

Physical, Proximate and Toxicological Properties of *Andrographis Paniculata* Herbal Powder Beverage Mix

Research Article

Etti CJ^{1*}, Etti I C², Sani D³

¹ Department of Agricultural and Food Engineering, University of Uyo, Uyo, Nigeria.

² Department of Pharmacology and Toxicology, University of Uyo, Uyo, Nigeria.

³ Department of Veterinary Pharmacology and Toxicology, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria, Nigeria.

Abstract

This study investigated the physical, proximate and toxicological properties of *Andrographis paniculata* (*A. paniculata*) herbal powder beverage mix. The herbal powder, *A. paniculata* with high medicinal value was formulated with non-dairy creamer and sugarto enhance the taste, nutritional and economic values, thus making it good and safe for human use. The physical properties of the formulated herbal beverage mix was determined: Particle size, pH, moisture content, bulk and tapped densities, were measured to determine Carr index and Hausner ratio which were indices of flowability. The proximate analysis such as ash, lipid, fibre, carbohydrate and crude protein contents of the beverage mix was determined. Toxicological study on the formulated beverage mix was performed using healthy male wistar rats to ascertain the safety of the product. The formulation of the pure *A. paniculata* herbal powder into a beverage mix enhanced the particle sizes with reduction in moisture content making the beverage to be “free flowing”. The formulated *A. paniculata* beverage mix had a pH of 7.49 ± 0.11 which is suitable for the human system. The formulated beverage mix was a good source of carbohydrate ($87.81 \pm 0.30\%$) and protein ($8.00 \pm 0.24\%$). However, the data revealed that the formulation was not a rich source of fat, making it recommendable to people with high lipid profile. The safety of the mix was ascertained after the acute oral and sub-chronic toxicity studies carried out for 28 days revealed no apparent adverse effect on the histology of both the liver and kidney of experimental animals.

Keywords: Physical Properties; Proximate Analysis; Toxicological Properties; *Andrographis Paniculata*; Herbal Powder; Beverage Mix.

Introduction

Herbal products, which are increasing worldwide are often classified as dietary supplements, but are not subject to premarketing approval unlike pharmaceutical products [1]. Companies and individuals who market these products have the sole responsibility to ensure the safety of their products. Most often, manufacturers produce, sell, and market herbs without first demonstrating safety and efficacy [2]. The setback in the production of herbal products and medicine is standardization, a process involving the production of herbal resources like extracts or phytochemicals with guaranteed products potency and stability in active compound content level [3]. Thus, high level of knowledge and skills in phytochemical analysis and process technology are necessary to ensure the required quality assurance. There is a large global market for herbal products because of their nutritive and medicinal properties [1,

4]. In fact, an estimated 70,000 species of plants are used for medicinal purposes globally [5, 6]. Finished herbal products are presented in various dosage forms like decoctions, herbal powders, alcoholic beverages, capsules, tablets, ointments and creams [7]. Generally, the therapeutic usage of herbs is enhanced in powder forms owing to increase absorption due to the large surface area [8]. The bulk behaviour of herbal powders are influenced by their physical properties such as particle sizes and shapes distribution, weights, chemical composition as well as their moisture contents [9]. Herbal powders with very fine particle size ranges may give rise to problems in the course of their industrial processing [10]. Ethno-botanically, as reported by Ayodele et al., [11], herbs and spices have been significantly utilised traditionally due to their flavour enhancement properties and their medicinal values [1].

Andrographis Paniculata (*A. paniculata*) also known as “king of bit-

*Corresponding Author:

Etti CJ,
Department of Agricultural and Food Engineering, University of Uyo, Uyo 520271, Nigeria.
E-mail: christopheretti@uniuyo.edu.ng

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ters", is a herbal plant that is widely used in traditional medicines for centuries in the treatment of certain diseases like skin eruptions, boils, scabies, and chronic undetermined fevers. *A. paniculata* has been reported to possess antibacterial, antifungal, antiviral, hypoglycemic, anti-cancer, anti-inflammatory and antipyretic properties [12]. The major modern use of *A. paniculata* is for the prevention and treatment of cold as it possesses antithrombotic actions, suggesting a likely advantage in cardiovascular disease [13].

The bitter taste of *A. paniculata* may influence its usage, thus, necessitating its formulation with creamer and sugar into a beverage mix in order to enhance its acceptability while ensuring the safety. A key stage in ensuring the safety of a product is to conduct toxicity tests in appropriate animal models [14]. Acute toxicity studies and repeated dose toxicity tests were employed to predict the safety in humans. The aim of this research was to investigate the Physical, Proximate and toxicological properties of *A. paniculata* herbal powder mix beverage.

Materials and Methodology

The herbal powder, *A. paniculata*, used in this study was acquired from Ethno Resources Sdn. Bhd., Sungai Buloh, Malaysia. The powder was produced after the herb was oven dried and ground to smaller standard particle sizes to obtain the powder. The material properties used in this work are summarized in Table (1). Sugar (MSM Perlis Sdn. Bhd. brand) and the nondairy creamer (Carnation brand) were bought from KK supermarket in Malaysia with particle size (D0.5) of $349.1 \pm 1.88\mu\text{m}$ and $190.7 \pm 2.15\mu\text{m}$ respectively. *A. paniculata* powder of particle sizes (less than $100\mu\text{m}$), was formulated into herbal powder mix by mixing it with other materials like sugar and creamer in a ratio of 1:10:10 respectively using a tumbler mixer (Glas-col, TERRE HAUTE, USA) at 30 rpm for 30 minutes per each formulation to ensure consistency and homogeneity of the herbal powder beverage mix. The ratio of "1" for the *A. paniculata* herbal powder was chosen to ensure the safety of the herbs [15]. The ratio "10" for sugar was chosen to enhance the sweet taste of the mix and also for nutrients enhancement (Carbohydrates) [16], and the ratio "10" for the nondairy creamer was chosen for nutrients enhancement as well. A commercial "3 in 1" Ipoh white coffee powder bought from KK supermarket was used to compare with the results of the formulated herbal powder mix in this study.

pH

The pH of the materials was checked using the pH meter (mV/ORP, METTLER TOLEDO, USA) in the Department of Process and Food Engineering Laboratory, UPM. 5 grams of powder was weighed and transferred into a measuring flask, 100 ml of distilled water was added into the flask and shaking was done for a minute. The solution was allowed to settle for one hour. The pH meter was calibrated and an appropriate amount of the clear aqueous solution was transferred from the flask into the beaker. The pH value was then measured and reported.

Moisture content (% dry basis)

The moisture content of *A. paniculata* beverage mix powder was determined according to AOAC [17], with the use of a digital

moisture analyzer (OHAUS MB45, UK). The *A. paniculata* beverage mix powder (1.0 ± 0.01 g) was weighed and kept in a sample plate, then measurement was made in triplicate. The result is given in Table 1.

Bulk and tapped densities

Bulk density (ρ_{bulk}) can be identified as the volume occupied by the solid plus the volume of voids when divided into powder. Whereas, tap density (ρ_{tab}) is a different type of bulk density obtained by tapping or vibrating the container in a particular method to achieve more effective particle parking and therefore, it is usually higher than bulk density [18],

$$\rho_{bulk} = W_t / V_{bulk} \text{ ---- (1)}$$

Where W_t is weight of the powder, V_{bulk} is volume of the powder obtained from tarred graduated cylinder without tapping. The tapped density (ρ_{tab}) of the powders was calculated by using the following equation;

$$\rho_{tab} = W_t / V_{tab} \text{ ---- (2)}$$

Where W_t is the weight of powder, V_{tab} is the volume of the powder bed after 500 taps.

Carr index and Hausner ratio

Carr Index and Hausner Ratio are used in describing the flowability of powder. Carr Index (CI) can be determined as the ratio of the difference of the tapped and the bulk densities to the tapped density [19]. According to Carr [19], who introduced the flowability index, an excellent flowability is between the Carr Index of 5% to 15% while Carr Index of above 25% normally shows poor flowability.

$$C.I = \rho_{tap} - \rho_{bulk} / \rho_{tap} \text{ ---- (3)}$$

Hausner Ratio (HR) are also used to characterize the flowability of powder, which can be determined by the ratio of the tapped density to that of bulk density [20]. HR of 1.0 to 1.1, indicates free flowing powder, HR greater than 1.1 to 1.25, indicates powder that is medium flowing, HR greater than 1.25 to 1.4, indicates powder that is difficult to flow and HR higher than 1.4, indicates powder that is very difficult to flow [21];

$$H.R = \rho_{tap} / \rho_{bulk} \text{ ---- (4)}$$

Proximate composition

Proximate composition of the samples was carried out using official AOAC [22] methods for moisture content, crude fat, crude fibre, ash, crude protein. Nitrogen to protein conversion factor of 6.25 was used. Carbohydrate content was calculated by difference. The result of the proximate analysis of the formulated herbal powder mix beverage is shown in Table 2.

Toxicological studies

Experimental animal: Healthy, mature male Wistar rats, weighing between 150-170g and aged 10-12 weeks were used for this experiment. The animals were procured from Saintik Enterprise,

No 5, Jalan 1/4 Taman Kembang Sari, 43300, Seri Kembangan, Selangor, Malaysia. The rats were kept in stainless steel cages for a period of 10 days to adapt to laboratory condition at an ambient temperature of $25 \pm 2^\circ\text{C}$ with 12h light: 12 h dark cycle. They were fed on commercial rat/mouse pellet diet (Specialty feeds, Glen forest, Western Australia) and water ad libitum throughout the study duration. All animal experiments were conducted in compliance with the internationally accepted principles of laboratory animal care specified and approved by UPM Animal Care Use Committee (UPM/IACUC/AUP-R061/2014).

Acute oral toxicity study: The limit dose test (LD50), up and down procedure [23] originally outlined by the Organization for Economic Co-operation and Development [24] was adopted with slight modification to evaluate the acute oral toxicity of *A. paniculata* extract mixed beverages following oral administration in adult male rats. A total of five (5) male rats were randomly selected and used for the study. The rats were maintained on standard feed and water provided ad libitum. They were marked and caged individually in the laboratory for 7 days to allow for acclimatization to the laboratory conditions. The rats to be treated were fasted overnight but allowed free access to water prior to dosing on each occasion. Each of the rats was picked, weighed and dosed orally with a single high dose of 3000mg/kg body weight of the extract beverages suspended in water (vehicle). Similar treatment was done for another set of rats with distilled water and was assigned control group. All the animals were observed thoroughly for instant death and then watched for the successive 24 hours for the short-term outcome and finally for the next 14 days for any delayed toxic effects. The LD50 was predicted if three or more rats survived after the experimental period [23].

Sub chronic toxicity studies: Male Wistar rats were randomly selected and used for the experiment. The rats were assigned into four groups (n=6 per group). Groups C, D, and E were administered graded doses (50, 100 and 200mg/kg respectively) of the extract beverages suspended in water orally for 28 days, while group A (the control) and B (positive control) received distilled water and 200mg of the commercial preparation for the same period. The weight of the rats were measured prior to administration of the extract and then weekly thereafter. Similarly, toxic manifestations and mortality were monitored daily for 28 days.

At the end of the experimental period (29th day), blood samples were collected via cardiac puncture from the rats in each group, transferred into plain and EDTA containing tubes for biochemical and haematological analysis respectively prior to sacrifice. The liver, kidney, heart, lung, intestine, stomach and pancreas of the sacrificed animals were also removed, physically examined for possible lesions and samples collected for histopathological analysis using standard Methods [25].

Hematologic and biochemical analysis: Estimation of haematological parameters such as red blood cells count (RBC), white blood cells count (WBC), haemoglobin concentration (Hb) and platelet (PLT) were carried out using a fully automated haematological analyser Abbott Cell-Dyn 3500 (Abbott Laboratories, IL, USA), while serum biochemistry tests were performed using a COBAS Integra 800 (Roche, Germany).

Histopathological analysis: Samples of liver, kidney, and spleen isolated from individual rats were fixed in 10% buffered formalin. The tissues were then dehydrated through graded concentrations of ethanol (70%, 95% and absolute), cleared in xylene and embedded in paraffin wax. The embedded tissues were sectioned at 5 μm thickness and stained with Haematoxylin and Eosin (H&E) for light microscope examination [25-27]. The lesions observed under microscope were captured for further analysis.

Results and Discussions

Physical properties

Table 1 below shows the physical Properties of herbal powder beverage mix and the commercial 3 in 1 coffee. From the table, the particle size analysis (D0.5) of pure herbal powder, sugar, creamer and the formulated herbal powder beverage mix product is shown. The formulation of the pure *A. paniculata* herbal powder into a beverage mix enhanced the particle sizes from $50.3 \pm 0.4\mu\text{m}$ of *A. paniculata* pure powder to $256.4 \pm 0.7\mu\text{m}$ of *A. paniculata* beverage mix. It was observed that based on Carr index [19] and Hausner ratio [20], the formulated beverage mix was "Free flowing" in terms of flowability properties. The enhancement in particle size enhanced the flowability because the smaller the particle size, the more difficult it is for the particle to flow [28]. From Table 1, a commercial 3 in 1 coffee mix was also analyzed

Table 1. Physical Properties of Herbal Powder Beverage Mix and commercial 3 in 1 coffee.

Material properties	<i>A. paniculata</i>	3 in 1 coffee
Powder Particle size before mixing (μm) (D 0.5)	50.3 ± 0.4	-
Particle size for formulated mix (μm) (D 0.5)	256.4 ± 0.7	232.0 ± 0.6
Particle size for Sugar (μm) (D 0.5)	349.1 ± 1.88	-
Particle size for Creamer (μm) (D 0.5)	190.7 ± 2.15	-
pH	7.49 ± 0.11	6.44 ± 0.13
Moisture content (% dry basis)	2.12 ± 0.09	2.26 ± 0.53
Bulk density (kg/m^3)	661.2 ± 2.1	532.0 ± 1.6
Tap density (kg/m^3)	799.0 ± 3.1	652.0 ± 1.8
Hausner Ratio (1967) (HR)	1.21 ± 0.98	1.23 ± 0.97
Carr Index (1965) (%)	17.25 ± 1.02	18.41 ± 0.87
Categorization based on HR	Free flowing	Free flowing

and the result showed that it was also “Free flowing”. The free flowing nature of the formulated beverage will reduce the cost of controlling caking problem in the industry. Also, considering the pH analysis, the formulated *A. paniculata* was seen to have a pH of 7.49 ± 0.11 which was neutral to basic in nature compared to the commercial 3 in 1 coffee mix with pH of 6.44 ± 0.13 which was acidic in nature. Alkaline foods help in countering the risks of acidity and acid refluxes, bringing some sort of relief to the body system [29].

Proximate analysis

Proximate analysis plays important role in assessing the nutritional significance of food [30]. The world health organization (WHO) had emphasized the need and importance of determining the proximate analysis of herbal formulations for standardization purposes [31]. The proximate analysis of *A. paniculata* herbal powder beverage formulation is shown in Table 2 below. *A. paniculata* herbal powder beverage mix was high in the crude protein content ($8.00 \pm 0.24\%$). Generally, the data revealed that the formulation was not a rich source of fats and can therefore be recommended to people that fat is a risk factor. Also, the low fat contents is a reason why all the herbal powders beverage mix is free flowing (see Table 1) because fat content can influence the flowability of powders, high fat contents will make the powders to be cohesive, posing a problem to flow [32]. *A. paniculata* herbal powder beverage mix is recommended for people that have protein deficiency

because of its rich protein content. The herbal powder beverage mix could also serve as an energy buster due to its high carbohydrate content ($87.81 \pm 0.30\%$) (Table 2). The low moisture content of the herbal powder beverage mix ($2.12 \pm 0.09\%$) is also responsible for its free flowing nature (Table 1) because high moisture contents increase powders cohesive strength [33].

Toxicology Studies

Acute Toxicity Study: In this study, administration of 3000mg/kg of the extract beverages did not cause any visible behavioural change and death of the rats within the short and long outcome of the limit dose test (Table 3). All five rats survived until the end of the experiment with no mortality recorded. The LD50 was determined to be greater than 3000mg/kg body weight [23].

Effect of oral administration of different doses of AP extract formulation on body weight change: Figure 1 depicts changes in body weight of rats fed with different doses (50, 100 and 200 mg/kg) of *A. paniculata* extract beverage mix for 28 days. There was significant ($P < 0.05$) dose dependent increase in the mean body weight in both the control and treated groups compared to respective day 0 values.

Subchronic toxicity study: In subchronic toxicity study, there were no observable changes in the general behaviour of all the treated rats (groups 50mg/kg, 100mg/kg and 150mg/kg) as com-

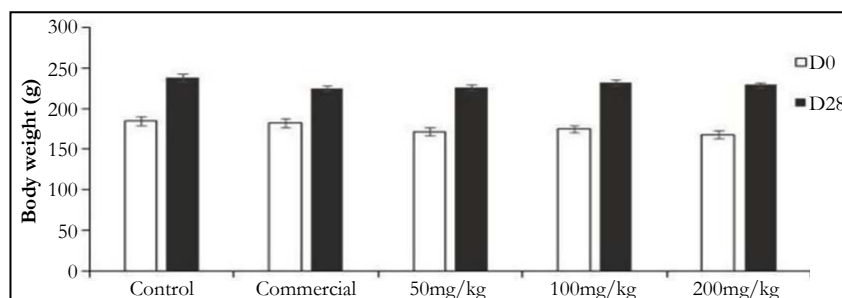
Table 2. Proximate analysis of the formulated herbal powder mix beverage.

Formulated <i>A. paniculata</i> beverage mix	Values
Crude fibre (%)	0.52 ± 0.09
Crude fat (%)	1.46 ± 0.09
Crude protein (%)	8.00 ± 0.24
Moisture content (% dry basis)	2.12 ± 0.09
Ash (%)	0.09
Carbohydrate (%)	87.81 ± 0.30

Table 3. Result of limit dose test of *A.paniculata* extract beverages in rats.

Test sequence	Animal ID	Dose (mg/kg)	Short term Effect (24h)	Long term Effect (14days)
1	A1	3000	Survival	Survival
2	A2	3000	Survival	Survival
3	A3	3000	Survival	Survival
4	A4	3000	Survival	Survival
5	A5	3000	Survival	Survival

Figure 1. Mean body weight of rats fed with different doses of *A. paniculata* extract beverages for 28 days.



pared to the control groups (Control and Commercial control). Both controls and the treated rats appeared uniformly healthy till the end of the study and throughout the 28 days treatment period.

Blood Analyses: Exposure of rats to sub chronic treatment with varied doses (50, 100 and 200mg/kg) for 28 days showed significant ($P < 0.05$) increase in the haematological parameters (red blood cell count (RBC), haemoglobin concentration (HGB), total white blood cell count (WBC), white blood cell differential count and platelet counts) of the extract formulated treated rats when compared to control rats. Exposure of rats to sub chronic treatment with varied doses (50, 100 and 200mg/kg) for 28 days showed significant ($P < 0.05$) increase in the haematological parameters (red blood cell count (RBC), haemoglobin concentration (HGB), and platelet counts (PLT)) of the extract formulated treated rats when compared to control rats. With the increasing questioning of the safety of herbal (medicinal plant) usage sequel to frequent report of illness and fatalities, research into evaluating the safety profile on medicinal plant becomes necessary. Haematological analysis of blood parameters in animal study is necessary to evaluate the risk of alterations of the hematopoietic system in toxicity studies, for necessary application to humans [34]. Haematopoiesis is the process of blood cell formation including an erythrocyte (RBC), a leukocyte (WBC), or a thrombocyte (platelet). In healthy adults, stem cells in hematopoietic sites undergo a series of divisions and maturational changes to give rise to mature cells found in the blood [35]. In this study, administration of the herbal powder formulated beverage mix after 28 days up to a dose of 200mg/kg body weight resulted in dose-dependent significant increase in RBC, HGB and PLT in *A. paniculata* formulated beverage mix (Table 4). This could be as a result of the activation of the hematopoietic system, leading to the production of RBC (erythropoiesis) and platelets [21]; although, all the haematological parameters (WBC, RBC, HGB and PLT) were within rat haematologic reference ranges [36]. There was a slight insignificant increase in WBC for the formulated beverages mix compared with the control. The WBC protects the body from infection by foreign organisms, the RBC boost the immune system and the platelets protect blood vessels from endothelial damage as well

as initiate repair of these vessels. This therefore suggests a strong immuno-modulatory, antioxidant and endothelial protection and repair activity of these formulated beverage mix.

Effect of oral administration of different doses of AP extract formulation on some biochemical parameters

Biochemical analysis did not reveal any significant difference after 28 days of exposure of rats to different doses of *A. paniculata* extract formulation when compared to control group. However, there were increases in the levels of AST, ALT and ALP in the group treated with 200mg/kg of the extract formulation when compared to control although not significant. Tables 5 showed the biochemical analysis of the different formulated herbal powder beverage mix. Biochemical analysis did not reveal any significant difference after 28 days of exposure of rats to different doses of all formulated beverages mix when compared to control group. Liver is the major organ involved in drug biotransformation. Levels of serum liver biomarker enzymes are biochemical parameters usually performed in order to evaluate any toxic effects on the liver [37]. Increases in the levels of AST, ALT and ALP in the serum are associated with liver toxicity by drugs or any other hepatotoxin [38]. More so, ALT is more specific to liver and thus a better parameter for detecting liver injury as ALP is present mostly in cells lining the biliary duct of the liver and is used to diagnose obstruction to the biliary system. Therefore, its elevation in the blood indicates cholestatic diseases such as gallstone or tumor blocking the bile duct [39]. Urea and creatinine are considered as important markers of kidney dysfunction [40]. In this study, chronic exposure of rats to different doses (50, 100 and 200mg/kg) of herbal powder formulated beverage mix did not revealed significant changes in all the biochemical parameters tested over the 28 days treatment compared to control group, signifying normal functioning of the liver and kidney. It also confirms with the theory of target organ toxicity [41], since the kidney is the major organ of excretion, suggesting that the toxic principles in these beverages mix are not high enough to induce significant health hazard [25].

Table 4. Haematological Values of Rats Treated with *A. paniculata* Herbal Powder Beverage Mix for 28 Days.

Parameters	Control	Commercial	50mg/kg	100mg/kg	200mg/kg
WBC ($\times 10^9/L$)	9.25 \pm 0.25	10.6 \pm 0.5	10.83 \pm 0.29	11.31 \pm 0.18	11.98 \pm 0.24
RBC ($\times 10^{12}/L$)	5.44 \pm 0.18	6.53 \pm 0.18	7.21 \pm 0.15 ^a	7.35 \pm 0.20 ^a	7.65 \pm 0.2 ^{ab}
HGB (g/dL)	10.53 \pm 1.33	11.45 \pm 2.76	13.13 \pm 0.34 ^a	13.9 \pm 0.84 ^{ab}	13.7 \pm 1.03 ^{ab}
PLT ($\times 10^9/L$)	237.00 \pm 16.36	272.00 \pm 12.89 ^a	348.33 \pm 4.30 ^{ab}	385.17 \pm 5.65 ^{ab}	389.33 \pm 11.19 ^{ab}

The data represents the Mean \pm SD for each group of rats, n = 6. ^ap < 0.05 and ^{ab}p < 0.01 compared to the appropriate control group.

Table 5. Biochemical Parameters of Rats Treated with *A. paniculata* Herbal Powder Beverage Mix for 28 Days.

Parameters	Control	Commercial	50mg/kg	100mg/kg	200mg/kg
AST (U/L)	147.8 \pm 5.5	135.4 \pm 3.3	144.5 \pm 6.9	145.3 \pm 3.1	150.8 \pm 3.8
ALT (U/L)	32.63 \pm 1.4	30.18 \pm 0.7	30.93 \pm 2.2	31.60 \pm 2.3	32.24 \pm 1.7
ALP (U/L)	233.38 \pm 3.8	200.68 \pm 7.6	221.75 \pm 2.0	229.4 \pm 3.6	233.21 \pm 5.1
UREA (U/L)	5.15 \pm 0.3	4.38 \pm 0.3	4.43 \pm 0.1	4.59 \pm 0.17	4.46 \pm 0.92
CRE (mg/dL)	0.47 \pm 0.2	0.39 \pm 0.2	0.42 \pm 0.2	0.43 \pm 0.1	0.44 \pm 0.1

Note: Aspartate transaminase (AST); Alanine aminotransferase (ALT); Alkaline Phosphatase (ALP)

Histopathological evaluation of rat organ sections (kidney, liver and lungs) exposed to graded (50, 100 and 200 mg/kg) of *A. paniculata* extract

Histological evaluations of the livers and kidneys did not show any morphological changes after administration of the aqueous

extracts formulation for 28 days. The herbal powder formulated beverages mixes are relatively safe as they reveal no apparent adverse side effect on the function of both the liver and kidney (see Figures 2 and 3). However care should be taken with prolonged consumption of higher doses (>200mg/kg) of this herbal powder formulated beverages.

Figure 2. Liver of normal control (A), 50mg/kg (B), 100mg/kg (C) and 200mg/kg (D) rats treated with *A. Paniculata* herbal powder beverage mix for 28 days showing apparently normal architecture with central vein (CV), hepatocytes and hepatic lobules (section x100).

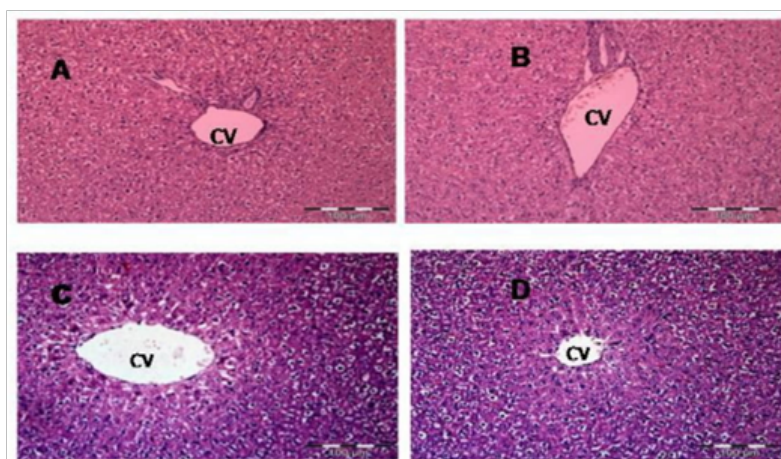
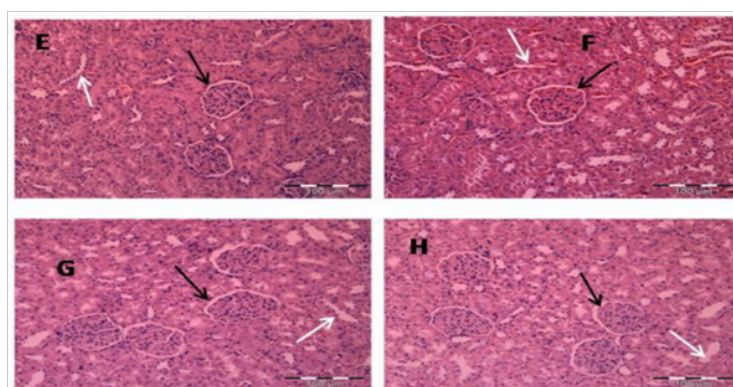


Figure 3. (E) Histologic section of normal rat kidney showing normal glomerulus (black arrow) with intact tubules (white arrows). (F, G, H): Photomicrograph of kidney section from experimental rats treated with *A. Paniculata* formulated beverage mix (50mg/kg, 100mg/kg and 200mg/kg respectively) showing nearly normal architecture with intact glomerulus (black arrow) and renal tubules (white arrow) (section x100).



Conclusion

In conclusion, this study enhances the understanding of powder physical property, which can improve the development and formulation of herbal powder beverage mix. The formulated beverage mix could serve as an energy buster and body building beverage because it is a good source of carbohydrate and protein. The extract formulation is relatively safe as the administration of 3000mg/kg of the aqueous beverage did not elicit any sign of toxicity or cause any visible behavioural change and death of the animals within the short and long outcome of the limit dose test. Analysis of the haematological, biochemical and histological parameters of the rats after the administration of the aqueous beverage formulation for 28 days revealed the safety of the beverage mix. However care should be taken with prolonged consumption of higher doses (> 200mg/kg) of this extract formulation.

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