

# Heavy Metal Infiltration and its Effect on the Liver Upon Intake of Marketed Herbal Supplements in Nigeria

Arit Okechukwu Nwogu<sup>1\*</sup>; E. O. Anyalebechi<sup>2</sup>; I. Elekima<sup>3</sup>

<sup>1,2,3</sup>Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Rivers State University, Port-Harcourt, P.M.B 5080, Nigeria

Corresponding Author: Arit Okechukwu Nwogu\*

Publication Date: 2026/06/03

**Abstract:** Herbal supplements are slowly becoming an important part of primary healthcare worldwide with a lot of persons coming down with hepatotoxic disease of the liver. This study aims to provide a significant correlation between increased concentrations of toxic heavy metals in marketed herbal supplement in Port Harcourt and liver cells and tissues. This study evaluated the hepatotoxic activity and heavy metal content of some marketed herbal supplements (Deep Seed, Omega Roots, and Jalin Herbal) in Port Harcourt which were analysed for heavy metals (Cadmium, Lead, Nickel, Arsenic and Mercury). Sixty-six (66) albino rats, weighing 150g were randomly selected and acclimatised, after which they were grouped into different treatment groups. All treatments were administered orally once daily for 28 days. After this administration period, blood and liver tissue samples were obtained and used for the analysis of liver function parameters (AST, ALT, ALP, bilirubin, total protein, and albumin) using spectrophotometric methods. Data was analysed using SPSS version 24, and results were expressed as mean  $\pm$  SD and analysed using one-way ANOVA and Tukey's post-hoc test at  $p < 0.05$ . Results revealed significantly elevated levels of cadmium, nickel, and lead exceeding permissible limits. Biochemical findings revealed significantly elevated levels of AST ( $26.33 \pm 1.53$ U/L) across all herbal supplement and elevated ALT ( $11.67 \pm 1.53$ U/L) in omega root indicating hepatocellular injury. This study reveals a hepatocellular injury highlights the hepatotoxic risks associated with the consumption of herbal supplements contaminated with heavy metals and encourages regulatory agencies to enforce stricter quality control and regulatory measures with regards to herbal supplement use and consumption.

**Keywords:** Heavy Metal, Infiltration, Liver, Marketed, Herbal Supplements.

**How to Cite:** Arit Okechukwu Nwogu; E. O. Anyalebechi; I. Elekima (2026) Heavy Metal Infiltration and its Effect on the Liver Upon Intake of Marketed Herbal Supplements in Nigeria. *International Journal of Innovative Science and Research Technology*, 11(5), 3018-3024. <https://doi.org/10.38124/ijisrt/26may1392>

## I. INTRODUCTION

The use of herbal supplements as an alternative to conventional pharmaceutical drugs has gained increasing global relevance over the past few decades. The World Health Organization (WHO) estimates that about 80% of the world's population relies on herbal supplements for their primary healthcare needs, particularly in developing countries where accessibility to conventional drugs is limited (WHO, 2013). This global trend is evident in countries like Nigeria, where herbal supplements are a key component of the primary healthcare delivery system, serving as the first line of treatment for a wide range of conditions, including infectious diseases, such as malaria and typhoid fever, some chronic conditions, and general body wellness.

However, the practice of herbal medicine in Nigeria is slowly undergoing a significant change. While freshly prepared traditional remedies are still common, there is currently a shift towards more conveniently packaged herbal supplements in the form of capsules, tablets, and syrups. However, despite their therapeutic benefits, these herbal supplements are at a higher risk of being contaminated with toxic substances, such as heavy metals like lead (Pb), cadmium (Cd), mercury (Hg), arsenic (As), and nickel (Ni). Several reports have been published on the harmful effects of herbal supplements and reports by Nwokediuko *et al.*, 2013 gives a statistic of 46% of Nigerians down with liver toxicity due to herbal usage.

These herbal supplements can be easily accessed through traditional healers, open markets, and unregulated vendors, which, in most cases, have not undergone the standard testing procedures often seen in conventional drugs. The World Health Organization estimates that for millions of people, traditional medicine is their main or only source of medical care. Its significance is further enhanced by culture and traditions, where knowledge of medicinal plants is passed down through generations.

Socio-economic factors such as poverty, limited access to modern healthcare, and the high cost of conventional drugs further drive their widespread use. However, the lack of standard production procedures and inadequate regulation has raised concerns regarding the safety of these herbal supplements. Urban centres like Port Harcourt are at greater risk because these products are being sold in markets without standard testing and adequate quality control analysis. Even at very low concentrations, these toxins accumulate and cause severe damage to cells and tissues. (Mazumder *et al.*, 2026)

Herbal medicines are made from herbs, plant extracts, and plant-based materials, and these can be contaminated during plant growth, harvesting, processing, transport, and storage, which makes the final herbal drug contaminated with these toxic metals. The lack of a strict regulatory framework and the inability to enforce these laws and guidelines make this issue of serious public health concern. Consumers of these contaminated herbal supplements are often not aware of the risks associated with these drugs. The primary routes of exposure are inhalation and ingestion via contaminated food and herbal supplements. Upon ingestion, these metals accumulate in the tissues and vital organs like the liver, bones, brain and kidneys, leading to chronic damage over time (Luo *et al.*, 2021).

Studies have shown that different plants have different capacities to absorb and retain specific metals, this is evident in regions like Port Harcourt, where there is heavy industrial activity, gas flaring, and oil exploration, which leads to pollution of the surrounding soil and water with heavy metals, accumulation of heavy metal is on the increase in these regions (Vinogradova *et al.*, 2023).

In some cases, heavy metals are intentionally included in the production of certain traditional remedies as it is claimed that small amounts of lead can calm stomach upsets, arsenic can be used in the treatment of cancer and mercury can be used to kill bacteria cells (Alharbi *et al.*, 2024). There are acceptable limits for levels of heavy metals in herbal supplements, which are set up by international bodies such as the World Health Organization (WHO), Food and Agriculture Organization (FAO), and national agencies such as the National Agency for Food and Drug Administration and Control (NAFDAC) (Mahmudi *et al.*, 2023). Mercury has a minimum level of 0.1ppm, Lead has a minimum level of 10 ppm, cadmium has a minimum level of 0.3 ppm, arsenic recommended minimum level is 10 ppm while Nickel's recommended minimum limit is 8ppm (WHO, 2006).

The liver is the major organ in the body responsible for the metabolism and detoxification of foreign substances. These metabolites can be excreted, and, in some cases, it can convert xenobiotics into highly toxic intermediates, which can often be a source of toxicity in the body (Phang-Lyn & Llerena, 2023). Hence heavy metals accumulate since they cannot be metabolized by the liver, overtime these metals overwhelm the liver's detoxification ability, resulting in severe damage to the liver cells and tissues.

## II. MATERIALS AND METHOD

### ➤ *Study Area*

The study was conducted in Port Harcourt metropolis, Rivers State, Nigeria from August 2025 to October 2025. Port Harcourt is the capital and biggest city of Rivers State and it is one of the states that make up the South-South geopolitical region in Nigeria.

### ➤ *Experimental Animal*

A total of sixty-six (66) randomly selected healthy albino rats of both male and female sexes, weighing around 150-250g, were used for toxicity study. They were housed in standard plastic cages with wire mesh tops, under controlled environmental conditions and allowed food and water ad libitum. The study lasted for 42days.

### ➤ *Herbal Supplements*

Three (3) commonly sold herbal supplements, namely Jalin Herbal Supplements, Omega Roots and Ginseng and Deep Seed Sperm Booster, were identified and obtained from major commercial markets in Port Harcourt.

### ➤ *Acute Toxicity Study*

A Pilot study was done to establish the minimum dose that caused 50% deaths (LD50) in the experimental animals. The LD50 of these herbal supplements administered intraperitoneally were carried out using 30 albino rats in two phases as described by Lorke, 1983.

### ➤ *Determination of Therapeutic Doses of Herbal Supplements:*

Following the results of the acute toxicity study, three doses were selected. low dose, medium dose and high dose. All doses were below the threshold that caused observable acute toxicity.

### ➤ *To Determine the Medium Dose of Jalin, Omega Root and Deep Seed,*

The therapeutic doses of the herbal supplements were extrapolated from human doses, and this was determined based on the method of Paget and Barnes (1964) conversion table. Therein, the daily dose of all three herbal supplements was determined using the OECD's guidelines (OECD, 2001) as reputed by Nwogu *et al.*, 2023.

### ➤ *Dose Calculation for Jalin Herbal*

Each Sachet of Jalin contains 5000mg, using the conversion formula, rat dose = 5000mg x 0.018 x 5 = 450mg. Since 450g can be given to a 1000kg rat, the dose for a 150g rat

$$\text{Dose} = (150\text{g} \times 450\text{mg}) / 1000\text{g} = 67.5\text{mg/kg}$$

According to the OECD guidelines for volume selection, 67.5mg/kg was dissolved in 1.5ml of distilled water which ensured accurate administration throughout the period of study. The doses for the low and high treatment groups were calculated from the medium dose.

➤ *Dose Calculation for Omega Roots and Ginseng*

Each capsule weighs 320mg, and 2 capsules are taken morning and evening. Therefore, the human dose per day = 320mg x 4 = 1280mg

For a rat weighing 170g, dose to be given = 1280mg x 0.018 x 5 = 115.2 mg

$$\text{Dose} = (170\text{g} \times 115.2\text{mg}) / 1000\text{g} = 19.58\text{mg/kg}$$

➤ *Dose Calculation for Deep Seed Sperm Booster*

Each capsule weighs 530mg, and 1 capsule is taken morning and evening.

Therefore, the human dose per day = 530mg x 2 = 1060mg for a man of weight 70kg = 1060mg x 0.018 x 5 = 95.4mg

Since 95.4mg can be given to a 1000kg rat, the dose for a 150g rat

$$\text{Dose} = (150\text{g} \times 95.4\text{mg}) / 1000\text{g} = 14.31\text{mg/kg}$$

The doses obtained are the medium doses for each herbal supplement, the low and high doses were calculated therein.

➤ *Experimental Design*

A total of twenty-seven (27) healthy albino rats, weighing 150g - 200g, were purchased from the animal house selected and grouped into 3 treatment groups (low, medium and high) with 3 animals per group (per herbal supplement), and the doses were administered as follows: Jalin Herbal low ( 33.75mg/0.75ml), Jalin Herbal medium (67.5mg/1.5ml), Jalin Herbal high (35mg/3ml), Deep Seed Sperm Booster low (7.15mg/0.75ml), Deep Seed Sperm Booster medium (14.31mg/1.5ml) and Deep Seed Sperm Booster high- (28.62mg/3ml)

Omega Roots and Ginseng low (8.64mg/0.75ml), Omega Roots and Ginseng medium (17.28mg/1.5ml), Omega Roots and Ginseng high (34.56mg/3ml) and a negative control group. Treatment was given for 28 days.

➤ *Sample Collection:*

At the end of the 28-day administration period, the animals were anaesthetised and 3ml of the blood samples were collected via cardiac puncture into lithium heparin sample bottles. The samples were then centrifuged at 3000 rpm for 10 minutes. The plasma was then carefully separated and transferred into another plain sample bottle and used for the laboratory analysis of liver function biomarkers.

➤ *Laboratory Analysis*

Analysis of aspartate amino transferase (AST), alanine amino transferase (ALT), Alkaline Phosphatase (ALP), total protein and albumin was estimated quantitatively by the colorimetric method of Reitman and Frankel, (1957). Heavy metal analysis was done using AAS and the histology of the liver was carried out.

➤ *Statistical Analysis*

The data generated from the analysis were expressed as Mean ± standard deviation, and the data were analysed using the Statistical Package for Social Sciences (SPSS) Version 24 tool. Comparison of the mean and standard deviation values was made for the various parameters for the various groups using one-way ANOVA and the Tukey test. The results were considered statistically significant at 95% confidence interval with a p-value less than 0.05 (P<0.05).

### III. RESULTS

The result of the heavy metal composition of the three herbal supplements as shown on table 1.0 reveals that Nickel and Cadmium showed the highest metal concentrations with significantly high levels in all three herbal supplements.

Table 1.: Heavy Metal Concentrations in Herbal Supplements

Supplement	Ni (mg/kg)	Cd (mg/kg)	Pb (mg/kg)	As (mg/kg)	Hg (mg/kg)
Jalin Herbal	43.30	2.70	-9.40	-2.70	-0.70
Omega Roots	19.50	1.70	-15.20	-1.50	-0.80
Deep Seed	40.80	9.10	2.60	-6.00	-0.40

Table 2 compares the AST, ALT, ALP, total Protein and Albumin parameters of control, Jalin Herbal (JH)-treated rats, Omega roots and Deep Seed herbal at high, medium, and low doses. The result reveals significant elevation of AST across the high and medium group, and this was significantly different from the control group at p= 0.000 and F = 44.33. ALT was not significantly elevated in all the groups but in omega root while ALP decreased significantly in all treatment group but not significantly. Total protein was not significantly increased in all groups; this was same for albumin. A significant difference was observed in total bilirubin levels (F = 4.13; p = 0.004) and conjugated bilirubin at F = 3.49; p = 0.010.

Table 2.: Comparison of Liver Function Parameters Among the Three Experimental Groups (Jalin Herbal, Omega Roots and Deep Seed)

Parameter	Control	JH High	JH Medium	JH Low	DS High	DS Medium	DS Low	OR High	OR Medium	OR Low	F-value	p-value	Remark
AST (U/L)	12.33 ± 2.08 <sup>a</sup>	15.33 ± 1.53 <sup>b</sup>	14.67 ± 1.16 <sup>b</sup>	6.00 ± 1.00 <sup>c</sup>	26.33 ± 1.53 <sup>d</sup>	13.67 ± 1.53 <sup>b</sup>	9.00 ± 1.00 <sup>c</sup>	14.33 ± 2.31 <sup>b</sup>	11.00 ± 0.00 <sup>a</sup>	10.00 ± 0.00 <sup>a</sup>	44.33	0.000	SS
ALT (U/L)	6.00 ± 3.46 <sup>a</sup>	7.00 ± 2.65 <sup>a</sup>	5.00 ± 1.00 <sup>a</sup>	6.67 ± 4.16 <sup>a</sup>	8.33 ± 1.53 <sup>a</sup>	11.67 ± 1.53 <sup>b</sup>	8.67 ± 4.04 <sup>a</sup>	7.67 ± 4.62 <sup>a</sup>	7.00 ± 0.00 <sup>a</sup>	15.00 ± 0.00 <sup>c</sup>	3.31	0.012	SS
ALP (U/L)	33.33 ± 4.16 <sup>a</sup>	26.00 ± 2.00 <sup>a</sup>	30.00 ± 5.57 <sup>a</sup>	25.33 ± 5.69 <sup>a</sup>	30.67 ± 7.10 <sup>a</sup>	30.33 ± 8.15 <sup>a</sup>	27.67 ± 8.96 <sup>a</sup>	23.33 ± 2.31 <sup>a</sup>	29.00 ± 0.00 <sup>a</sup>	33.00 ± 0.00 <sup>a</sup>	1.12	0.393	NS
TP (g/dL)	74.00 ± 1.73 <sup>a</sup>	74.00 ± 5.57 <sup>a</sup>	66.00 ± 6.00 <sup>a</sup>	70.33 ± 4.04 <sup>a</sup>	76.67 ± 5.13 <sup>a</sup>	72.67 ± 3.06 <sup>a</sup>	78.00 ± 4.58 <sup>a</sup>	75.33 ± 6.35 <sup>a</sup>	76.00 ± 0.00 <sup>a</sup>	71.00 ± 0.00 <sup>a</sup>	2.06	0.085	NS
ALB (g/dL)	37.00 ± 2.65 <sup>a</sup>	36.33 ± 4.16 <sup>a</sup>	30.67 ± 2.08 <sup>b</sup>	34.67 ± 2.52 <sup>a</sup>	39.33 ± 5.69 <sup>a</sup>	36.67 ± 2.08 <sup>a</sup>	39.33 ± 4.04 <sup>a</sup>	37.00 ± 3.46 <sup>a</sup>	36.00 ± 0.00 <sup>a</sup>	37.00 ± 0.00 <sup>a</sup>	1.81	0.128	NS
TB (µmol/L)	10.00 ± 2.00 <sup>a</sup>	7.67 ± 1.53 <sup>a</sup>	9.33 ± 1.53 <sup>a</sup>	7.67 ± 2.52 <sup>a</sup>	7.33 ± 2.52 <sup>a</sup>	5.33 ± 1.16 <sup>b</sup>	7.00 ± 2.00 <sup>a</sup>	8.00 ± 1.73 <sup>a</sup>	11.00 ± 0.00 <sup>a</sup>	12.00 ± 0.00 <sup>a</sup>	4.13	0.004	SS
CB (µmol/L)	4.67 ± 0.58 <sup>a</sup>	6.00 ± 1.00 <sup>a</sup>	4.33 ± 1.53 <sup>a</sup>	5.00 ± 1.73 <sup>a</sup>	4.00 ± 1.73 <sup>a</sup>	2.67 ± 0.58 <sup>b</sup>	3.33 ± 2.08 <sup>b</sup>	4.67 ± 0.58 <sup>a</sup>	6.00 ± 0.00 <sup>a</sup>	7.00 ± 0.00 <sup>a</sup>	3.49	0.010	SS

KEY: AST = Aspartate Aminotransferase; ALT = Alanine Aminotransferase; ALP = Alkaline Phosphatase; TP = Total Protein; ALB = Albumin; TB = Total Bilirubin; CB = Conjugated Bilirubin. SS = Statistically Significant (p < 0.05); NS = Not Significant (p > 0.05). Values are expressed as Mean ± Standard Deviation. Means with different superscripts (a, b, c, d) within a row differ significantly (Tukey HSD, p < 0.05), JH = Jalin Herbal, DS = Deep Seed, OR = Omega Root

#### IV. DISCUSSION

The study aims to investigate the presence of heavy metals in marketed herbal supplements in Port Harcourt upon administration and its hepatotoxicity on albino rats. The acute toxicity tests reveal the effect of these herbal supplements on the health of albino rats at different concentration. At a concentration of 5000mg/kg, noticeable signs of inactivity and sluggishness were seen on the rats. A lower dose in contrast does not produce any noticeable sign of toxicity. Although the absence of fatalities at high dose suggests that the overall survival of the rats was not compromised at this dosage. The heavy metal analysis reveals that Lead, Arsenic and Mercury concentrations were undetectable in the herbal supplements, though Deep Seed Sperm Booster has a significant concentration of about 2.60mg/kg which is quite lower than the permissible limit of lead (10mg/kg) whereas cadmium and nickel were higher than permissible limits in all the three herbal supplements with nickel seen to be in greater concentration in Jalin herbal (43.30mg/kg) and deep seed (40.80mg/kg) compared to the permissible standard (5mg/kg). Studies by Nwogu *et al.*, 2025 using fertility herbal supplements on male albino rats reveal higher levels of cadmium concentration compared to permissible limits. The use of herbal supplements is not regulated in Nigeria, and its safety is poorly understood. The populace is at the mercy of the use

of just any substance due to ignorance. Studies by Fawehinmi *et al.*, 2024 also reveals heavy metal contamination in herbal prepared product. Heavy metals are nonbiodegradable such that their accumulation in cells and tissues become overwhelming thus damaging cell membrane, inhibiting protein activity, inhibiting ATP synthesis which in turns brings about mitochondria oedema. There are diverse routes Nickel enters the body which include inhalation, ingestion and dermal absorption, and these routes is determined by its chemical form. Water soluble nickel is easily absorbed into the body especially via inhalation, Fat soluble nickel can cross cell membranes by diffusion or through calcium channels making it extremely toxic while insoluble nickel particles are soluble in body fluids so tend to accumulate in tissues. Highest concentrations are found in bone, lung, kidney, liver, brain and endocrine glands. Nickel accumulation can cause a variety of adverse effects on human health, such as contact dermatitis, lung fibrosis, cardiovascular, kidney and liver diseases. Just drinking water polluted by Nickel can cause accumulation of Nickel as seen by Apiamu *et al.*, 2024. Cadmium appears to have the capability to damage genetic material particularly chromosomes in mammalian cells since they generate reactive oxygen species, hence quite harmful. Several studies prove that cadmium affect several developmental stages, studies by Nwogu *et al.*, 2024 shows that cadmium affects reproductive development in man. The

liver is the core target since it is the primary site of metal accumulation and metabolic transformation. HDS (herbal and dietary supplement)-induced liver injury now accounts for 20% of cases of hepatotoxicity in the United States based on research data. (Navarro *et al.*, 2014, Fotana *et al.*, 2023) whereas in Nigeria, most cases are not documented. The rate of liver injury in our hospital is quite alarming with unknown aetiology. Our study reveals an hepatotoxic stress upon intake of Jalin Herbal (JH), Omega Roots, and Deep Seed extracts across three dosage levels. The findings show a clear and significant elevation of AST in the medium- and high-dose groups ( $F = 44.33$ ;  $p = 0.000$ ), suggesting dose-dependent stress. Elevated AST is a well-recognized marker of liver cell injury, and similar patterns have been reported in animals and humans exposed to hepatotoxic herbal or dietary supplements. Several studies reveal liver induced injury with sharp increases in AST and ALT due to mitochondrial and immune-mediated hepatotoxicity due to frequent usage of herbal product used for weight loss, fertility, bone improvement and several other illness. (Zhang *et al.*, 2022, Nwogu *et al.*, 2023).

From this study, ALT levels did not show significant elevation across all treatment groups. ALT is generally more liver-specific than AST, and its lack of significant change may indicate that hepatic injury remains mild at this stage probably due to shorter duration of administration such that as intake progresses, ALT levels may likely be elevated. Several literatures support this case of supplement-induced toxicity with disparity levels of disproportionately of higher AST relative to ALT, especially in early hepatocellular irritation or when extrahepatic factors contribute to AST elevation. (Navarro *et al.*, 2017, Zheng *et al.*, 2015)

ALP levels across all treatment groups were statistically not significant, suggesting that these herbal extracts do not induce cholestatic injury. ALP elevation is typically associated with biliary obstruction; therefore, its downward trend may indicate inhibitory or non-cholestatic hepatic responses. Similar studies reveal that herbal supplement tend to produce hepatocellular damage rather than cholestatic patterns of injury, this is consistent with the findings of Huang *et al.*, 2021

Total protein and albumin levels were not significantly different across all treated groups revealing the fact that albumin synthesis often remains normal in early or mild liver injury, due to its long half-life. Similar observations have been reported by Kalas *et al.*, 2021 and Paar *et al.*, 2021 in which chronic liver injury studies where early hepatocellular damage elevates only enzyme markers without significantly altering protein synthesis.

In contrast, total and conjugated bilirubin levels showed significant differences among treatment groups (total bilirubin:  $F = 4.13$ ,  $p = 0.004$ ; conjugated bilirubin:  $F = 3.49$ ,  $p = 0.010$ ). Elevation of bilirubin often reflects impaired bilirubin uptake, conjugation, or excretion as seen by Erlinger *et al.*, 2014 and Ramakrishnan *et al.*, 2022. Herbal supplement induced hepatotoxicity can impair bilirubin handling, particularly in cases of hepatocellular

injury or early cholestatic involvement. Green tea extract, anabolic steroids, and other hepatotoxic supplements have been associated with bilirubin disturbances accompanying elevated liver enzymes. Moreover, bilirubin abnormalities can be seen in cases of stable ALT levels as seen in a study by Šuk *et al.*, 2019 revealing hepatocellular injury models where early conjugation or transport mechanisms are impacted.

## V. CONCLUSION

The heavy metal and biochemical results derived from the three herbal supplement purchased in the open market in port Harcourt revealed an inflammatory and gradual loss of liver cells due to heavy metal toxicity with early damage on bilirubin metabolism rather. These findings align with documented patterns of herbal-induced liver injury reported in several literature.

## DECLARATION BY AUTHORS

- Ethical Approval: Approved
- Acknowledgement: Department of Pharmacology faculty of pharmaceutical sciences, university of Port Harcourt. Department of Chemistry, faculty of Sciences, Rivers State University, Port Harcourt
- Source of Funding: None
- Conflict of Interest: The authors declare no conflict of interest.

## REFERENCES

- [1]. Alharbi, S. F., Althbah, A. I., Mohammed, A. H., Alrasheed, M. A., Ismail, M., Allemalem, K. S. & Alkhalifah, A. (2024). Microbial and heavy metal contamination in herbal medicine: a prospective study in the central region of Saudi Arabia. *BMC Complementary Medicine and Therapies*, 24(1), 3-6.
- [2]. Apiamu, A., Awwioroko, O.J., Evuen, U.F. *et al.* Exposure to Nickel–Cadmium Contamination of Drinking Water Culminates in Liver Cirrhosis, Renal Azotemia, and Metabolic Stress in Rats. *Biol Trace Elem Res* 202, 1628–1643 (2024). <https://doi.org/10.1007/s12011-023-03777-y>
- [3]. Arit Okechukwu Nwogu, Davies G. Tamuno-Emine, Adline E. Ben-Chioma, Ebirien-Agana Samuel Bartimaeus. Evaluation of the hepatotoxic effect of some commonly sold male herbal fertility supplements in Port Harcourt on male albino rats. *Int J Health Sci Res.* 2023; 13(9):194-200. DOI: <https://doi.org/10.52403/ijhsr.20230928>
- [4]. Arit Okechukwu Nwogu, Onengiyeofori Ibama and Ebirien-Agana Samuel Bartimaeus. (2025). Evaluation of Heavy Metal Contamination and Antioxidant Efficacy of Polyherbal Male Fertility Supplements in Lead-Acetate-Induced Albino Rats. *Sokoto Journal of Medical Laboratory Science*; 10(2):139 – 146. <https://dx.doi.org/10.4314/sokjmls.v10i2.16>

- [5]. Erlinger S., Arias I. M., Dhumeaux D. Inherited disorders of bilirubin transport and conjugation: New insights into molecular mechanisms and consequences. *Gastroenterology*. 2014;146(7):1625–1638. doi: 10.1053/j.gastro.2014.01.046
- [6]. Fawehinmi, A. B., Hassan Lawal, E. U. Chimezie A. T. Ola-Adedoyin, and C.O Ahonsi. 2024. "Determination of Heavy Metal Contamination of Some Commercially Available Herbal Preparations in Nigeria". *Journal of Pharmaceutical Research International* 36 (8):46-54. <https://doi.org/10.9734/jpri/2024/v36i87557>
- [7]. Fontana, R.J.; Liou, I.; Reuben, A.; Suzuki, A.; Fiel, M.I.; Lee, W.; Navarro, V. AASLD practice guidance on drug, herbal, and dietary supplement-induced liver injury. *Hepatology* 2023, 77, 1036–1065. [Google Scholar] [CrossRef] [PubMed]
- [8]. Huang YS, Chang TT, Peng CY, Lo GH, Hsu CW, Hu CT, Huang YH. Herbal and dietary supplement-induced liver injury in Taiwan: comparison with conventional drug-induced liver injury. *Hepatol Int*. 2021 Dec;15(6):1456-1465. doi: 10.1007/s12072-021-10241-3. Epub 2021 Aug 11. PMID: 34382132.
- [9]. International Programme on Chemical Safety (IPCS) (1992). Cadmium. *Environmental Health Criteria* 134. World Health Organisation. Geneva. <http://www.inchem.org/documents/ehc/ehc/ehc134.htm>
- [10]. Kalas MA, Chavez L, Leon M, Taweesedt PT, Surani S. Abnormal liver enzymes: A review for clinicians. *World J Hepatol* 2021; 13(11): 1688-1698 [PMID: 34904038 DOI: 10.4254/wjh.v13.i11.1688]
- [11]. Lorke, D. (1983). A new approach to practical acute toxicity testing. *Archives of Toxicology*, 54 (4), 275-287.
- [12]. Luo, L., Wang, B., Jiang, J., Huang, Q., Yu, Z., Li, H., Zhang, J., Yang, C., Zhang, H., Dong, L. & Chen, S. (2021). Heavy metal contamination in herbal medicines: determination, comprehensive risk assessments, and solutions. *Frontiers in Pharmacology*, 11(595335), 7-16.
- [13]. Mahmudi, M., Annisa, M., Farida, M., Yusuf, M., Azhari, S. & Fachrunniza, Y. (2023). Assessing heavy metal contamination in traditional herbal medicine (JAMU) by atomic absorption spectrophotometry. *Grimsa Journal of Science Engineering and Technology*, 1(1), 35-39.
- [14]. Mazumser, S., Bhattacharya, D., Lahiri, D., Nag, M., Maity, S., Raja, C., Sharma, S., Dwivedi, SP., Rajeev, M. & Kadirov, I. (2026). Lead and cadmium induced toxicity under prolonged low-dose exposure: Food chain source, Molecular Mechanism Signaling cascade and health implications. *Journal of Applied Toxicology*, 10.1002/jat.70136. Epub ahead of print.
- [15]. Navarro VJ, Barnhart H, Bonkovsky HL, Davern T, Fontana RJ, Grant L, Reddy KR, Seeff LB, Serrano J, Sherker AH, Stolz A, Talwalkar J, Vega M, Vuppalanchi R. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. *Hepatology*. 2014 Oct;60(4):1399-408. doi: 10.1002/hep.27317. Epub 2014 Aug 25. PMID: 25043597; PMCID: PMC4293199.
- [16]. Navarro VJ. Supplement-Induced Liver Injury. *Gastroenterol Hepatol (N Y)*. 2017 Apr;13(4):245-247. PMID: 28546798; PMCID: PMC5441028.
- [17]. Nwogu, A. O., Sunday, O. E., Odinga, T.-B., Homa, C. P., Nyebuchi, J., Okwuchi, A. E., & Akuru, U. B. (2024). Evaluation of the ameliorative potential of some fertility herbal supplements on male fertility hormones and semen parameters of lead acetate-induced toxicity in albino rats. *Trends in Medical Research*, 19(1), 103–111.
- [18]. Nwokediuko S.C., Osuala P.C., Uduma U.V., Alaneme A.K., Onwuka C.C., Mesigo C. Pattern of liver disease admissions in a Nigerian tertiary hospital. *Niger. J. Clin. Pract.* 2013;16:339–342. doi: 10.4103/1119-3077.113458. [DOI] [PubMed] [Google Scholar]
- [19]. Paar, M., Fengler, V.H., Rosenberg, D.J. *et al.* Albumin in patients with liver disease shows an altered conformation. *Commun Biol* 4, 731 (2021). <https://doi.org/10.1038/s42003-021-02269-w>
- [20]. Phang-Lyn, S. & Llerena, V. A. (2023, August 14). Biochemistry, biotransformation. Retrieved from <https://www.ncbi.nlm.nih.gov/books/NBK544353/>
- [21]. Ramakrishnan, N., Bittar, K., & Jialal, I. Impaired bilirubin conjugation. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. Last updated: September 12, 2022. Available from: Europe PMC. Europe PMC link: <https://europepmc.org/books/n/statpearls/article-18282/>
- [22]. Reitman, S. & Frankel, S. (1957) A colorimetric method for determination of serum glutamate oxaloacetate and glutamic pyruvate transaminase. *American Journal of Clinical Pathology*, 28, 56-58.
- [23]. Šuk, J., Jašprová, J., Biedermann, D., Petrásková, L., Valentová, K., Křen, V., Muchová, L., & Vítek, L. Isolated silymarin flavonoids increase systemic and hepatic bilirubin concentrations and lower lipoperoxidation in mice. *Oxidative Medicine and Cellular Longevity*. 2019;2019:6026902. <https://doi.org/10.1155/2019/6026902> PMCID: PMC6390243 PMID: 30891115
- [24]. Vinogradova, N., Glukhov, A., Chaplygin, V., Kumar, P., Mandzhieva, S., Minkina, T. & Rajput, V. D. (2023). The content of heavy metals in medicinal plants in various environmental conditions: a review. *Horticulturae*, 9(2), 239.
- [25]. World Health Organization (WHO) (2006). Supplementary guidelines on good manufacturing practices for the manufacture of herbal medicine. Geneva.
- [26]. World Health Organization. (2013). *WHO traditional medicine strategy: 2014-2023*. Retrieved from <https://iris.who.int/handle/10665/92455>
- [27]. Zhang, L.; Niu, M.; Wei, A.-W.; Tang, J.-F.; Li, P.-Y.; Song, D.; Bai, Z.-F.; Liu, Y.-P.; Xiao, X.-H.; Wang, J.-B. Clinical correlation between serum cytokines and the susceptibility to *Polygonum multiflorum*-induced liver injury and an experimental study. *Food Funct*. 2022, 13, 825–833. [Google Scholar] [CrossRef] [PubMed]

- [28]. Zheng EX, Navarro VJ. Liver injury from herbal, dietary, and weight loss supplements: a review. *J Clin Transl Hepatol.* 2015;3(2):93–98. doi: 10.14218/JCTH.2015.00006. [DOI] [PMC free article] [PubMed] [Google Scholar]