja	Baidyanath	Herbomineral (Herbs + Lohasara, Abhraka- Mica, Mandoora- Iron, Gandhaka- Sulphur)	Vanga (Tin), Ropya (Silver), Naga (Lead), Rasa Sindoora, Parada (Mercury), Suvarna (Gold)	Lead (37,000 mg/g); Mercury (22, 800 mg/g); Arsenic (8100 mg/g)
11.	Navratna Rasa (Navratna Kalpamruta rasa)	Unjha	Bhasmas of precious/ semiprecious stones	Calcs of tourmaline, Coral, Cat's eye, Emerald, Sapphire, Ruby, Diamond, Topaz, Coral, Gold, Onyx, Black sulphide of mercury	Lead (600 mg/g); Iron pyrites, Mercury (104, 000 mg/g); Arsenic (60 mg/g)
12.	Safi	Hamdard Pakistan	Herbal	Nil	Arsenic (54 mg/ml)
13.	Shilajit	Syncom	Mineral	-	Lead (8 mg/g)
14.	Swarna Mahayogaraja Guggulu with gold	Baidyanath	Herbo-Mineral (Herbs + Lohasara, Abhraka- Mica, Mandoora- Iron, Gandhaka- Sulphur)	Vanga (Tin), Ropya (Silver), Naga (Lead), Rasa Sindoora	Lead (7870 mg/g); Mercury (4380 mg/g); (Mercury), Suvarna (Gold) Arsenic (800 mg/g)

Table 4—Heavy metal limits in few countries

	Arsenic	Lead (As)	Cadmium (Pb)	Chromium (Cd)	Mercury (Cr)	Copper (Hg)	Total Toxic (Cu)	Metals as Lead
For herbal medicines								
Canada	Raw medicinal plant materials	5 ppm	10 ppm	0.3 ppm	2 ppm	0.2 ppm		
	Finished herbal products	0.01 mg/day	0.02 mg/day	0.006 mg/day	0.02 mg/day	0.02 mg/day		
China to be changed	Medicinal plant materials	2 ppm	10 ppm	1 ppm		0.5 ppm	20 ppm	
Malaysia	Finished herbal products	5 mg/kg	10 mg/kg			0.5 mg/kg		
Republic of Korea	Medicinal plant materials							30 ppm
Singapore	Finished herbal products	5 ppm	20 ppm			0.5 ppm	150 ppm	

(Contd.)

- b. Does mere presence of heavy metals in plant makes it toxic or the presence of heavy metals in trees may be contributing to therapeutic activity as well?
- c. There is a need to conduct a comparative study of a plant material containing heavy metals from the soil v/s the plant material which does not contains heavy metals from the soil but the similar quantity of heavy metals are added from out side. Both these samples should be subjected to compare their toxicity to answer the above two questions.
- d. In India, we do not have any systematic study basis by which the limit of heavy metals can be decided. It is recommend therefore to first screen the plant materials available in India for heavy metal presence from various geographical locations and then decide the limits.

To emphasize this point, the country specific limits for heavy metals <sup>6</sup> have been enumerated (Table 4).

It is also possible that sometimes these heavy metals may come as contaminant during processing in improper vessels or from the water used. These are probable sources of contamination and Good Manufacturing Practices should be able to take care of it.

### 3. Improper use of Ayurvedic medicine

Following factors are very important with respect to Ayurvedic medicine consumption.

- i. The vehicle e.g. honey, water etc.
- ii. Relationship with food
 

There are 10 different timing of taking the medicine as per Ayurveda which are given below

  1. *Abhukta* (early morning empty stomach)
  2. *Pragbhukta* (immediately before food)
  3. *Adhobhukta* (immediately after food)
  4. *Madhyabhukta* (mid way in the meal)
  5. *Antarabhukta* (between morning meal and evening meal)
  6. *Sabhukta* (with food or mixed in food)
  7. *Samudagbhukta* (before and after intake of light meal)
  8. *Muhur-muhur* (with food or without food, with food or w/o infrequent intervals)
  9. *Sagras* (with every bite or with some of the bite)
  10. *Grasantar* (between subsequent bite)

Table 4—Heavy metal limits in few countries

	Arsenic	Lead (As)	Cadmium (Pb)	Chromium (Cd)	Mercury (Cr)	Copper (Hg)	Total Toxic (Cu)	Metals as Lead
Thailand	Medicinal plant material, finished herbal products	4 ppm	10 ppm	0.3 ppm				
WHO recommendations		10 mg/kg	10 mg/kg	0.3				
For other herbal products								
National Sanitation Foundation draft proposal (Raw dietary supplement)		5 ppm	10 ppm	0.3 ppm	2 ppm			
National Sanitation Foundation draft proposal (Finished Dietary Supplement)		0.01 mg/day	0.02 mg/day	0.006 mg/day	0.02 y mg/day	0.02		

- iii. Improper dose
- iv. Incompatible formulations- though Ayurvedic physicians always take care for any incompatible formulations, however this possibility over ruled in OTC products.

#### 4. Quality of Ayurvedic medicine

Maintaining quality of Ayurvedic medicine is of paramount importance. Government of India has after almost 30 years efforts developed Ayurvedic Pharmacopoeia of India giving the quality standards of certain raw materials. Since Ayurvedic medicines cover a large number of ingredients and formulations, generation of quality specifications of all the ingredients and formulations is an uphill task and will take its own time. In the meantime, most of the Indian Ayurvedic industries use their own in-house standards to maintain the quality. However, presence of unscrupulous manufactures can't be ruled out. GMP guidelines for Ayurvedic medicines in India have recommended implementations of quality control measures as well.

#### 5. Abuse

*Charaka Samhita* has classified physicians into 3 categories; genuine physician, feigned physician, and pseudo-physician. Due to socio economic reasons quackery is also prevalent in certain parts of India in the name of Indigenous System practitioners.

In one study, the presence of phenytoin and phenobarbital in the Ayurvedic tablets given to the patients of epilepsy has been reported<sup>7</sup>. Presence of corticosteroids in some of the Ayurvedic preparations prescribed by the so-called traditional medicinal physicians in India has been reported<sup>8</sup>. In this study almost 42% Ayurvedic medicine samples were found to be adulterated with corticosteroids.

This is to be noted that these kind of malpractice usually happen at the physician's end rather than at the manufacturer's end.

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