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HEAVY METAL CONTENTS AND ASSOCIATED HEALTH RISK OF SOME GHANAIAN AND ASIAN HERBAL DRUGS

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ABSTRACT: This study looked at heavy metal levels in selected registered herbal drugs of Asian and unregistered Ghanaian herbal drugs sold in Kumasi. It examined the health risks of the metals. It provided authorities with data to ensure that herbal drugs are strictly monitored and their metal levels evaluated to safeguard patrons' health. Dry ashing method was used on 10g of each of the herbal drug samples. Ashes were digested at 95 ºC with 70% HNO_3 and 70% $HClO_4$ (2:5v/v), and then metals were analyzed using Atomic Absorption Spectrophotometer (AAS). The Asian drugs recorded 27.42E-01 mg/kg (Fe), 28.17E-0 4 mg/kg (Pb), 27.43E-0 4 mg/kg, 12.06E-06E-0 2 mg/kg (As) and 79.72E-0 2 mg/kg (Cu) whilst the Ghanaian drugs recorded mean levels of 15.43E-01 mg/kg (Fe), 24.99E-02 mg/kg (Pb), 16.04E-03 mg/kg, 47.70E-0 4 mg/kg (AS) and 12.37E-0 4 mg/kg. Metal levels in drugs were below WHO and Pharmacopeia (China) permitted levels. HI and HQ were below 1, indicating that risk linked to the metals were acceptable.

INTRODUCTION: Globally, approximately 80% of the population depend on herbal remedies to treat and manage diseases such as diabetes, stroke, and hypertension, among others [1]. Herbal drugs play a vital role in the healthcare delivery schemes of numerous countries and are either self-prescribed or recommended by herbal practitioners [2]. For instance, in some Asian countries (China, Japan and India), herbal remedies have cooperated into healthcare schemes [3]. In Ghana, herbal remedies are also vital in the healthcare schemes for treating and managing ailments and conditions such as malaria, numbness, hypertension, ulcers, infertility, and sexual weakness, among others [1].

Currently, Ghana is overwhelmed with varieties of herbal drugs and other plant products of varied therapeutic values, and most Ghanaians depend on herbal medicines for their healthcare need. However, herbal drugs could have intrinsic health risks as various studies have documented metal poisoning in individuals using herbal remedies [4].

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Other studies [5] have also reported Lead (Pb), Cadmium [6, 7,] and Arsenic (As) at levels dangerous to humans and the environment. More studies [8] have similarly seen Pb, Hg, and As poisoning in patrons of herbal remedies. Investigations conducted on different herbal drugs showed elevated levels of Pb, Hg, and As [9, 10] sufficient to prompt injurious health issues. Lead levels (3290 µg/L and 795 µg/L) respectively have been found in blood samples of diabetic patients who experienced severe abdominal pains after consuming some herbal drugs [11, 12]. Chinese and Indian registered herbal remedies are being sold on the Ghanaian markets.

These herbal remedies treat diabetes, stomach ache, hypertension, prostate cancer, stomach ulcer, piles, sexual weakness, and infertility problems, among others. However, Chinese and Indian herbal drugs have been found to have caused lead, arsenic, and mercury poisonings in a substantial number of global patrons [13, 15]. Food and Drugs Authority, Ghana, is instructed by law to scrutinize and test drugs (herbal or orthodox) for safety and efficacy prior to public use. However, not all herbal drugs are scrutinized and tested due to ingress *via* unapproved routes and local productions in remote areas. Thus, the population may be at risk from contaminants (mainly elevated heavy metal levels) that may exist in the herbal drugs *via* absorption and storage in plant tissues [13, 15].

Upon ingesting the herbal drugs, these stored heavy metals are transferred to patrons [16.] Heavy metals are extensively investigated [17] and damage or affect the kidneys, endocrine glands, lungs, liver, hearts, skin, and the brain [18]. Heavy metals also damage the normal functioning of the nervous systems [19], cause hearing and speech difficulties [20], lack of coordination [17], memory loss, unusual heart rhythm [21], stunted growth, learning disabilities [22], cancers [23] and even death [24]. Heavy metals levels above maximum permissible limits have been detected in herbal drugs globally [25]. These metals are harmful and could be detrimental to the health of consumers [26]. Based on the severity of health effects associated with heavy metals and the fact that huge portions of herbal drugs in Ghana do not undergo safety checks before consumption, it is prudent to investigate the herbal drugs to safeguard human health and preserve lives. The main aim of the present study was to provide data on the levels of Fe, Pb, Cd, As, and Cu in some registered herbal drugs of Chinese and Indian origin on the Ghanaian market and some unregistered Ghanaian herbal drugs. A further attempt was made to assess the health risk associated with consuming these herbal drugs. Furthermore, the study seeks to furnish authorities with data and the need to implement stringent examination and testing regimes to ensure that the health of patrons of herbal drugs is protected.

MATERIALS AND METHODS:

Description of Study Area: Kumasi is the second-largest city in Ghana [27]. Kumasi has an estimated population of 2,069, 350 [28]. Geographically, Kumasi is located at latitude 6.350-6.400N and longitude 1.30-1.350W [29]. It is approximately 254 km from Accra. Kumasi is located in the forest-savannah zone at an altitude of 250 m. The metropolis shares boundaries with Kwabre East to the north, Atwima District to the west, Ejisu-Juaben Municipal to the east, and Bosomtwe to the south. Kumasi is a cosmopolitan city and is the center of the Ashanti region [28]. Commercial activities in the area are varied and include but are not limited to the sale of farm produce herbal remedies, and jewelries. Kumasi receives traders from Cote d'Ivoire, Burkina Faso, Mali, Niger, and Togo [28].

Sample Collection: Selected registered Chinese and Indian herbal drugs samples and unregistered Ghanaian herbal drugs samples were purchased into plastic zipper bags from different locations within the Kumasi metropolitan area. The zipper bags were firmly sealed and properly labelled. The registered Chinese and Indian herbal drugs samples were labelled CHI and IND, respectively whilst the unregistered Ghanaian herbal drugs samples were GHA. Samples were transported in brown paper bags to the laboratory for metal extraction and analysis.

Sample Treatment and Metal Analysis: The dry ashing method 30 was adopted and used in this study. A 10 g of each herbal drug was put into 20 g capacity porcelain crucibles, and 20 mL of 2M aqueous solution of magnesium nitrate was added. The magnesium nitrate (Merck, Germany) treated samples were put into a muffled oven and heated at

450 ºC until samples were completely ashed. The ashes were dissolved in 20 mL of 70 % HNO_3 and 70% $HClO_4$ (BDH, UK) (2:5v/v) mixture in 200 mL digestion tubes and boiled gently at 95 ºC until dense white fumes appeared. Twenty milliliters of de-ionized water were added to the boiled ashes and continuously stirred for 5 minutes. The mixtures were filtered under gravity through Whatman No.1 filter paper. Filtrates were made to 50 mL with de-ionized water and analyzed in triplicates with Atomic Absorption Spectrophotometer (VARIAN SPECTRA AA220).

Spike Sample Preparation: To determine the efficiency of metal extraction method employed, 20% of the samples were subjected to quality control analysis. A 10 g sample of each herbal drug was spiked with 0.1g of an apple leaves standard reference material (NIST®SRM 1515) (Sigma-Aldrich) to prepare the quality control samples. The powdered apple leaves SRM had Fe (8.3 ± 5.00 mg/kg), Pb (0.47± 0.024 mg/kg), Cd (0.013 ± 0.002 mg/kg), as (0.038 ± 0.007mg/kg) and Cu (5.64 ± 0.24 mg/kg). Spiked samples were prepared at the time drug samples were being prepared. Spiked samples were treated, digested, and analyzed exactly as described for herbal drug samples. Percentage recoveries of the metals were calculated using equation (1).

$$\% \text{ Recovery} = (\text{Spiked result} - \text{Unspiked result}) / (\text{Amount of metal added}) \times 100 \quad (1)$$

Blank Samples Preparation: Blank samples were prepared to check cross-contamination of drug samples by chemicals/reagents and/or glassware used. To prepare the blank samples, 20 mL each of 2M aqueous magnesium nitrate solution was put into five different 20 g capacity porcelain crucibles. The crucibles and contents were put into the muffled oven and heated at 450 ºC until solutions were dried. Reconstitution of solutions was with 20 mL of 70% HNO_3 and 70% $HClO_4$ mixture (2:5v/v). The reconstituted solutions were put into five different 200 mL digestion tubes and boiled gently at 95 ºC until dense white fumes appeared. After digestion, 20 mL of de-ionized water was added to each digestion tube, shaken vigorously for 5 minutes, and filtered under gravity through Whatman No.41 filter paper. Filtrate volumes were made to 50 mL with de-ionized water and then analyzed exactly as done for herbal drug samples.

Human Health Risk Estimation: The health risk of Fe, Pb, Cd, As, and Cu in the herbal drugs were assessed using the expected daily intake (EDI) of the metals, Hazard Index (HI), and Hazard Quotient (HQ) as employed elsewhere [31, 32]. The EDI of Fe, Pb, Cd, As, and Cu were calculated to assess expected average quantities of each metal that patrons are likely to be exposed to daily. The EDIs were calculated using equation (2) as used in analogous studies [33].

$$EDI = (C_{metal} * IR) / BW, \quad (2)$$

Where C metal (mg/kg) is the average concentration of heavy metals in the herbal drugs, IR is the ingestion rate of the herbal drug, EDI is the expected daily intake of the metal for an adult (gram/day/person), and BW is the average body weight of an adult (kg) as used in an analogous [34]. The ingestion rate of Chinese herbal drugs (CHI-01, CHI-02, CHI-03, CHI-05, CHI-08, CHI-09, and CHI-10) is 20 g (dry weight)/day whilst that of (CHI-04 and CHI-06) is 10 g (dry weight)/day. The ingestion rate of Indian herbal drugs (IND-10, IND-02, IND-03, IND-06, and IND-08) is 20 g (dry weight) /day whilst that of (IND-01 IND-04, IND-05, IND-07, and IND-09) is 10g (dry weight) /day. Ghanaian herbal drugs (GHA-01, GHA-02, GHA-03, GHA-05, GHA-06, GHA-07, GHA-08, GHA-09 and GHA-10) have ingestion rate of 10 g (dry weight) /day whilst that of (GHA-04) is 20 g (dry weight) /day. Sixty-five kilograms (65 kg) were employed as the average body weight of an adult consumer of the herbal drugs used in analogous studies [35, 37].

Hazard Quotient (HQ) Estimation: The likelihood of non-carcinogenic illnesses emerging among patrons of the herbal drugs was investigated via hazard quotient (HQ). Hazard quotient (HQ) was calculated *via* equation (3) as used in analogous studies [38, 39]. Hazard quotient (HQ) less than 1 as interpreted in comparable studies indicates that likely occurrence of non-cancerous diseases amongst patrons of the herbal drugs from long-term usage of the drugs investigated is non-existence. Hazard quotient (HQ) greater than 1 as established in analogous studies [39] is indicative of the likelihood of patrons to surfer non-cancerous illnesses from long-term usage of the herbal drugs. Hazard quotients (HQs) were calculated as the ratio

of EDI (mg/kg/day) to reference dose (R_fD) (mg/kg/day) of metals using equation (3) as used in analogous studies elsewhere [32, 39]. The reference dose (R_fD) 9.0E-03 mg/kg/day (Fe), 3.5E-03 mg/kg/day (Pb), 1.0E-03 mg/kg/day [6] and 3.0E-03 mg/kg/day (As) and 1.20E-02 mg/kg/day (Cu) were used in equation (3) to estimate HQ data of each metal in each herbal drug.

$$HQ = EDI/R_{fD}, \quad (3)$$

Health Indices (HIs) Estimation: To assess contribution of Fe, Pb, Cd, As and Cu to the non-cancerous illnesses that could emerge from ingesting the herbal drugs, health indices (HIs) were estimated as summation of hazard quotient (HQ) connected to each metal as done in similar studies [40] using equation [4]. The health indices were estimated to reflect the additive effect of the manifold heavy metals in the herbal drugs as presented in analogous studies [31, 32]. The HI data as interpreted in similar studies [41] shows an unacceptable risk level at values equal to or greater than 1. The risk level is considered acceptable at HI less than 1as described in various studies [31, 32].

$$HI=\Sigma (HQFe + HQPb + HQCd + HQAs + HQCu), \quad (4)$$

RESULTS AND DISCUSSION: Quality control processes included blank sample analysis, triplicate herbal drug samples analysis, and metals recovery assessment. Data generated were analyzed by Microsoft Excel 2016. Levels of Fe, Pb, Cd, As, and Cu achieved in the recovery assessment were expressed as mean ± standard error of measurement (Mean ± SE) (mg/kg/dry weight of sample) and presented in **Table 1.** Dry ashing method 30 used to extract Fe, Pb, Cd, As and Cu from the herbal drugs was very efficient (95% CL). Percentage recoveries ranged from 93.92% (Cu) to 99.26 % (Pb). The dry ashing method was also accurate and precise as exhibited by lesser uncertainty between 2.99E-03 (mg/kg) [6] to 39.20E-03 (mg/kg) (Cu) and insignificant error margin between 1.0E-03 (mg/kg) [6] to 1.0E-02 (mg/kg) (Fe and Pb) **Table 1.**

TABLE 1: ASSESSMENT OF EFFICIENCY OF HEAVY METAL EXTRACTION METHOD

Metal	Certified Value (mg/kg)	Recovered Value (mg/kg)	Recovery (%)	Expanded Uncertainty (mg/kg)
Fe	8.3 ± 5.00	8.18 ± 1.0E-02	98.74	22.63E-03
Pb	0.47± 0.024	0.45 ± 1.0E-02	99.26	27.46E-03
Cd	0.013 ± 0.002	0.011 ± 1.0E-03	96.82	2.99E-03
As	0.038 ± 0.007	0.036 ± 2.0E-03	95.77	3.92E-03
Cu	5.64 ± 0.24	5.29 ± 2.0E-03	93.92	39.20E-03

Metal Levels in Herbal Drugs: Iron [42,] Lead (Pb), Cadmium [6], Arsenic (As) and Copper [43] levels in registered herbal drugs of Chinese (CHI) and Indian (IND) origin and unregistered ones of Ghanaian (GHA) origin were investigated for likelihood to exert unwanted ailments on persons relying on them for their healthcare need. The herbal drugs were used to treat and manage health illnesses such as waist pain, chest pain, diabetes, and sexual weakness. Data generated from AAS analysis of the herbal drug samples were statistically treated (95% CL) using Microsoft Excel 2016. Iron [42, 44], Pb, Cd, As and [43] levels calculated were also reported as Mean ± SD (mg/kg/dry weight of sample) and presented in **Tables 2, 3** and **4.** Iron [42, 44], Pb, Cd, As, and [43] levels in the herbal drugs were compared with WHO and Pharmacopeia (China) permitted levels of the metals as done in comparable study [42, 44].

The concentration of Fe, Pb, Cd, As, and Cu in registered Chinese herbal drugs sold in Ghana Mean levels of metals in Chinese herbal drugs (registered) ranged from 12.06E-02 (As) to 27.42 E-01 mg/kg (Fe). Although Fe levels were high (14.78 E-02 to 47.56 E-0 1 mg/kg) in all drugs, levels were below WHO and pharmacopeia (China) permitted limits **Table 2** and appeared not to exert damaging effect(s) on the gastrointestinal system. In addition, Fe levels appeared insufficient to cause vomiting, diarrhea, and stomach ache linked to Fe toxicity. Iron [42, 44] in herbal drugs is non-heme Fe, and its bioavailability is approximately 5 to 12%. Hence, persons using the Chinese drugs would have roughly 13.71E-03 (5% of mean levels of Fe) to 32.90 E-0 3 mg/kg (12% of mean levels of Fe) of Fe absorption into their system. Thus, iron accumulation in organs of the body and its' subsequent damage to the liver and or brain is eliminated. Copper [43] levels in 70% of drugs (CHI-

01) for liver purification, Kidney purification (CHI-02), rheumatism (CHI-03), malaria (CHI-04 and CHI-09), sexual weakness (CHI-05), diabetes (CHI-06) were below WHO, and Pharmacopeia (China) permitted levels **Table 2.** Low Cu levels in CHI-01, CHI-02, CHI-03, CHI-04, CHI-05, CHI-06 and CHI-09 show that health problems linked to Cu toxicity may not occur in patrons of the drugs as Cu levels were far below WHO and Pharmacopeia (China) allowable limit. The remaining 30 % of drugs for gout (CHI-07), arthritis (CHI-08), and migraine (CHI-10) had Cu levels above WHO and Pharmacopeia (China) allowable limit and ranged between 25.70E-01 to 61.70 E-0 1 mg/kg **Table 2.** Hence, as seen in similar studies, frequent intake of CHI-07, CHI-08, and CHI-10 could cause liver and kidney damage. Thus, patrons prone to diseases such as Wilson's disease might show signs of the illness as high Cu contents in CHI-07, CHI-08 and CHI-10 could encouragement Cu build-up in the liver when Cu homeostasis is hugely impaired. Lead (Pb), Cd, and As levels in the Chinese drugs (registered) were below WHO and pharmacopoiea (China) permitted limits **Table 2.** Although the Chinese drugs appear not to have inherent negative health conditions linked to Pb, Cd, and As, their existence in the drugs is worrying as Pb, Cd, and As could progressively bioamplify in people relying on the drugs for their healthcare needs. Hence, drug regulatory authorities in Ghana must establish and implement rigorous drug scrutinization and testing systems to ensure that only herbal drugs with infinitesimal heavy metal contents are permitted entry into Ghana.

TABLE 2: CONCENTRATIONS OF METALS (MG/KG) IN CHINESE HERBAL DRUG SAMPLES

Metal	Minimum	Maximum	Mean	SE	WHO Limit	Pharmacopoiea China
Fe	14.78E-02	47.56E-01	27.42E-01	49.39E-03	10	0.20
Pb	8.87E-04	7.7E-03	28.17E-04	83.65E-05	0.30	0.50
Cd	5.10E-05	11.08E-03	27.43E-04	10.30E-04	0.20	0.03
As	53.70E-03	201.47E-03	12.06E-02	16.16E-03	0.20	0.20
Cu	12.76E-03	35.58E-01	79.72E-02	40.32E-02	0.04	0.20

Concentration of Fe, Pb, Cd, As and Cu in Registered Indian Herbal Drugs Sold in Ghana: Fe, Pb, Cd, As, and Cu levels in the Indian herbal drugs were analyzed and presented in **Table 3.** Metal levels ranged between 10.67E-04 mg/kg (Pb) to 82.50E-0 2 mg/kg (As) **Table 3.** Sixty percent of drugs for malaria (IND-02), hemorrhoids (IND-03), stomachaches (IND-06), toothaches (IND-07), jaundice (IND-08), and loss of appetite (IND-10) had Cu above WHO and Pharmacopeia (China) recommended levels **Table 3.**

TABLE 3: CONCENTRATIONS OF METALS (MG/KG) IN INDIAN HERBAL DRUG SAMPLES

Metal	Minimum	Maximum	Mean	SE	WHO Limit	Pharmacopoiea China
Fe	12.72E-02	42.51E-01	21.24E-01	4.23E-01	10	0.20
Pb	10.67E-04	12.67E-04	11.77E-04	2.28E-05	0.30	0.50
Cd	11.67E-04	25.00E-04	17.03E-04	1.67E-04	0.20	0.03
As	6.84E-02	82.50E-02	25.01E-02	6.99E-02	0.20	0.20
Cu	12.19E-03	74.80E-01	15.05E-01	6.43E-01	0.04	0.20

Mean levels of the metals ranged between 11.77E-0 4 mg/kg (Pb) to 15.05E-0 1 mg/kg (Cu) **Table 3.** The high Cu contents in IND-02, IND-03, IND-06, IND-07, IND-08, and IND-10 might have originated from low pH and high Cu contents of soils in areas raw materials were sourced.

This observation agreed favourably with that made in analogous studies [45]. The possible low soil pH might have resulted in highly mobile and spontaneous accessible Cu-ions for absorption by roots of the plant as seen in similar studies [45].

Past or present unrestricted anthropogenic Cu discharge into the environments of plants from mining, smelting, manufacturing, agriculture, or improper waste disposal technologies might have also played a vital role in high Cu levels in IND-02, IND-03, IND-06, IND-07, IND-08 and IND-10. The herbal drugs (IND-02, IND-03, IND-06, IND-07, IND-08 and IND-10) could also be hyper-accumulators of Cu due to the presence of highly water-soluble and low-molecular-weight metal-receptors compounds in the herbal drugs.

These metal-receptors provided trafficking pathways for Cu-ions uptake by plants. The trafficked Cu-ions might have been coordinated to organic acids in the herbal drugs (IND-02, IND-03, IND-06, IND-07, IND-08, and IND-10), which ensured that high enough Cu levels were available to the plants to perform its biological functions before plants were used for IND-02, IND-03, IND-06, IND-07, IND-08, and IND-10. The elevated Cu levels in IND-02, IND-03, IND-06, IND-07, IND-08, and IND-10 suggest that frequent ingestion could activate liver damage, abdominal pain cramps, nausea diarrhea and vomiting, as reported a similar study [45].

Concentration of Fe, Pb, Cd, As, and Cu in Unregistered Ghanaian Herbal Drugs: The unregister Ghanaian herbal drugs origin had mean levels of metals between 12.37E-0 4 mg/kg (Cu) to 15.34E-0 1 mg/kg (Fe) **Table 4.** The mean levels of the metals were below [46] and Pharmacopeia China levels protective of human health **Table 4.** Twenty percent of the drugs (GHA-03) (for gonorrhea) and GHA-09) (for sexual weakness) had recorded Pb levels consistent with 0.30 mg/kg allowed by [46] but below 0.50 mg/kg permitted by Pharmacopeia (China). Seventy percent of the herbal drugs for various illnesses *viz:* chest pain (GHA-01), dysentery (GHA-02), syphilis (GHA-05), fever (GHA-06), jaundice (GHA-07), malaria (GHA-08), and diabetes (GHA-10) had lead levels below WHO and Pharmacopeia (China) recommended levels **Table 4.**

TABLE 4: CONCENTRATIONS OF METALS (MG/KG) IN GHANAIAN HERBAL DRUG SAMPLES

Metal	Minimum	Maximum	Mean	SE	WHO Limit	Pharmacopoiea China
Fe	13.12E-02	1003.15E-02	15.34E-01	9.60E-01	10	20
Pb	10.12E-02	35.54E-02	24.99E-02	2.38E-02	0.30	0.50
Cd	2.22E-03	31.86E-03	16.04E-03	2.96E-03	0.20	0.03
As	14.33E-04	80.34E-04	47.70E-04	7.06E-04	0.20	0.20
Cu	11.33E-04	13.67E-04	12.37E-04	2.14E-05	0.04	0.20

Lead level (35.00E-0 2 mg/kg) in the remaining 10% of the drugs (GHA-04) (for dyspepsia) was above 30.00E-0 2 mg/kg permitted by WHO **Table 4.** This shows that GHA-04 could prompt unwanted health situations such as intellectual disability, abdominal pain, constipation, headaches, irritability, memory problems, infertility, tingling in hands and feet, and other conditions linked to elevated Pb levels when GHA-04 is ingested over an extended period.

Human Health Risk Assessment of Herbal Drugs: To evaluate the probable health effect of Fe, Pb, Cd, As, and Cu that could arise upon recurrent and prolonged ingestion of the herbal drugs investigated, background concentrations of Fe, Pb, Cd, As and Cu in the herbal drugs were assessed. The mean background concentrations were used to compute each metal's health Index (HI) and hazard quotient (HQ) in the various herbal drugs. The HI and HQ calculated were presented in **Tables 5, 6,** and **7** and values compared with those reported in similar studies [39, 42, 44].

Health Indices and Hazard Quotients for Metals in Herbal Drugs: Health effects of Fe, Pb, Cd, As and Cu on humans via incessant and recurrent ingestion of the herbal drugs (CHI, IND, and GHA) were investigated via health indices (HI) and hazard quotient (HQ) assessment models. The HQs were used to analyze the non-cancerous hazard of each metal on consumers over lifetime exposure to the metals via ingestion of the drugs herbal drugs (CHI, IND, and GHA). The health indices (HIs) were employed to evaluate the combined effects of Fe, Pb, Cd, As, and Cu on the exposed population. The HI computation was a vigorous phase in the health risk assessment procedure as diverse heavy metals occurred in the herbal drugs. The HIs and HQs calculated are presented in **Tables 5, 6,** and **7.**

The HIs for the Chinese herbal drugs (CHI) ranged between 2.515E-06 [6] to 253.00E-03 (Fe) whilst the HQs were between 7.83E-04 (Pb) to 371.00E-03 (As). The HIs and HQs calculated (Table 5) were less than 1, indicating that risk levels linked to the metals in the Chinese herbal drugs (CHI-01 to CHI-10) are satisfactory, as reported in analogous studies [39]. The HI and HQ data for the Chinese (CHI-01 to CHI-10) **Table 5** also suggest that though Fe, Pb, Cd, As, and Cu occurred in the drugs, they were inadequate to trigger any health risk (carcinogenic or non-carcinogenic) linked to

them. Hence, consumers of the Chinese herbal drugs (CHI-01 to CHI-10) are unlikely to be hurt by Fe, Pb, Cd, As and Cu contents (CHI-01 to CHI-10) over time of continuous consumption.

TABLE 5: HI AND HQ FOR METALS IN HERBAL DRUGS OF CHINESE HERBAL DRUGS

Metal	Total metal concentration (mg/kg) in herbal drug samples	HI	HQ
Fe	2743.00E-03	253.00E-03	281.20E-03
Pb	2.87E-03	2.584E-06	7.83E-04
Cd	2.74E-03	2.515E-06	2.53E-03
As	120.60E-03	1.11E-04	371.00E-03
Cu	797.20E-03	7.35E-04	18.30E-03
Total	3665.00E-03	261.60E-03	673.90E-03

Health Indices and Hazard Quotients for Metals in Herbal Drugs: The Indian herbal drugs (IND-01 to IND -10) were also investigated for the possibility to exert any of the unwanted health conditions linked with Fe, Pb, Cd, As and Cu. The HI and HQ were calculated and presented for individual metals **Table 6.** The HIs for the Indian herbal drugs (IND-01 to IND -10) ranged between 1.08E-06 (Pb) to 25.31E-03 (Fe) whilst the HQs ranged from 3.08E-04 (Pb) to 76.95E-02 (As). The HI and HQ were below 1 for each metal **Table 6** indicating that risk levels of Fe, Cu, As, Cd and Pb in the Indian herbal drugs (IND-01 to IND -10) are acceptable as reported elsewhere [39, 42, 44]. Based on the HI and HQ data generated (HI < 1 and HQ <1) in **Table 6,** the Indian herbal drugs (IND-01 to IND -10) appear to be safe, as presented in analogous investigations [45]. Fe, Pb, Cd, As, and Cu levels in the drugs (IND-01 to IND -10) were inadequate to provoke any negative health issues often associated with Fe, Pb, Cd, As, and Cu on an exposed population.

TABLE 6: HI AND HQ FOR METALS IN HERBAL DRUGS OF INDIAN ORIGIN

Metal	Total metal concentration (mg/kg) in herbal drug samples	HI	HQ
Fe	212.40E-02	25.31E-03	217.84E-03
Pb	11.77E-04	1.08E-06	3.08E-04
Cd	17.03E-03	1.57E-06	15.72E-04
As	25.01E-02	2.30E-05	76.95E-02
Cu	150.50E-02	13.89E-04	34.70E-03
Total	388.19E-02	21.22E-02	102.39E-02

Health Indices and Hazard Quotients for Metals in Herbal Drugs of Ghanaian Origin: The unregistered Ghanaian herbal drugs (GHA-01 to GHA-10) were subjected to similar HI and HQ evaluation procedures **Table 7.**

This was imperative in order to check for possibilities of the metals (Fe, Pb, Cd, As, and Cu) in the drugs (GHA-01 to GHA-10) to activate undesirable health conditions on consumers of the drugs (GHA-01 to GHA -10).

The HIs for the metals were between 1.14E-06 (Cu) to 14.16E-03 (Fe), whereas the HQs ranged between 2.85E-05 (Cu) to 157.33E-03 (Fe) **Table 7.**

The HI and HQ for the metals (Fe, Pb, Cd, As, and Cu) were less than 1 for each metal **Table 7.**

The HI and HQ evidence suggest that while Fe, Pb, Cd, As, and Cu were in the drugs (GHA-01 to GHA -10), their associated risk levels were satisfactory and the health conditions of consumers of the drugs (GHA-01 to GHA-10) would not be affected negatively by the levels of Fe, Pb, Cd, As and Cu in the Ghanaian herbal drugs.

TABLE 7: HI AND HQ FOR METALS IN HERBAL DRUGS OF GHANAIAN ORIGINS

Metal	Total metal concentration (mg/kg) in herbal drug samples	HI	Health Quotient (HQ)
Fe	15.34E-01	14.16E-03	157.33E-03
Pb	24.99E-02	23.06E-05	65.90E-03
Cd	16.04E-03	1.48E-05	14.80E-03
As	4.77E-03	4.40E-06	14.67E-03
Cu	12.37E-04	1.14E-06	2.85E-05
Total	180.59E-02	14.40E-02	25.27E-02

CONCLUSION: This study assessed levels, health indices (HIs) and hazard quotients (HQs) of Fe [42, 44], Pb, Cd, As and Cu in selected unregistered Ghanaian herbal drugs (GHA-01 to GHA -10) and selected registered Chinese and Indian (CHI-01 to CHI-10) and (IND-01 to IND-10) respectively. Metal levels in the drugs (CHI-01 to CHI-10) ranged from 5.10E-05 mg/kg [6] to 47.56 E -01 mg/kg (Fe) whilst their mean levels were 27.42 E-01 ± 49.39 E -0 3 mg/kg (Fe), 28.17 E -04 ± 83.65 E -05 mg/kg (Pb), 27.43 E -04 ± 10.30 E -04 mg/kg [6], 12.06 E -02 ± 16.16 E -03 mg/kg (As) and 79.72 E -02 ± 40.32 E -0 2 mg/kg (Cu). The mean levels were generally below WHO and pharmacopoiea china recommended levels. Iron (Fe) [42, 44], Pb, Cd, as and Cu contributions to the total metal burden (3665.00 E -0 3 mg/kg) of the (CHI -01 to CHI -10) were 55.501% (2743.00E-03, Fe), 0.075% (2.87 E -03 mg/kg, Pb), 0.074% (2.74 E -03 mg/kg, Cd), 3.290% (120.60 E -03 mg/kg, As) and 41.060% (150.50 E -02 mg/kg, Cu).

Iron (Fe) [42, 44], Pb, Cd, As and Cu input to the total health indices (HI, 261.60 E-03) was 99.244% (253.00 E -03, Fe), 9.87 E -04 % (2.584 E -06, Pb), 9.61 E -04% (2.515 E -06, Cd), 42.43 E -03% (1.11 E -04, As) and 53.09 E -02% (13.89E -04, Cu) whereas their contributions to total HQ (673.90E-03) were 41.72% (281.20E-03, Fe), 1.11 % (7.83E-04, Pb), 0.37% (2.53E-03, Cd), 54.09 % (371.00E-03, As) and 2.71% (18.30E-03, Cu). Metal levels in the Indian drugs (IND-01 to IND-10) ranged from 10.67E-04 mg/kg (Pb) to 74.80E-01 mg/kg (Cu) whilst their mean levels were 21.24E-01 ± 4.23E-01 mg/kg (Fe), 11.77E-04 ± 2.28E-05 mg/kg (Pb), 16.04E-03 ± 2.96E-03 mg/kg [6], 25.01E-02 ± 6.99E-02 mg/kg (As) and 15.05E-01 ± 6.43E-01mg/kg (Cu).

Aside Cu which had mean level above WHO and Pharmacopoiea (China) acceptable levels in 60% of drugs (IND-02, IND-03, IND-06, IND-07, IND-08, IND-10), mean levels of Fe, Pb, Cd and As were below WHO and Pharmacopoiea (China) recommended levels **Table 3.** Iron (Fe), Pb, Cd, As and Cu contributions to total metal load (388.19E-02 mg/kg) of (IND-01 to IND-10) were 54.33 % (212.40E-02 mg/kg, Fe), 0.030% (11.77 E -04 mg/kg, Pb), 0.438% (17.03 E-03 mg/kg, Cd), 6.44% (25.01 E -02 mg/kg, As) and 38.76% (150.50E-02 mg/kg, Cu). The metals (Fe [42], Pb, Cd, As and Cu) inputs to the total health indices (HI, 21.22 E -02) were 99.98% (25.31 E-03, Fe), 0.00050% (1.08E-06, Pb), 0.0026% (1.57 E -06, Cd), 0.010% (2.30 E -05, As) and 0.00053% (1.14 E -06, Cu). Iron (Fe), Pb, Cd, As and Cu) contributions to the total HQ (102.39E-02) were 21.27% (217.84 E -03, Fe), 0.030% (3.08 E -04, Pb), 0.153% (15.72 E -04, Cd), 75.15% (76.95 E-02, As) and 3.389% (34.70 E -03, Cu). Metal levels in the drugs (GHA-01 to GHA -10) were between 11.33 E -04 mg/kg (Cu) to 1003.15 E -02 mg/kg (Fe). mean levels of Fe, Pb, Cd, As and Cu were 15.34 E -01± 9.60 E -01 mg/kg (Fe), 24.99 E -02 ± 2.38 E -02 mg/kg (Pb), 16.04 E -03 ± 2.96 E -03 mg/kg [6], 47.70 E -04 ± 7.06 E -04 mg/kg (As) and 12.37 E -04 ± 2.14 E -05 mg/kg(Cu). The mean levels of Fe, Pb, Cd, As and Cu were generally below WHO and Pharmacopoiea (China) suggested levels. Only 1% GHA-04) of the unregistered Ghanaian herbal drugs had recorded Pb level 30.00 E -02 mg/kg permitted by WHO **Table 4.**

Iron (Fe) [42], Pb, Cd, As and Cu contributions to the total metal load (180.59 E -02 mg/kg) of the (GHA-01 to GHA -10) were 84.35% (15.34 E -01 mg/kg, Fe), 13.83 % (24.99 E -02 mg/kg, Pb), 0.88% (16.04 E -03 mg/kg, Cd), 0.26% (4.77 E -03 mg/kg, As) and 0.68% (12.37 E -04 mg/kg, Cu). Iron (Fe) [42], Pb, Cd, As and Cu contributions to the total health indices (HI, 14.40 E -02) were 99.82% (14.16E-03, Fe), 0.16% (23.06 E -05, Pb), 0.01% (1.48E-05, Cd), 0.003% (4.40 E -06, As) and 0.0007% (1.14 E -06, Cu) whereas their contributions to total HQ (25.27 E -02) were 62.26% (157.33 E -03, Fe), 26.07% (65.90 E -03, Pb), 5.85% (14.80 E -03, Cd), 5.80 % (14.67 E -03, As) and 0.011% (2.85 E -05, Cu).

The registered Indian herbal drugs (IND-01 to IND-10) had the higher total metal burden (388.19 E -02 mg/kg) followed by the unregistered Ghanaian herbal drugs (GHA-01 to GHA -10) (180.59E-02 mg/kg) followed by the registered Chinese herbal drugs 3665.00 E -0 3 mg/kg (CHI-01 to CHI-10) (3665.00 E -03 mg/kg). The HI and HQ for individual metals were less than 1 **Tables 5, 6,** and **7**. The total HI and HQ for the metals in each herbal drug sample were also less than 1. These indicate that the individual metals and the combined effects of the metals, cannot induce any of the health conditions often linked to the metals.

Thus, all herbal drugs appeared safe for managing and treating the various health conditions and illnesses indicated for them. Although herbal drugs appear harmless when ingested, it is vital for authorities in Ghana to institute strict and robust regulatory control systems to ensure that herbal drugs sold in Ghana are duly registered. Authorities must further subject these herbal drugs to the instituted regulatory systems to safeguard the wellbeing of people that depend on the herbal drugs for their healthcare needs.

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