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Risk Assessment of Cadmium and Lead in Herbal Remedies Produced in North Western Nigeria

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ABSTRACT: This study aimed at determining the concentration of Cd and Pb in some herbal remedies prepared in North Western Nigeria followed by assessing their potential health risk via computation of the Hazard quotient (HQ) and Hazard index (HI). Samples were purchased from wholesalers to ensure wide coverage of herbs used in the region. Samples were treated according to standard methods and analysed by atomic absorption spectroscopy. The results revealed that Cd concentration range was 0.60 to13.45 mg/kg while Pb was 20.45 – 86.40 mg/kg. All samples exceed the WHO maximum permissible limit of Pb and greater percentage exceeds that of Cd. Generally there is significant ($p < 0.05$) safety difference between adult and children. HQ values of all samples in adult for Cd was less than 1 with 55.17% samples for children. HQ values for Pb indicated that the safety of 48.28% of the samples is questioned for adult use while a meagre 6.90% samples are safe for children. Results of the HI values showed that 34.48% of the samples are safe for adult while all the samples are not safe for children. Based on the concentrations of the metals and HQ/HI studied, the herbal are unsafe for consumption.

Key words: Herbal remedies, heavy metals, hazard quotient, risk assessment, atomic absorption spectroscopy.

INTRODUCTION

Herbal remedies or medicine connotes use of raw plant underground or aerial materials such as root, rhizome, stem, leaf, flower seed, fresh juice or processed into powder extract, poultice, tinctures by extraction, fractionation, purification, concentration, fermentation and other biological and physical processes [1]. Studies have shown that people around the globe used herbal for it being accessible, affordable, good efficacy and safe [2]. Although there are still people who use herbal remedies exclusively, many practice both herbal and orthodox. A study found 41% respondents prefer herbal medicine as their first choice of medication [3].

Like other parts of the world, in North Western Nigeria herbs are involved in the practice of traditional medicine. For instance, it was reported that *bori* (cult) practitioners prescribe herbs to patients as inspired by *iskoki* (spirit) [4].

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However, research have shown that herbal remedies should be used with caution as they resulted in adverse effects due to among other factors, use of wrong plant species, adulteration, over dosage, misuse by health-care providers or consumers, concomitant administration with other medicines and presence of toxic substances either from the metabolites or through deliberate or unintentional contamination. These substances include pesticides, radioactive particles, microbes and heavy metals [1]. Studies have confirmed high heavy metals concentration in herbal preparations such as in Chinese herbs [5] and also in Nigerian herbs [6].

The case of a child who was treated with remedies containing high concentration of Fe, Mn, and to a lesser extent As and Pb suffered from diarrhoea, vomiting and severe metabolic acidosis which was clinically found to be renal failure symptom is a typical example [7]. This is in line with claim that Pb accounts for most of the cases of pediatric heavy metal poisoning [8]. Other reports indicated metals poisoning causing morbidity and death in children [9,10], with Cd

and Pb being the most toxic elements for man [11].

Some studies were reported for use of herbs in Northern Nigeria which often paid attention to phytochemicals content and therapeutic potentials of individual plants [12,13,14], whereas in many cases multiple plants are formulated for a given remedy, particularly the practice of local herbalists in the area. For instance, *Mangifera indica, Cymbopogan citrates* and *Alchonea cordifolia* are formulation for body fever while *Euphorbia prostrate* and *Baphia nitida* are for irregular menstruation [15].

Hence, the aim and objective of the study was to determine concentration of Pb and Cd metals in herbal remedies produce in North Western Nigeria. The interest in these metals lies with the report that some plants e.g. *Triticum turgidum* var. *duram, Hypericum perforatum etc* accumulate Cd and also Cd and Pb are common airborne foliar contaminants [16].

EXPERIMENTAL

All glass and porcelain wares were scrupulously cleaned with 10% HNO_3, rinse several times with deionised water and dried at 120°C. Reagents of analytical grades were used except otherwise stated.

A total of 29 samples out of which 6 are packaged were purchased from wholesalers herbalists in Kurna Kano, Chiranci, Maigatari, Kawo Kaduna and Zaria towns of Kano, Katsina, Jigawa and Kaduna State, respectively. Table1 showed the herb samples and their cures as claimed by the herbalists. Some herbs constituents were undisclosed as the practice is sometimes kept with secrecy.Samples were air dried and grinded to powder. 0.5g of a sample was weighed into a pre-weighed porcelain crucible and placed in a muffle furnace set at 500°C. Sample was heated for four hours at the temperature, then removed and cooled. 10ml of 6 M HCl was added covered with watch glass and heated for 15min on a steam bath. Another 1ml HNO_3 was added and evaporated to dryness with further heating for 1hour to dehydrate silica and digest organic compounds completely. 5ml of 6M HNO_3 and 10ml of deionized water were added and the mixture heated on a steam bath to complete dissolution. The mixture was cooled and filtered through Whatman No. 1 filter paper into a 50ml volumetric flask and made up to the mark with deionized water [17].

The analyte solutions, a blank and calibration solutions of 0.000, 1.000, 2.000 and 3.000mg/l for Lead and 0.000, 0.500, 1.000, 2.000 and 3.000mg/l for Cadmium were aspirated into AA500 pginstrument atomic absorption spectrometer as recommended by manufacturer's format at the Soil Science Laboratory, Ahmadu Bello University Zaria, Nigeria. Detection limits were 0.0015mg/kg for both Cd and Pb respectively. In absence of reference materials for the herbal remedies, spiking experiment was conducted on some samples to validate the experimental protocol. Percentage recoveries on spiking revealed 103.47±0.56% and 95.71±29.77% for Cd and Pb, respectively.

HAZARD QUOTIENT AND HAZARD INDEX

The potential health risk of the metals was assessed by parameters of hazard quotient (HQ) for individual metals and the hazard index (HI) for overall metals. The HI assumes that the magnitude of the adverse effect will be proportional to the sum of multiple metal exposures. It also assumes similar working mechanisms that linearly affect the target organ.

$$HQ = (Dih) \times (C_{metal}) / R_fD \times Bo \text{ (Adapted from [18])}$$

$$HI = \Sigma\, HQ = HQCd + HQPb$$

Where Dih is the daily intake of herb (kg / person/day) which is 3.0 g for this study as the herbalists usually prescribe an average of 1.5g which is equivalent to a teaspoonful of formulation twice a day, Cmetal is the concentration of metal in the herb ($mgkg^{-1}$), RfD is the oral reference dose for the metal (mg/kg/day) and Bo is the human body mass (kg) The average Bo was taken as 70 kg for adults [19] and 19.25 kg for children 0-6 years old [20]. RfD is an estimation of the daily exposure to which the human population is likely to be without any appreciable risk of deleterious effects during a lifetime. Values of RfD for Cd is 0.001 mg/kg/day [21], while for Pb is 0.0035 mg/kg/day [19]. The HQ is a highly conservative and relative index. When HQ is < 1, there is no obvious risk from the substance over a lifetime of exposure, while HQ is > 1, the toxicant may produce an adverse effect.

The daily intake of the herb samples was used to compute the hazard quotient and hazard index as reported in table 2.

RESULTS AND DISCUSSION

Concentrations of the metals in the herbal remedies were presented in figures 1 and 2.

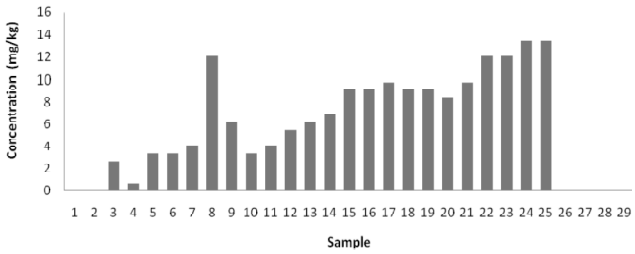

Figure 1: Cd mean concentration

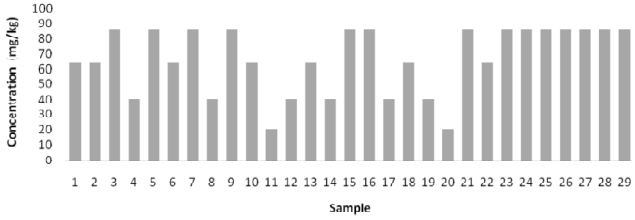

Figure 2: Pb mean concentration

Figure 1 shows that Cd concentration range from 0.60-13.45mg/kg. The highest concentrations of Cd were associated with the packaged herbs samples 24 and 25, even though the packaged samples 26-29 have concentration below detection. It is obvious that packaging alone improves hygiene but the study shows that it does not ensure safety of herbal medicine. This agrees with the report that the accumulation of heavy metals in herbal plants depends on climatic factors, plant species, and air and soil pollution. [22]. Therefore, other factors such as contamination of the plant during cultivation, transportation or storage could be responsible. Also, since the information on recipe of the formulation was not disclosed, the likelihood that the remedies may contain inorganic substance in the formulation is plausible as it is sometimes practiced. The highest concentration of 13.45mg/kg concentration observed in this study is much higher than the highest value of 0.360mg/kg Cd recorded for samples of Saudi Arabia [23]. Also, this study range is wider than 0.19mg/kg in Anethum to 1.75mg/kg Cd in Galega as reported [24]. However, it is lower compared to Cd highest concentration of 40.29 mg/kg in some herbs [25]. The fact, that 79.31% of the samples have their Cd concentration exceeding the permissible limit of 0.3 mg/kg [1] indicates taking caution in the use of the herbal remedies.

Cd affects the kidney, the skeletal system and the respiratory system and is classified as a human carcinogen. Kidney is most affected by the renal tubular dysfunction, which results in increased excretion of low molecular weight proteins in the urine when it accumulates in the kidney; this is generally irreversible [26].

The result indicates that all the samples contain Pb at varying concentration in the range of 20.45 – 86.4mg/kg with highest concentration being in about 50% of the samples which cut across, packaged and unpackaged. This range is lower than 35 – 624mg/kg Pb in some herbs reported by Garba *et al* [27]. However, it is comparable to Pb range of 4.12-73.56mg/kg in herbs reported by [28] and 9.61 mg/kg - 52.74 mg/kg Pb [24], even though the highest concentration of the study area is higher. All the samples exceed the maximum permissible limit for Pb set by WHO [29]. The prevalence of Pb might be due to aerial deposition from airborne and mode of transportation. Exposure to Pb is of concern mainly because of its acute toxicity even at trace levels and numerous studies have revealed that it can adversely affects the central nervous systems, cognitive development, renal system, blood circulation, mental retardation, reproductive health, growth and development, and can even cause death [30, 31].

The two metals Cd and Pb did not show significant correlation ($p>0.05$) which indicate that they are from different sources.

HAZARD QUOTIENT

Cd was found to be safe for use in adult as all the HQs are less than 1. Conversely, the HQ values showed that 44.83% samples in children are of safety concern. The HQ values of Pb indicated that the safety of 48.28% is questioned for adult use while 6.90% is safe for children use. The safety difference between adult and children for both metals is significant ($p < 0.05$) The Pb concentration in the herbal remedies and its HQ values showed that there is need for concern about regulation of the herbal formulations.

HAZARD INDEX (HI)

Result of the HI values showed that 34.48% of the samples are safe for adult while all the samples are not safe for children consumption. Another study has shown that 98% of herbal remedies used

in South Eastern Nigeria violated the regulatory limits of heavy metals [6].

CONCLUSION

The study showed that packaged and unpackaged herbal remedies from North Western Nigeria are contaminated with Cd and Pb in excess of WHO recommended limits. Furthermore, the HQ and HI values showed potential risk in the use of large portion of samples especially for children. It is therefore recommended that, the herbalists should be enlightened on the best practices of herbal preparations and the consumers on precautionary measures.

Table 1
Herb formulation samples with their plants constituents and treatments.

Sample	*Local Name*	*Treatments*	*Plants with Local Names Used in Formulation**
1	Maganin malaria da shawara	Malaria, jaundice	*Anogeissus leiocarpus(Marke), Cassia singueana (Runfu), Ximenia americana (Tsada)*
2	Maganin sanyin mara	Waist weakness,	*Anogeissus leiocarpus(Marke), Cassia singueana (Runfu),*
3	Maganin basir	Pile	*Prosopis africana (kirya), Detarium microcarpum (Taura)*
4	Danbashanana	Sexual stimulant	Undisclosed
5	Maganin basir	Pile	*Anogeissus leiocarpus(Marke), Mangifera indica (mangwaro),Diospyros mespiliformis(Kanya),Lannea microcarpa (Faru), c*
6	Maganin kurajen baki	Mouth boils	*Acacia Senegal*
7	Maganin gyanbon ciki	Endo abdominal wound	Undisclosed
8	Maganin ciwon ciki	Stomach ache	*Lannea microcarpa (Faru), Piliostigma reticulatum (Kalgo),*
9	Maganin shawara	Jaundice	*Anogeissus leiocarpus(Marke), Guiera senegalensis (Sabara),*
10	Maganin majina	Moderate mucus	*Albizia chevalieri (Katsari), Senna italic (Filasko)*
11	Maganin basir da zafi	Haemorrhoids	*Prosopis africana (kirya), Commiphora kerstingii (*ÁrárráSíí*)*
12	Maganin shawara	Jaundice	*Cochlospermum tinctorium (Rawaya)*
13	Maganin kasala	Body weakness	*Combretum micranthum (Geza)*
14	Maganin shawara	Jaundice	*Anogeissus leiocarpus (Marke), Cochlospermum tinctorium (Rawaya)*
15	Maganin basir	Pile	*Commiphora kerstingii(*ÁrárráSíí*), Ficus ovate (Gamji), Detarium microcarpum* (Taura)
16	Maganin rana	Sun burn	*Prosopis africana (kirya)*
17	Maganin jinni	Haemorrhage	*Detarium microcarpum* (Taura)
18	Maganin basir	Haemorrhoids	*Cochlospermum tinctorium (Rawaya), Detarium microcarpum* (Taura), *Ficus ovate (Gamji)*
19	Maganin daji	Cancer	*Ficus ovate (Gamji), Detarium microcarpum* (Taura), *Cassia singueana (Runfu), Ficus spp(*áuréé*)*
20	Dan kadafi	Sexual stimulant	Undisclosed
21	Maganin kaikai	Itches	*Tamarindus indica*
22	Maganin mura	Catarrh	*Anogeissus leiocarpus (Marke)*
23	Dan kadafi	Sexual stimulant	Undisclosed
24	Maganin basir	Haemorrhoids	Undisclosed
25	Sanamaki	Headache, spirit	“
26	Maganin gudawa	Diarrhoea	“
27	Maganin sihiri	Spirit	“
28	Zaiti	Pain, typhoid fever, yellow fever, worms, pile	“
29	Nauriyya	Ulcer, pile, jaundice, asthma, cold, typhoid	“

*Information on formulated plants was given by the herbalists. Samples 1-23 were unpackaged while 24-29 were packaged.

Table 2
Values of daily intake, hazard quotient and hazard index of heavy metals in the herb formulations

Sample	*Cd*			*Pb*				
	Daily Intake	*Hazard Quotient*		*Daily Intake*	*Hazard Quotient*		*Hazard Index*	
		Adult	*Children*		*Adult*	*Children*	*Adult*	*Child*
1	0	0	0	0.191	0.78	2.83	0.78	2.83
2	0	0	0	0.191	0.78	2.83	0.78	2.83
3	0.008	0.11	0.41	0.259	1.06	3.85	1.17	4.26
4	0.002	0.03	0.09	0.123	0.50	1.82	0.53	1.91
5	0.010	0.14	0.52	0.259	1.06	3.85	1.20	4.37
6	0.010	0.14	0.52	0.191	0.78	2.83	0.92	3.36
7	0.012	0.18	0.64	0.259	1.06	3.85	1.23	4.49
8	0.036	0.52	1.88	0.123	0.50	1.82	1.02	3.70
9	0.019	0.27	0.97	0.259	1.06	3.85	1.32	4.81
10	0.011	0.14	0.52	0.191	0.78	2.83	0.92	3.36
11	0.012	0.18	0.64	0.061	0.25	0.91	0.43	1.55
12	0.017	0.24	0.86	0.123	0.50	1.82	0.74	2.68
13	0.019	0.27	0.97	0.191	0.78	2.83	1.05	3.80
14	0.021	0.30	1.08	0.123	0.50	1.82	0.80	2.90
15	0.027	0.39	1.42	0.259	1.06	3.85	1.45	5.27
16	0.027	0.39	1.42	0.259	1.06	3.85	1.45	5.27
17	0.029	0.42	1.53	0.123	0.50	1.82	0.92	3.35
18	0.027	0.39	1.42	0.191	0.78	2.83	1.17	4.25
19	0.027	0.39	1.42	0.123	0.50	1.82	0.89	3.24
20	0.025	0.36	1.31	0.062	0.25	0.91	0.61	2.22
21	0.029	0.42	1.53	0.259	1.06	3.85	1.48	5.37
22	0.036	0.51	1.87	0.191	0.78	2.83	1.29	4.70
23	0.036	0.51	1.87	0.259	1.06	3.85	1.57	5.72
24	0.041	0.58	2.10	0.259	1.06	3.85	1.63	5.94
25	0.041	0.58	2.10	0.259	1.06	3.85	1.63	5.94
26	0	0	0	0.259	1.06	3.85	1.06	3.85
27	0	0	0	0.259	1.06	3.85	1.06	3.85
28	0	0	0	0.259	1.06	3.85	1.06	3.85
29	0	0	0	0.259	1.06	3.85	1.06	3.85
Range	0-0.040	0 – 0.58	0 – 2.10	0.061 – 0.259	0.25 – 1.06	0.91 – 3.85		

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References

[1] WHO, Guideline for Assessing Quality of Herbal Medicines with Reference to Contaminants and Residues 11-13, **(2007)**.

[2] Gyasi, R.M., Mensah,C.M., Adjei, C.O. and Seth Agyemang, S., Public Perception of the Role of Traditional Medicine in the Health Care Delivery System in Ghana. Global Journal of Health Science. Vol. 3, No. 2, **(2011)**.

[3] Osemene, K.P., Elujoba, A.A., and Ilori, M.O. A Comparative Assessment of Herbal and Orthodox Medicine in Nigeria. *Research Journal of Medical Sciences.* Vol 5 Issue 5 pp 280-285, **(2011)**.

[4] Andersson, U. Working with Spirits Among Muslim Hausa in Nigeria. A Study of Bori in Jos. Working Papers in Cultural Anthpology, No. 11 pp. 1-14, **(2002)**.

[5] Li S., Fang Y., Ning H. and Wu Y.X. Heavy metals in chinese therapeutic foods and herbs. *J. Chem. Soc. Pak.*, Vol. 34, No.5, 1091-1095, **(2012)**.

[6] Nwoko,C.O. and Mgbeahuruike, L. Heavy Metal Contamination of Ready-to-use Herbal Remedies in South Eastern Nigeria. *Pakistan Journal of Nutrition* 10 (10): 959-964, **(2011)**.

[7] Steenkamp, V., Stewart, M.J., Curowska, E. and Zuckerman, M., A Severe Case of Multiple Metal Poisoning in a Child Treated With a Traditional Medicine. *Forensic Science International* 128, 123-126, **(2002)**.

[8] Roberts, J. R., Metal toxicity in children. In Training Manual on Pediatric Environmental Health: Putting It into Practice 1999 Jun. Emeryville, CA: Children's Environmental Health Network (*http://www.cehn.org/cehn/trainingmanual/pdf/manual-full.pdf,* **(1999)**.

[9] Wood, R., Mills, P., Knobel, G., Hurlow, W. and Stokol, J., Acute Dichromate Poisoning After Use of Traditional Purgatives. A Report of Seven Cases. *S. Afr. Med. J.,* Vol. 77, 640-642, **(1990)**.

[10] Michie, C., Hayhurst, M., Knobel, G., Stokol, J. and Hensley, B., Poisoning with a Traditional Remedy Containing Potassium dichromate. *Hum. Exp. Toxicol.* Vol. 10(2) pp. 129-131, **(1991)**.

[11] Volpe, M.G.; La Cara, F.; Volpe, F.; De Mattia, A.; Serino, V.; Pettito, F.; Zavalloni, C.; Limone, F.; Pellecchia, R.; De Prisco, P.P.; Di Stasio, M., Heavy metal uptake in the ecological food chain. *Food Chemistry* 117: 553-560, **(2009)**.

[12] Aliyu, A.B., Musa, A.M. M. S. Abdullahi, M.S. and A. O. Oyewale, A.O. and Gwarzo, U.S., Activity of Plant Extracts Used In Northern Nigerian Traditional Medicine Against Methicillin-Resistant Staphylococcus Aureus (MRSA). *Nigerian Journal of Pharmaceutical Sciences* Vol. 7, No. 1, **(2008)**.

[13] Garba, S. and Okeniyi, S. O., Antimicrobial activities of total alkaloids extracted from some Nigerian medicinal plants. *Journal of Microbiology and Antimicrobials* Vol. 4(3), pp. 60-63, **(2012)**.

[14] Amupitan, T. A., Ethnobotanical Survey of Medicinal Plants in Biu Local Government Area, Borno State, Nigeria. *Comprehensive Journal of Herbs and Medicinal Plants* Vol. 2(1), pp. 7-11, **(2013)**.

[15] Bhat, R. B., Medicinal Plants and Traditional Practices of Xhosa People in the Traskei Region of Eastern Cape, South Africa. *Indian Journal of Traditional Knowledge.* Vol. 13(2), 292-298, **(2014)**.

[16] American Herbal Products Association APHA, Heavy Metals: Analysis and Limits in Herbal Dietary Supplements, **(2009)**.

[17] Dzomba, P., Chayamiti, T. and Togarepi, E., Heavy Metal Content of Selected Raw Medicinal Plant Materials: Implication for Patient Health. *Bull. Environ. Pharmacol. Life Sci.*; Volume 1 [10] PP 28 - 33, **(2012)**.

[18] Guerra F., Trevizam A.R., Muraoka T., Marcante N.C. and Canniatti-Brazaca S.G., Heavy metals in vegetables and potential risk for human health. Sci. Agric. v.69, n.1, p.54-60, **(2012)**.

[19] World Health Organization [WHO]., Evaluation of Certain Food Additives and Contaminants. In: Forty-First Report of the Joint FAO/WHO Expert Committee on Food Additives., WHO, Geneva, Switzerland. (WHO Technical Series, 837), **(1993)**.

[20] Brazilian Institute of Geography and Statistics [IBGE]. Anthropometry and Children and Teenager Nutritional State Analysis in Brazil: Familiar Budget Survey; 2002-2003. IBGE, Rio de Janeiro, RJ, Brazil (in Portuguese), **(2006)**.

[21] U.S. Environmental Protection Agency [US EPA]. (2010). Integrat-ed risk information system. Available at: http://cfpub.epa.gov/ncea/iris/compare.cfm [Accessed Jan. 08, 2010].

[22] Lasisi A.A., Yusuff A.A., Ejelonu B.C., Nwosu E.O. and Olayiwola M.A., Heavy metals and macronutrients content in selected herbal plants of Nigeria. *INT. J. Chem.* Vol. 15 147-154, **(2005)**.

[23] Maghrabi, I.A., Determination of Some Mineral and Heavy Metals in Saudi Arabia Popular Herbal Drugs Using Modern Techniques. *African Journal of Pharmacy and Pharmacology* 8(36):893-898, **(2014)**.

[24] Mousavi, Z., Ziarati, P., Dehaghi1, M.E. and Qomi, M., Heavy Metals (Lead and Cadmium) in some Medicinal Herbal Products in Iranian Market. *Iranian Journal of Toxicology* Volume 8, No. 24, **(2014)**.

[25] Adepoju-Bello, A. A., Issa, O. A., Oguntibeju, O. O., Ayoola, G. A. and Adejumo, O. O., Analysis of some selected toxic metals in registered herbal products manufactured in Nigeria. *African Journal of Biotechnology,* Vol. 11(26), pp. 6918-6922, 29, **(2012)**.

[26] WHO, Preventing Disease Through Healthy Environments Exposure to Cadmium: A Major Public Health Concern, **(2010)**.

[27] Garba, M.A., Musa, A., Mohammed, L. and Musa, H.A. The Concentrations of Lead in Some Herbs in Makarfi, Nigeria. *Nigerian Journal of Pharmaceutical Sciences* Vol. 9, No. 1, pp. 1-5.

[28] Baranowska, I., Srogi, K., W³ochowicz, A and Szczepanik, K., Determination of Heavy Metal Contents in Samples of Medicinal Herbs. *Polish Journal of Environmental Studies,* Vol. 11, No. 5, 467-471, **(2002)**.

[29] WHO.WHO, Monographs on Selected Medicinal Plants: Bulbus Allii Cepae: World Health Organization, **(1999)**.

[30] Barbosa, A. C. and Dorea, J. G., *Environmental Toxicology and Pharmacology*, **6**,71. IARC-International Agency for Research on cancer (2004) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Inorganic and organic lead compounds, **87**, 10, **(1998)**.

[31] International Agency for Research on cancer. IARC (2004) Monographs on the Evaluation of Carcinogenic Risks to Humans: Inorganic and organic lead compounds, **87**, 10.