# DEVELOPMENT AND ASSESSMENT OF A SYNERGY-BASED COMBINED EXTRACTS OF *Spondias mombin* L., *Spilanthes filicaulis* (SCHUMACH. & THONN.) C.D.ADAMS and *Piper guineense* THONN. FOR LEARNING AND MEMORY ENHANCEMENT.

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**MEDICINAL PLANTS RESEARCH AND DRUGS DEVELOPMENT**

Memory challenges and cognitive decline, linked to neurodegenerative illnesses, continue to rise worldwide without effective remedies. Earlier research indicates that traditional medicinal plants may offer potential benefits in addressing these conditions. The three plants investigated in this study have been documented for memory enhancement.The current study is aimed at developing a synergy-based combined extracts of *Spondias mombin, Spilanthes filicaulis,* and *Piper guineense* in different ratios for learning and memory enhancement in order to suggest the ratio with the best pharmacological effect and toxicological profile that could be formulated into a herbal product.

Mice were pretreated with 2 mg/kg scopolamine intraperitoneally for three consecutive days. Thereafter, the synergistic combination of *S. mombin, S. filicaulis* and *P. guineense* in ratio 2:2:4 (H1) or ratio 2:2:2 (H2) at 50, 100, or 150 mg/kg, and piracetam (200 mg/kg) was given orally, respectively, for fourteen (14) consecutive days. From day 11 post-treatment, mice were subjected to neurobehavioural studies (Morris water maze test (MWM), Y-maze test, and Elevated plus maze test), respectively. The mice's hippocampus were isolated for biochemical analysis or histopathological examination following the neurobehavioural task. The synergistic combinations were also evaluated for total phenolic content, total flavonoid content, antioxidant activity (using 2, 2- diphenyl-1-picrylhydrazyl (DPPH), and ferric ion reducing power (FRAP) assays), GC-MS analysis, and acute toxicity testing. The statistical level of significance was determined by one- or two-way ANOVA followed by Tukey post hoc multiple comparison tset (whichever is applicable).Differences between means at 5% level ($P \leq 0.05$) were considered significant.

Administration of both combinations significantly ameliorated scopolamine-induced cognitive impairment in mice, evident in enhanced performance in Y-maze and MWM tests, while also attenuating anxiety-related behavior in the Elevated Plus Maze test. Combination H1 and H2 significantly decreased oxidative stress markers (MDA, H2O2) and restored antioxidant defenses by elevating glutathione and superoxide dismutase activity. Additionally, they restored hippocampal tissue integrity altered by scopolamine. Because of their high phenolic and flavonoid contents especially H1, the combinations demonstrated favourable effects in scavenging free radicals, demonstrated by their action against DPPH and displayed moderate antioxidant capabilities in FRAP tests. The GC-MS analysis revealed 30 peaks within H1 and 20 peaks withing H2 with phytochemical compounds associated with antioxidant and acetylcholinesterase inhibition.

The combined-extract H1 consistently demonstrated superior performance across most of the experiments and assays conducted, suggesting its promising potential for enhancing memory and learning.

**Keywords:** Medicinal plants, Synergistic combination treatment, Neurodegenerative disorders, Antioxidant activity, Acetylcholinesterase activity.

# EVALUATION OF ANTIDIABETIC AND HEPATOPROTECTIVE ACTIVITIES OF *Laportea aestuans* (L.) CHEW LEAVES AND *Telfairia occidentalis* HOOK.F. STEM IN HIGH-FAT DIET/STREPTOZOTOCIN-INDUCED DIABETES IN RATS

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Diabetes mellitus (DM) comprises a set of metabolic disorders marked by persistent hyperglycaemia, leading to damaging effects to other organs including the liver. Its global prevalence is rapidly increasing. The limitations associated with the antidiabetic drugs necessitate the search for novel bioactive alternatives from natural plant origin. This study evaluated the antidiabetic and hepatoprotective properties of the hydroethanolic extracts of *Laportea aestuans* (L.) Chew leaves (LA) and *Telfairia occidentalis* Hook.f. Stem (TO) in high- fat diet and streptozotocin (HFD/STZ) induced diabetic rats. Forty-two male Wister rats (150-180 g) were divided into seven groups (n=6). Group 1 served as the healthy control and was provided with a normal diet. Groups 2 to 7 were given HFD for 21 days followed by two intraperitoneal injections of Streptozotocin (35 mg/kg) administered in one week interval. Group 2 served as the diabetic control, group 3 was administered metformin (250 mg/kg), group 4 and 5 were given the hydroethanolic extract of LA (200 and 400 mg/kg, respectively), and group 6 and 7 were administered the hydroethanolic extract of TO (200 and 400 mg/kg, respectively). All the treatments were administered to the rats orally for 21 days. Fasting blood sugar (FBS) was measured every 7 days using the glucometer. The serum liver enzymes (ALT and AST), serum inflammatory markers (CRP, TNF-α, and IL-6) and oxidative stress markers in the liver and kidney were assayed using standard methods. LA and TO were partitioned sequentially in *N*-hexane, diethyl ether, ethyl acetate, and *N*-butanol. Qualitative phytochemical screening and thin layer chromatography analysis were done following the standard procedures. The *in vitro* α-amylase and α- glucosidase inhibitory activities of the crude extracts and the fractions were also investigated. The data with P values below 0.05 were considered statistically significant. Treatment of the diabetic rats with LA produced a dose-dependent significant ($p < 0.05$) reduction in FBS relative to the diabetic control, while the extract of TO stem did not cause a significant ($p > 0.05$) decrease. TO extract showed antihepatotoxic effect by significantly decreasing the elevated level of serum AST, whereas LA extract did not change the level of the liver enzymes. Inflammatory parameters in serum and liver were significantly reduced by both extracts. Malondialdehyde levels in kidney and liver were reduced, while antioxidant parameters were improved by both extracts. The diethyl ether fraction of TO exhibited the highest activity against α-amylase and α- glucosidase enzymes (IC50 8.19±0.39 and 49.74±0.35, respectively). The phytochemical analysis of the hydroethanolic extracts of LA and TO revealed the presence of flavonoids, alkaloids, phenols, terpenoids, and tannins but the absence of anthraquinones. Saponins and cardiac glycosides were detected only in the extract of LA. The GC-MS analysis of the diethyl ether fraction of TO showed oleic acid as the major component (70.94%). *Laportea aestuans* leaves and *Telfairia occidentalis* stem exhibited protective potential against type-2 diabetes in rats via mechanism related to inhibition of carbohydrate digesting enzymes, antihepatotoxic, anti-inflammatory and antioxidant activities which is attributed to their phytochemicals.

**Key words**: Antidiabetic plants, hepatoprotective, *Laportea aestuans*, *Telfairia occidentalis*, oleic acid.

# ANTIMICROBIAL ACTIVITY OF *Terminalia leiocarpa* Baill. (Combretaceae) AND *Terminalia avicennioides* Guill. & Perr. (Combretaceae) EXTRACTS IN RESISTANT CLINICAL ISOLATES.

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**MEDICINAL PLANTS RESEARCH AND DRUG DEVELOPMENT**

The utilisation of plants as a reservoir for potential chemotherapeutic and antimicrobial agents is a common practice in ethnomedicine. However, folkloric use of *Terminalia leiocarpa* and *Terminalia avicennioides* in treatment of microbial infection has prompted various pharmacological investigations especially antimicrobial studies. The current study seeks to investigate, assess antimicrobial activity and the bioactive compounds of *Terminalia leiocarpa* and *Terminalia avicennioides* roots bark extracts on clinical isolates.

The root bark of *Terminalia leiocarpa* and *Terminalia avicennioides* were dried and pulverized. Methanol extracts of the two plants were obtained from 900 g of the pulverized root barks through maceration. Antimicrobial activities of 500 mg/mL of each of the extracts were performed through agar well diffusion method on selected microorganisms. The most active methanol extract of *Terminalia leiocarpa* was fractionated into Aqueous methanol, methanol, dichloromethane and hexane fractions. Compounds present in dichloromethane fraction of *T. leiocarpa* were identified utilising gas chromatography-mass spectrometry (GC-MS). The statistical difference in the mean zone of inhibition was determined by one-way analysis of variance. Differences between means at a $P\text{-}_{value} \leq 0.05$ were considered significant.

The inhibition zone diameter (IZD) of the extracts on selected microorganisms were within(18-24mm) and (13-21 mm) with *T. leiocarpa* having better activity (24mm) on *Acinetobacter baumannii*. The GC-MS revealed 15 peaks in dichloromethane fraction. The use of compounds as great synergetic compounds could be a potential resistance-free template in future antimicrobial drug discovery.

**Keywords**: *Terminalia avicennioides*, *Terminalia leiocarpa*, Antimicrobial, *Acinetobacter baumannii*, Gas chromatography-mass spectrometry.

# ANTHELMINTIC ACTIVITY OF *Vernonia purpurea* (ex Walp) Sch. Bip. (Asteraceae) AND CHEMICAL PROFILING USING GC-MS AND LC-MS.

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**MEDICINAL PLANTS RESEARCH AND DRUG DEVELOPMENT**

Soil-transmitted helminthiasis (STH) is a parasitic disease affecting poor and deprived communities with a high death rate; however, the treatment of STH is associated with drug resistance and side effects, which result into treatment failures; thus, the need for new drug molecules. Vernonia genus is a reservoir of anti-parasitic agents, and *Vernonia purpurea* plant was subjected to successive extraction by maceration, using n-hexane (HEX), dichloromethane (DCM), ethyl acetate (EA) and methanol (MeOH), in addition to aqueous extraction of the plant sample. Phytochemical screening on the sample was carried out using qualitative and quantitative methods. The crude extracts were screened for *in vitro* anthelmintic activity on earthworms using Albendazole as positive control, and the most active extract was subjected to metabolite profiling through GC-MS and LC-MS. In addition, oral acute toxicity studies and granules formulation were carried out on the most active extract (EA). The phytochemical screening allowed the identification of flavonoids, saponins, terpenoids, phenolics and tannins, while alkaloids, anthraquinones and cardiac glycosides were not detected. Quantitative estimation of the most active extract (EA) revealed the total phenolics to be higher than total flavonoids and total tannins contents. The *in vitro* anthelmintic activity revealed EA as the most potent anthelmintic agent on helminths paralysis and death. The anthelmintic activity of EA was comparable to standard drug (Albendazole) indicating the significance of this study. This can be attributed to the chemical compounds present in EA and identified through GC-MS, predominantly fatty acid and their esters, in addition to flavonoids and flavonoid glycosides identified through LC-MS. The oral acute-toxicity studies on EA showed an $LD_{50}$ > 5,000 mg/Kg, indicating safety for consumption. The granules formulated exhibited excellent flow properties, good percolation and high aqueous solubility. The findings have demonstrated the suitability of *V. purpurea* EA as a potential candidate for drug development against STH.

**Keywords**: *Vernonia purpurea*, soil-transmitted helminthiasis, anthelmintic. GC-MS, LC-MS