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## Research Article

# Assessment of Heavy Metal Content of Branded Pakistani Herbal Products

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## Abstract

**Purpose:** To investigate the heavy metals present in branded Pakistani herbal medicines used in the management of various human ailments.

**Method:** The herbal dosage forms assessed were tablets, capsules and syrups. The samples were prepared for analysis by wet digestion method using nitric acid and perchloric acid treatment and then analyzed using a flame atomic absorption spectrometer.

**Results:** Most of the products exceeded the permissible limits for lead (100 %), cadmium (68 %), chromium (96 %) and nickel (100 %). However, the contents of copper, manganese, zinc and iron were below toxic limits in several of the products. Some of the products, including Arq-e-badian, Bazori, Banafsha and Arq-Mako, exhibited toxic concentration of almost all the metals assessed.

**Conclusion:** There is need to design suitable quality control parameters for the validation of herbal products and/or implement already existing rules and regulations for the safety of end-users.

**Keywords:** Heavy metals, Branded herbal products, Validation, Toxicity

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## INTRODUCTION

Over the years, herbal products have been used in various civilizations of the world for the cure of human ailments. Advocates of herbal therapies say that these products are safe and efficacious due to long empirical usage and natural origin [1]. In Pakistan, the practice of traditional medicine is in the form of hikmath and homeopathy, which is regulated by the Federal Government through Unani, Ayurvedic and Homeopathic (UAH) Practitioners Act, 1965; the National Council of Tibb and National Council for Homeopathy were established as corporate bodies under section 3 of the Act to promote and popularize the traditional system of medication [2]. Pakistan's Ministry of Health (MOH) estimates that there are 39,584 registered hakims and 82,375 homeopathic practitioners in various rural and urban areas of the country. A large segment of population has benefited from these therapies due to low cost and easy access [3-4].

Although phytomedicines are often claimed to be beneficial and free of side effects, there have been reports of acute and chronic toxicity resulting from their use. The World Health Organization (WHO) recommends that herbal products should be evaluated for efficacy, potency as well as safety to protect public health. One of the leading causes of toxicity of herbal medicines is the presence of toxic heavy metals [5-6]. The plants imbibe toxic metals in various ways including the environment they grow in, contaminated water, agricultural expedients, storage environment and manufacturing processes [7]. The purpose of this study was to evaluate the heavy metals contents of some selected herbal products available in the Pakistani market.

## EXPERIMENTAL

### Materials

Nitric acid and perchloric acid (both from Sigma), deionizer (Elga, B 114), Whatman 42 filter paper, glass ware, hot plate (Lab Tech), and atomic absorption spectrometer (Parkin Elmer AAnalyst 700).

### Collection of herbal samples

The herbal products were purchased from a local market in the district of Swabi, Pakistan. Selection of the products used was based on the popularity of the products among the general public and the reputation of the manufacturers. The list of the twenty-five herbal products selected is given in Table 1.

### Prevention of contamination

Standard experimental conditions were followed through out the analysis. In order to prevent contamination, all the glassware were soaked in chromic acid for 24 h and thoroughly washed with deionized water and/or distilled water. They were then dried in an oven at 60 °C and stored in dust free environment without touching their interior.

### Sample preparation

Twenty five commercial herbal products of various brands were analyzed for their toxic metal concentrations. They were available in both solid and liquid dosage forms. For solid formulations, 1 g of the powdered sample was taken in a flask, 10 ml of concentrated nitric acid (67 %) was added and kept at room temperature for 24 h in a fume hood. Perchloric acid (4 ml) was added to the sample and concentrated on a hot plate at 60 °C until a suspension of approximately 1 ml was left in the flask. The residue was cooled, diluted with deionized water up to 50 ml and filtered through Whatman filter paper no. 42. Sufficient deionized water was added to make the volume up to 100 ml (stock solution) [8] and was kept in a transparent bottle until analyzed by atomic absorption spectrometer (AAS) for various heavy metals with the results expressed in parts per million (ppm). AAS operating parameters are as shown in Table 2. For liquid dosage forms, 1 ml of the liquid sample was taken in a 100 ml flask and made up to 100 ml with deionized water [9]. For viscous suspensions, a few drops of nitric acid (65 %) were added to digest the particles, In either case, the

**Table 1:** Basic information on the herbal products

Product	Batch no.	Manufacturer	Indication(s)	Dose
Anab	060308	Qurshi	Blood purifier	30 ml BD
Arq-e-badian	071107	Qurshi	GIT, UTI	40 ml BD
Arq-Mako	–	Qurshi	Anti-inflammatory	80 ml BD
Asthmina	231107	Qurshi	Anti-asthmatic	5-10 ml TDS
Banafsha	221107	Qurshi	RTI	30 ml BD
Bazori	0104408	Qurshi	Diuretics	30 ml BD
Colgesic	275	Galen lab	Anti-spasmodic	10-15 ml TDS
Colic	172 B	Brick	GIT disorders	15-30 ml TDS
Demaghoon	TT062007	TT Lab	Enhance memory	30 ml BD
Digical	–	Green lab	GIT disorders	5-15 ml TDS
Dinar	–	Qurshi	Liver disorders	30 ml BD
Hazmeena tab	9810039	Hamdard	Digestive	4 tab daily
Injabar	180907	Qurshi	GIT disorders	30 ml BD
Mansofar tab	080108	Qurshi	Menstrual disorder	2 tab OD
Masturin	023	Hamdard	Menstrual disorder	10 ml OD
Pathri tore tab	230607	Qurshi	Kidney stone	2 tab TDS
Sposmodin	091	Hamdard	Blood purifier	10 ml BD
Sharbate foulad	170408	Qurshi	Tonic	15-30 ml BD
Sharbate foulad	12	Aqsa lab	Tonic	15-30 ml BD
Sharbate sadar	–	Qurshi	RTI	5-10 ml TDS
Suduri	122	Hamdard	Cough	10 ml TDS
Supari pak	290308	Qurshi	Leucorrhoea	10 mg BD
Toot siah	03117	Qurshi	Cough	10 ml TDS
Urosinal	–	Qurshi	UTI	5 ml BD
Y-lin	001	Brick	Cough	15 ml TDS

**Key:** tab = tablet, OD = once daily, BD= twice daily, TDS= thrice daily

**Table 2:** Operating parameters for atomic absorption spectrometry

Metal name	Wave-length (nm)	Slit width (nm)	Acetylene flow (L/min)	Cathode lamp current (mA)
Pb	283.3	0.7H	2.0	10
Cd	279.5	0.2H	2.0	20
Zn	213.9	0.7H	2.0	15
Cr	357.9	0.7H	2.5	25
Fe	248.3	0.7H	2.0	30
Ni	232	0.2H	2.0	25
Mn	279.5	0.2H	2.0	20
Cu	324.5	0.7H	2.0	15

**Note:** Flame type was air-acetylene while air oxide flow was 17 L/min

solution was filtered, processed and analyzed as described above for solid dosage forms.

## Statistical analysis

Data are expressed as mean  $\pm$  SEM (n = 3) and were analyzed using GraphPad, San Diego, CA, USA)

## RESULTS

The concentration levels of the various metals in the products are summarized in Table 3. Almost all the samples exceeded the permissible limit for lead (5 ppm). In the case of cadmium, 17 products (i.e., 68 %) exceeded the permissible limit (0.5 ppm). Chromium was found in 96 % of the samples to have exceeded the permissible limit (30–35 ppm) while nickel concentration exceeded the permissible limit (1.5ppm) in all the samples. Manganese, zinc and iron were found within permissible limits in all the herbal products. The highest Pb concentration was found in *Banafsha*

**Table 3:** Heavy metal content (ppm, mean  $\pm$  SEM) of some herbal products used Pakistan

Product	Pb	Cd	Cr	Cu	Ni	Mn	Zn	Fe
Anab	28.2 $\pm$ 0.01	5.2 $\pm$ 0.02	128.8 $\pm$ 0.01	1.1 $\pm$ 0.03	9.3 $\pm$ 0.00	ND	6.6 $\pm$ 0.01	21.3 $\pm$ 0.02
Arq-e-badian	28.9 $\pm$ 0.02	7.2 $\pm$ 0.01	146.4 $\pm$ 0.00	1.6 $\pm$ 0.01	11.2 $\pm$ 0.02	ND	9.0 $\pm$ 0.01	16.1 $\pm$ 0.02
Arq-Mako	25.4 $\pm$ 0.01	5.1 $\pm$ 0.00	142.7 $\pm$ 1.39	ND	6.1 $\pm$ 0.01	ND	5.7 $\pm$ 0.01	9.8 $\pm$ 0.01
Asthmina	31.8 $\pm$ 0.01	5.0 $\pm$ 0.01	133.5 $\pm$ 1.33	0.1 $\pm$ 0.00	5.7 $\pm$ 0.02	ND	5.1 $\pm$ 0.02	9.7 $\pm$ 0.03
Banfsha	46.4 $\pm$ 0.04	6.9 $\pm$ 0.00	154.2 $\pm$ 0.00	2.7 $\pm$ 0.03	12.3 $\pm$ 0.01	1.1 $\pm$ 0.00	7.6 $\pm$ 0.03	33.8 $\pm$ 0.05
Bazori	30.7 $\pm$ 0.01	6.3 $\pm$ 0.01	148.2 $\pm$ 0.06	0.7 $\pm$ 0.00	14.9 $\pm$ 0.00	ND	11.5 $\pm$ 0.03	19.3 $\pm$ 0.04
Colgesic	27.4 $\pm$ 0.01	5.5 $\pm$ 0.05	136.3 $\pm$ 0.07	0.9 $\pm$ 0.00	5.9 $\pm$ 0.02	ND	6.4 $\pm$ 0.00	18.3 $\pm$ 0.01
Colic	28.2 $\pm$ 0.01	6.3 $\pm$ 0.03	126.7 $\pm$ 0.08	2.0 $\pm$ 0.01	4.4 $\pm$ 0.00	0.6 $\pm$ 0.00	18.3 $\pm$ 0.01	19.5 $\pm$ 0.03
Demaghoon	30.0 $\pm$ 0.04	6.9 $\pm$ 0.00	141.2 $\pm$ 0.05	1.0 $\pm$ 0.00	5.5 $\pm$ 0.01	ND	8.7 $\pm$ 0.00	23.3 $\pm$ 0.04
Digical	20.9 $\pm$ 0.05	5.3 $\pm$ 0.00	127.7 $\pm$ 0.06	2.5 $\pm$ 0.01	1.2 $\pm$ 0.00	ND	6.1 $\pm$ 0.00	29.3 $\pm$ 0.07
Dinar	28.6 $\pm$ 0.00	5.6 $\pm$ 0.01	136.8 $\pm$ 0.02	0.6 $\pm$ 0.00	3.9 $\pm$ 0.00	ND	5.9 $\pm$ 0.02	10.9 $\pm$ 0.01
Hazmeena tab	35.2 $\pm$ 0.03	5.9 $\pm$ 0.03	94.5 $\pm$ 0.02	18.0 $\pm$ 0.03	9.3 $\pm$ 0.00	26.5 $\pm$ 0.07	87.9 $\pm$ 0.11	697.8 $\pm$ 1.09
Injabar	24.6 $\pm$ 0.06	1.9 $\pm$ 0.00	125.3 $\pm$ 0.07	1.3 $\pm$ 0.00	6.7 $\pm$ 0.01	ND	5.6 $\pm$ 0.00	8.6 $\pm$ 0.01
Mansofar tab	4.6 $\pm$ 0.00	4.0 $\pm$ 0.00	87.2 $\pm$ 0.04	10.5 $\pm$ 0.02	7.4 $\pm$ 0.00	346.4 $\pm$ 1.0	253.8 $\pm$ 0.90	2731.8 $\pm$ 2.02
Masturin	31.2 $\pm$ 0.03	5.3 $\pm$ 0.00	132.8 $\pm$ 0.04	3.9 $\pm$ 0.00	4.5 $\pm$ 0.00	6.6 $\pm$ 0.00	35.4 $\pm$ 0.41	1580.4 $\pm$ 1.25
Pathri tore tab	22.7 $\pm$ 0.03	4.2 $\pm$ 0.00	144.6 $\pm$ 0.05	12.1 $\pm$ 0.01	56.3 $\pm$ 0.01	38.8 $\pm$ 0.50	31.4 $\pm$ 0.40	634.3 $\pm$ 1.01
Sposmodin	20.0 $\pm$ 0.11	ND	50.2 $\pm$ 0.05	1.0 $\pm$ 0.01	4.3 $\pm$ 0.00	ND	ND	ND
Sharbate foulad	26.9 $\pm$ 1.01	6.8 $\pm$ 0.05	150.3 $\pm$ 0.05	0.8 $\pm$ 0.00	7.9 $\pm$ 0.00	ND	6.2 $\pm$ 0.02	159.5 $\pm$ 1.00
Sharbate foulad	29.2 $\pm$ 1.03	4.7 $\pm$ 0.00	147.7 $\pm$ 0.00	ND	9.3 $\pm$ 0.09	ND	9.4 $\pm$ 0.21	80.7 $\pm$ 0.70
Sharbate sadar	23.1 $\pm$ 1.04	4.9 $\pm$ 0.00	127.7 $\pm$ 0.00	1.1 $\pm$ 0.00	3.5 $\pm$ 0.02	ND	8.4 $\pm$ 0.05	11.8 $\pm$ 0.00
Suduri	29.9 $\pm$ 1.00	6.1 $\pm$ 0.01	139.4 $\pm$ 0.00	1.5 $\pm$ 0.02	9.1 $\pm$ 0.09	1.2 $\pm$ 0.01	5.3 $\pm$ 0.01	15.5 $\pm$ 0.11
Supari pak	23.1 $\pm$ 1.04	23.8 $\pm$ 1.00	86.0 $\pm$ 0.03	7.7 $\pm$ 0.02	5.3 $\pm$ 0.11	23.4 $\pm$ 0.11	37.8 $\pm$ 0.02	446.2 $\pm$ 0.60
Toot siah	26.9 $\pm$ 0.05	5.9 $\pm$ 0.08	142.3 $\pm$ 1.03	0.1 $\pm$ 0.02	7.0 $\pm$ 0.16	ND	6.6 $\pm$ 0.00	21.8 $\pm$ 0.04
Urosinal	26.5 $\pm$ 0.00	6.6 $\pm$ 0.12	133.6 $\pm$ 0.03	1.3 $\pm$ 0.02	5.4 $\pm$ 0.06	ND	7.9 $\pm$ 0.07	16.4 $\pm$ 0.01
Y-lin	31.6 $\pm$ 0.01	7.1 $\pm$ 0.02	139.5 $\pm$ 0.09	0.6 $\pm$ 0.02	9.7 $\pm$ 0.14	2.0 $\pm$ 0.02	7.4 $\pm$ 0.21	26.1 $\pm$ 0.03

ND = Not detected

(46.4ppm) followed by *Hazmeena tab* (35.2 ppm), *Asthmina* (31.8 ppm), *Y-lin* (31.6 ppm) and *Masturin* (31.2 ppm). The Cd concentration range in the tested samples was 1.9 - 23.8 ppm with the highest concentration in *Supari pak* (23.8 ppm), followed by *Arq-e-badian* (7.2 ppm), *Y-lin* (7.1 ppm), *Banfsha* (7.1 ppm), *Demaghoon* (6.9 ppm), *Sharbate foulad* (6.8 ppm) and *Colic* (6.3 ppm). These values show that all the samples exceeded the permissible limit for cadmium. The highest Cr concentration was found in *Banfsha* (154.2 ppm) followed by *Sharbate foulad* (150.3 ppm), *Bazori* (148.2 ppm). The

highest concentration of copper was found in *Hazmeena tab* (18 ppm) followed by *Pathri tore tab* (12.1 ppm), *Mansofar tab* (10.5 ppm), *Supari pak* (7.7 ppm), *Masturin* (3.9 ppm), *Banfsha* (2.7 ppm), and *Colic* (2 ppm).

## DISCUSSION

To appreciate the implications of the findings of this study, the recommended daily limits of some of the more significant metals are shown in Table 4 while the hypothetical intake of the metals by patients who consume

the herbal products has been computed and listed in Table 5.

**Table 4:** Recommended daily limits for some metals

Metal	Recommended daily limit	Reference
Pb	20–514 ug	14
Cd	70 ug	14
Cr	11-25 ug (child), 30 -35 ug (adult)	17, 18
Cu	340–400 ug (child), 900 ug (adult)	17, 18
Ni	35 ug	20
Mn	8–11 mg	17
Zn	3-8 mg	17
Fe	8-10 mg	17

### Lead

Lead is one of the most toxic among toxic heavy metals. It enters the human body in

various ways including inhalation, drinking water, ingestion of food polluted with lead and absorption by skin. It accumulates in the body has no known useful biological function [10]. It has adverse effects on various body systems such as the reproductive, renal, digestive, cardiovascular and immunological systems [11].

The concentration of lead in the tested products was in the range of 4.6 – 46.4 ppm. The recommended limit for finished herbal products is 5 ppm while for crude herbal materials, it is 10 ppm [12]. Since our study was conducted on finished herbal products, we consider the 5 ppm as the applicable limit. Thus, only one product out of the twenty five assessed had lead concentration below the recommended limit. It is clear, therefore, that these products are potentially toxic to man.

**Table 5:** Daily consumption of metals ( $\mu\text{g}/\text{day}$ ) based on manufacturers' recommended dose of the respective products

Product	Pb	Cd	Cr	Cu	Ni	Mn	Zn	Fe
Anab	1692	312	7728	66	558	ND	396	1278
Arq-e-badian	2312	576	11712	128	896	ND	720	1288
Arq-Mako	2032	408	11416	ND	488	ND	456	784
Asthmina	477–954	75–150	2002.5–4005	1.5–3	85.5–171	ND	76.5–153	145.5–291
Banfsha	2784	414	9252	162	738	66	456	2028
Bazori	1842	378	8892	42	894	ND	690	1158
Colgesic	822–1233	165–247.5	4089–6133.5	27–40.5	177–265.5	ND	192–288	549–823.5
Colic	423–846	94.5–189	1900.5–3801	30-60	66-132	9-18	274.5–549	292.5–585
Demaghoon	1800	414	8472	60	330	ND	522	1398
Digical	313.5–627	79.5–238.5	1915.5–5746.5	37.5–112.5	18–54	ND	91.5–274.5	439.5–1318.5
Dinar	1716	60	8208	36	234	ND	354	654
Hazmeena tab	140.8	23.6	378	72	37.2	106	351.6	2791.2
Injabar	1476	114	7518	78	402	ND	336	516
Mansofar tab	5.4	4.72	102.8	12.39	8.7	408.7	299.4	3223.5
Masturin	312	53	1328	39	45	66	354	15804
Pathri tore tab	90.8	15.3	529.2	44.2	206	142	114.9	2321.5
Sposmodin	400	ND	1004	20	86	ND	ND	ND
Sharbate foulad	403.4–807	204–408	4509–9018	24–48	237–474	ND	186–372	9570-4785
Sharbate foulad	438–876	141–282	4431–8862	ND	279–558	ND	282–564	2415–4830
Sharbate sadar	354–708	73.5–149	1915.5–3831	16.5–33	52.5–105	ND	126–252	177–354
Suduri	897	183	4182	45	273	36	159	465
Supari pak	46.2	47.6	1.7	0.1	0.1	0.4	0.7	8.9
Toot siah	807	177	4269	3	210	ND	198	654
Urosinal	265	66	1336	13	54	ND	79	164
Y-lin	1422	319	6277.5	27	439.5	90	333	1174.5

Incidentally, all these products are very popular among the people and adult and children chronically use some of them such as Sharbate foulad and Colic. There is a large body of data on the adverse effect of lead in herbal formulations human health [13]. The daily consumption of lead, based on the recommended dose of the products, was computed and is shown in Table 5. The recommended daily consumption of lead is 20 – 514  $\mu\text{g/day}$  [14]. Based on this limit, 19 out of the 25 products exceeded the permissible limit. The highest daily consumption of lead was found for *Banafsha* (2784  $\mu\text{g/day}$ ), followed by *Arq-e-badian* (2312  $\mu\text{g/day}$ ) and *Arq-Mako* (2032  $\mu\text{g/day}$ ). The consumption of the metals is directly proportional to the dose of the products.

### Cadmium

Cadmium is a toxic metal of occupational and environmental concern. Cadmium exposure leads to a variety of adverse effects due to its extremely long biological half-life. The rate of cadmium transfer from soil to plants is very high and the metal is considered to have carcinogenic effects on liver, pancreas and stomach [15]. Its recommended concentration in plant is 3 ppm while for finished plant products, it is 0.5 ppm [12]. The computed daily intake of cadmium due to the consumption of these products is given in Table 4. The recommended consumption of cadmium is 70  $\mu\text{g/day}$  [14]. Based on this, 17 products out of 25 exceeded the permissible limit. The highest Cd consumption are: *Arq-e-badian* (576  $\mu\text{g/day}$ ) followed by *Demaghoon* and *Arq-Mako* (414  $\mu\text{g/day}$ ), and *Banafsha* (408  $\mu\text{g/day}$ ).

### Chromium

Chromium exists in two ionic forms, trivalent and hexavalent, the latter being toxic and is correlated to human carcinogenesis and acute toxicity of aquatic organisms [16]; on the other hand, its reduced form (trivalent) is an essential element for animals. The concentration of chromium was in the range

of 86 - 154.2 ppm. There is no recommended limit for chromium in herbal finished products. Its daily intake for these products is shown in Table 4. The highest consumption was observed for *Arq-e-badian* (11712  $\mu\text{g/day}$ ) followed by *Arq-Mako* (11416  $\mu\text{g/day}$ ). The recommended limit of chromium is 11 - 25  $\mu\text{g/day}$  for children and 30 - 35  $\mu\text{g/day}$  for adults [17,18]. Only one product had chromium concentration below the recommended limit. Such a high concentrations could be toxic due to the chronic use of some of the tested products. Copper

Copper has both beneficial and toxic effects depending on its level of consumption. Monitoring of copper limit is essential as it is beneficial in low concentrations but exhibit various toxic effects above the safety limit. In this study, copper was found in the products in the concentration range of 0.1 - 18 ppm. The calculated daily consumption of copper for the products is shown in Table 4. The recommended consumption of copper is 900 and 340 - 400  $\mu\text{g/day}$  for adult and for child, respectively [17,18]. Thus, all the tested products were safe with regard to copper content.

### Nickel

Nickel is abundant in nature. Possible exposure sources of nickel are food, drinking water, absorption by contact and inhalation in nickel-polluted area [19]. Ingestion of large amounts of nickel affects stomach, liver, kidneys, immune system and reproduction in rats and mice [19]. The most common toxic effect is dermatitis while lung cancer has also been reported in some studies [19]. Nickel was found in a concentration range of 1.2 - 56.3 ppm as shown in Table 3. The highest concentration was found in *Pathri tore tab* (56.3 ppm), followed by *Bazori* (14.9 ppm), *Banafsha* (738 ppm). The daily intake of nickel by patients, calculated on the basis of the products' recommended doses is shown in Table 5. The recommended consumption limit of nickel is 35  $\mu\text{g/day}$  [20]. Therefore, the

highest consumption of the metal would occur for *Arq-e-badian* (896 µg/day), followed by *Bazori* (894 µg/day) and *Banafsha* (738 µg/day). Thus, almost all the tested samples exceeded the daily allowed limit for nickel.

### Other metals

The contents of Mn, Zn and Fe in the tested products were within their permissible limits, as shown in Table 3; they did not exceed the daily consumption limits of these metals.

### CONCLUSION

Among the tested herbal products, the levels of lead, cadmium, chromium and nickel exceeded recommended limits. Based on the results, it is strongly recommend to that regulatory authorities should make and enforce regulations for pre-marketing safety studies on herbal products in order to protect the health of the public. Like conventional drugs, herbal products should be subjected to adequate quality control requirements, such as those recommended by WHO, to ensure their efficacy, potency and safety.

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