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Acute Toxicity and *IN VIVO* Antischistosomal Effects of *Entada africana* Guill & Perott (Fabaceae) Methanol Stem Bark Extract in Albino Mice

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Abstract:- The study was aimed at determining the acute toxicity and schistosomicidal effects of methanol extract (ME) of *Entada africana* (*E. africana*), in albino mice. Fresh stem bark of *E. africana* was shade-dried and extracted by Soxhlet extraction. Acute toxicity was carried out on 6 groups of mice (n=3) of 6-week-old, sizes 27-30g; to determine the therapeutic index, piloerection signs and possible mortality (LD_{50}) in 24h exposure period. Cercaria from *B. globosus* snails were shed under a 100W bulb for 2 hours. *In vivo* antischistosomal assays was by used of 6-weeks old (27-30g) mice. Set I (n=10) involved investigation on schistosomules infection in the mice, 3-7 days post infection (PI). Set II (n=10) was infected and treated with *E. africana* ME extract, at concentrations 10-100mg/l, 35th day, PI for 5 consecutive days. Set III (n=10), were infected and treated with praziquantel– PZQ (positive control). While set IV (n=10) were infected and untreated (negative control). All were sacrificed, 75th day of PI. Data were analyzed by GraphPad® prism 8.4, version 2020. Findings revealed that *E. africana* ME did not generate any harmful or clinical effect within 24h, post administration; and there were no obvious reactions such as paw licking, stooling, piloerection or immediate death, except at phase II, 5000mg/kg bwt, (⅓) being the highest dosage. Worm burden decreased with increase in concentrations, especially at 70-100mg/l. Lower concentrations (10mg/l), had high worm population (76.00±21.28). Infected and untreated group had highest worm population (189.67±32.52). *E. africana* ME stem bark extract, showed antischistosomal effect and worm reduction in a dose-dependent pattern.

Keywords:- *Acute Toxicity, Entada Africana, Methanol Extract, Schistosomiasis.*

I. INTRODUCTION

Schistosomiasis infection is still a significant health problem especially in low-income societies of sub-Saharan African (Basha and Mamo, 2021). The disease has caused morbidity and mortality in humans, mostly in underdeveloped countries such as Africa and Asia, caused by three primary parasitic species, which are *S. mansoni*, *S. haematobium*, and *S. japonicum* (Xiao et al., 2007; and Coeli *et al*., 2013). Prolong use of praziquantel (PZQ) – the drug of choice, even though not effective against the larval form; is expensive, with consequent cases of drug resistance that poses constant threat due to its continued usage (Crellen et al., 2016; Molehin, et al., 2022 and Asante-Kwatia et al., 2023). There is no single vaccine against schistosomiasis that has been developed, whether for human or animals (Molehin, et al., 2022). Overdependence on the only drug of choice (PZQ), especially it repetitive used on a wide scale in endemic areas, has led to selective resistance, more so that PZQ is less efficient against schistosomules (Coeli et al., 2013).

Plant biocomponents of *Jathropa curcas* (Adamu et al., 2006); and *Catropis procera* (Khalil et al., 2016), have demonstrated high potentials of antischistosomal properties that have shown considerable worm reduction, including other developmental stages of the parasite (Mohammed et al., 2005). Other researchers (Tonuci et al., 2012); worked on *Tagetes erecta* essential oil; and stem bark of *Rauwolfia vomitoria* (Tekwu et al., 2017) also, had demonstrated reduced worm population and decreased in motor activity respectively. The extracts of *Tagetes erecta* are known to inhibited egg development similar to PZQ (Tonuci et al., 2012). Further, after 72 hours of post-exposure to crude dichlomethane extract and aqueous fraction of *Baccharis trimera*; caused mortality of the adult worms with morphological changes on the tegument, suckers, oral, and acetabulum of both male and female *S. mansoni*, with hundred percent inhibition of oviposition in the female (Oliveira et al., 2014). When experimental mice were treated with *Chroocuccus turgidus* extract, it demonstrated significant reduction in the number of eggs both in the liver and intestine; and reduction in worm burden as well as significant changes such as loss of spines and swollen suckers (Ali et al., 2016).

In view of the high cost of PZQ, and often not easily accessible especially in poor-developing countries that are often endemic with the disease; emphasis has been on bioregulation of the snail intermediate hots (Kiros et al., 2014; and; Prabhakaran et al., 2017). The stem bark of *E. africana* has shown to have bioactive molluscicidal effect (Daben et al., 2023). As such, using plant extracts is more conducive, safe, and has a low environmental impact, as well

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as less expensive with greater chance of sustainability (Prabhakaran et al., 2017). Utilization of natural products as potential novel treatments for both enteric and urinary schistosomiasis has grown in popularity; in particular, is the effects of secondary metabolites such as alkaloids, terpenes, phenols, tannins, and flavonoids, which are known to have antischistosomal activities (Yusuf and Abdullahi, 2019). Saponins are the main active ingredients found in these plants (Daben and Mwansat, 2024). Numerous literatures showed beneficial effects of *E. africana* such as antidiarrheal effect in mice (Mu'azu and Usman, 2020). Mvondo et al., (2017); had established several ethnobotanical and ethnopharmacological usage of *E. africana* plant parts, which includes the leaves that is used for treatment of burn wounds, the stem bark, used for treatment of lower abdominal pains, malaria, cough and hemorrhoids; while the roots for elimination of intestinal worms. This make the search for novel drug or antischistosomal therapy that is plant-base and are rich source of secondary metabolites, of great necessity (Dube et al., 2022). Therefore, we set out to investigate the antischistosomal effects of the candidate plant (*E. africana*) as a potential schistosomicidal agent, considering its rich primary and secondary metabolites (Daben and Mwansat, 2024). Ease of Use.

II. MATERIALS AND METHODS

- *Ethical Clearance*

Ethical permission was obtained from the Animal Experimental Unit (AEU) of the Faculty of Pharmaceutical Sciences, University of Jos. No. UJ/FPS/F17-00379, according to the regulations of the Institutional of Animal Care and Use (IACU); in partnership with the Office of Laboratory Animal Welfare (OLAW). Reference number: F17-00378.

- *Sample Collection*

Plant materials were collected at Dangshang and Rom, that is, sites A and B in Mushere-Central in Bokkos Local Government Area of Plateau State, Nigeria. Geographical coordinates of site A were at Latitude $9^0$08'31.66 N and Longitude $09^0$04'55.09 E, at an elevation of 903.122m, eye altitude 7.199m. While that of site B was at Latitude $9^0$08'27.70 N and Longitude $9^0$06'00.75 E, elevation 1005.23m and an eye altitude of 7.199m.

- *Preparation of Samples*

The *E. africana* stem bark (Plate 1) was peeled and shade-dried for 2 weeks, before it was pulverized (Plate 2), by use of mortar and pestle. It was then sieved using wire mesh of 0.5 mm sizes, and measured for Soxhlet extraction.

Plate 1: Young Fresh Stem Bark

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Plate 2: Pulverised Sample

➢ *Soxhlet Extraction And Rotary Evaporation*

Five hundred gram (500 g) of the powdered sample was weighed and put in a thimble and place in a Soxhlet extractor. Seven hundred (700 cm^3) of methanol solvent was poured into a 1000 cm^3 capacity, quick-fit flask. The Soxhlet extractor was then fixed onto the quick-fit flask and the condenser connected to the tap, then mounted on the Soxhlet extractor. This setup was carefully clamped and mounted on the thermostatically controlled heating mantle. The process of extraction continued for 8 hours until all the active components from the sample were extracted, indicated by clear appearance of the solvent at the thimble end point (Daben et al., 2023). The extracted sample was further concentrated by use of a Rotary Evaporator (RE-52A), based on set temperature of the solvent (64.9 ℃). The stem bark extract was poured into a quick-fit flask (250 cm^3), and fixed onto the rotary evaporator, then dipped into a thermostatically-controlled water bath. Evaporation process was done continually until minimum quantity of about 50 ml of the sample, was left in the flask. This was further allowed to air-dry in a fume cupboard or refrigerated pending use.

➢ *Toxicity Profile: Dosage Preparation*

Methanolic extract was first diluted in tween 80 using a 10-dilution factor: 1: 9ml v/v (Tween 80 and water), and administered to the mice via oral gavage, for bioevaluation of acute toxicity according to Salawu et al., (2009); and Chinedu et al., (2013).

➢ *Determination of LD_{50}*

Mice obtained from AEU, were randomly divided into 3 groups (n=3) before a single-dose oral administration of *E. africana* ME was carried out in two phases. This was done after withdrawing their feed (fasted) for a 12h-period; and were observed for 24 hours. No feeding was done after the extracts was administered. The LD_{50} was assessed for toxicity signs such as loss of appetite, raised fur, paw licking, stooling, micturition, lying flat on belly, raised fur, salivation, reduced activity and possible mortality within the 24h exposure period (Yakubu *et al*., 2015). Mice were properly labeled in order to allow for easy identification and administration of the respective dosages base on their kilogram body weight (kg/bwt).

Nine mice were allocated into three groups (n=3) each. In phase I, group A: labelled Head (H), Back (B), and Tail (T). These were administered 10 milligrams/kg bwt. The respective kg/bwt doses were H (0.27ml), B (0.27ml), and T (0.33ml). Group B: were administered 100mg/kg bwt labelled, Right Ear (RE), Left Ear (LE), and Two Ears (TE), doses 0.30ml for all the three mice in the group. While the last, Group (C): were given 1000mg/kg bwt, labeled Right Leg (RL), Left Leg (LL), and Two Legs (TL), dosages given were 0.25, 0.30, and 0.28ml, respectively.

Similarly, in Phase II, mice were labeled Head and Back (HB), Head and Tail (HT), and Blank (B) and given 1600, 2900, and 5000mg/kg bwt, calculated administered dosages were 0.44, 0.77, and 1.20ml respectively. At both phase I and II, the controls were usually given 1ml of normal saline (Pomogyi et al., 2023).

The LD_{50} was determined based on the formula:

$$LD_{50} = \sqrt{D_0 \times D_{100}}$$

Where:
D_0 = Highest dose that produce no mortality
D_{100} = Lowest dose that produce mortality.
Note: these outcomes were compared to Hodge and Sterner Toxicity Scale – Appendix I, Ahmed, (2015).

➢ *Inoculation and Percutaneous Penetration of Cercaria*

This was carried out according to Metwally et al., (2018), where 120 six-week-old adult male and female mice, ranging between 21-31g were used. Prior to treatment, the animals were maintained and acclimatized in normal cages at room temperature (28 ℃ ± 2), for 3 weeks, with a 12-hour light-dark cycle to simulate the natural environment. The AEU provided a balanced diet that was fed *ad libitum*. Inoculation was by natural route; that is exposure of cercaria through skin penetration (Tucker *et al*., 2001), with slight modification to suit researcher's procedures; that is the mice snipped between fingers, while exposing shaved abdomen to

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water containing *S. haematobium* cercaria in relatively stable position for 15 minutes. The abdomen was first wipe by use of a gauze sponge, soaked with conditioned water. Mice were put on its abdomen in a 10-cm watch glass; being careful to maintain serenity to ensure no disturbance due to involuntary movement that may disrupt cercarial penetration. The desired cercarial inoculum (seven drops of cercarial water) was pipetted onto the watch glass with the shaved abdomen facing it. During this length of exposure, the mice were kept warm by natural radiation, since the ambient temperature was favorable. Mice were returned to their cages without wiping or washing the exposed sites.

➢ *In Vivo Antischistosomal Bioassays*

In vivo antischistosomal bioassays was according to Metwally, et al., (2018) and Wang et al., (2019). Set I (n=10) involved preliminary investigation for the establishment of schistosomules. Five (5) mice were infected but untreated and 5 uninfected (control). This was carried out to determine the success of infectivity and establishment of the *S. haematobium* schistosomules in the lungs of the mice, 3-7 days post infection – PI (El-Ridi et al., 2010), before being euthanized and sacrificed to assess the presence of schistosomules. The lungs were minced and the tissues were placed in normal saline and observe for tiny "black" rod-like schistosomules under the microscope. Set II (n=10) was the experimental group (infected and treated) with methanolic stem bark extract of *E. africana* at different concentrations (10-100 mg/L). Administration of the *E. africana* ME per mouse was on the 35th day post inoculation (PI); for 5 consecutive days. This was for *in vivo* assessment of antischistosomal efficacy of the *E. africana* ME stem bark extract on the mice, at a baseline standard value of 200mg/kg body weight (Partrick-Iwuanyanwu et al., 2012). Prior to administration of the extract, the mice were reweighed to check for weight gain or loss, which determined the dosages in mg/kg bwt administered. Set III (n=10), were infected and treated with PZQ (positive control) also on the 35th day PI, side by side ME. Whie set IV (n=10) was infected but not treated (negative control) and sacrificed on the 75th day of PI to compare the number of worms with the infected and treated groups (set II and III). All experiments were done in triplicate. Animals were euthanized and sacrificed to determine worm burden in the experimental group (treated with *E. africana* ME), compared to the negative and positive controls. Perfusion of the perivesical (venous plexus) or renal vein and veins surrounding the bladder, hepatic portal vein, and liver was used to assess worms. The percentage reduction of worms challenged and treated with *E. africana* ME versus the infected but treated with PZQ (positive control); was compared to that of infected but untreated (negative control) groups, under a stereo microscope. These were valued by use of the formula: Q = R – S/R x 100 (Metwally, 2006).

Where:
Q = % of worm reduction
R = mean number of parasites recovered from infected animals
S = mean number of parasites recovered from treated animals.

III. DATA ANALYSIS

The therapeutic index – ratio between the pharmacologically acceptable dosage and the dosage within which it produces lethal effect (LD_{50}); based on acceptable protocol in order to assess the safety of extract for *in vivo* administration and/or the antischistosomal bioassay was compared to the standard – Hodge & Sterner Toxicity scale (Ahmed, 2015). The effect of *E. africana* ME on the adult population of *S. haematobium* were assessed using one-way ANOVA. A Brown-Forsythe test was used to determine the level of significance by used of GraphPad® prism 8.4.2 version 2020, the level of significance was calculated at $p = 0.05$, where $p < 0.05$ was considered significant, CI was at 95%.

IV. RESULTS

➢ Acute toxicity evaluation of the stem bark extract

The solvent extracts of *E. africana* did not generate any harmful or clinical effects within the 24-h observation period. There were no obvious reactions such as paw licking, stooling, micturition, lying flat on belly, raised fur, salivation, reduced activity, sedation, convulsion, or quick death. At the second phase, being the highest dosage (5000mg/kg bwt), resulted in reduced activity at about 12 hours of post exposure and one death at 24 hours of post exposure (Table 1). The LD_{50} value showed no toxicity effects at 10-100mg/kg body weight. At phase II (5000mg/kg bwt), revealed slight toxicity, valued at 3807.88mg/kg, comparable to the standard, Hodge & Sterner Toxicity Scale (Appendix I). The LD_{50} value was 3807.88mg/kg bwt; falls within the normal range of 500-5000mg/kg standard scale, indicative that it is slightly toxic. The therapeutic index for ME extract was relatively safe, when administered to albino mice via oral gavage; base on the range value as compared to the standard (Appendix I).

Table 1: Mean Acute Lethal Concentrations (LD_{50}) of *E. Africana* Methanol Stem Bark Extract

Experiment	Dose (mg/kg bwt)	Conc. (mg/ml)	Mortality after 24h
Phase I	10	1	0/3
	100	10	0/3
	1000	100	0/3
Phase II	1600	100	0/3
	2900	100	0/3
	5000	100	1/3

Number of mice per group = 3, Number of deaths per group = 1.

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- *In vivo antischistosomal bioactivities of E. africana methanol stem bark extract*

On Table 2 below, the infected but untreated (negative control group) had high worm burden (189.67±32.52); whereas the positive control that is, treated with praziquantel (PQZ) had the lowest worm burden (0.67±1.16). The worm burden in *E. africana* ME-treated group, decreased with increase in concentration, especially at 70-100mg/l. However, lower concentrations of 10mg/l, revealed that the worm population was relatively high (76.00±21.28), compared to the worm burden at 100mg/l (11.00±3.61), which was significantly less. The infected but untreated group (negative control) had the highest worm population (189. 67±32.52). Worm population reduction followed a relatively dose-dependent pattern.

Antischistosomal *in vivo* bioactivities of *E. africana* methanolic extracts were significantly different ($p \leq 0.0001$, LSD 20.1, CI = 95%) across the different concentrations among the experimental groups, administered intraperitoneally for a 5-day continuous period. The R^2 = 0.96; and F-ratio was 51.33. Overall, worm burden, was largely concentration-dependent in reverse proportion that is, worms burden decreases with increase in concentrations. The maximum worm burden (76.00±21.28) was found at the lowest concentration of 10mg/l, followed by 50.00±15.00 at 20mg/l concentration. While that of 100mg/l concentration, was 11.00±3.61 being the least in the treated groups (Table 2). The total numbers of worms collected at the various concentrations were not substantially different. Ranking across showed values with the same super script were not significantly different. Tukey's multiple comparisons test revealed a significant difference ($p < 0.05$) between 10–100mg/l concentrations, comparable to the negative and positive controls, which had very high and least worm burden respectively.

Table 2: *In vivo* Antischistosomal Bioactivities of *E. africana* Methanol Stem Bark Extract on *S. haematobium* Adult Stage

Concentration (mg/l)	Worm burden (M±SD)*
10	76.00 ± 21.28^{b}
20	50.00 ± 15.00^{c}
30	38.00 ± 5.57^{cd}
40	33.67 ± 6.11^{cd}
50	23.33 ± 5.77^{d}
60	26.00 ± 11.53^{d}
70	18.33 ± 3.06^{d}
80	14.33 ± 3.06^{d}
90	13.67 ± 5.79^{d}
100	11.00 ± 3.61^{d}
Negative Control	189.67 ± 32.52^{a}
Positive control**	0.67 ± 1.16^{e}
LSD	20. 1

** Standard drug (PZQ)

*Mean values ± standard deviation from 3 replicates. There is no significant difference between averages with the same superscript. Superscript with different letters a, b, c, d and e are significantly different at $p < 0.05$ (Turkey's multiple comparison). While cd indicates that true mean value lies between c and d.

V. DISCUSSION

It is a well-known fact that that praziquantel (PZQ) does not guard against reinfection and it is ineffective against the juvenile stage of the schistosomes' parasites (Dejon-Agobe, et al., 2019). Moreover, it has long been established that the continuous use of PZQ has inherent weaknesses elsewhere (Wang et al., 2019; and Acheampong et al., 2020); and this, in addition to the fact that there is currently no vaccine for the treatment of schistosomiasis infection (Molehin, 2020). The aforementioned reasons serve as incentive and driving force in the local search for alternative sources of schistosomiasis treatment that are cheap, easily accessible, and possible sustainability by the locals. This is important for the very fact that most rural farmers, particularly in Northern Nigeria, are involved in fadama or dry season irrigation farming and/or swamp rice cultivation (depending on the season). These groups of farmers are constantly in contact with water environment; hence, are prone to infection and reinfection by the *S. haematobium* parasites. Similarly, occupational practices such as fishing, majorly in riverine communities; who cannot do without regular water-contact (Awosolu et al., 2020); served as occupational risk factors and predispose individuals to continual infection by *S. haematobium*. These are exacerbated by the fact that, most of these farmers have little understanding of the disease and its transmission dynamics. Even individuals who are familiar with the schistosome's disease do not consider it as life-threatening as cases of diseases like malaria. In the course of verbal interactions with some of the residents during snail vector collection, they acknowledge the fact that schistosomiasis is a "water disease"; and that it comes and goes and does not kill. This was with particular reference to cases of haematuria. As such, they have learned to live with it. All of these buttressed the necessity for continual search for alternative schistosomiasis control strategy that could be adaptable to every locality.

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Therefore, the toxicity of *E. africana* stem bark methanol solvent extracts as assessed on the experimental mice by oral gavage and watched for 24 hours, for *in vivo* administration in order to evaluate its antischistosomal properties, was generally found to be safe. The LD_{50} valued at 3807.88mg/kg, was found to be within the acceptable pharmacological – therapeutic index ratio, based on the established protocol (Patrick-Iwauanyanwu et al., 2012; and Ahmed, 2015). This is similar to the work of Saad El-Din, et al., (2023); in *Moringa oleifera* that are known to have less toxicity yet effective in control of *S. mansoni*. Moreover, there was no observable toxicological or clinical effect(s), and/or reaction such as paw licking, stooling, micturition, lying flat on belly, raise hair, salivation, reduce activity, drowsiness, convulsion, or instant death caused by *E. africana* methanol extract on the experimental mice. Thus, the methanol extract was considered safe, since the baseline dose of 200mg/kg body weight utilized; was far less than 5000mg/ml dose that resulted in slight toxicity as compared to Hodge & Sterner Toxicity Scale (Ahmed, 2015).

Again, Tiwari et al., (2011), earlier identified the anthelminthic properties of *E. africana*, which could be responsible for vacuolization and disintegration of the teguments. More so that the phytochemical analysis of *E. africana* plant, revealed the presence of secondary metabolites such as saponins, alkaloids, flavonoids, tannins, and terpenoids (Yusuf and Abdullahi 2019; and Daben and Mwansat, 2024). These metabolites could be associated with significant anthelminthic bioactivities of the plant. Besides, Jatsa et al., (2019), had posited that these metabolites are directly linked to active agents against helminths; and might possibly affect the viability, mobility and fecundity of the adult schistosome worms. Furthermore, findings of this work were also consistent with the works of Santos et al., (2014), who used *Schinopsis brasiliensis*; and Yusuf and Abdullahi (2019), that worked on the phytochemical and pharmacological actions of *E. africana.* These authors, established that the methanolic extract does not show any cytotoxicity effect nor produced any significant modification on the haematological and biochemical parameters. These positions consolidate on the safety and use of *E. africana* extract on the experimental animals. Considering the several health-promoting reports of the major components of some plants such as saponins that is said to reduce cancer risk, lower blood cholesterol level, decrease blood lipids, inhibition of dental caries and reduce incidence of renal stones (Roopashree and Naik, 2019) and as well, having anti-inflammatory effects (González-Madariaga et al., 2020); with wide pharmacological properties (Juang, and Liang, 2020); underscores the importance of *E. africana* for possible drug formulations that can be used in humans, which may serve as a substitute for the conventional and commonly used praziquantel that is usually expensive and inaccessible by most rural communities, especially in Nigeria.

Thus, *in vivo* administration of *E. africana* methanolic stem bark extract to control the schistosome's adult stage; was an attempt at validating the ethnobotanical and ethnopharmacological use of the plant, for probable treatment of urinary and/or intestinal adult schistosome's forms. The resultant effect of treatment of mice (with the *E. africana* extract) infected with *S. haematobium* cercaria; with consequent reduction in number of worms in the infected and treated group, which was lower than those obtained in the untreated group. This could be due to the inducement of tegument damage or a reduction in oviposition and/or worm pairing. Hence, the high potential of *E. africana* methanolic stem bark extract; to contain schistosomicidal property on the adult stage of *S. haematobium* worm parasites. Therefore, this study's findings elucidated the multiple therapeutic properties of the *E. africana* plant, earlier established by Yusuf and Abdullahi (2019).

Moreover, Mvondo et al., (2017) demonstrated experimentally, other medicinal potentials such as decreased dysmenorrhea associated with endometriosis, and also the treatment of female infertility as recorded by Yusuf and Abdullahi, (2019), portrays a high possibility for its use in human population without any adverse side effects. This agrees with the low toxicity level and lack of a toxic effect of *E. africana* extracts in the experimental mice. By implication, with further research such as evaluation of the extracts' sub-acute toxicity effects; denotes a promising antischistosomal agent that can be used among human population. Given that the worm can survive in its human host for more than 10 years (Colley et al., 2014; and Krautz-Petersen et al., 2017); most likely related to host resistance and/or histocompatibility of the human system with the antigens produced by the parasites, as well as immunopathological consequences because of long-term association of the schistosome parasites with its human host. This limits vaccine production that is based on immune responses to schistosome infection in modeled animals as posited by Krautz-Peterson et al., (2017).

The findings in this investigation, compares favorably with the works of Kiros et al., (2014) and Acheampong et al., (2020), who employed ethyl acetate extracts of *Glinus lotoides* fruits and methanolic extracts of several Ghanaian medicinal herbs, respectively. Both studies indicated positive adult worm reduction, however, Kiros et al., (2014) discovered that at a very low concentration of 3.7mg/L, it reduces worm load per mouse by 35.8 percent. Furthermore, the dose-dependent relationship of worm reduction in this study is also related to the discovery made by Oliveira et al., (2014); even though their most effective dosage of 30µg/mL was much lower than the 100mg/l used in this study, it compared favorably with the positive control (treatment with PZQ) of our investigations. It was also consistent with the findings of Yones et al., (2016); and Acheampong et al., (2020), who carried out *in vivo* and *in vitro* administration of ethanolic stem bark extracts of *E. africana* and *Punica granatum* L., respectively. All the authorities posited that the ethanol extracts disrupted the adult male and female pairing of *S. haematobium* worms, rather than the fact that it suppressed oviposition as posited by Oliveira et al., (2014). Additionally, worm population that declines with increasing concentrations of the *E. africana* methanolic plant extract; was in consonant with the results of Tonucci et al., (2012) using *Tagetes erecta* and Muema et al., (2015), used red apple fruits (*Malus domestica*); lemon fruits (*Citrus limon*)

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and onion (*Allium cepa*) bulbs. However, Muema et al., (2015) used a much higher dosage, their minimum (100mg/l) being the highest of this study, underscores the efficacy of *E. africana* extracts. While Tonuci et al., (2012), on the other hand, utilized a significantly lower concentration of 10-100µg/mL; by *in vitro* administration of *Tagetes erecta* essential oils that compared favorably with both the treated group and positive controls of this study. Again, the work by Tekwu et al., (2017) in an *in vitro* administration of stem bark and roots of *Rauwolfia vomitoria* ethanolic extracts resulted in significant a worm reduction following a dose-dependent pattern similar to the findings of this study; even though theirs was at an exposure period of 120h. The strong antischistosomal property of *E. africana* could have been due to separation of adult worm pairs, related to the earlier work recorded by Mohammed et al., (2005); using crushed seeds of *Nigella sativa*, as most worms were not in copula form.

On the contrary, in an earlier study by Abdel-Hameed et al., (2008), discovered earlier that ethyl acetate extract of *Curcuma longa* had more bioactive properties and is more effective in worm reduction than methanol extract, which was used in this study as well as by other authorities (Ismail et al., 2016; and Acheampong et al., 2020). This again, suggests that the biopotency of a plant may not just be related to the solvent employed for extraction, but also to the amounts of secondary metabolites and/or the plants' part in used.

All of these, strongly support the ethnopharmacological and bioactive potential of the *E. africana* plant, which might be employed in drug formulations or antischistosomal agent that can be used in humans. Moreover, there has been no reported illness and/or clinical case among the local population based on the ethnobotanical usage, used in harvesting fish, "piscicidal function" in natural ponds, among the Mushere people of Bokkos LGA in Plateau State (Daben et al., 2023).

VI. CONCLUSION

The methanol stem bark extract of *E. africana* had shown strong potential for antischistosomal therapy that resulted in worm reduction in a dose-dependent pattern. This work provides cheap alternative control measure against schistosomiasis. Further work like sub-acute evaluation, could validate its safety as an antischistosomal agent that is inexpensive and has a high potential for sustainability in rural communities; particularly those with high water-contact activities.

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