Antiplasmodial and Toxicological Properties of *Pentaclethra macorphylla*, *Cnidoscolus aconitifolius* and Semicarbazone (imine derivative)

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INTRODUCTION

- Malaria, a vector borne infectious disease in human, caused by five species of *Plasmodium* and transmitted by female *Anopheles* mosquitoes (WHO, 2015).

- Taylor-Robinson (2014) stated that 3.4 – 3.7 billion of the world population were at risk of contracting malaria and 1 – 3 million death resulting from it.

- Malaria prevention is important to the achievement of sustainable development goal number two, however, it remains a major public healt challenge (WHO, 2015).
- Artemisinins combination therapies (ACTs) are now first line antimalarial drugs, but, recent report shows some challenges (Cui and Su, 2009; Enserink, 2010).

- Hence, efforts are being made to discover alternatives to ACTs through different drug discovery processes, thus, the essence of this research to determine the potential of synthetic and natural products as an alternative antimalarial drug candidate(s).

- New drugs introduced into the therapeutic arsenal are mostly derived from natural products (Newman and Cragg, 2012).

- Plants provide secondary metabolites that are useful for the treatment of protozoan diseases such as Malaria (Pohlit *et al*., 2013).

- Quinine and Artemisinin are both products of traditionally used antimalarial plants (Frausin *et al*., 2015);

- The African oil bean (Ugba/Ukpaka (common local name)/ *Pentaclethra macrophylla*) is a tropical tree crop found mostly in Southern and Middle-belt regions of Nigeria.
- Seed extract has a wide range of activity against infectious agents with minimal toxicity (Okorie et al., 2006).
- *Cnidoscolus aconitifolius* (Tree spinach), particularly the shoots and leaves are used traditionally against a number of ailments(Rates, 2001).
- Semicarbazone is a derivative of imines formed by a condensation reaction between a ketone or aldehyde and semicarbazide.
- Ahsan *et al*. (2011), reported that Semicarbazones has a wide range of biological activity; also Beraldo and Gambino (2004) reported that Semicarbazones has anti-protozoal properties.

Figure 1a: African Oil Bean Plant

Figure 1b: Tree Spinach Plant

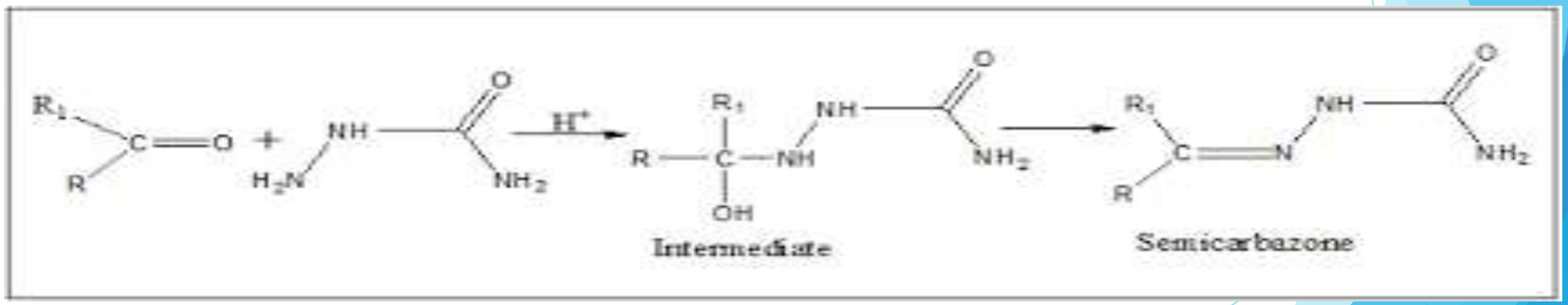

Figure 1c: Chemical synthesis and structure of Semicarbazone

Source: Google Images.

AIM

- The aim of this study was to determine the Lethal Dose (LD50) and antiplasmodial activities of semicarbazone and the crude extracts of *Pentaclethra macrophylla* seeds and, leaves of *Cnidoscolus aconitifolius*

MATERIALS & METHODS

- PLANT COLLECTION AND AUTHENTICATION: seeds of *Pentaclethra macrophylla* and leaves of *Cnidoscolus aconifolus* plants were collected from within Covenant university, Ota, Ogun state; identified and authenticated by a Plant taxonomist from Covenant Univesity Biological Sciences department.

- EXPERIMENTAL ANIMALS: Swiss albino mice (*Mus musculus*) of either sex between 18 -25g were used.

- PARASITES: Chloroquine-Sensititive *Plasmodium berghei berghei* NK65 was obtained from National Institute for Medical Research (NIMR), Lagos, Nigeria.

- ETHICAL APPROVAL: sought and given by Covenant University Biological Science Ethical Review Committee.

MATERIALS & METHODS

- PLANT EXTRACTION: based on the method as described by Nwodo et al., 2010 and Oyegbami and Odetola, 2010; for *Pentaclethra macrophylla* and *Cnidoscolus aconifolus* respectively.

- COMPOUND (Semicarbazone) FORMULATION: as described by the method of Shriner *et al*., 1999.

- TOXICITY TEST: $LD_{50\ of}$ the test compound and plant extracts were determined according to the method by Lorke (1983).

- ANTIPLASMODIAL ACTIVITY: determined by modified Peter's (1965) chemosuppressive method.

RESULTS

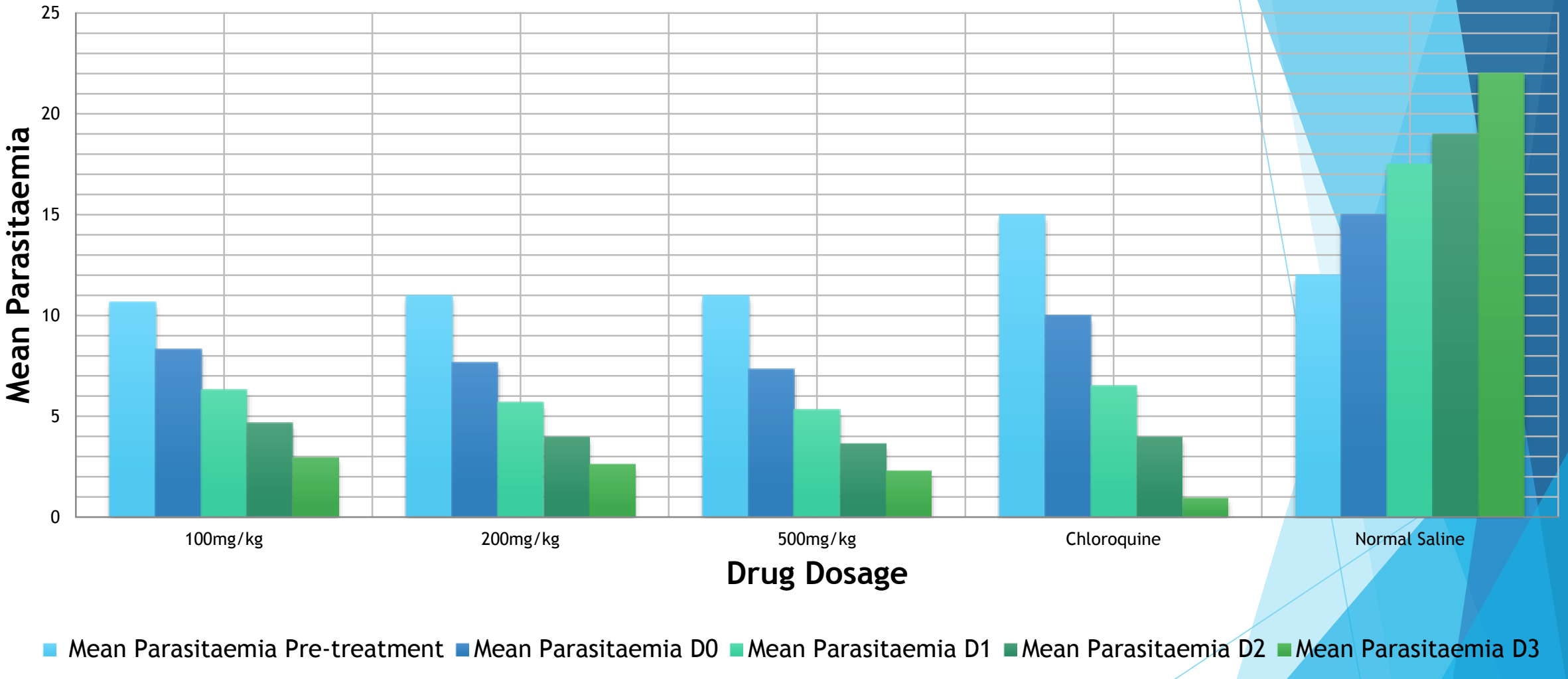

Figure 2: Mean daily parasitaemia at various concentrations of Semicarbazone

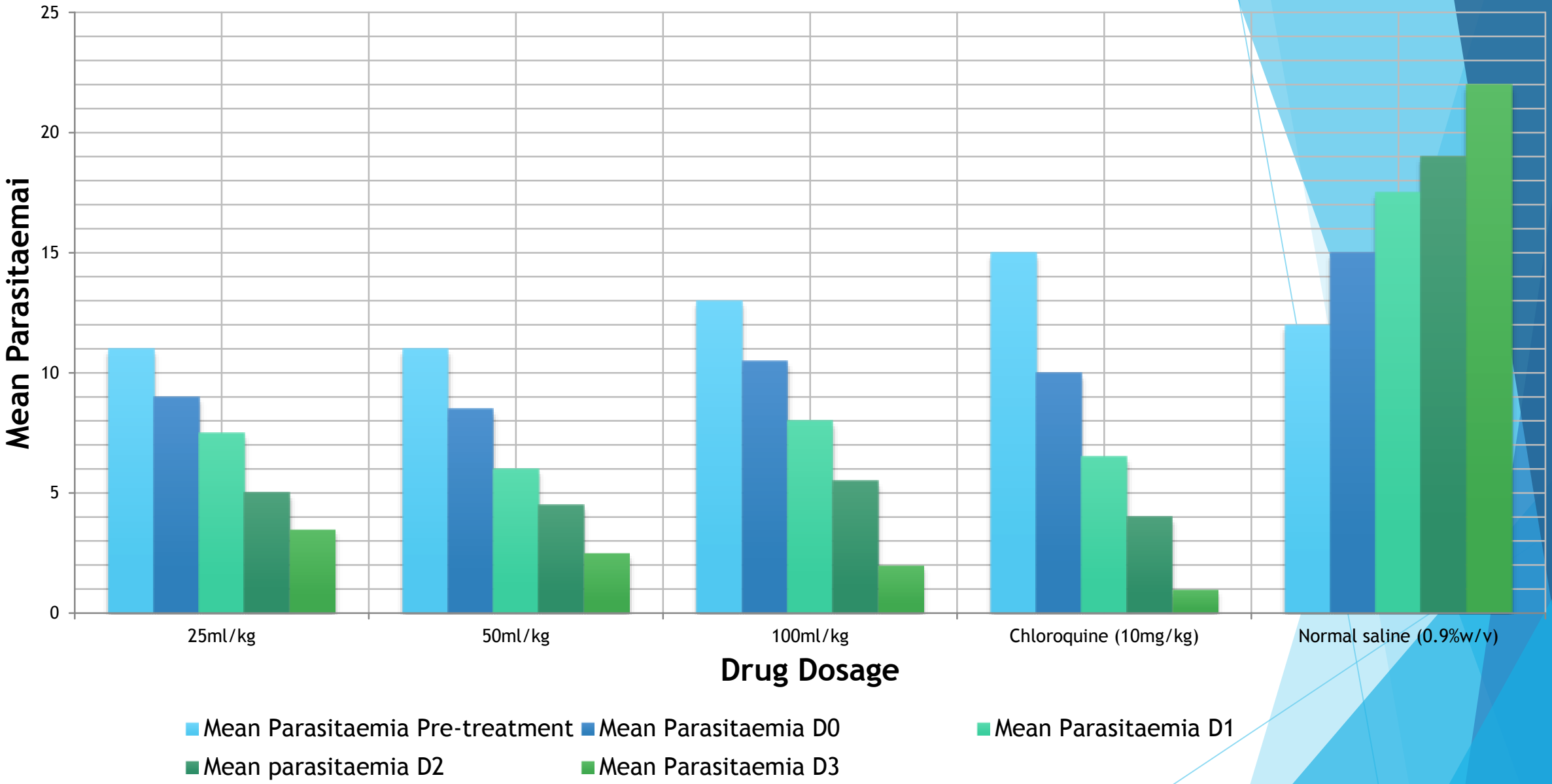

Figure 3: Mean daily parasitaemia at various concentrations of ethanolic extract of *Penthaclethra macrophylla*

Table 1: Percentage chemosuppression of the Semicarbazone

Drug	Dose	Percentage chemo-suppression (%)
Physiological saline	0.5ml/kg	0
Semicarbazone	100mg/kg	86.36
	200mg/kg	87.86
	500mg/kg	89.41
Chloroquine Phosphate	10mg/kg	95.45

Table 2: Percentage Chemo-suppression of the ethanolic extract of *P. macrophylla* seed

Drug	Dose	Percentage chemo-suppression (%)
Physiological saline	0.5ml/kg	0
P. macrophylla	25mg/kg	84.09
	50mg/kg	88.63
	100mg/kg	90.90
Chloroquine Phosphate	10mg/kg	95.45

Table 3: Percentage Chemo-suppression of the Ethanolic Extract *C. aconitifolius* leaf

Drug	Dose	Percentage chemo-suppression (%)
Physiological saline	0.5ml/kg	0
C. aconitifolius	25mg/kg	85.0
	50mg/kg	79.09
	100mg/kg	94.09
Chloroquine Phosphate	10mg/kg	95.45

DISCUSSION

- Many therapeutic medications can be acutely toxic, but are beneficial when used at the appropriate concentrations .This was determined in this study by oral administration of the test substances.
- Oral administration of Semicarbazone at concentrations of 100mg/kg, 200mg/kg and 500mg/kg attested to be safe, no lethality was experienced after 72 hours after dose administration in the test animals.
- For the Ethanolic extract of *Pentaclethra macorphylla and Cnidoscolus aconitifolius* , oral acute toxicity performed at 25, 50, and 100mg/kg had no lethal effect on the test animals after 72 hours.
- Upon physical examination of the test animals during the first 4 hours until the end of 72 hour observations, there was no trembling, changes in skin and eye colour, no falling off of fur, no unusual sleep.

- The *in vivo* animal models was used in consideration of the possible pro-drug effect and a likely involvement of the immune system in eradicating the parasites (Waako *et al.*,2005).
- The chemo-suppressive activity of Semicarbazone , *Pentaclethra macrophylla and Cnidoscolus aconitifolus* as presented in tables 1-3 respectively showed that the test substances have a good potential as an antimalarial candidate when compared to the result of the standard antimalarial drug (Chloroquine) used in the test.
- The antiplasmodial effect or the chemosuppressive activity demonstrated by the chemically synthesized Semicarbazone confirms the previously evaluated antimalarial activity of Semicarbazone with a percentage chemosuppression of 61% at 20mg/kg (de Oliveira *et al.*, 2008).

- The results from this study are comparable with earlier studies where the percentage chemosuppression was above 50% for ethanolic and other extracts of indigenous medicinal plants (Deharo *et al*., 2001; Okorie *et al*., 2006; Olasehinde *et al*., 2012, 2014).

- While the standard drug chloroquine caused chemosuppressions of 95.45%. This was obviously higher than the groups treated with the plant extracts. The observed higher efficacy of Chloroquine may in part be due to non-selectivity of the extract or slow absorption and poor bio-availability of the extract. This is common with medicinal plant extracts (Adzu and Haruna, 2007)

CONCLUSION

The study showed that the synthesized compound, semicarbazone, the ethanolic extracts of *Pentaclethra macorphylla and Cnidoscolus aconitifolius* possess potent antimalarial effect and as such may be a good antimalarial candidates. However, Further research should be done in a bid to determine the bioactive compound s from each plant extract, re-validate their potential and determine their mechanism of action.


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