Comparison of toxic heavy metals concentration in medicinal plants and their respective branded herbal formulations commonly available in Khyber Pakhtunkhwa

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Abstract: The present study was conducted on fifteen medicinal plants and their respective branded formulations, commonly used in Khyber Pakhtunkhwa, for the evaluation of toxic heavy metals. The purpose of the study was to assess the toxic profile of the crude medicinal plants with respect to the worldwide permissible limits of metal concentrations and to correlate it with their respective herbal formulations available on the market. Chromium (Cr), Copper (Cu), Lead (Pb), Manganese (Mn) and Nickel (Ni) content were evaluated using wet digestion and Atomic Absorption Spectrophotometry technique. The results exhibited that in 100% of the analyzed medicinal plants Cr and Ni are present in excess of the maximum limits, Cu and Pb in 73% and 60% respectively, while Mn is in the normal range. Likewise in the respective branded formulations Cr and Ni exceed the normal limit in 100% of the products, Cu and Pb in 27% and 20% of the products respectively, while Mn is in the normal range. It indicates that majority of people in Pakistan who frequently use herbal drugs in various forms are exposed to the hazardous elements, which may pose serious health effects. Regulatory measures should therefore be taken to protect the general public from their hazardous health effects.

Keywords: Hazardous heavy metals, Medicinal plants, Herbal formulations, Toxicity.

INTRODUCTION

The word "conventional medicine" is a medical system developed over centuries in different period of modern medicine (Shinwari, 2010). Traditional or conventional practices include Homeopathy, Tib-E-Nabvi, Ayurvedic, Traditional medicines, Chinese-medicine, South African Muti, as well as other such medical practices all over the world (Saeed *et al*., 2011). According to WHO the conventional medicines are defined as: "The health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral- based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses or maintain well-being" (WHO, 2002). Herbal products have been employed for the treatment of various ailments in both eastern and western civilizations for many hundreds years ago (Chaudhury, 1992). More than 2000 varieties of minor and major illness were studied and it was noticed that more than 40% were recovered using conventional orthodox pharmaceuticals (Abbot *et al*., 1996). The importance and emerging market demand of herbal products cannot be ignored. At the same time certain aspects concern with the safety, efficacy and quality of natural and herbal products are challenges (Chan, 2003). In the United States most of the herbal products are kept under the category of dietary supplements and thus are not regulated as a medicine. These products are not required to meet the standard for drugs specified in the Federal Food, Drugs and Cosmetic Act. These preparations are bound to the Dietary Supplements and Health Act (DSHEA) 1994. According to the DSHEA the responsibility for the quality control and safety parameters of the herbal preparation is on the manufacturer (Ang-Lee *et al*., 2001). In Pakistan, the conventional medicine is practiced 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 conventional medicine system. According to Pakistan's Ministry of Health (MOH) there are 39,584 hakims and 82,375 homeopathic practitioners in the rural and urban areas. Due to low cost and easy access a large population of the country has approached them for treatment (Saeed *et al*., 2011).

The safety or their use has recently been questioned due to the reports of illness and fatalities (Saeed *et al*., 2011; Stewart *et al*; 1999; Ernst, 2002). Toxicity due to the toxic metals in medicinal plants has been reported in various countries of the world and even in Pakistan (Dunbabin *et al*., 1992; Olujohungbe *et al*., 1994). Although these herbal preparations are claimed for their efficacy and lack of side effects, yet they are reported for acute and chronic toxicity resulting from their use. According to World Health Organization these herbal preparations should be evaluated for their efficacy, potency and safety to protect public health. The presence of toxic heavy metals in the

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crude drugs as well as in herbal products causes severe health risk to the consumers. The major and basic source of metal contamination are the plants raw materials, while leeching of metal from containers and different chemical used in various stage of manufacturing and intentional use of heavy metals in Chinese and Indian traditional medicines for their therapeutic claims are the other sources (Ernest *et al*., 2002; Saper *et al*., 2004). In Singapore arsenic poisoning has been observed in children using Chinese herbal products (Saper *et al*., 2004). Similarly toxicity of Pb, Cd, As, and Hg associated with various Chinese and Indian herbal preparations has been documented across the world (Ernst, 2003; Dargan *et al*., 2008).

As it has been proven that in developing countries the users of alternative medicine are high in number, the protection and effectiveness of the herbal medicine is a challenge to the researchers. This study was therefore conducted to evaluate the potential for harm of these products. Toxic heavy metals namely Chromium (Cr), Copper (Cu) Lead (Pb), Nickel (Ni), and Manganese (Mn) were determined in fifteen medicinal plants and their respective branded formulations most commonly used in Khyber Pakhtunkhwa and all over Pakistan in general.

MATERIAL AND METHODS

Fifteen medicinal plants as identified and collected by their suppliers in market and their respective branded formulations were collected from reputed manufacturers of Khyber Pakhtunkhwa, Pakistan (names not disclosed), in March 2012 (table 1). The plants materials were powdered finely. It was stored in glass bottles with appropriate labeling. Wet digestion method, as discussed below, was used for the preparation of samples for analysis. Fine-grounded powder (1gm) of each plant was taken in a small beaker; concentrated nitric acid (Sigma-Aldrich) (10ml) was transferred to each beaker and was allowed to digest for 24 hrs. Each beaker was heated on hot plate, until the production of red NO_2 fumes ceased. After cooling, perchloric acid (Sigma) (2-4 ml) was added and heated, then aqua regia (10ml) was added and heated till evaporate to small volume, it were cooled by adding distilled water and filtered with what man filter paper no. 42. The final volume of the filtrate was made by double distilled water (Fazli *et al*., 2012). Each branded liquid formulation (1ml) was transferred to beaker and was treated similarly as in case of medicinal plants powder to prepare sample. Likewise, each branded solid dosage form (1gm) was taken and sample was prepared by applying the same procedure as in case of medicinal plant powder to prepare sample. The stock solutions marked with names and code numbers and were analyzed through atomic absorption spectrophotometer for quantitative detection of the following trace elements and heavy metals; namely Chromium (Cr), Copper (Cu) Lead (Pb) Manganese (Mn) and Nickel (Ni). Standard working conditions were used for individual elements as described in literature previously (Saeed *et al*., 2011).

RESULTS

Chromium (Cr)

Concentration of chromium in medicinal plants and their respective branded formulations is given in table 2. Similarly its daily intake calculated on the basis of recommended daily dose of the branded formulation is given in table 3. In medicinal plants the range of chromium was 41.3-74.2 ppm, while in respective branded formulations it was found in the range of 36.5-63.0 ppm.

Copper (Cu)

Concentration of copper in medicinal plants and their respective branded formulations are given in table 2. Similarly its daily intake calculated on the basis of recommended daily dose of the branded formulation is given in table 3.

Lead (Pb)

Concentration of lead in medicinal plants and their respective branded formulations is given in table 2. Similarly its daily intake calculated on the basis of recommended daily dose of the branded formulation is given in table 3. The concentration of lead was found in the range of 7.5-18.0ppm in the medicinal plants, while the metal content in the branded formulations was found in the range of 5.0-13.5ppm.

Manganese (Mn)

Concentration of manganese in medicinal plants and their respective branded formulations is given in table 2. Similarly its daily intake calculated on the basis of recommended daily dose of the branded formulation is given in table 3.Concentration of manganese was found in the range of 12.1-48.5 ppm in the medicinal plants, while the metal content in the branded formulations was found in the range of 5.0-11.5ppm. Calculated daily intake was in the range of 0.028-1.150mg/day.

Nickel (Ni)

Concentration of nickel in medicinal plants and their respective branded formulations is given in table 2. Similarly its daily intake calculated on the basis of recommended daily dose of the branded formulation is given in table 3. Calculated daily intake was in the range of 0.027-7.150 mg/day.

DISCUSSION

In the current study the level of toxic metals in medicinal plants and their respected branded formulations available in the local market were evaluated. The daily consumption of these metals was calculated on the basis

Table 1: Medicinal plants and their respective branded formulation

S. No	Botanical name of plant	Part use	Branded Product Daily dose (ml)	Medicinal uses
1	*Sphaeranthusindicus* (Gulemundi)	Flowers	100	Jaundice, Helminthiasis, Skin disease
2	*Trachyspermumammi* (Ajwainekhrasani)	Fruit	80	Colic pain, Anthelmentic, Antihyperlipidemic
3	*Santalum album* (Sandal)	Bark	40	Coolant, Expectorant, Tonic
4	*Morousnigra* (Shahtoot)	Fruit	40	Purgative, hypoglycemic, anti-inflamatory
5	*Oleaeuropea* (Zaitoon)	Fruit	5	Cardiotonic, Antiarrthmic
6	*Foeniculum vulgaris* (Sonf)	Seeds	100	Carminative, Diuretic
7	*Plantagoovate* (Ispaghol)	Seeds	5	Anti-diarrheal, antihyperlipidemic
8	*Fumariaofficinalis* (Shahtarah)	Whole plant	100	Bile stone, Psoriasis
9	*Ziziphus jujube* (Unnab)	Fruit	40	Diarrhea, Hypoglycemia
10	*Ricinuscommunis* (Arandi)	Seeds	20	Anti-inflamatory, Larvicidal
11	*Solinumnigrum* (Kachmach)	Fruit	100	Anti-inflamatory, Diuretic
12	*Menthaarvensis* (Podina)	Leaves	100	Flatulence, Constipation
13	*Chichriunintybus* (Kasni)	Whole plant	100	Antibacterial, amenorrhea, dysmenorrheal
14	*Cuminumcyminum* (zeera)	Fruit	80	Jaundice, Diuretic
15	*Rosa demascena* (Gulab)	Flower	30	Laxative, Digestive disorders

of the manufacturer recommended doses indicated in the labels as shown in table 2. The metals content of the plants and brands were compared with international recommended limits and the daily consumption of the metals were compared with recommended daily allowance. Discussion regarding each of the studied heavy metal is as given below.

Chromium (Cr)

Chromium may exist either as trivalent or hexavalent. The former is essential for human and nontoxic, while the latter is carcinogenic and its acute toxicity has been observed in aquatic organisms. There is no recommended limit for plant materials in literature. The recommended daily allowance of chromium is 11-25µg/day for children and 30-35µg/day for adults (Trumbo *et al.*, 2001) (table 4). It is clear from table 3 that all samples are exceeding the daily recommended limit. Such a high concentrations could be toxic due to the chronic use of some of the tested products.

Copper (Cu)

Copper is an essential trace metal. However it is toxic if it exceeds allowable concentrations. Monitoring of copper limit is essential as it is beneficial in low concentrations but exhibit various toxic effects above the safety limit. The recommended limit for Copper is 10 ppm (Srivastava *et al.*, 2006). Similarly the recommended consumption of copper is 0.9 mg/day and 0.35 mg/day for adult and for child, respectively **[**IOM, 2001, ATSDR, 2008**]**. In our tested plants samples the Cu was observed in the range of 4.5-18.5 ppm. Only four samples were found with Cu level within permissible limit.

Lead (Pb)

Lead is one of the most toxic substances known. It can enter the human body through inhalation, ingestion and skin absorption. It accumulates in the body has no known useful biological function (Venkatesh, 2004). It has adverse effects on various body systems such as cardiovascular, digestive, immunological, renal, and reproductive systems (Jalili *et al*., 2009). The recommended limit for finished herbal products is 5 ppm while for crude herbal materials; it is 10 ppm (Kosalec *et al*., 2009). Similarly the recommended daily allowance for lead is 20-514 µg. The concentration of lead in the tested products was in the range of 10-13 ppm, which shows that all the brands possess toxic levels of lead.

Manganese (Mn)

The human body contains about 10mg of *Mn*, most of which is concentrated in the liver, bones and kidneys. It is a cofactor for a number of important enzymes, including arginase, cholinesterase, phosphor glucomutase, pyruvate carboxylase, mitochondrial super oxide dismutase and several phosphates, peptidases and glycosyltransferases. Manganese functions with vitamin K in the formation of prothrombin (Fell *et al*., 1996). Manganese is an essential nutrient, required in trace amounts for human health. The recommended permissible limit for *Mn* is 200 ppm in the plants (Srivastava *et al*., 2006). Similarly the recommended daily allowance for Mn is 8-11mg (Trumbo *et al*., 2001). Manganese was found in the range of 12.1-48.5 ppm in the medicinal plants, while the metal content in the branded formulations was found in the range of 5.0 -6.5 ppm. Daily intake due to branded formulation was in the range of 0.028-1.150 mg/day. It means that all the medicinal plants and branded formulations contain the

Table 2: Concentration of heavy metals in medicinal plant and their respective branded formulation.

S. No.	Medicinal plant	*Cr (ppm)		*Cu (ppm)		*Mn (ppm)		*Ni (ppm)		*Pb (ppm)	
		Plant	Brand	Plant	Brand	Plant	Brand	Plant	Brand	Plant	Brand
1	*Sphaeranthusindicus* (Gulemundi)	45.0	57.5	6.5	4.0	12.1	5.0	55.2	71.5	8.5	7.0
2	*Trachyspermumammi* (Ajwainekhrasani)	43.5	56.5	11.3	3.0	25.2	5.5	47.3	76.0	9.0	5.0
3	*Santalum album* (Sandal)	57.1	36.5	4.5	1.0	13.1	5.0	50.2	57.5	9.0	5.5
4	*Morousnigra* (Shahtoot)	48.1	53.0	11.5	1.5	20.5	7.0	44.2	73.5	18.0	13.0
5	*Oleaeuropea* (Zaitoon)	59.2	62.0	9.0	1.5	25.3	7.0	55.5	74.5	13.5	7.5
6	*Foeniculum vulgaris* (Sonf)	52.2	52.54	10.5	3.0	25.5	6.0	58.1	6.65	7.5	5.5
7	*Plantagoovate* (Ispaghol)	53.1	63.0	13.3	6.5	22.3	7.0	50.2	67.5	10.5	6.5
8	*Fumariaofficinalis* (Shahtarah)	47.1	51.0	16.1	3.0	23.0	11.5	58.5	69.5	10.2	13.5
9	*Ziziphus jujube* (Unnab)	41.3	52.1	10.0	2.0	26.5	7.0	51.5	68.5	5.0	10.0
10	*Ricinuscommunis* (Arandi)	60.2	56.0	11.5	4.0	43.5	6.0	49.5	65.5	14.0	9.0
11	*Solinumnigrum* (Kachmach)	50.5	63.0	18.5	1.5	33.3	6.0	50.5	69.5	14.0	9.0
12	*Menthaarvensis* (Podina)	74.2	61.5	13.0	3.5	39.5	6.5	53.5	70.0	11.0	10.0
13	*Chichriunintybus* (Kasni)	70.5	58.0	18.1	4.0	48.5	6.5	50.5	65.5	10.5	8.0
14	*Cuminumcyminum* (zeera)	50.5	56.5	12.5	3.0	38.5	5.0	50.0	60.5	15.0	12.0
15	*Rosa demascena* (Gulab)	62.3	61.5	6.5	4.0	42.5	5.5	47.3	55.5	15.5	8.0

Table 3: Calculated daily intake of heavy metals on the basis of dose taken of the branded formulation

S. No	Medicinal plant	Cr (mg/day)	Cu (mg/day)	Mn (mg/day)	Ni (mg/day)	Pb (mg/day)
1	*Sphaeranthusindicus* (Gulemundi)	5.750	0.400	0.500	7.150	0.700
2	*Trachyspermumammi* (Ajwainekhrasani)	4.520	0.240	0.440	6.080	0.400
3	*Santalum album* (Sandal)	1.460	0.040	0.200	2.300	0.220
4	*Morousnigra* (Shahtoot)	2.120	0.060	0.280	2.940	0.520
5	*Oleaeuropea* (Zaitoon)	0.310	0.007	0.035	0.372	0.375
6	*Foeniculum vulgaris* (Sonf)	52.54	0.300	0.600	6.650	0.550
7	*Plantagoovate* (Ispaghol)	0.252	0.026	0.028	0.270	0.026
8	*Fumariaofficinalis* (Shahtarah)	5.100	0.300	1.150	6.950	1.350
9	*Ziziphus jujube* (Unnab)	2.084	0.080	0.280	2.740	0.400
10	*Ricinuscommunis* (Arandi)	1.120	0.080	0.120	1.31	0.180
11	*Solinumnigrum* (Kachmach)	6.300	0.150	0.600	6.950	0.900
12	*Menthaarvensis* (Podina)	6.150	0.350	0.650	7.000	1.000
13	*Chichriunintybus* (Kasni)	5.800	0.400	0.650	6.550	0.800
14	*Cuminumcyminum* (zeera)	4.520	0.240	0.400	4.840	0.960
15	*Rosa demascena* (Gulab)	1.845	0.160	0.165	1.665	0.320

Table 4: Recommended limit of metals for plants and Recommended Daily Allowance (RDA)

S. No	Metal	Limit ppm	Reference	RDA	Reference
1	Cr	1.5	(Srivastava *et al.*, 2006)	11-35ug	Trumbo *et al.*, 2001
2	Cu	10	(Srivastava *et al.*, 2006)	400-900ug	Trumbo *et al.*, 2001
3	Pb	10	(Caldas & Machado, 2004)	20-514ug	Obi *et al.*, 2006
4	Mn	200	(Srivastava *et al.*, 2006)	8-11mg	Trumbo *et al.*, 2001
5	Ni	1.5	(Srivastava *et al.*, 2006)	35ug	Förstner *et al.*, 1979

permissible limit for Mn. The daily consumption for manganese is also in the permissible limit and may serve as supplement in manganese deficient patients.

Nickel (Ni)

Nickel is abundant in nature. Possible exposure sources of nickel are food, drinking water, absorption by contact and inhalation in nickel-polluted area (Trumbo, 2001). Ingestion of large amounts of nickel affects stomach, liver, kidneys, immune system and reproduction in rats and mice (Trumbo, 2001). The most common toxic effect is dermatitis while lung cancer has also been reported in some studies. The recommended limit for nickel in plant materials is 1.5 ppm, while its recommended daily

allowance is 35 µg (Srivastava *et al.*, 2006; Saeed *et al.*, 2010b). The concentration of nickel in the tested products was in the range of 44.2-58.5 ppm, while the daily intake was in the range of 0.27-7.150 mg/day. This shows that the daily intake is well above the toxic levels and may pose serious threats to those consuming these products.

In light of this research work, it can be said confidently that most of the medicinal plants used in the Unani or Ayurvedic systems of medicines in Pakistan may produce severe long-term toxic effects in human beings who are blindly taking it due to a common perception that they are safe. The significance of this become manifold when there is no control of the government over its quality during, trade, manufacture storage and sale due to the absence of legislation as observed for allopathic drugs. Our current work will, on one hand create awareness in the general masses regarding safe use of herbal drugs and at the same time it will provide guidelines to Government to make legislation and tools of Standardization for Manufacture, trade and use of Herbal preparation. Our work indicates that a large population is exposed to the toxic effects of the metals, which are in high concentrations. It has been confirmed from the company sources that they are using raw materials, which are purchased from the local market (Pansari Shops) in Pakistan.

CONCLUSION

In the light of this research it can be concluded that blind use of herbal products based on the belief that they are always safe needs to be considered. It has been recommended that the collection of medicinal herbs should be made a profession and not be left for the causal collectors as presently practiced. The collection of herbal drugs from the habitat by skilled professionals at a proper time and proper way will ensure the availability of standard raw materials for the manufacturer, hakims and public in general. The crude drugs before being subjected to manufacture, must be analyzed for detection of toxic heavy metals. Like allopathic drugs, herbal medicine should be subjected to all pharmaceuticals and pharmacological tests to ensure safety, potency and efficacy of these products to protect the ultimate users from the toxic effects. The Pakistan Tibb council is needed to make a comprehensive plan to evolve policies for standardized Tibb education curricula in tibia colleges throughout Pakistan so that well educated and trained Hakims are produced who can skillfully handle the patients. Similarly regulations such as those for allopathic medicines should be devised for their manufacture and use etc., and Good Manufacturing Practices (GMP) should be adopted to ensure uniform quality of the these products, such that to protect the general public from their hazardous health effects.

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