# Studies on the medical safety of botanical medicines: Novel toxic metals and microbial contamination approach

Roqayah Hassan Kadi<sup>1</sup>, Uguru Hilary<sup>2</sup>, Akpokodje Ovie Isaac<sup>3</sup>, Idama Omokaro<sup>4</sup>, Rokayya Sami<sup>5</sup>\*, Suha Abduljawad<sup>6</sup>, Fayez Alsulaimani<sup>7,8</sup>, Ahmed Basri<sup>7,8</sup>, Ola Abu Ali<sup>9</sup> and Mahmoud Helal<sup>10</sup>

**Abstract**: The utilization of herbal therapies is increasing globally, prompting investigations into the health complications that may arise from drug side effects. A total of 160 herbal medicines (HMs), were used for this study, and their toxic heavy metal content, microbial load and dielectric properties were evaluated. The results obtained revealed that the crude HMs exhibited a greater proportion of heavy metals, microorganisms and a higher dielectric constant ( $\epsilon'$ ) value, in comparison to the refined HMs. Particularly, the powdered HMs contained high heavy metals and microbial contaminations. For the unrefined powders, HM samples exceeded the safety limits of  $cfu/g \le 10^5$ , approved by World Health Organization for herbal medications. Regarding the electrical properties, the  $\epsilon'$  for the crude unrefined HMs ranged from 9.19 to 92.67; while the refined HMs  $\epsilon'$  values varied from 7.35 to 39.15. The hazard index (HI) analysis showed that unrefined HMs have higher non-carcinogenic toxicity than refined ones, with children facing serious health risks as their HI values surpass 1. Crude heavy metal consumption increases a child's risk of developing cancer. This research's findings highlighted the importance of consistent monitoring of herbal products, as heavy metals can accumulate, resulting in toxicity after prolonged use of these drugs.

Keywords: Drug safety, heavy metals, medicinal herbs, microbial contamination, public health practice

Submitted on 3-2-2025 – Revised on 30-3-2025 – Accepted on 23-6-2025

# INTRODUCTION

The increasing global health issues are closely associated with anthropogenic activities such as pollution, urbanization, lifestyle patterns, and self-medication (Ellwanger et al., 2023). Millions of people die annually, from non-communicable diseases (NCDs), and diseases that could be prevented (WHO, 2024). In numerous lowand middle-income nations, challenging economic conditions and distrust in conventional treatments drive patients to seek herbal remedies (Okaiyeto and Oguntibeju, 2021; Wu et al., 2022; Lima et al., 2023). Herbal medicine (HM) is an extract derived from plant products, which has nutritional and therapeutic benefits (WHO, 2008; AJerohoet al., 2018; Amir et al., 2023). Globally, around \$60 billion is spent annually on herbal medications, often used without proper prescriptions, risking under-dosing or overdosing challenges (Barkat et al., 2021; Wu et al., 2022). Overdosing can cause drug toxicity, leading to serious health problems, including

\*Corresponding author: e-mail: rokayya.d@tu.edu.sa

neurological damage, kidney problems and liver issues (Picot *et al.*, 2022; Antar *et al.*, 2023).

Herbal medicines fall into two main types: crude herbal medicines, which are not registered by the Food and Drug Administration (FDA), and refined herbal medicines, which are FDA-registered (Muyumba et al., 2021). They come in creams, soaps, powders, water-extracted liquids and ethanol-extracted liquids forms (de Sousa et al., 2020). Some herbal medicine practitioners assert their products are registered; however, they lack the rigorous testing and safety evaluations of pharmaceuticals (Hassen et al., 2022; Mssusa et al., 2023). These medicines often contain various toxic substances, including heavy metals, benzene, formaldehyde, cyanogenic glycosides, ephedrine, phytates, tannins, and pyrrolizidine alkaloids, as well as pathogens (Quan et al., 2020; Lis-Cieplak et al., 2024).

Herbal medicines are widely sold and consumed globally, and in most cases, these products lacks adequate regulations and clinical evidence to support their public

<sup>&</sup>lt;sup>1</sup>Department of Biological Sciences, College of Science, University of Jeddah, Jeddah, Saudi Arabia

<sup>&</sup>lt;sup>2</sup>Department of Agricultural Engineering, Delta State University of Science and Technology, Ozoro, Nigeria

<sup>&</sup>lt;sup>3</sup>Department of Civil and Water Resources Engineering, Delta State University of Science and Technology, Ozoro, Nigeria

<sup>&</sup>lt;sup>4</sup>Department of Computer Engineering, Delta State University of Science and Technology, Ozoro, Nigeria

<sup>&</sup>lt;sup>5</sup>Department of Food Science and Nutrition, College of Sciences, Taif University, Taif, Saudi Arabia

<sup>&</sup>lt;sup>6</sup>Department of Clinical Nutrition, College of Applied Medical Sciences, Taibah University, Medina, Saudi Arabia

<sup>&</sup>lt;sup>7</sup>Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia

<sup>&</sup>lt;sup>8</sup>Embryonic Stem Cell Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia

<sup>&</sup>lt;sup>9</sup>Department of Chemistry, College of Science, Taif University, Taif, Saudi Arabia

<sup>&</sup>lt;sup>10</sup>Department of Mechanical Engineering, Faculty of Engineering, Taif University, Taif, Saudi Arabia

safety and efficacy (AJeroho *et al.*, 2018; Okaiyeto and Oguntibeju, 2021; Hassen *et al.*, 2022). Though certain HMs have high efficacy managing protracted ailments, materials used for their production may contain harmful substances and pathogens (Okaiyeto and Oguntibeju, 2021; Jităreanu *et al.*, 2023). Alghamdi *et al.* (2023) reported that some herbal drugs can interfere with conventional drugs, resulting in life-threating side effects. Likewise, improper formation tends to reduce the efficacy and public health safety of herbal products (Hassen *et al.*, 2022; Wang *et al.*, 2023; Balkrishna *et al.*, 2024). Furthermore, HMs' electrical properties can be correlated to their parent materials' physicochemical characteristics (Brini *et al.*, 2017; Schafer and Lerner, 2022).

Although numerous studies have investigated the effectiveness of herbal therapies, there has been relatively little comprehensive research conducted on the potential health hazards associated with these herbal treatments. It is now paramount to conduct an in-depth examination of the health risks associated with herbal medicines. Therefore, this study combines many aspects such as microbial load, heavy metal contamination, and electrical properties, to evaluate the public health safety of herbal products. Information obtained from this study will proffer possible solutions, to health risks allied to HMs consumption.

# **MATERIALS AND METHODS**

## Sample size and sampling technique

To accomplish the goals of this study: 40 powders, 40 water-based extracts, 40 ethanol-based extracts, 20 creams and 20 soaps samples, were randomly selected from Saudi Arabia. Among the sampled specimens, 20 powders, 20 ethanol- based extracts, 5 creams and 5 soaps samples were refined products (certified by Food and Drugs Administration), while the remaining samples were from local/crude unrefined sources. The medicines were placed in coded glass bottles, placed in dark containers at ambient temperature (25±3°C), and promptly taken to the laboratory for analysis. The study was conducted from January 2024 to October 2024.

#### Chemicals, reagents and instruments

The chemicals used for this research were of the analytical grade procured from Fisher Scientific (Thermo Fisher Scientific, America). The Atomic absorption spectrometry (AAS) system used for the heavy metals analysis was purchased from Fisher Scientific Ltd.

#### Determination of heavy metals

The metals (cadmium "Cd", arsenic "As", lead "Pb", chromium "Cr", nickel "Ni", copper "Cu", zinc "Zn" and mercury "Hg") levels in the herbal samples were determined, by employing the appropriate ASTM approved procedures (ASTM D1971-16, 2021). 10 mL or

its equivalent of each HM, was digested with 50 mL of a prepared mixture, that contained concentrated HNO<sub>3</sub> and H<sub>2</sub>O<sub>2</sub>, mixed at a ratio of 4:1. A temperature of 100±5°C was used for the digestion until a clear product was achieved. The digested specimen was cool to room temperature (25±4°C), sieved, and diluted to 100 mL using deionized water (Uguru *et al.*, 2023). Thereafter, elemental contents of the digested sample as measured, by using atomic absorption spectrophotometer (AAS) system. The detection limits of elements were 1, 3, 1, 2, 3, 1 and 3 ppb, for Cd, Pb, Cr, Hg, Cu, Ni, As and Zn, respectively.

# Microbial population

The microbial evaluation of the herbal materials was conducted in accordance with standard strategies (WHO, 2007). After the incubating period, the colony-forming units per gram (cfu/g) were computed, through multiplication of the mean colonies quantity by the dilution factor, and the total bacterial count (TBC) and total fungal count (TFC) population documented.

## Electrical properties

The HMs dielectric constant ( $\varepsilon'$ ) levels were determined at 1 MHz frequency, though the processes employed by these authors (Hong *et al.*, 2024; Šegatin *et al.*, 2020). The  $\varepsilon'$  value was calculated through the formula shown in Equation 1.

$$E' = \frac{Cps}{kc}$$

Where Cps = sample parallel capacitance corrected for 'stray' capacitance, and Kc = average cell constant (Šegatin *et al.*, 2020)

# Health risk assessment

The oral absorption (ingestion) method assessed the serious internal health risks of heavy metal exposure in humans, focusing solely on herbal products extracted with powder, water, and ethanol during evaluation (Luo *et al.*, 2021).

# Daily intake dose (EDI)

The EDI was calculated through Equation 2.

$$BDI = \frac{C \times IR}{BW}$$

Where C = metal level in the herbal preparations, IR = mean daily ingestion rate and was taken to be 20 g/person/day (Meseret *et al.*, 2020), BW = individual body weight, which was taken to be 25 kg for children and 75 kg for adults (Uguru *et al.*, 2023), CF = conversion factor from g/person/day to mg/person/day, and it was 0.001.

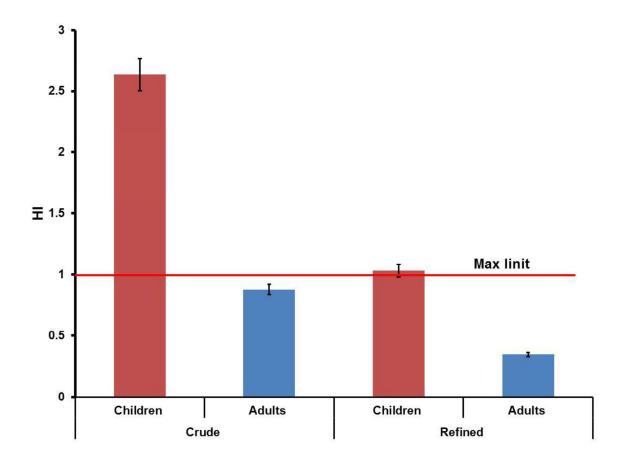


Fig. 1: The HI values of the herbal medicines

Table 1: Heavy metals levels in the herbal medicines (mg/kg)

Metal		Powder	Water	Ethanol	Cream	Soap	WHO*
Cd	L	0.772 <sup>b</sup> ±0.929	0.760 <sup>b</sup> ±0.779	0.675°a±0.758	0.681a±0.893	0.651°±0.754	0.3
	R	$0.142^{c}\pm0.248$	ND	$0.104^{b}\pm0.171$	$0.044^a \pm 0.058$	$0.063^a \pm 0.079$	0.3
Pb	L	$0.968^{c} \pm 1.353$	$0.848^{b} \pm 1.066$	$0.764^{a}\pm0.919$	$0.951^{c}\pm1.083$	$0.733^a \pm 1.053$	10
	R	$0.317^{c}\pm0.459$	ND	$0.215^{b}\pm0.322$	$0.092^{a}\pm0.119$	$0.093^a \pm 0.126$	10
Cr	L	$0.737^{d} \pm 0.831$	$0.567^{b} \pm 0.649$	$0.462^{a}\pm0.411$	$0.579^{b} \pm 0.638$	$0.615^{c}\pm0.726$	2
	R	$0.201^{c}\pm0.349$	ND	$0.133^{b}\pm0.240$	$0.139^{b}\pm0.161$	$0.069^{a}\pm0.116$	2
As	L	$0.406^{c} \pm 0.487$	$0.446^{d} \pm 0.435$	$0.346^{a}\pm0.376$	$0.362^{b} \pm 0.446$	$0.350^a \pm 0.402$	10
	R	$0.236^{\circ} \pm 0.370$	ND	$0.180^{b} \pm 0.257$	$0.014^a \pm 0.018$	$0.017^{a}\pm0.022$	10
Ni	L	$1.419^{c}\pm1.468$	$1.185^{d}\pm1.170$	$1.038^{a}\pm1.068$	1.315°±1.164	$1.140^{b}\pm1.113$	NA
	R	$0.055^{b} \pm 0.088$	ND	$0.040^{a}\pm0.061$	$0.073^{c}\pm0.057$	$0.053^{b} \pm 0.058$	NA
Hg	L	$0.194^{c}\pm0.257$	$0.183^{b} \pm 0.229$	$0.148^a \pm 0.208$	$0.182^{b}\pm0.231$	$0.178^{b}\pm0.219$	1.0
_	R	$0.036^{b} \pm 0.045$	ND	$0.025^{a}\pm0.031$	$0.054^{c}\pm0.045$	$0.027^{a}\pm0.045$	1.0
Cu	L	$10.698^{d} \pm 8.981$	$8.962^{b} \pm 6.883$	$7.887^{a}\pm6.233$	$9.159^{c}\pm6.262$	$8.893^{b} \pm 7.039$	20
	R	$8.753^{\circ} \pm 6.981$	ND	$5.671^{b}\pm4.121$	$4.917^{a}\pm4.340$	5.365 <sup>b</sup> ±5.113	20
Zn	L	$13.495^{d} \pm 9.889$	$10.629^{b} \pm 6.73$	$11.380^{\circ} \pm 6.803$	$10.967^{b} \pm 8.751$	$9.855^a \pm 7.906$	50
	R	$10.132^{c} \pm 6.737$	ND	$7.252^{a}\pm3.937$	$7.883^{b} \pm 3.860$	$7.586^{b} \pm 3.927$	50

L = Crude HMs, R = Refined HMs, ND = not determined, WHO\* = (WHO, 2007), Mean  $\pm$  standard deviation, NA = not available, for same metal and HM type- columns with the same common letter (superscript) indicate that they are not significantly differ at p  $\leq$ 0.05 using DMRT,

Table 2: Estimated Daily Intake (mg/kg/day) and HQ values of the heavy metals

	EDI (mg/kg/day)				HQ			
	Crude		Refined		Crude		Refined	
	Children	Adults	Children	Adults	Children	Adults	Children	Adults
Cd	5.89E-04	1.96E-04	9.84E-05	3.28E-05	5.89E-01	1.96E-01	9.84E-02	3.28E-02
Pb	6.88E-04	2.29E-04	2.13E-04	7.09E-05	4.91E-01	1.64E-01	1.52E-01	5.07E-02
Cr	4.71E-04	1.57E-04	1.34E-04	4.45E-05	1.57E-01	5.24E-02	4.45E-02	1.48E-02
As	3.19E-04	1.06E-04	1.66E-04	5.55E-05	1.06	3.55E-01	5.55E-01	1.85E-01
Ni	9.71E-04	3.24E-04	3.80E-05	1.27E-05	4.86E-02	1.62E-02	1.90E-03	6.33E-04
Hg	1.40E-04	4.67E-05	2.44E-05	8.13E-06	7.00E-02	2.33E-02	1.22E-02	4.07E-03
Cu	7.35E-03	2.45E-03	5.77E-03	1.92E-03	1.84E-01	6.12E-02	1.44E-01	4.81E-02
Zn	9.47E-03	3.16E-03	6.95E-03	2.32E-03	3.16E-02	1.05E-02	2.32E-02	7.73E-03

Table 3: The CR and TCR values of the toxic metals

Metal	Unre	fined	Refined		
	Children	Adults	Children	Adults	
Cd	2.24E-04	7.46E-05	3.74E-05	1.25E-05	
Pb	5.85E-06	1.95E-06	1.81E-06	6.03E-07	
Cr	2.36E-04	7.85E-05	6.68E-05	2.23E-05	
As	4.79E-04	1.60E-04	2.50E-04	8.32E-05	
Ni	8.16E-04	2.72E-04	3.19E-05	1.06E-05	
		TCR			
	Children	Adults	Children	Adults	
	1.76E-03	5.87E-04	3.88E-04	1.29E-04	

**Table 4**: Microbial population of herbal medicines (x10<sup>4</sup>cfu/g)

State		Bacteria	Fungi	WHO*
Powder/dried	Crude	28.93 <sup>d</sup> ±39.60 (0.2-152)	25.09°±32.36 (0.3-135)	$cfu/g \le 10^5$
	Refined	$9.95^{b}\pm3.38(0-51)$	9.18 <sup>a</sup> ±9.86 (0-38)	$cfu/g \le 10^5$
Liquid - WE	Crude	$19.36^{b} \pm 27.45 \ (0.06 - 106.82)$	12.84 <sup>a</sup> ±19.97 (0.04-84.8)	$cfu/g \le 10^5$
Liquid - EE	Crude	$14.77^{d} \pm 20.65 \ (0.05-81.05)$	9.60°±14.37 (0.03-62.75)	$cfu/g \le 10^5$
	Refined	3.25 <sup>b</sup> ±4.94 (0-18.26)	2.04°±2.64 (0-11.97)	$cfu/g \le 10^5$
Cream	Crude	$14.19^{d} \pm 18.79 (0.05-76.86)$	11.25°±14.69 (0.17-64.98)	$cfu/g \le 10^5$
	Refined	2.57°a±2.39 (0.02-8.67)	$3.05^{b}\pm2.90 (0.01-12.86)$	$cfu/g \le 10^5$
Soap	Crude	$8.80^{d}\pm8.70\ (0.04-41.54)$	$6.49^{\circ}\pm6.81\ (0.09-28.19)$	$cfu/g \le 10^5$
	Refined	2.43°±2.61 (0.05-10.17)	$2.67^{b}\pm2.76$ (0.03-11.25)	$cfu/g \le 10^5$

WE  $\sim$  Water extracted, EE  $\sim$  Ethanol extracted, Mean  $\pm$  standard deviation and range in parentheses, rows having the same common letter (superscript) specify that they are significantly similar (p  $\leq$ 0.05) using DMRT, \*  $\sim$  WHO Standards (WHO, 2007).

Table 5: The HMs dielectric properties

State	Level	Dielectric constant
Powder/dried	Crude	50.29 <sup>h</sup> ±9.43 (34-69)
	Refined	$39.15^{g}\pm8.21$ (27-55)
Liquid – WE	Crude	92.67 <sup>±</sup> 7.82 (78-106)
Liquid – EE	Crude	$32.14^{f}\pm7.09$ (24-52)
_	Refined	24.05°±5.71 (18-41)
Cream	Crude	$20.76^{d} \pm 4.92 (14-34)$
	Refined	15.85°±4.91 (9-27)
Soap	Crude	$9.19^{b}\pm3.33$ (4-16)
-	Refined	$7.35^{a}\pm2.76(4-13)$

Mean  $\pm$  standard deviation and range in parentheses; rows sharing similar superscript letter designate no significant differences (p  $\leq$  0.05) according to DMRT.

# Non-carcinogenic risk

The hazard quotient (HQ) and hazard index (HI) of the metals were computed using Equations 3 and 4.

$$HQ = \frac{EDI}{RfD}$$

$$HI = \Sigma HQ$$
3
4

Where RfD = Reference dose, with Cd, Pb, Cr, As, Ni, Hg, Cu and Zn values of 0.001, 0.0014, 0.003, 0.0003, 0.002, 0.002, 0.04 and 0.3 mgkg<sup>-1</sup>day<sup>-1</sup>, respectively (Meseret *et al.*, 2020; Uguru *et al.*, 2024).

## Carcinogenic risk

The carcinogenic risk values were calculated using Equations 5 and 6 (Uguru *et al.*, 2023).

$$CR = EDI \times CSF$$
 5  
 $TCR = \Sigma CR$  6

Where CSF= cancer slope factor (oral) for the PTMs - Cd (0.38), Pb (0.0085), Cr (0.5), As (1.5) and Ni (0.84) (Uguruet al., 2023).

# **DATA ANALYSIS**

The data obtained from this research were analyzed through Analysis of variance by employing SPSS software (version 22). Additionally, the average results were separated using the Duncan's Multiple Range Test (DMRT) at 5% significant level (p  $\leq$ 0.05). All the tests were conducted in triplicates.

#### **RESULTS**

## Heavy metals content

The results of the heavy metals concentrations for HMs are presented in table 1. It was observed that there were significant differences among the mean values of the different herbal products (table 1). Notably, Zn recorded the maximum concentration in the local powdered, refined powdered and water-solvent extracted botanical medicines, with values of 13.495, 10.132 and 10.629 mg/kg, respectively. Similarly, it was noted that in the crude ethanol extracted, refined ethanol extracted, unrefined soap, and refined soap herbal medicines, zinc still maintained the maximum concentration, with an average value of 11.380, 7.252, 9.855 and 7.586 mg/kg, respectively. Additionally, the results revealed that the unrefined cream (pomade) and refined herbal cream medicines, exhibited the highest zinc concentrations, with a mean value of 10.967 and 7.8832 mg/kg, respectively.

#### Health risk assessment

Non - carcinogenic risk

Table 2 presents the EDI and HQ values of the PTMs investigated in this study. For the crude herbal products, the EDI values ranged from 4.67 x10<sup>-5</sup> to 9.47 x10<sup>-3</sup> mg/kg/day, while for their refined counterparts, the EDI values varied from 8.13 x10<sup>-6</sup> to 6.95 x10<sup>-3</sup> mg/kg/day. The HQ values depicted that the crude products ranged

from  $1.05 \times 10^{-2}$  to 1.06, while the refined products HQ values varied between  $6.33 \times 10^{-4}$  and  $5.55 \times 10^{-1}$ . Similarly, the HI results presented in fig. 1 revealed that HI values for the crude HMs were 2.635 and 0.878 for children and adults, respectively; while for the refined HMs, the values for the children and adults were 1.031 and 0.344, respectively.

# Carcinogenic risk

The calculated CR and TCR results of the PTMs evaluated in this study are presented in table 3 shows that in the crude HMs, the CR values ranged from  $5.85 \times 10^{-6}$  to  $8.16 \times 10^{-4}$  for children and  $1.95 \times 10^{-6}$  to  $2.72 \times 10^{-4}$  for adults. Then in the refined HMs, the CR values varied from  $1.81 \times 10^{-6}$  to  $2.50 \times 10^{-4}$  and  $6.03 \times 10^{-7}$  to  $8.32 \times 10^{-5}$  for the children and adults, respectively. Additionally, the total carcinogenic risk (TCR) results depicted that the TCR values for the children and adult for unrefined HMs were  $1.76 \times 10^{-3}$  and  $5.87 \times 10^{-4}$ , respectively. However, in the refined HMs, it was noted that the TCR values for the children and adult categories were  $3.88 \times 10^{-4}$  and  $1.29 \times 10^{-4}$ , respectively.

#### Microbial load

The results of the microbial population in the herbal medications are presented in table 4. It was observed that the TBC and TFC in the HMs varied from 2.43 x10<sup>4</sup> to 28.93 x10<sup>4</sup>cfu/g, and from 2.04 x10<sup>4</sup> to 25.09 x10<sup>4</sup>cfu/g, respectively. The crude HMs exhibited higher microbial levels compared to the refined products, which can be attributed to the higher hygienic procedures strictly adopted during refined products preparation and packaging unit operations (de Sousa *et al.*, 2020; Alharbi *et al.*, 2024).

# Electrical properties

The results of the dielectric constant ( $\epsilon'$ ) are presented in table 5. It was noted that the dielectric constant varied widely among the medical products. The  $\epsilon'$  values of the herbal materials studied varied between 7.35 and 92.67, which is an indication of wide electrical behavior of the herbal mediations.

# **DISCUSSION**

# Heavy metals concentration

This research has established that the refined HMs recorded lower metals levels. This situation can be correlated with effective refining and storage operations (Kandić *et al.*, 2023; Hu *et al.*, 2024). Fascinatingly, the results revealed that apart Cd concentration degree in the crude powder herbal product, the concentrations of the remaining heavy metals, regardless of the HMs nature were below the World Health Organization approved maximum allowable limits for metals. Notably, most HMs tend to have higher Cd levels, as earlier buttressed and published by these researchers (AJeroho *et al.*, 2018; Kandić *et al.*, 2023; Bhalla and Pannu, 2020).

The mean Hg levels recorded in this study were lower than those reported by Bhalla and Pannu (2020), higher than the findings of Kandić *et al.* (2023), and within the range of values obtained by Wu *et al.* (2022). Also, the Pb concentrations obtained for this study were smaller than the values reported by Wu *et al.* (2022) and Meseret (2020). However, the Cr, Zn and Cu concentrations observed in this study were below the WHO maximum limits (Cr = 2 mg/kg, Cu = 20 mg/kg, Zn = 50 mg/kg). The presence of toxic heavy metals in the HMs may be related to environmental pollution in the area, where the herbal plants thrived or during the production processes (Wu *et al.*, 2022; Uguru *et al.*, 2023; Asiminicesei *et al.*, 2024).

Toxic metals like Pb, As, Cd, and Hg, noted in significant levels in this study, are deemed hazardous by the US Agency for Toxic Substances and Disease Registry (ATSDR) (ATSDR, 2019). Long-term Cd exposure can cause issues in cancer, kidneys, lungs, and renal tract (Uguru *et al.*, 2023). Chronic As exposure is linked to cancer diseases; Hg toxicity affects kidney and the nervous system; while Zn toxicity can lead to mucormycosis (Bhalla and Pannu, 2020; Yao *et al.*, 2024).

#### Health risk assessment

The calculated health hazards associated with the HMs consumption indicated that the medications are largely safe for human ingestion. Generally, the EDI values indicate that the refined medicines pose lower health risks, aligning with the findings reported by Kandic' et al. (2023). Except for arsenic in children, human exposure to heavy metals poses no significant health risks, since hazard quotient values exceeded 1 in all age groups. The high Pb and As HQ values documented in this research are similar to the findings of Wu et al. (2022) and Kandic' et al. (2023), indicating that great concern should be given to contamination these by metals phytomedicines. Furthermore, the HI results (table 2) indicated significant non-cancerous health risks for children exposed to these phytomedicines, as their HI values exceeded 1 for both crude and refined forms (USEPA, 1986; Uguru et al., 2023). This study's findings align with those of Meseret et al. (2020) and Kandić et al. (2023), highlighting the dangers of toxic metal contamination in herbal medicines. The close proximity to the critical threshold of 1 necessitates urgent attention to mitigate potential heavy metal toxicity risks (Yang et al., 2021).

This study's Carcinogenic risk results outcome revealed that the refined HMs exhibited lower carcinogenic risks compared to their unprocessed counterparts. This aligned with previous authors (Yang *et al.*, 2021 and Wu *et al.*, 2022) reports, which stipulated that refining processes tend to reduce the toxicity and carcinogenic potentials of

HMs. This research's TCR values revealed that intake of these crude HMs posed serious carcinogenic health risks to the children, as the TCR values were below  $1.00 \times 10^{-4}$ . According to World Health Organization, TCR values below  $1.00 \times 10^{-4}$  is considered dangerous and carcinogenic (Uguru *et al.*, 2024). The study's outcomes have highlighted the potential health hazards associated with crude biomedicines.

#### Microbial load

The pathogenic evaluation results depicted that the TBC and TFC population in most of the un-refined herbal medicines exceeded the safe borders (cfu/g  $\leq 10^5$ ) approved by the WHO for herbal medications (WHO, 2007). This shows that un-refined biomedicines have a lot of health complications, observation aligning with previous reports of these scientists (Yesuf *et al.*, 2016; de Sousa *et al.* 2020). Remarkably, the microbial populations obtained in this investigation, were comparatively less than outcomes reported by Yesuf *et al.* (2016), regarding HMs in Ethiopia.

Additionally, the pathogenic levels detected in the refined biomedicines, might be caused by cross contamination, primarily due to insanitary (de Sousa *et al.*, 2020; Ekeleme *et al.*, 2024; Alharbi *et al.*, 2024). Furthermore, ethanol's antiseptic characteristics can be attributed to the lower pathogenic growth observed mostly in the ethanol based biomedicines formation (Gonelimali *et al.*, 2018). The large microbial population thieving in the crude HMs, will reduced their efficacy, and can also results in adverse health challenges (Yesuf *et al.*, 2016).

# Electrical properties

Interestingly, this research's verdicts illustrated that most herbal drugs have substantial dielectric properties, which will affects their efficiency. Lesser dielectric constant identified in the refined products, may be attributed to the lower impurities they have. Dielectric properties can alter drugs absorption and dissemination rates; and higher  $\varepsilon'$  tends to increases the possibilities of adverse drugs side effects (Hong *et al.*, 2024). The elevated  $\varepsilon'$  recorded from water based products, can be linked to water's polarity, which increases solubility and mobility of bioactive compounds (Brini *et al.*, 2017).

Furthermore, the  $\varepsilon'$  of the biomedicines appraised in this study, were lower than Abdul *et al.* (2018) findings; however, they aligned with Hong *et al.* (2024) and Lahane (2016) reports. The discrepancies noted among the dielectric properties values - as obtained by various researchers, might be linked to environmental factors, processing approaches, moisture content, and the machines settings (Kandić *et al.*, 2023. According to Abdul *et al.* (2020), dielectric constant of materials is highly dependent on the frequency used for the measurement, and lower frequency tends to produce

higher  $\epsilon'$  values. Dielectric constant has been identified as an indispensable factor that is employed to identify drugs safety.

#### **CONCLUSION**

The increasing demand for alternative medications has spawned considerations, regarding their efficacy and health implications. This research was conducted to assess the safety of herbal medicines (HMs), and to propose solutions to their limitations. The microbiological, heavy metals and electrical properties of biomedical drugs were measured in harmony with standard approaches. Interestingly, the laboratory outcomes depicted that crude herbal drugs posed serious health implications. The results further shown that, the refined herbal medications have lower toxic metals concentrations, pathogenic loads, and dielectric constant ( $\epsilon'$ ) values. Notably, the crude HMs microbial loads, surpassed the WHO's approved maximum limits for drugs safety. The findings highlighted that refined HMs, cannot be directly correlated to either non-carcinogenic or carcinogenic diseases, which portrays their safeness. Findings of this study have underscored that caution should be taken, when taking unregistered biomedicines, and consistent monitoring of herbal drugs formulation and medication. Also, children should be given special attention when administering herbal medications.

# Funding

This research was funded by Taif University, Saudi Arabia, Project No. (TU-DSPP-2024-79).

#### **ACKNOWLEDGMENTS**

The authors extend their appreciation to Taif University, Saudi Arabia, for supporting this work through project number (TU-DSPP-2024-79).

# Conflict of interest

There are no conflict of interest.

# REFERENCES

- Abdul JAH, Abdullah BM, Pawa NP and Shaikh YH (2018). High quality dielectric properties of four medicinal herbs at different frequencies. *IJRAR*, **5**(4): 636-641
- Abdul JAH, Sayyeda RN, Shaikh IF and Shaikh YH (2020). Dielectric properties of drugs at lower frequency range from 3 KHz to 5 MHz by using impedance analyzer. *J. Chem.*, **6**: 209-214.
- AJeroho O, Achara F, Adewoyin B and Abo K (2018). Determination of cadmium, chromium and lead in four brands of herbal bitters preparation sold in Benin-city, Southern Nigeria. *Afr. J. Environ. Sci. Technol.*, **12**(5): 186-190.

- Alghamdi W, Al-Fadel N, Alghamdi EA, Alghamdi M and Alharbi F (2023). Signal detection and assessment of herb-drug interactions: Saudi food and drug authority experience. *DRWO*, **10**(4): 577-585.
- Alharbi SF, Althbah, AI, Mohammed AH, Alrasheed MA, Ismail M, Allemailem KS, Alnuqaydan AM, Baabdullah AM and Alkhalifah A (2024). Microbial and heavy metal contamination in herbal medicine: A prospective study in the central region of Saudi Arabia. *BMC Complement. Med. Ther.*, **24**(1): 2-7
- Amir M, Vohra M, Raj RG, Osoro I and Sharma A (2023). Adaptogenic herbs: A natural way to improve athletic performance. *Health Sci. Rev.*, 7: 100092.
- Antar SA, Ashour NA, Sharaky M, Khattab M, Ashour NA, Zaid RT, Roh EJ, Elkamhawy A and Al-Karmalawy AA (2023). Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. *Biomed. Pharmacother.*, **168**: 115734 115754
- Asiminicesei DM, Fertu DI and Gavrilescu M (2024). Impact of heavy metal pollution in the environment on the metabolic profile of medicinal plants and their therapeutic potential. *Plants*, **13**(6): 913-927
- ASTM D1971-16 (2021). Standard practices for digestion of water samples for determination of metals by flame atomic absorption, graphite furnace atomic absorption, plasma emission spectroscopy, or plasma mass spectrometry.
- ATSDR (2019). Agency for toxic substances and disease registry substance priority List
- Balkrishna A, Sharma N, Srivastava D, Kukreti A, Srivastava S and Arya V (2024). Exploring the safety, efficacy, and bioactivity of herbal medicines: Bridging traditional wisdom and modern science in healthcare. *FIM.*, **3**(1): 35-49.
- Barkat Md. A, Goyal A, Barkat HA, Salauddin M, Pottoo FH and Anwer ET (2021). Herbal medicine: Clinical perspective and regulatory status. *CCHTS Journal*. 24(10): 1573-1582.
- Brini E, Fennell CJ, Fernandez-Serra M, Hribar-Lee B, Lukšič M, Dill KA (2017). How water's properties are encoded in its molecular structure and energies. *Chem. Rev.*, **117**(19): 12385-12414.
- Bhalla A and Pannu AK (2022). Are Ayurvedic medications store house of heavy metals? *Toxicol. Res.* **11**(1): 179-183.
- De Sousa CM, Fujishima MAT, de Paula B, Mastroianni PC, de Sousa FFO and da Silva JO (2020). Microbial contamination in herbal medicines: A serious health hazard to elderly consumers. *BMC Complement. Med. Ther.*, **20**(1): 252-271
- Ekeleme UG, Ikwuagwu VO, Chukwuocha UM, Nwakanma JC, Adiruo SA, Ogini IO and Ude IU (2024). Detection and characterization of microorganisms linked to unsealed drugs sold in Ihiagwa

- community, Owerri, Imo State, Nigeria. *Access Microbiol.*, **6**(2): 000752
- Ellwanger JH, Veiga ABG, Kaminski VL, Valverde-Villegas JM, Freitas AWQ and Chies JAB (2021). Control and prevention of infectious diseases from a One Health perspective. GMD., **44**(Suppl 1): e20200256 e20200271
- Gonelimali FD, Lin J, Miao W, Xuan J, Charles F, Chen M and Hatab SR (2018). Antimicrobial properties and mechanism of action of some plant extracts against food pathogens and spoilage microorganisms. *Front. Microbiol.*, **9**: 1639-1662.
- Hassen G, Belete G, Carrera KG, Iriowen RO, Araya H, Alemu T, Solomon, Bam DS, Debele T, Zouetr M and Jain N (2022). Clinical implications of herbal supplements in conventional medical practice: A US perspective. *Cureus*, 14(7): e26893.
- Hong LO, Ee Meng C, Mohamad CWS.R, Mohd Nasir, NF, Xiao Jian T, Chong You B, Ziezie Mohd Tarmizi E, Kim Yee L, Kok Yeow Y, Shing Fhan K, Kim Fey L, Kian Keong T, Mohd Roslan MR and Baharuddin, SA (2024). Frequency-dependent dielectric spectroscopic analysis on phytochemical and antioxidant activities in radix glycyrrhizae extract. *Heliyon*, **10**(17): e37077.
- Hu Y, Wang J, Yang Y, Li S, Wu, Q, Nepovimova E, Zhang X and Kuca K (2024). Revolutionizing soil heavy metal remediation: Cutting-edge innovations in plant disposal technology. *Sci. Total Environ.*, **918**: 170577 170592
- Jităreanu A, Trifan A, Vieriu M, Caba IC, Mârţu I and Agoroaei L (2023). Current trends in toxicity assessment of herbal medicines: A narrative review. *Processes*, **11**(1): 83-105
- Kandic I, Kragovic M, Petrovic J, Janackovic P, Gavrilovic M, Momcilovic M and Stojmenovic M (2023). Heavy metals content in selected medicinal plants produced and consumed in Serbia and their daily intake in herbal infusions. *Toxics*, **11**(2): 198 215
- Lahane UR (2016). Dielectric parameters of herbal medicines (2016). *IJSER*., 7(3): 1109-1112.
- Lima MBA and Yonamine M (2023). Counterfeit medicines: Relevance, consequences and strategies to combat the global crisis. *Braz. J. Pharm. Sci.*, **59**: e20402 e20418
- Lis-Cieplak A, Trześniowska K, Stolarczyk K and Stolarczyk EU (2024). Pyrrolizidine alkaloids as hazardous toxins in natural products: Current analytical methods and latest legal regulations. *Molecules*, **29**(14): 3269-3281
- Luo L, Wang B, Jiang J, Fitzgerald M, Huang Q, Yu Z, Li H, Zhang J, Wei J, Yang C, Zhang H, Dong L and Chen S. (2021). Heavy metal contaminations in herbal medicines: Determination, comprehensive risk assessments, and solutions. *Front. Pharmacol.*, 11:1-14
- Mssusa AK, Holst L, Kagashe G and Maregesi S (2023). Safety profile of herbal medicines submitted for

- marketing authorization in Tanzania: A cross-sectional retrospective study. J. Pharm. Policy Pract., 16(1): 241
- Meseret M, Ketema G and Kassahun H (2020). Health Risk Assessment and determination of some heavy metals in commonly consumed traditional herbal preparations in Northeast Ethiopia. *J. Chemistry*, **4**: 1-7
- Muyumba NW, Mutombo SC, Sheridan H, Nachtergael A and Duez P (2021). Quality control of herbal drugs and preparations: The methods of analysis, their relevance and applications. *Talanta Open*, **4**: 100070-100085
- Okaiyeto K and Oguntibeju OO (2021). African herbal medicines: Adverse effects and cytotoxic potentials with different therapeutic applications. *Int. J. Environ. Res. Public Health.*, **18**(11): 5988-6006
- Picot S, Beugnet F, Leboucher G and Bienvenu AL (2022). Drug resistant parasites and fungi from a one-health perspective: A global concern that needs transdisciplinary stewardship programs. *One health*, **14**: 100368-100382.
- Quan NV, Dang Xuan T and Teschke R (2020). Potential hepatotoxins found in herbal medicinal products: A systematic review. *Int. J. Mol. Sci.*, **21**(14): 5011.
- Schafer G and Lerner BL (2022). Physical and chemical characteristics and analysis of plant substrate. *Ornam. Hortic.*, **28**(2): 181-192
- Segatin N, Pajk Zontar T and Poklar Ulrih N (2020). Dielectric properties and dipole moment of edible oils subjected to 'Frying' thermal treatment. *Foods*, **9**(7): 900-917
- Uguru H, Essaghah AE, Akwenuke OM, Akpokodje OI, Rokayya S and Mahmoud H (2023). Environmental impact of wasteyard leachate pollution, it's health risks with some microbial and ecological implications. *J. Biobased Mater. Bioenergy.* **17**: 270-285
- Uguru H, Efeoghene EA., Issac AO, Sami R, Baakdah F and Pareek S (2024). Exposure to airborne pollutants in urban and rural areas: Levels of metals and microorganisms in PM10 and gaseous pollutants in ambient air. *Air Qual. Atmos. Hlth.*, **1**: 40-61
- USEPA (United States Environmental Protection Agency) (1986). Guidelines for the health risk assessment of chemical mixtures. *Fed. Regist.*, **51**: 34014-34025.
- Wang H, Chen Y, Wang L, Liu Q, Yang S and Wang C (2023). Advancing herbal medicine: Enhancing product quality and safety through robust quality control practices. *Front. Pharmacol.*, **14**: 1265178.
- World Health Organization (2008). Traditional Medicines. Geneva
- WHO (2024). Noncommunicable diseases, Geneva
- WHO (2007). WHO Guidelines for Assessing Quality of Herbal Medicines with Reference to Contaminants and Residues. Geneva
- Wu X, Wu P, Gu M and Xue J (2022). Trace heavy metals and harmful elements in roots and rhizomes of herbs: Screening level analysis and health risk assessment. *Chin. Herb. Med*, **14**(4): 622-629.

- Yang CM, Chien MY, Chao PC, Huang CM and Chen CH (2021). Investigation of toxic heavy metals content and estimation of potential health risks in Chinese herbal medicine. *J. Hazard. Mater.* **412**: 125142.
- Yao Z, Liang M and Zhu S (2024). Infectious factors in myocarditis: A comprehensive review of common and rare pathogens. *Egypt. Heart J.*, **76**(1): 1-20
- Yesuf A, Wondimeneh Y, Gebrecherkos T and Moges F (2016). Occurrence of potential bacterial pathogens and their antimicrobial susceptibility patterns isolated from herbal medicinal products sold in different markets of Gondar town, Northwest Ethiopia. *Int. J. Bacteriol*, doi.org/10.1155/2016/1959418.