African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

SAFETY EVALUATION OF MARKETED ANTI-DIABETIC HERBAL MEDICINES IN GHANA

Ayembilla, J. A.[1], Dzotefe, G. B.[2], Gordon, A.[3], Botchway, F. A.[4], Antwi, E. O.[5], Akotesie, G. A.[6], Dartey, D.[7], Abayateye, S.[8], and Osei-Adjei, G.[9]

[1,3,5,6,7,&8]Department of Science Laboratory Technology, Faculty of Applied Sciences, Accra Technical University, Accra, Ghana.

[2,4,&9]Department of Medical Laboratory Technology, Faculty of Applied Sciences, Accra Technical University, Accra, Ghana.

[6,7&8]Department of Pharmacology/Toxicology, Centre for Plant Medicine Research, Mampong-Akuapem, Ghana.

[1]jayembilla@atu.edu.gh

ABSTRACT

Purpose: Despite readily available over-the-counter drugs, most herbal products are not scientifically validated for their safety profile. The study aimed to evaluate the safety profile of marketed anti-diabetic herbal medicines in Ghana.

Design/Methodology/Approach: Four antidiabetic herbal medicines were purchased from herbal shops at Okaishie market in Accra. The mixtures were dried at 70^{o}C in a water bath to obtain powdered extracts. A single dose of 5000mg/kg body weight of each extract was administered to 10 female Sprague Dawley rats once for the acute toxicity studies, and signs of toxicity were observed. Histopathological examination of essential organs was conducted after sacrificing the rats. $P < 0.05$ was considered statistically significant after multiple comparison tests.

Findings: No mortality or adverse side effects were recorded. The rats ' normal growth, food, and water consumption were observed during the study period. No significant biochemical or haematological differences were observed, and no significant histological alterations were observed in the tissues studied.

Research Limitation: This study used a specific batch of screened antidiabetic herbal medicines, and the results cannot be generalised to all batches of these herbal medicines.

Practical Implication: It will help the Food and Drugs Authority, Ghana Standard Authority, Ministry of Health, and Ghana Health Service to intensify their surveillance of these antidiabetic herbal medicines.

Social Implication: Safety evaluation of herbal medicines is vital in protecting society from serious adverse health effects from harmful herbal products.

Originality/Value: The study employs laboratory animals to assess these herbal medicines for safety evaluations. Rats have almost the same physiology and anatomy as humans.

Keywords: *Acute toxicity. antidiabetic. herbal medicine. rat. subchronic toxicity*

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

INTRODUCTION

There is a global upsurge in the usage of herbal medicines, especially in developing countries. In Ghana, the widely patronised herbal products include antidiabetic, antimalarial, and antifungal agents, which may come in different forms such as capsules, mixtures, or creams (Tetteh et al., 2020). Many authors have attributed the patronage of herbal formulations to their readily availability and affordability, cultural acceptability, high cost of orthodox drugs, perceived safety, and effectiveness. (Mensah et al., 2019; Zaidi et al., 2022).

In some communities' people believe that allopathic drugs cannot cure some disease conditions, and some diseases have a spiritual origin and can only be cured by herbal medicines (Ameade et al., 2018; Aziato & Antwi, 2016; Mensah et al., 2019; Nketia et al., 2022). Almost every herbal practitioner in Ghana has one herbal formulation or other for the treatment of various diseases such as infectious diseases, immunological disorders, non-communicable diseases, reproductive issues, etc (Adinortey et al., 2019; Ameade et al., 2018; Aziato & Antwi, 2016; Nketia et al., 2022; Tetteh et al., 2020; Wilmot et al., 2017) probably due to their acceptability and the rich biodiversity of plants in Ghana. Despite their availability as over-the-counter drugs, most herbal products are not scientifically validated for their safety profile (Gyasi & Dwumoh, 2024). Aside from developing countries, herbal medicine is acclaimed in developed countries such as the United Kingdom, North America, Australia, China, etc, due to the introduction of complementary and alternative medicine (Ekor, 2014).

LITERATURE REVIEW

Plants, by nature, produce bioactive compounds that are toxic and distasteful to ward off predators from their habitats. For example, plants such as *Datura spp., Tropa belladonna. Aconitum spp* and *Digitalis spp* are known to be naturally poisonous (Nasri & Shirzad, 2013). Therefore, herbal preparations must be appropriately screened for their safety and efficacy before being allowed into the market.

Most orthodox drugs in modern-day medicine, such as artemisinin, aspirin, ephedrine, paclitaxel (Zhang et al., 2015), morphine, and digoxin (Zaidi et al., 2022) were extracted from plants, emphasising the importance of herbs in disease treatment and management. Diabetes threatens life globally and poses a severe economic burden to patients, households, communities, and the world at large.

Allopathic drugs have not proven to be effective in the treatment of diabetes since the drugs are unable to restore average glucose balance and have deleterious side effects (Balogun et al., 2016).

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

The current antidiabetic synthetic medications such as sulfonylureas, metformin, dipeptidyl peptidase four inhibitors, thiazolidinediones, and sodium-glucose cotransporter-2 all have severe side effects (Keezhipadathil, 2019). For example, biguanide and thiazolidinedione are nephrotoxic and can result in weight gain (He et al., 2019; Sukhikh et al., 2023). Incretin-based drugs cause gastrointestinal problems (He et al., 2019; Sukhikh et al., 2023). Thus, the quest to search for effective alternative drugs with minimal adverse side effects must be supported.

In most countries, plants known to have antidiabetic activity include *Azadirachta indica A. juss*, *Trigonella foenumgraecum L., Eugenia Jambolana Lam., Momordica charantia*, *Coccinia indica Wight & Arn*, *Allium sativum L.* (Mangesh et al., 2014; J. Sun et al., 2021; Tariq et al., 2020). These plants have been scientifically proven to contain sterols, flavonoids, saponins, tannins, and polyphenols for diabetes management (Kamau et al., 2017; Rizvi & Mishra, 2013). A study by Kavishankar et al. (2011) revealed that ethanolic and aqueous leaf extracts of *Aloe vera, Aegle marmelose, Ocimum sanctum,* and *Mangifera indica* increased superoxide dismutase (SOD) and glutathione levels in diabetic rats. Besides that, some active medicinal plant principles act as antidiabetic agents by stimulating insulin release, reducing insulin resistance, and enhancing pancreatic β-cells regeneration (Adinortey et al., 2019; Joseph & Jini, 2013). Some also have antioxidant and anti-inflammatory activity, which prevent diabetes-related hepatic and renal damage (Adinortey et al., 2019). Since herbal medicines are thought to be safe, they can be potentially toxic to vulnerable populations such as pregnant women and children.

The acceptability of herbal medicines in formal healthcare systems hinges on the scientific evidence of their safety and effectiveness, which is often lacking in most cases. The study aimed to evaluate the clinical safety of Ghana's four most patronised herbal medicines in treating diabetes.

METHODOLOGY

Antidiabetic herbal medicines

Four popular and over-the-counter antidiabetic herbal medicines, Bridelia tea, Dietes control, Osompa Dp, and Alive Diabelex mixtures, were purchased from herbal shops at the Okaishie market in the Greater Accra region of Ghana. The samples were transported to the Science Laboratory Technology of the Accra Technical University for analysis. The herbal plants used for the preparation of the herbal mixtures as presented on the labels include the following: Bridelia tea (*Bridelia ferruginea*), Dietes control (*Morinda lucida, Spathodea camolat*e), Osompa Dp (*Carica papaya, Vernonia amygdalina, Musah paradisiaca*), Alive Diabelex (*Vernonia amygdalina, Momordica charantia, Strophanthus hispidus*).

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

Study Setting

The purchased antidiabetic herbal medicines were dried into extracts at the Department of Science Laboratory Technology of Accra Technical University, Ghana. The toxicity studies were conducted at the Centre for Plant Medicine Research, Akwapim Mampong, Ghana, between June 2023 to November 2023.

Extract preparation

The extracts for the study were prepared by pouring 1L of each antidiabetic herbal mixture (Dietes control, Osompa Dp, and Alive Diabelex mixtures) into labelled stainless-steel plates and dried in a water bath at 70ºC. The dried extracts obtained were stored at -20ºC until analysis. The bridellia tea was prepared by soaking 100mg of pulverised *Bridelia ferruginea* in hot water for 10 minutes. The decoction was sieved with porcelain cloth and filtered with a No.1 Whiteman filter paper with a diameter of 110mm. The filtrate obtained was poured into a stainless-steel plate and dried on a water bath at 70ºC until dried. The dried extract was stored at -20ºC until analysis.

Ethical Approval

The Accra Technical University ethics committee approved the study, and the ARRIVE guidelines 2.0 for reporting animal studies was followed for this research. Food and water were regularly provided to the animals to ensure that we minimised animal suffering and use. Their bedding was cleaned every other day, and they could sleep in a dark, calm environment at night. They were monitored throughout the study period for any sign of stress.

Sample size calculation

To determine the total number of animals and the number of animals per group required for the study, the resource equation approach was used to calculate the sample size, and the data were analysed with analysis of variance (ANOVA) and t-test (Arifin & Zahiruddin, 2017; Charan & Kantharia, 2013).

$$n = \frac{DF}{k} + 1 \quad \text{.......(1)}$$

where n = number of rats per group, DF = degrees of freedom (range between 10 – 20), k = number of groups. For the thirteen (13) groups used for this study, a sample size of 2 - 3 rats per group was calculated. Thus, to increase the accuracy and power of the study, six (6) rats per group were used.

Experimental animals

A total of seventy-eight (78) healthy nonpregnant female Sprague Dawley rats weighing (150-180) g were purchased from the Animal Experimental Unit at the Centre for Plant Medicine Research (CPMR) because of their better sensitivity to toxicants than male rats based on OECD guidelines

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

test No. 423 and No. 408 (OECD, 2001, 2018). They were caged and allowed free access to water, and standard rodent pelleted chow was bought from Agricare Limited, Kumasi, Ghana, *ad libitum.* The rats were maintained at a humidity of 55 ± 10% and room temperature of 22 ± 2ºC with a 12h light/dark cycle (Ayembilla et al., 2023). They were allowed one week to acclimatise after grouping before the commencement of the study.

Acute toxicity study

The acute toxicity study was conducted following the guidelines of the Organization of Economic Cooperation and Development (OECD) guidelines 423 and 408 for testing chemicals (OECD, 2001, 2018). Thirty (30) Female (nonpregnant and nulliparous) Sprague Dawley rats were randomised into five groups (n=6) and acclimatised for one week before the study began. They were allowed access to water and feed *ad libitum*. The rats fasted overnight before treatment. The groups were orally gavaged with 5000mg/kg of the respective extracts and normal saline doses. After the oral gavage of the drugs, the rats were monitored and observed every hour for the next 12 hours and then at 24 hours, 48 hours until the 14th day for salivation, mortality, asthenia, diarrhoea, aggressiveness, hypoactivity, piloerection, aggressiveness, hyperventilation, loss of fur, grooming, lacrimation, tremor, and convulsions. The Irwin test procedure was followed for reporting signs of toxicity (Irwin, 1968).

Subchronic toxicity study

The experimental design was a randomised block design module. The animals were randomised into thirteen (13) blocks. The rats were orally administered 200mg/kg, 600mg/kg and 1200mg/kg bw.t dosage of the respective extract daily for six weeks (42 days). Any signs of toxicity were monitored daily throughout the study period. Abnormalities in food and water intake, appearance, and behavioural changes were recorded according to the primary observation procedure of the Irwin test (Irwin, 1968)The rats' weight was recorded at baseline, third, and sixth weeks. Blood and urine samples will be collected at baseline, third, and sixth weeks for analysis. The heart, liver, lungs, spleen, and kidney will be excised after the rats are sacrificed at the end of the experiment.

Blood sample collection and organ excision

Blood was sampled into ethylene diamine tetra acetate (EDTA) tubes and serum gel separator (SST) tubes at baseline, third, and sixth weeks. The EDTA samples were inverted about 5–10 times to allow for homogenous mixing of the anticoagulated with blood to prevent coagulation. The EDTA samples were used for haematological analysis. The SST samples were allowed to stand at room temperature for 30 minutes to allow the sample to clot. They were centrifuged at 5000rpm for 5min, and the serum was collected into Eppendorf tubes and stored at -20ºC for biochemical analysis.

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

Estimation of serum biochemical parameters

The effect of the extract on lipid profile was determined, and coronary risk was estimated by calculating the ratio of total cholesterol to high-density lipoprotein. The effect of the drugs on liver function was evaluated based on the total protein, albumin, alkaline phosphate, alanine aminotransferase, direct bilirubin, aspartate aminotransferase, total bilirubin, gamma-glutamyl transferase. Besides that, renal function following the extract consumption was assessed by measuring urea, sodium, creatinine, chloride, and potassium.

Estimation of haematological parameters

Fresh EDTA blood samples were analysed to determine haematological parameters such as Red Blood Cells (RBC), Haemoglobin (Hb), Haematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW), Platelet crit (PCT), White Blood Cells (WBC), Lymphocytes (Lymph#), Granulocytes (Gran#), Platelet Distribution Wide (PDW), Platelet (PLT), Mean Platelet Volume (MPV)

Measurement of body weight and relative organ weight

At baseline, third, and sixth weeks, the body weights of the rats were measured, and the percentage body weight gain was determined using equation 1:

$$\text{Percentage body weight gain} = \frac{\text{Weekly weight (g)} - \text{Baseline weight(g)}}{\text{Baseline Body Weight (g)}} \text{ x } 100\% \quad \text{.....(2)}$$

Additionally, the relative organ weight (ROW) of the examined organs was calculated using Equation 2:

$$\text{Relative Organ Weight} = \frac{\text{Absolute Organ Weight (g)}}{\text{Rat Body Weight (g)}} \text{ x } 100\% \quad \text{.....(3)}$$

Histological evaluation

The harvested organs: liver, heart, kidney, spleen, and lung tissues were cleaned with normal saline and preserved in 10% buffered formalin. Tissue sections were then processed into paraffin blocks using labelled tissue processing cassettes. They were treated with increasing concentrations of alcohol (70, 80, 90) % and absolute. The tissues were further cleared in three changes of xylene and embedded in paraffin wax. A thickness of 4µm of each tissue was cut and placed on microscope slides stained with haematoxylin and eosin and examined with an Olympus microscope for morphological and histological alterations (Abotsi et al., 2011; Ayembilla et al., 2023).

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

Data handling and statistical analysis

The data was analysed with GraphPad prism. The quantitative data were presented as mean ± SEM. A multiple comparison test was performed with ANOVA, followed by Turkey's post hoc test, which will be performed to compare for significant differences among the groups. Statistical significance was considered at $p < 0.05$.

RESULTS AND DISCUSSION

Acute toxicity assessment of the antidiabetic herbal medicines

In assessing the acute toxicity of the extracts, the rats were orally gavaged with extracts according to the doses described in Table 1. They were then monitored for any potential sign of toxicity for the first 12 hours, then 24 hours, 48 hours up to 14 days. At the end of the study, no rats died, and no sign of toxicity such as asthenia, salivation, piloerection, convulsion, lacrimation, diarrhoea, hyperventilation, grooming, tremor, or loss of fur was recorded. There was no loss of appetite, and the rats had normal food and water consumption. No behavioural changes were noted (Table 3). Thus, a single oral dose of 5000mg/kg bw.t of the studied antidiabetic herbal medicines was not fatal to rats over six weeks.

Body weight and relative organ weight

The body weights of the rats were recorded weekly. Over the six-week study period the body weights of the rats in both the control and treatment groups linearly increased (Figure 1). However, the body weights of the rats in all the treatment groups were statistically significantly higher than the control. In the case of the relative organ weight the liver of the Alive high (Alive_1200mg/kg) and Osompa high (Osompa_1200mk/kg) treatment groups were higher than the control. This was statistically significant at $P<0.05$. A similar trend was observed for the relative heart and lung body weight ratio. The alive high (Alive_1200kg) and Osompa high (Osompa_1200mg/kg) had their heart and lung body weight ratios statistically significantly different from the control group (Table 4).

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

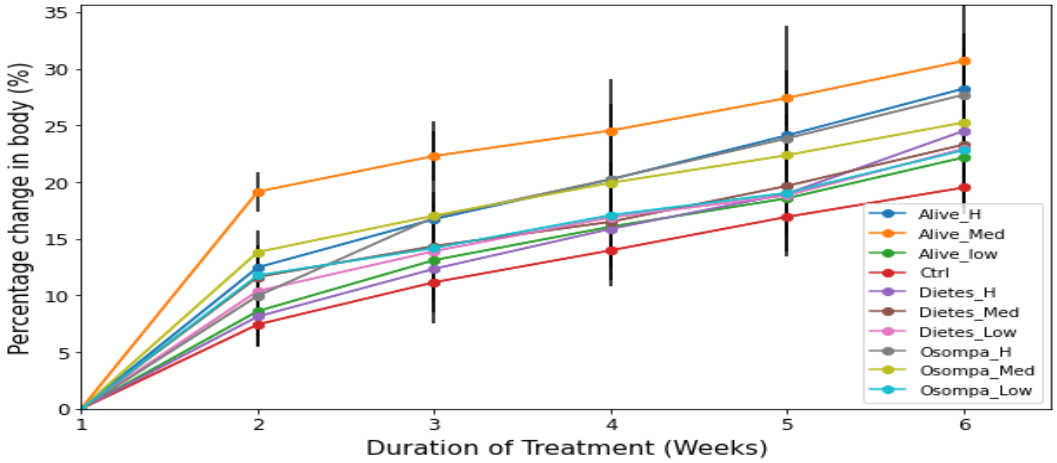

Figure 1: Percentage change in body weight after a subchronic oral administration of antidiabetic herbal medicine in Ghana to Sprague Dawley rats.
The legend represents the dosage of the drugs:
Alive_H- Alive 1200mg/kg, Alive_Med- Alive 600mg/kg, Alive_low- Alive 200mg/kg, Ctrl- control, Dietes_H- Dietes 1200mg/kg, Dietes_Med- Dietes 600mg/kg, Dietes_Low- Dietes 200mg/kg, Osompa_H- Osompa 1200mg/kg, Osompa_Med- 600mg/kg, Osompa_Low- 200mg/kg.

Table 4: Relative organ to body weight ratio

Treatment	Organs				
	Liver	Heart	Lungs	Kidney	Spleen
Control	2.12 ± 0.23^{ac}	0.49 ± 0.02^{ac}	0.26 ± 0.02^{ac}	0.52 ± 0.05	0.31 ± 0.04
Alive_200mg/kg	2.61 ± 0.23	0.32 ± 0.02	0.81 ± 0.12	0.58 ± 0.04	0.29 ± 0.05
Alive_600mg/kg	2.43 ± 0.10^{b}	0.28 ± 0.03^{ab}	0.55 ± 0.03^{b}	0.55 ± 0.03	0.22 ± 0.02
Alive_1200mg/kg	3.14 ± 0.23^{a}	0.40 ± 0.08	0.72 ± 0.11^{a}	0.63 ± 0.04^{a}	0.23 ± 0.02
Dietes_200mg/kg	2.60 ± 0.05	0.31 ± 0.02	0.71 ± 0.08	0.54 ± 0.02	0.23 ± 0.02
Dietes_600mg/kg	2.44 ± 0.17^{d}	0.32 ± 0.05^{d}	0.58 ± 0.07^{d}	0.46 ± 0.03^{ab}	0.29 ± 0.03
Dietes_1200mg/kg	2.78 ± 0.24	0.29 ± 0.02	0.76 ± 0.11	0.55 ± 0.04	0.35 ± 0.08
Osompa_200mg/kg	2.93 ± 0.12	0.32 ± 0.04	0.79 ± 0.24	0.54 ± 0.03	0.25 ± 0.02
Osompa_600mg/kg	2.67 ± 0.06	0.29 ± 0.02	0.58 ± 0.03	0.57 ± 0.01	0.26 ± 0.02
Osompa_1200mg/kg	3.31 ± 0.07^{bcd}	0.33 ± 0.01^{bcd}	0.82 ± 0.04^{bcd}	0.63 ± 0.03^{b}	0.29 ± 0.03

Data points represent mean ± SD and those with the same superscript are statistically significantly different at $p<0.05$.

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

Serum Biochemical Analysis

In the subchronic toxicity studies, the rats were orally administered daily with the antidiabetic herbal medicines extracts for six weeks. Serum biochemical analysis of the blood samples of the rats shows that except ALP and DBil for Osompa 600mg/kg bw.t and Osompa 1200mg/kg, which were statistically significantly different from the control group, all the other liver parameters were not statistically different from the control (Table 6).

Haematological analysis

The control group haemoglobin was statistically significantly different from Alive 200mg/kg, Alive 1200mg/kg, and Osompa 200mg/kg bw.t treatment group. Except for Dietes 200mg/kg and Osompa 1200mg/kg the RBCs were not statistically significantly different between the control and treatment groups. The MCH of Alive 200mg/kg, Dietes 200mg/kg, Dietes 1200mg/kg, Osompa 200mg/kg, and Osompa 600mg/kg were statistically significantly different from the control. All the other treatment groups of MCH were not statistically different from the control group.

Table 5: Effect of antidiabetic herbal medicines on differential, full blood count

Parameter	Control	Alive_200mg/kg	Alive_600mg/kg	Alive_1200mg/kg	Dietes_200mg/kg	Dietes_600mg/kg	Dietes_1200mg/kg	Osompa_200mg/kg	Osompa_600mg/kg	Osompa_11200mg/kg	P-Value
WBC	9.8 7 ± 1.6 1	10.62 ± 0.68	9.10 ± 1.81	9.38 ± 1.66	9.39 ± 1.14	9.48 ± 1.08	7.72 ± 0.42	11.47 ± 1.05	10.80 ± 0.97	11.89 ± 2.03	0.5 72
LYM	5.8 2 ± 0.9 1	4.98 ± 0.67	4.94 ± 1.20	4.63 ± 0.64	5.50 ± 0.88	5.02 ± 0.65	4.25 ± 0.08	5.14 ± 0.56	5.46 ± 0.36	7.67 ± 1.34	> 0.05
MID	1.0 0 ± 0.2 7	0.82 ± 0.06	0.90 ± 0.20	0.89 ± 0.15	0.80 ± 0.35	0.93 ± 0.19	0.71 ± 0.11	1.17 ± 0.24	0.81 ± 0.11	1.01 ± 0.21	> 0.05
GRA	3.0 6 ±	4.83 ± 1.01	3.27 ± 0.43	3.86 ± 0.94	3.10 ± 0.14	3.53 ± 0.39	2.77 ± 0.48	5.16 ± 0.31	4.54 ± 0.55	3.22 ± 0.66	> 0.

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

	0.48										05
LYM%	59.03 ± 1.82	47.65 ± 7.55[a]	52.83 ± 2.61	50.45 ± 3.60	58.23 ± 1.90	52.75 ± 1.12	55.58 ± 3.43	44.65 ± 1.00[b]	50.93 ± 1.77	64.38 ± 1.41[ab]	< 0.05
MID%	9.68 ± 1.29	7.70 ± 0.55	9.73 ± 0.83	9.68 ± 0.95	7.68 ± 2.27	9.78 ± 1.82	9.25 ± 1.63	9.85 ± 1.19	7.43 ± 0.60	9.10 ± 2.46	> 0.05
GRA%	31.30 ± 1.40	44.63 ± 7.55[a]	37.43 ± 3.00	39.85 ± 3.18	34.08 ± 3.40	37.50 ± 2.60	35.18 ± 4.59	45.50 ± 2.05[b]	41.68 ± 1.58	26.53 ± 1.36[ab]	< 0.05
RBC	7.97 ± 0.21[d]	8.35 ± 0.14[b]	8.13 ± 0.19[c]	8.58 ± 0.19[a]	8.47 ± 0.10[e]	7.94 ± 0.33[cf]	6.70 ± 0.31[abd efgh]	8.16 ± 0.16[g]	8.39 ± 0.22[h]	7.59 ± 0.15	< 0.01
HGB	15.05 ± 0.20[ac ehijk l]	15.68 ± 0.34[cd]	15.60 ± 0.19[ef]	15.98 ± 0.27[ab]	16.00 ± 0.27[in]	15.10 ± 0.29[jo]	13.98 ± 0.39[hm]	15.35 ± 0.12[bdf mnopq]	15.43 ± 0.14[lq]	15.25 ± 0.12[kp]	< 0.01
HCT	42.82 ± 0.79	44.59 ± 1.00[a]	44.25 ± 0.51	46.29 ± 0.85	46.45 ± 0.92	43.75 ± 0.98	39.56 ± 0.92[abc]	43.50 ± 0.39[b]	44.12 ± 0.53[c]	42.76 ± 0.75	< 0.05
MCV	54.00 ± 1.23	53.25 ± 1.03[a]	54.25 ± 0.75	54.00 ± 0.41	55.00 ± 0.71	55.50 ± 1.56	59.50 ± 2.84[abc]	53.00 ± 0.82[b]	52.75 ± 0.75[c]	56.50 ±0.29	< 0.05

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

MCH	18.90 ± 0.42^{ac}	18.78 ± 0.26^{b}	19.28 ± 0.33	18.63 ± 0.12^{a}	18.90 ± 0.17^{d}	19.08 ± 0.57	21.00 ± 0.87$^{bcd ef}$	18.88 ± 0.37^{e}	18.40 ± 0.38^{f}	20.10 ± 0.25	< 0.05
MCHC	35.13 ± 0.25	35.10 ± 0.41	35.28 ± 0.32	34.53 ± 0.17	34.45 ± 0.45	34.50 ± 0.45	35.33 ± 0.43	35.35 ± 0.38	34.95 ± 0.37	35.70 ± 0.20	> 0.05
MPV	6.20 ± 0.11	5.98 ± 0.06	6.18 ± 0.14	6.48 ± 0.35	6.53 ± 0.14	6.40 ± 0.09	5.98 ± 0.09	6.18 ± 0.08	6.33 ± 0.13	6.43 ± 0.23	> 0.05
PLT	579.00 ± 90.81	730.50 ± 81.68	772.75 ± 82.31	771.50 ± 113.88	736.75 ± 53.32	659.25 ± 46.24	898.00 ± 96.49	664.50 ± 43.83	709.50 ± 74.50	593.75 ± 72.98	> 0.05
PCT	0.36 ± 0.06	0.44 ± 0.05	0.48 ± 0.05	0.49 ± 0.06	0.48 ± 0.04	0.43 ± 0.03	0.54 ± 0.05	0.41 ± 0.03	0.45 ± 0.04	0.38 ± 0.04	> 0.05
RDWc%	21.15 ± 0.37^{a}	19.43 ± 0.21	18.90 ± 0.12	19.10 ± 0.31	18.90 ± 0.25	19.43 ± 0.73	19.95 ± 1.04	20.45 ± 1.23^{b}	18.58 ± 0.50	17.20 ± 0.27^{ab}	< 0.05

Data points represent mean ± standard error of the mean. Means with superscripts alphabets are significant and those with the same alphabet are significant different from each other.

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

Table 6: Comparative assessment of the effect of antidiabetic herbal medicines on liver function in Sprague Dawley rats

Parameter	Ctrl	Alive_Low	Alive_Med	Alive_H	Diets_Low	Diets_Med	Diets_H	Osompa_Low	Osompa_Med	Osompa_H	P-value
ALT	67.78 ± 7.21	89.05 ± 5.72	85.15 ± 3.93	58.50 ± 16.99	75.33 ± 9.75	101.80 ± 19.47	61.13 ±11.46	65.58 ± 11.81	62.55 ± 8.31	60.27 ± 8.04	>0.05
AST	244.58 ± 9.17	314.15 ± 21.09	306.85 ± 16.74	274.25 ± 13.06	245.20 ± 37.60	315.30 ± 27.79	292.08 ± 12.25	264.70 ± 17.70	284.83 ± 16.00	195.93 ± 100.49	>0.05
ALP	406.30 ± 10.33[a]	342.13 ± 58.52	218.33 ± 16.61	299.75 ± 28.01	329.98 ± 28.30	322.68 ± 62.22	229.85 ± 58.50	255.10 ± 77.76	142.45 ± 48.31[a]	217.30 ± 41.47	<0.05
GGT	1.60 ± 0.60	3.78 ± 1.23	3.53 ± 1.42	0.83 ± 0.28	1.88 ± 0.68	3.35 ±1.13	1.93 ± 0.58	2.40 ± 1.57	1.18 ± 0.32	1.83 ±1.00	>0.05
TP	86.40 ± 1.43	83.18 ± 3.24	86.25 ± 2.30	87.83 ± 1.19	87.93 ± 3.35	87.88 ± 0.93	90.30 ± 4.09	83.90 ± 3.46	86.98 ± 2.65	92.13 ± 2.44	>0.05
ALB	37.28 ± 0.44	41.25 ± 3.67	37.35 ± 1.40	34.85 ± 2.99	38.28 ± 0.86	38.08 ± 2.26	39.63 ± 2.37	36.08 ± 2.91	40.40 ± 1.56	45.43 ± 7.04	>0.05

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

TBil	3.53 ± 0.39	4.24 ± 0.62	4.23 ± 0.22	2.94 ± 0.23	2.54 ± 0.05	3.42 ± 0.34	3.86 ± 0.41	12.01 ± 9.73	2.77 ± 0.32	3.40 ± 0.37	>0.05
DBil	1.46 ± 0.13	2.30 ± 0.29[a] [b]	1.61 ± 0.24	1.39 ± 0.05	1.33 ± 0.09	1.66 ± 0.15	1.36 ± 0.26	1.40 ± 0.24	1.20 ± 0.32[b]	1.25 ± 0.20[a]	<0.05
AST/ ALT	3.73 ± 0.36	3.58 ± 0.34	3.53 ± 0.03	3.43 ± 0.33	3.33 ± 0.37	3.58 ± 0.91	5.33 ± 1.00	4.53 ± 0.95	4.78 ± 0.69	2.90 ± 1.47	>0.05

Each data point represents mean ± standard error of the mean. The superscripts represent significant differences and means with the same superscript are significantly different from each other.

ALT- Alanine aminotransferase, AST-Aspartate aminotransferase, ALP-Alkaline phosphatase, GGT-gamma glutamyl transferase, TP-Total protein, ALB-Albumin, TBil-Total Bilirubin, Dbil- direct bilirubin, AST/ALT- AST/ALT ratio.

3.5 Histopathological Examination

Figure 2 represents the histopathological evaluation of the cardiac tissues stained with H &E. Where A1-A3, B1-B3, and C1-C3 indicate the low (200mg/Kg bw.t), medium (600mg/Kg bw.t), and high (1200mg/Kg bw.t) respectively. A, B, C, and D represent the Dietes, Alive, Osompa, and the Control group, respectively. After the treatment duration, the D (normal group) presents normal cardiac morphology with well-arranged myocardial fibres and little or no exposure to the endomysium. Also, no pathology was realised in the cardiomyocytes, with minimal occurrence of the fibrocytes. The cardiomyocytes present moderate striations with no infiltration or inflammatory cells in the tissue.

Not many morphological discrepancies were observed in the intra-group assessment of diabetes treatment at the low dose. The morphology of the cardiomyocytes and tissue presented similar observations as realised in the control group, though there was an insignificant exposure of the cardiac endomysium (star, A1).

Comparatively, the presentations in the low dose of Alive and Osompa present similar observations as seen in the 200mg/kg bw.t dietes. For the medium dosage, it was realised that the cardiac morphology was maintained after treatment of all treatment groups except for some exposures in the endomysium seen in all the treatment groups. Comparative analysis of the high dosage to the

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

standard group as well as the low dose indicates some abnormalities in the cardiac tissues of all treatment groups, with many abnormalities seen in the dietes and alive as compared to osompa group. From Figures 2 A3 to C3, it could be observed that there were a lot of disarranged cardiac myofibres with more significant exposure to the endomysium. Also, lots of fibrocytes could be seen, suggesting some form of cardiac fibrous with some level of myocardial death (loss of cardiocyte nuclei). The study suggests histological damage to cardiac tissue at higher doses than the medium and lower doses.

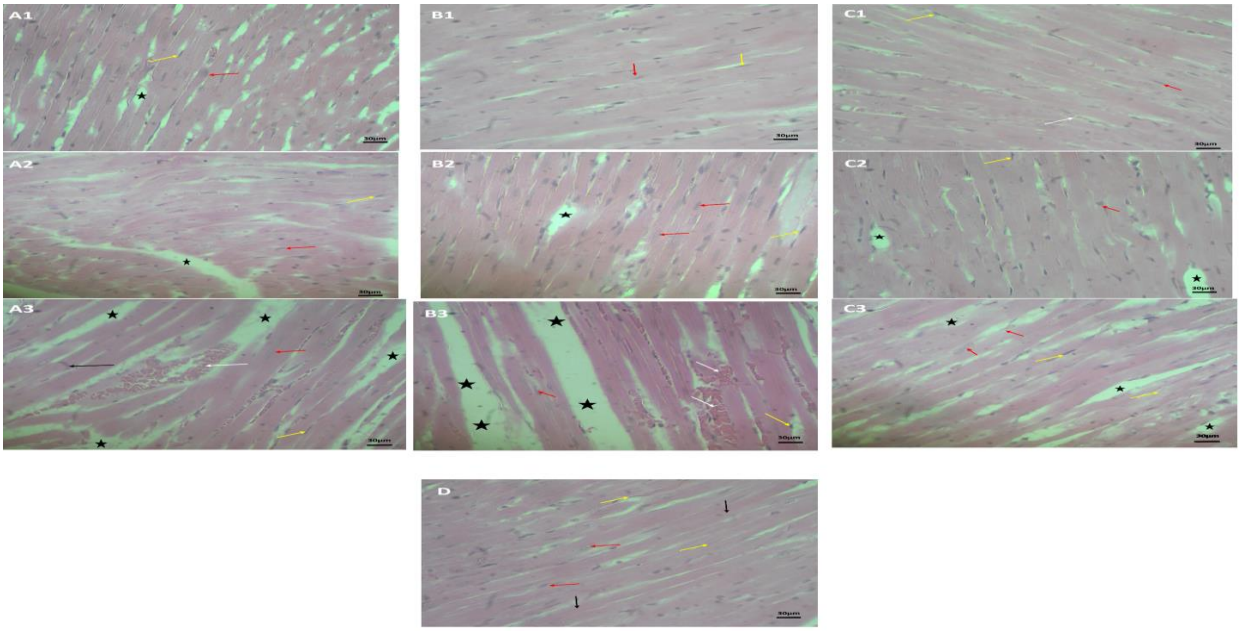

Figure 2: Histological appearance of the cardiac at the end of the experiment (Haematoxylin & Eosin) at 400 magnifications.
A, B, C, & D represent photomicrographs of Dietes, Alive, and Osompa anti-diabetic herbal medicines of heart tissue with different dosages 1(200 mg/Kg bw.t), 2(600mg/Kg bw.t) and 3(1200mg/Kg bw.t) and the control group. The white arrow indicates infiltration of red cells, the Black arrow indicates intercalated disk, the yellow arrow for fibrocytes, the red arrow for cardiomyocytes, and the star for endomysium exposure.

Figure 3, A to D, represents the H and E showing of the liver. The experiment demonstrates the effect of different doses of the drugs dietes (A1-A3), alive (B1-B3), and osompa (C1-C3). The

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

normal liver morphology can be seen in D with well-preserved hepatocytes and the central vein. The hepatic sinusoids are well preserved with no hepatic vacuolations. Also, there was an extensive presentation of pyknotic hepatocytes. However, in the drug-treated group, it was realised that the damage to the hepatic organ was dose-dependent, with the higher dose presenting a lot of vacuolations and infiltration of blood cells in the parenchyma of the liver. It was also observed that apoptosis could be observed with some chromatin condensations in the hepatocytes. Nonetheless, the damages were moderate to the wild in the medium dosage (600mg/kg) and low dosage (300mg/kg), respectively. This, therefore, suggests hepatic damage in a dose-dependent manner.

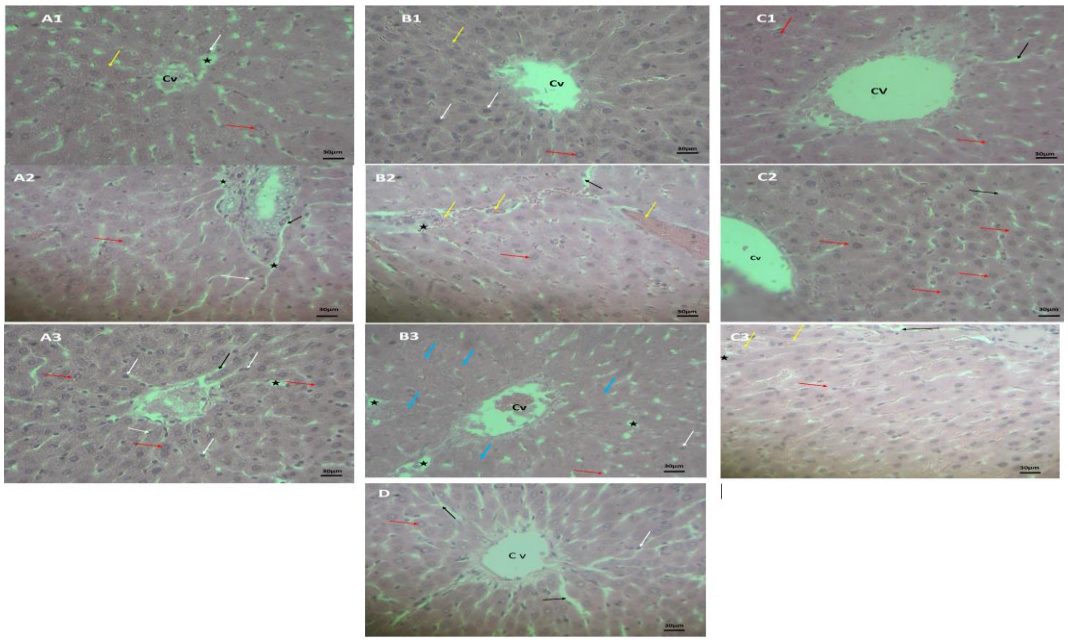

Figure 3: Histological appearance of the Liver at the end of the experiment (Haematoxylin & Eosin) at 400 magnifications.

A, B, C, & D represent photomicrographs of Dietes, Alive, and Osompa anti-diabetic herbal medicines with different dosages 1(200 mg/Kg bw.t), 2(600mg/Kg bw.t) and 3(1200mg/Kg bw.t and control group). The white arrow indicates pyknotic hepatocytes; the Black arrow indicates sinusoids; the yellow arrow infiltration of red cells; the red arrow for hepatocytes; the Black star indicates vacuolations; and the blue arrow for degenerated or dead hepatocytes; and the Cv for Central vein.

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

DISCUSSION

Herbal medicines are heavily patronised in Ghana, and following the approval by the Ministry of Health, herbal medicines are prescribed even in hospitals. Because of the immense biodiversity of plants in Ghana, herbal medicines are relatively cheaper than orthodox drugs. However, the challenge is that most of these herbal medicines are not preclinically tried before their sale in the market, especially over-the-counter ones. It thus poses a serious health risk to the consumers. This study sought to evaluate the acute and subchronic toxicity of a sample of antidiabetic herbal medicines in Ghana.

The main findings from the study are that (i) a single dose of 5000mg/kg bw.t extract of the studied antidiabetic herbal medicines was not fatal to the Sprague Dawley rats over 14 days. (ii) the rats exponentially gained body weight higher than the controls over six weeks. The relative to-body weight ratio was not statistically different between the control and treatment groups (ii) no mortality or any observable sign of toxicity was recorded in the study (iii) no severe alteration in lipid metabolism, renal or liver function was observed.

Mortality of animal models or cell lines in clinical trials is a significant criterion for indicating toxicity of a test substance, agrees with the finding of Baldrick et al. (2020). They are used as the first line of tests to prove the safety profile of test substances before human clinical trials can start. This study did not record any mortality during the acute or subchronic phase, suggesting that the tested antidiabetic herbal medicines were safe over the study duration in Sprague Dawley rats. Together with no mortality, the non-observable behavioural or physical signs of toxicity were recorded to demonstrate that these antidiabetic herbal medicines are tolerable and have no fatal, behavioural, or neuropsychological adverse effects in Sprague Dawley rats (Aliyu et al., 2020). The rats exhibited normal feeding behaviour, water consumption, and exponential growth throughout the study, suggesting good metabolic health and general well-being. The normal feeding behaviour suggests that the studied herbal antidiabetic herbal medicines did not cause gastrointestinal distress or anorexia to the rats. Similarly, typical water consumption indicates that drug-induced dehydration, polydipsia, or renal dysfunction did not occur. The renal function test data confirms this notion. The exponential growth of the rats, which is their normal characteristic, suggests that the herbal medicines did not disrupt metabolic activities related to growth and energy. Relative organ-to-body weight ratio indicates organ-specific toxicity and agrees with the findings of Panossian et al. (2021). A non-significant increase or decrease in the relative organ-to-body weight ratio of the rats indicates no significant adverse effect such as inflammation, atrophy, or hypertrophy was induced by the studied herbal medicines in the kidney, lungs, liver, heart, and

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

spleen. Our findings contrast with (Tetteh et al., 2020) who reported that Ghanaian herbal medicines are safe.

After six weeks, the histological examination of the organ sections revealed alterations in the heart, liver, and kidney architecture in the 1200mg/kg bw.t treatment groups. This was observed in a dose-dependent manner as concentration increased. This means that prolonged consumption of these herbal medicines might have some long-term complications.

CONCLUSION

The study revealed that consuming high dosages of these antidiabetic herbal medicines over a prolonged period might be toxic to specific organs such as the liver, heart, and kidney. It implies that the FDA should conduct regular surveillance of herbal medicines for their safety.
It will help the Food and Drugs Authority, Ghana Standard Authority, Ministry of Health, and Ghana Health Service to intensify their surveillance of these antidiabetic herbal medicines.

Safety evaluation of herbal medicines is vital in protecting society from serious adverse health effects from harmful herbal products.

The study employs laboratory animals to assess these herbal medicines for safety evaluations. Rats have almost the same physiology and anatomy as humans.

Limitations of the study

This study was conducted using a specific batch of antidiabetic herbal medicines. The observed results cannot be generalised to all batches of Ghana's antidiabetic or herbal medicines. The Resource Equation, as used in calculating the sample size for this study, is robust enough and does not consider effect size in the calculation. Assessment of other essential organ functions, such as lung function, clotting profile deficiency, histology of the spleen, lungs, etc, were not conducted in this study. Further evaluation of the products should be conducted to unravel the comprehensive safety profile of these antidiabetic herbal medicines.

Acknowledgement

We acknowledge the Department of Science Laboratory Technology of Accra Technology technicians for their unwavering support of our research.

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

REFERENCES

Abotsi, W. K. M. , Ainooson, G. K. , & Gyasi, E. B. ,. (2011). Acute and subacute toxicity studies of the ethanolic extract of the aerial parts of Hilleria Latifolia (Lam.) H. Walt. (Phytolaccaceae) in rodents. *West African Journal of Pharmacy*, *22*(1), 27–35. https://www.researchgate.net/publication/215794441

Adinortey, M. B., Agbeko, R., Boison, D., Ekloh, W., Kuatsienu, L. E., Biney, E. E., Affum, O. O., Kwarteng, J. , Nyarko, A. K. , & Carvalho, J. C. T. (2019). Phytomedicines used for diabetes mellitus in Ghana: A systematic search and review of preclinical and clinical evidence. *Evidence-Based Complementary and Alternative Medicine*, *2019*. https://doi.org/10.1155/2019/6021209

Adinortey, M. B., Agbeko, R., Boison, D., Ekloh, W., Kuatsienu, L. E., Biney, E. E., Affum, O. O., Kwarteng, J., Nyarko, A. K., & Carvalho, J. C. T. (2019). Phytomedicines used for diabetes mellitus in Ghana: A systematic search and review of preclinical and clinical evidence. *Evidence-Based Complementary and Alternative Medicine*, *2019*. https://doi.org/10.1155/2019/6021209

Aliyu, A., Shaari, M. R., Ahmad Sayuti, N. S., Reduan, M. F. H., Sithambaram, S., Noordin, M. M., ... & Hamzah, H. (2020). Subacute oral administration of Clinacanthus nutans ethanolic leaf extract induced liver and kidney toxicities in ICR mice. Molecules, 25(11), 2631.

Ameade, E. P. k., Baba, M. M., Iddrisu, N. U., Musah, A. A., Gbedema, S. y., & Gbedema, S. Y. (2018). Herbal pharmacovigilance: Are Ghanaian herbal medicine practitioners equipped enough to assist in monitoring the safety of herbal medicines? -A survey in Tamale. *Ghana. Chronic Complement Altern Integra Med: CCAIM-101. 1*, 101.

Ameade, E. P. K., Ibrahim, M., Ibrahim, H. S., Habib, R. H., & Gbedema, S. Y. (2018). Concurrent Use of Herbal and Orthodox Medicines among Residents of Tamale, Northern Ghana, Who Patronize Hospitals and Herbal Clinics. *Evidence-Based Complementary and Alternative Medicine*, *2018*. https://doi.org/10.1155/2018/1289125

Ameade, E. P. K., Zakaria, A. P., Abubakar, L., & Sandow, R. (2018). Herbal medicine usage before and during pregnancy – a study in Northern Ghana. *International Journal of Complementary & Alternative Medicine*, *11*(4). https://doi.org/10.15406/ijcam.2018.11.00405

Arifin, W. N. , & Zahiruddin, W. M. (2017). Sample size calculation in animal studies using resource equation approach. *Malaysian Journal of Medical Sciences*, *24*(5), 101–105. https://doi.org/10.21315/mjms2017.24.5.11

Ayembilla, J. A., Khalid, A. R., Abubakari, S. B., Adams, A. R., Botchway, F. A., Antwi, S., Otu, P. N. Y., Appiah, M., Osei-adjei, G., Kottoh, K. O., Ahiabenu-williams, P., & Quasie, O. (2023). Acute and subchronic toxicity assessment of conventional Soxhlet Cymbopogon

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

citratus leaves extracts in Sprague Dawley rats. *Journal of Toxicology*, *2023*. https://doi.org/https://doi.org/10.1155/2023/8575741

Aziato, L., & Antwi, H. O. (2016). Facilitators and barriers of herbal medicine use in Accra, Ghana: An inductive exploratory study. *BMC Complementary and Alternative Medicine*, *16*(1). https://doi.org/10.1186/s12906-016-1124-y

Baldrick, P., Cosenza, M. E., Alapatt, T., Bolon, B., Rhodes, M., & Waterson, I. (2020). Toxicology paradise: sorting out adverse and non-adverse findings in animal toxicity studies. International Journal of Toxicology, 39(5), 365-378.

Balogun, F. O., Tshabalala, N. T., & Ashafa, A. O. T. (2016). Antidiabetic medicinal plants used by the Basotho tribe of eastern free state: A review. *Journal of Diabetes Research*, *2016*. https://doi.org/10.1155/2016/4602820

Charan, J. , & Kantharia, N. (2013). How to calculate sample size in animal studies? *Journal of Pharmacology and Pharmacotherapeutics*, *4*(4), 303–306. https://doi.org/10.4103/0976-500X.119726

Ekor, M. (2014). The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. In *Frontiers in Neurology: Vol. 4 JAN*. https://doi.org/10.3389/fphar.2013.00177

Gyasi, W. K., & Dwumoh, J. S. (2024). Reading Difficulty of Consumer Medicine Information (CMI) Leaflets for Five Chronic Ailments in Ghana. African Journal of Applied Research, 10(1), 224-237.

He, J. H., Chen, L. X., & Li, H. (2019). Progress in the discovery of naturally occurring anti-diabetic drugs and in the identification of their molecular targets. *Fitoterapia*, *134*, 270–289. https://doi.org/10.1016/j.fitote.2019.02.033

IDF. (2021). *IDF Diabetes Atlas 10th edition*. www.diabetesatlas.org

Irwin, S. (1968). Comprehensive observational assessment: Ia. A systematic, quantitative procedure for assessing the behavioral and physiologic state of the mouse. *Psychopharmacologia (Berl.)*, *13*, 222–257.

Joseph, B., & Jini, D. (2013). Antidiabetic effects of Momordica charantia (bitter melon) and its medicinal potency. *Asian Pacific Journal of Tropical Disease*, *3*(2), 93–102. https://doi.org/10.1016/S2222-1808(13)60052-3

Kamau, L. N. , Mbaabu, P. M. , Karuri, P. G. , Mbaria, J. M. , & Kiama, S. G. (2017). Medicinal plants used in the management of diabetes by traditional healers of Narok County, Kenya. *Tang [Humanitas Medicine]*, *7*(2), 10.1-10.10. https://doi.org/10.5667/tang.2017.0008

Kavishankar, G. B., Lakshmidevi, N., Murthy, S. M., Prakash, H. S., & Niranjana, S. R. (2011). Diabetes and Medicinal plants – A review. *International JOurnal of Pharmacy Biomedical Science*, *2*(3), 65–80. www.pharmainterscience.com

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

Keezhipadathil, J. (2019). Evaluation of suspected adverse drug reactions of oral anti-diabetic drugs in a Tertiary Care Hospital for type II diabetes mellitus. *Indian Journal of Pharmacy Practice*, *12*(2), 103–110. https://doi.org/10.5530/ijopp.12.2.23

Mangesh, K., Ashwini, K., Srinivas, B., Shivram, G., & Aaditi, K. (2014). Phytochemical and Pharmacological Accounts of Some Reviewed Plants with Antidiabetic Potential. *Scholars Academic Journal of Pharmacy (SAJP)*, *3*(2), 162–177. www.saspublisher.com

Mensah, M. L. K., Komlaga, G., Forkuo, A. D., Firempong, C., Anning, A. K., & Dickson, R. A. (2019). Toxicity and Safety Implications of Herbal Medicines Used in Africa. In *Herbal Medicine*. IntechOpen. https://doi.org/10.5772/intechopen.72437

Nasri, H., & Shirzad, H. (2013). Toxicity and safety of medicinal plants. *Journal of HerbMed Pharmacology Journal Homepage: J HerbMed Pharmacol*, *2*(2), 21–22. http://www.herbmedpharmacol.com

Nketia, A., Nakua, E., Tetteh, A. W., Thomford, K. P., Boadu, K. O., Thomford, A. K., & Amo, R. (2022). Herbal medicine practice in Ghana: A cross-sectional study to understand the factors influencing patient utilization of herbal medicine services. *International Research Journal of Public and Environmental Health*, *9*(1). https://doi.org/10.15739/irjpeh.22.003

OECD. (2001). *Test no. 423: Acute oral toxicity-acute toxic class method*. https://www.oecd-ilibrary.org/environment/test-no-423-acute-oral-toxicity-acute-toxic-class-method_9789264071001-en.

OECD. (2018). *Test no. 408: Repeated dose 90-day oral toxicity study in rodents*. http://www.oecd.org/termsandconditions/.

Panossian, A. G., Efferth, T., Shikov, A. N., Pozharitskaya, O. N., Kuchta, K., Mukherjee, P. K., ... & Wagner, H. (2021). Evolution of the adaptogenic concept from traditional use to medical systems: Pharmacology of stress-and aging-related diseases. Medicinal research reviews, 41(1), 630-703.

Rizvi, S. I., & Mishra, N. (2013). Traditional Indian medicines used for the management of diabetes mellitus. In *Journal of Diabetes Research* (Vol. 2013). https://doi.org/10.1155/2013/712092

Sukhikh, S., Babich, O., Prosekov, A., Kalashnikova, O., Noskova, S., Bakhtiyarova, A., Krol, O., Tsvetkova, E., & Ivanova, S. (2023). Antidiabetic properties of plant secondary metabolites. *Metabolites*, *13*(4). https://doi.org/10.3390/metabo13040513

Sun, H. , Saeedi, P. , Karuranga, S. , Pinkepank, M. , Ogurtsova, K. , Duncan, B. B. , Stein, C. , Basit, A. , Chan, J. C. N. , Mbanya, J. C. , Pavkov, M. E. , Ramachandaran, A. , Wild, S. H. , James, S. , Herman, W. H. , Zhang, P. , Bommer, C. , Kuo, S. , Boyko, E. J. , & Magliano, D. J. (2021). IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Research and Clinical Practice*, *183*. https://doi.org/10.1016/j.diabres.2021.109119

ISSN: 2408-7920

African Journal of Applied Research
Vol. 10, No. 2 (2024), pp. 44-64
http://www.ajaronline.com
http://doi.org/10.26437/ajar.01.12.2024.03
Special Issue: Applied Research Conference of Technical Universities in Ghana 2024
Received: December 15, 2023
Peer reviewed: June 2, 2024
Revised: November 3 2024
Published: December 2024

Sun, J., Ren, J., Hu, X., Hou, Y., & Yang, Y. (2021). Therapeutic effects of Chinese herbal medicines and their extracts on diabetes. In *Biomedicine and Pharmacotherapy* (Vol. 142). Elsevier Masson s.r.l. https://doi.org/10.1016/j.biopha.2021.111977

Tariq, A., Sadia, S., Fan, Y., Ali, S., Amber, R., Mussarat, S., Ahmad, M., Murad, W., Zafar, M., & Adnan, M. (2020). Herbal medicines used to treat diabetes in southern regions of Pakistan and their pharmacological evidence. *Journal of Herbal Medicine*, *21*. https://doi.org/10.1016/j.hermed.2019.100323

Tetteh, A. W., Thomford, K. P., Mensah, M. L., Boadu, K. O., Thomford, A. K., Amposah, I. K., Amofa, G., Turkson, B. K., Agyemang, M. O., & Owusu-Ansah, E. D. J. (2020). Ghanaian herbal medicines for malaria: An Evaluation of the Clinical Safety and Effectiveness of "Time Herbal Mixture" in uncomplicated malaria. *Pharmacognosy Research*, *12*(1), 71. https://doi.org/10.4103/pr.pr_23_19

Wilmot, D., Ameyaw, E. O., Amoako-Sakyi, D., Boampong, J. N., & Quashie, N. Ben. (2017). In vivo efficacy of top five surveyed Ghanaian herbal anti-malarial products. *Malaria Journal*, *16*(1). https://doi.org/10.1186/s12936-017-1757-4

Zaidi, S. F., Saeed, S. A., Khan, M. A., Khan, A., Hazazi, Y., Otayn, M., Rabah, M., & Daniyal, M. (2022). Public knowledge, attitudes, and practices towards herbal medicines; a cross-sectional study in Western Saudi Arabia. *BMC Complementary Medicine and Therapies*, *22*(236). https://doi.org/10.1186/s12906-022-03783-y

Zhang, J., Onakpoya, I. J., Posadzki, P., & Eddouks, M. (2015). The safety of herbal medicine: From prejudice to evidence. *Evidence-Based Complementary and Alternative Medicine*. https://doi.org/10.1155/2015/316706