Original Research Article

ANTIPLASMODIAL PROPERTIES, TOXICITY AND NOVELTY-INDUCED BEHAVIOR OF A FORMULATION FROM PICRALIMA NITIDA AND ALSTONIA BOONEI

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ABSTRACT

Aims: This study aimed at investigating the antiplasmodial activities of the combination of A. boonei De Wild (Apocynaceae) stem-bark and P. nitida (Stapf) T.&H.Dur. (Apocynaceae) seed, which is currently being produced as MAMA Syrup (MS) for malaria treatment in Nigeria. The study has also provided information on the CNS and sub-chronic toxicity effects of MS. This is to justify the folkloric use of the mixture of the two plants as an antimalarial remedy as well as the safety of MS.

Methodology: Swiss albino mice of both sexes, (18-22 g), were used for the antiplasmodial experiments with the freeze-dried extractive from the decoction of the 1:1 mixture of the two plants against chloroquine-sensitive Plasmodium berghei NK65 strain. For the toxicity and novelty-induced behavioral (NIB) studies, twenty four rats were divided into four groups (n=6 per group) for three dose levels of MS and the vehicle. The NIB was observed on both day 1 and day 30 of administration of MS and the vehicle. The animals were sacrificed on day 30 and the blood sample obtained for biochemical assays.

Results: The results of the antiplasmodial investigation showed that 12.5 mg/kg extractive of the plant mixture gave antiplasmodial activity equivalent to 82% of the activity of chloroquine (5 mg/kg). The NIB results showed that acute oral administration of MS had no significant effects while the sub-chronic administration caused a significant (P<0.05) increase in rearing but decrease in grooming behaviours, dose-dependently. The biochemical parameters were not affected by the administration of MS at all doses used.
Conclusion: The extractive of the plant mixture possessed antiplasmodial activity while the oral sub-chronic administration of MAMA syrup had central excitatory effects but no significant toxicity potentials in rats.

Keywords: Mama syrup, antiplasmodial, mice, herbal, toxicity

1. INTRODUCTION

*Picralima nitida* (Stapf) Th. & H. Dur. (Apocynaceae) is commonly known as akuamma seeds and locally known in Nigeria by the Igbo as “Osi”, “Osu-Ogwe” and Yoruba as “Abere”. Extracts of the leaves, seeds or stem bark are used in the preparation of various fever-remedies for malaria. In Central Africa, it is used for the treatment of primary hypertension, malaria and jaundice. In the herbal markets of Ghana, Nigeria and Ivory coast, akuamma seeds, stem-bark and dried fruits are highly priced as antimalarial agents [1]. The plant has been reported to have antitrypanosomal [2], anti-inflammatory and analgesic [3], antidiarrhoeal [4], antimicrobial [5], *in vitro* and *in vivo* antiplasmodial [6, 7] activities. The seed monograph is already contained in the first edition of Nigerian Herbal Pharmacopoeia [8]. *Alstonia boonei* De Wild (Apocynaceae), commonly known as cheesewood, is widely distributed in Africa and it is used in folklore medicine to treat various ailments such as malaria, fever, intestinal helminthes, rheumatism, hypertension, etc. [9, 10, 11]. The plant is known in Nigeria as “ahun” in Yoruba and “egbu-ora” in Igbo, The stem-bark is commonly used for malaria and it is so listed in the West African Herbal Pharmacopoeia [12] as an antipyretic/antimalarial drug with anti-inflammatory and analgesic activities [12, 13, 14]. The extract of the stem-bark have been known to possess potent neuroleptic and anxiolytic properties in behavioral studies using mice [15]. Various studies have shown that the principal chemical constituents in the plant are indole alkaloids from which echitamine, alstonine, alstonidine, amyrin, lupeol, porphyrine, triterpenes and ursane have been isolated [16, 17]. Despite the favourable reports on *P. nitida* seed and *A. boonei* stem-bark individually, there has been no scientific study to verify the antimalarial efficacy and safety of their mixture which is already being exploited for MAMA Syrup production by the Village Chemist of Nigeria.

2. MATERIALS AND METHODS

2.1 Plant Materials

The stem-bark of *Alstonia boonei* was collected from Moremi Hall garden, Obafemi Awolowo University (OAU), Ile-Ife while the seed of *Picralima nitida* was purchased from Oja-Oba market Osogbo in January, 2014, identified and authenticated by comparison with the herbarium specimens of previously collected and preserved samples in the IFE Herbarium of Botany Department, OAU, Ile Ife, Nigeria with the herbarium numbers IFE 16536 (*A. boonei* De Wild [Apocynaceae]) and IFE 17430 (*P. nitida* [Stapf] T.&H.Dur. [Apocynaceae]). Both plant materials were oven dried at 50°C separately.
2.2 Sample of MAMA Syrup

The sample of MAMA Syrup, used for this study was supplied by the Village Chemist outfit in the Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Nigeria, where it is produced and sold as a paediatric dosage form for malaria.

2.2.1 Preparation of MAMA Syrup by the Village Chemist

Mixture of equal weight (500 g) of A. boonei stem-bark and P. nitida seed (ratio 1:1) was decocted in water, filtered and made to volume of 5 L with Syrup B.P. [18], preserved pharmaceutically and then packaged for the market and for sale.

2.3 Drugs

Anesthetic ether, sodium hydroxide pellets (BDH), sucrose (0.25 M), normal saline, absolute ethanol (BDH), freshly prepared distilled water, formalin, cholesterol, assay kits for: Alkaline phosphatase (ALP), triglyceride, Alkaline aspartate transaminase (AST), Alkaline transaminase (ALT) (Antrim, United Kingdom).

2.4 Antiplasmodial studies

2.4.1 Extraction of plant materials

Mixture of equal weight (150 g each) of A. boonei stem-bark (chopped into small pieces) and P. nitida whole seed, was boiled in 1.5 L of distilled water for 1 h [19]. The decoction was filtered, concentrated in vacuo at 70°C and followed by freeze-drying. The freeze-dried residue, labeled “extractive”, was stored in sealed amber bottles and stored in a dry cupboard until ready for use.

2.5. Animals for antiplasmodial activity

Swiss albino mice of both sexes, weighing 18-22 g, were purchased from the animal house of the Faculty of Basic Medical Sciences, College of Health Sciences, Obafemi Awolowo University, (OAU), Ile-Ife, Nigeria. The animals were housed under a 12 h light /dark cycle with free access to water and commercial food pellets, purchased from Capsfeed Limited, Osogbo, Nigeria. They were acclimatized for two weeks prior to the assay. For toxicity and novelty-induced behavioral studies, twenty four (24) young albino rats of both sexes were procured as above and brought to the animal house of the Faculty of Pharmacy, OAU, Ile-Ife. All the animals were kept under standardized environmental conditions and had free access to food and water. All authors hereby declare that “Principles of laboratory animal care” (NIH publication No. 85 – 23, revised 1985) were followed, as well as specific national laws where applicable.

All experiments have been examined and approved by the Faculty of Pharmacy Postgraduate ethical Committee, Obafemi Awolowo University, Ile-Ife, Nigeria.
2.6. Parasite strain.

Chloroquine-sensitive *Plasmodium berghei* NK65 strain was obtained from the Institute of Advanced Medical Research and Training, University of Ibadan, Nigeria. The parasites were maintained in continuous blood passage in mice. A standard inoculum of $1 \times 10^7$ parasitized erythrocytes was prepared by dilution of blood harvested from a donor mouse (> 30% parasitaemia) with normal saline and administered intraperitoneally (200 µL) to each mouse.

2.7. Early-infection (chemosuppressive) Test [20].

Thirty (30) animals were intraperitoneally inoculated, 4 h prior to dosing. The animals were grouped into 6 groups of 5 mice per group. Groups 1 - 4 were respectively given doses of the freeze-dried extractive at 1.56, 3.13, 6.25 and 12.5 mg/kg per mouse/day for 4 consecutive days ($D_0$ – $D_3$). Group 5 mice were similarly dosed orally with 5 mg/kg/day chloroquine as positive control while Group 6 received 0.2 ml distilled water/mouse/day as negative control. Doses were given once daily, using a metal feeding cannula. On the fifth day ($D_4$), the parasitaemia level of each mouse was assessed by examining and counting the cells in the Giemsa-stained blood smears. The percentage of parasitaemia was determined by recording the number of parasitized erythrocytes out of 500 red blood cells in random fields under light microscope and calculating the average percentage parasitaemia suppression using the formula $100 \cdot \frac{(\text{A} - \text{B})}{\text{A}}$, where $\text{A}$ is the average percentage parasitaemia in the negative control group and $\text{B}$ is the average parasitaemia in the test group.

2.8 Acute toxicity

The LD$_{50}$ of the freeze-dried extractive of the plant mixture was determined *in vivo* using the procedure described by Lorke [21]. In the first phase, nine mice were randomly divided into three groups of three mice each and each group received the freeze-dried extractive at 10, 100 and 1000 mg/kg body weight orally (via a feeding cannula), respectively. The mice were then observed for signs of adverse effects and deaths for 48 h and 14 days. In the second phase, four mice were divided into 4 groups of 1 mouse each and were each similarly treated with the extractive at doses of 1000, 1600, 2900 and 5000 mg/kg orally, respectively. The animals were then monitored for any toxic symptoms or mortality over a period of 14 days.

2.9. Administration of MAMA Syrup

Eighteen (18) of the 24 rats were administered with *MAMA Syrup* at three dose levels ($n=6$ per group) and the remaining six animals (3 males and 3 females) were administered with the vehicle (distilled water) as negative control and were subjected to the same conditions as the drug-treated animals. The three dose levels tested in the animals were based on the regular paediatric daily dose of 40 mL (in 2 divided doses), given to a child of 20 kg average weight as follows: Low Dose: 1 µL/g (150 mg/kg); Regular Dose: 2 µL/g (300 mg/kg); High Dose: 4 µL/g (600 mg/kg). The drug was administered to the animals.
using the oral syringe, twice daily for 30 days. The first dose was always administered at 8 a.m. while the second dose was always administered at 6.00 p.m. The animals were observed daily for any drug reaction having been provided with feed and water *ad libitum* for a period of 30 days and kept in the animal house of the Faculty of Pharmacy, OAU, Ile-Ife.

### 2.10. Novelty-induced Behavior

Novelty-induced behaviors (Locomotion, rearing and grooming) were scored one hour (1 h) after the second dose of drug or vehicle *as above* by oral administration (150, 300 or 600 mg/kg) on day 1 (acute) and on day 30 (sub-chronic). Each rat was separately placed in the open field box and was scored for locomotion, rearing and grooming behaviors. They were each scored for a period of 30 minutes at 10 minutes time intervals. Locomotion was scored when the animal crossed one floor unit or square into another, fully with all its four legs in the square. Rearing was scored when the animal stood on its hind limbs with its fore limbs against the wall or in the air. Grooming was scored when the animal picked its body with its mouth or washed its face with its limbs. After an animal has been studied for its novelty-induced behavior, the open field box was cleaned with cotton wool soaked with ethanol to prevent interference of any odor with the next animal.

### 2.11. Blood and organ collection

After 30 days, the animals were anaesthetized individually in the anaesthetizing chamber already saturated with anaesthetizing ether. The animals were carefully dissected after they have been confirmed anaesthetized. Cardiac puncture technique was used to obtain the blood, which was then transferred into the pre-labeled heparinised sample bottles and gently rolled to allow the blood to mix thoroughly with the anticoagulant. Part of the liver sample obtained was also used along with the blood samples for biochemical analysis.

### 2.12. Biochemical analysis

#### 2.12.1. Collection of plasma

The heparinised blood samples were centrifuged at 5000 rpm for 5 minutes. The supernatant layer (containing the plasma) was aspirated using a 1000 µL micropipette and transferred to a well labeled plastic container with a stopper. The entire plasma samples were kept in the freezer until needed for biochemical analysis. The following biochemical parameters were determined: Triglyceride (TAG), Total cholesterol, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) using a commercially available assay kits made by RANDOX laboratory Ltd, antrim UK.
2.12.2. Preparation of the liver homogenates
Each of the liver samples was taken out of the freezer, blotted out of any blood in it and the weight was determined by using the electronic balance. It was homogenized using an electronic homogenizer (stir-R) at 1600 rpm. A 10% homogenate was prepared in 0.25 M sucrose. The homogenates were kept in the freezer until needed for analysis.

2.13. Statistical analysis
The results were expressed as mean ± SEM. The variation in a set of data was analyzed through one-way analysis of variance and the difference among the means was considered at 95% confidence level using the post-hoc test of Dunnett.

3.0 RESULTS
The yield of freeze-dried extractive from the decoction of 1:1 mixture of *A. boonei* stem-bark and *P. nitida* seed was 6.5% w/w. The result of the acute toxicity study (LD$_{50}$) on the freeze-dried extractive showed no signs of toxicity or mortality at doses up to 5000 mg/kg, after 14 days of observation. In the chemosuppressive experiment, there was a dose-dependent reduction of parasitaemia in the extractive-treated mice which was significantly different from the untreated control at all the doses tested (Table 1 & Fig. 1).

Table 1: *In vivo* antiplasmodial activities of the extractive from the decoction of 1:1 mixture of *A. boonei* stem-bark and *P. nitida* seed in mice

<table>
<thead>
<tr>
<th>Doses of extractive (mg/kg)</th>
<th>Average % chemosuppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.56</td>
<td>35.5 ± 3.8*</td>
</tr>
<tr>
<td>3.13</td>
<td>39.5 ± 1.6*</td>
</tr>
<tr>
<td>6.25</td>
<td>50.3 ± 3.7*</td>
</tr>
<tr>
<td>12.5</td>
<td>52.4 ± 2.3*</td>
</tr>
<tr>
<td>Chloroquine (5 mg/kg)</td>
<td>65.3 ± 1.4</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± standard error of mean, (n=5) * P < 0.01,  a P < 0.05 compared to Chloroquine at 5 mg/kg.
Figure 1: Effects of different doses of the extractive from decoction of 1:1 mixture of *P. nitida* seed and *A. boonei* stem-bark on parasitaemia in *P. berghei*-infected mice using the early malaria infection test. Test drugs: significant from negative control, * P < 0.001

[NC = Negative control (distilled water), PC = Positive control (Chloroquine)]

Novelty - induced behavior

The novelty – induced behavior during acute administration of *MAMA syrup* showed no significant difference in rearing and grooming behavior in the treated rats compared with the vehicle-treated control (Table 2). However, there was a significant (*F* (3, 23) = 5.10, *P* < 0.05) effect on locomotor activity at the dose of 600 mg/kg (high dose). After sub-chronic administration of *MAMA syrup*, there were significant (*F* (3, 23) = 3.38 *P* < 0.05), (*F* (3, 23) = 14.46 *P* < 0.05 and *F* (3, 23) =17.84; *P* < 0.05) effects on locomotion, rearing and grooming behaviors in rats, respectively (Table 3). Locomotor activity was only significantly increased at the dose of 600 mg/kg, rearing behavior was only significantly increased at the dose of 150 mg/kg while grooming was significantly decreased dose-dependently.
Table 2: Effects of oral acute administration of MAMA Syrup on NIB in rats

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Locomotion (30 min)</th>
<th>Rearing (30 min)</th>
<th>Grooming (30 min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>44.20 ± 14.00</td>
<td>24.50 ± 6.40</td>
<td>16.30 ± 5.50</td>
</tr>
<tr>
<td>150</td>
<td>57.50 ± 2.60</td>
<td>22.50 ± 2.00</td>
<td>12.50 ± 0.70</td>
</tr>
<tr>
<td>300</td>
<td>36.00 ± 8.60</td>
<td>26.20 ± 6.60</td>
<td>13.00 ± 2.10</td>
</tr>
<tr>
<td>600</td>
<td>91.70 ± 3.10*</td>
<td>24.50 ± 3.10</td>
<td>10.80 ± 1.20</td>
</tr>
</tbody>
</table>

All Results are expressed in mean ± S. E.M. Number of rats used for each treatment group (n=6)

*P = 0.05 compared with control.

Table 3: Effects of oral sub-chronic administration of MAMA Syrup on NIB in rats

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Locomotion (30 min)</th>
<th>Rearing (30 min)</th>
<th>Grooming (30 min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>36.20 ± 7.00</td>
<td>25.50 ± 2.30</td>
<td>33.30 ± 3.10</td>
</tr>
<tr>
<td>150</td>
<td>35.20 ± 3.70</td>
<td>41.70 ± 4.30*</td>
<td>16.80 ± 2.40*</td>
</tr>
<tr>
<td>300</td>
<td>44.50 ± 2.30</td>
<td>18.50 ± 2.10</td>
<td>18.80 ± 1.90*</td>
</tr>
<tr>
<td>600</td>
<td>55.20 ± 5.80*</td>
<td>19.20 ± 2.00</td>
<td>10.80 ± 1.20*</td>
</tr>
</tbody>
</table>

All Results are expressed in mean ± S.E.M. Number of Rats used for each treatment group (n=6)

*P = 0.05 when compared with control.

Percentage Change in Body Weight

One–way ANOVA showed that there was no significant (F (3, 23) = 0.5949; P = .05) difference in the final body weights of animals in the various groups administered orally with MAMA syrup (Fig. 2) when compared with the control group (Vehicle-treated rats).
Fig.2: Effects of oral sub-chronic administration of MAMA Syrup on body weight in rats. All Results are expressed in mean ± S.E.M., n=6 per group.

Biochemical Assay for MAMA Syrup
One-way ANOVA indicated no significant difference in the biochemical assay for triglycerides, cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphates (ALP) for the various groups of control, lower dose, the normal dose, and higher dose in both the plasma and liver samples from the rats administered with MAMA Syrup (Tables 4 and 5).

Table 4: Biochemical analysis for MAMA Syrup (plasma)

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>TRIG (mg/dl)</th>
<th>CHOL (mg/dl)</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>ALP (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>153.37 ± 2.33</td>
<td>165.95 ± 6.23</td>
<td>38.37 ± 1.05</td>
<td>120.09 ± 1.00</td>
<td>122.87 ± 0.91</td>
</tr>
<tr>
<td>150</td>
<td>144.42 ± 2.88</td>
<td>151.80 ± 2.19</td>
<td>37.96 ± 1.21</td>
<td>118.06 ± 1.87</td>
<td>122.56 ± 2.05</td>
</tr>
<tr>
<td>300</td>
<td>152.39 ± 3.36</td>
<td>164.16 ± 6.62</td>
<td>38.95 ± 1.19</td>
<td>119.70 ± 1.67</td>
<td>120.98 ± 2.10</td>
</tr>
<tr>
<td>600</td>
<td>153.12 ± 2.57</td>
<td>158.36 ± 2.91</td>
<td>39.73 ± 1.20</td>
<td>120.49 ± 2.35</td>
<td>124.63 ± 1.83</td>
</tr>
</tbody>
</table>

All Results are expressed in mean ± S.E.M. Number of rats used for each treatment group (n=6)

TRIG – Triglycerides; CHOL – Cholesterol; ALT – Alanine aminotransferase; AST – Aspartate aminotransferase; ALP–Alkaline phosphates.
Table 5: Biochemical analysis for MAMA Syrup (liver)

<table>
<thead>
<tr>
<th>Group</th>
<th>TRIG (mg/dL)</th>
<th>CHOL (mg/dL Tissue)</th>
<th>ALT (U/L Protein)</th>
<th>AST (U/L Protein)</th>
<th>ALP (U/L Protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4.82 ± 0.32</td>
<td>11.85 ± 0.47</td>
<td>25.54 ± 1.07</td>
<td>15.65 ± 0.83</td>
<td>46.13 ± 2.03</td>
</tr>
<tr>
<td>150</td>
<td>4.35 ± 0.25</td>
<td>11.06 ± 0.79</td>
<td>23.12 ± 1.16</td>
<td>14.52 ± 1.04</td>
<td>42.35 ± 1.09</td>
</tr>
<tr>
<td>300</td>
<td>4.54 ± 0.28</td>
<td>11.33 ± 0.65</td>
<td>24.05 ± 1.57</td>
<td>15.32 ± 0.87</td>
<td>41.53 ± 1.20</td>
</tr>
<tr>
<td>600</td>
<td>4.76 ± 0.20</td>
<td>10.60 ± 0.47</td>
<td>23.93 ± 1.35</td>
<td>15.70 ± 0.87</td>
<td>43.00 ± 1.48</td>
</tr>
</tbody>
</table>

All Results are expressed in mean ±S.E.M. Number of Rats used for each treatment group (n=6)

TRIG – Triglycerides; CHOL – Cholesterol; ALT – Alanine aminotransferase; AST – Aspartate aminotransferase; ALP – Alkaline phosphates.

4.0 DISCUSSION

The LD_{50} (safety) test, carried out on the freeze-dried extractive from the decoction of ratio 1:1 mixture of P. nitida seed and A. boonei stem-bark showed no sign of acute toxicity in mice. All the doses tested produced considerable antiplasmodial activities in mice. Although the values were lower than the positive control (chloroquine at 5 mg/kg) \((P > 0.05)\), at 6.25 mg/kg dose of the freeze-dried extractive, up to 77\% of chloroquine activity was achieved while at 12.5 mg/kg, the extractive gave up to 80\% of the activity of chloroquine in mice. Thus, at these doses of the extractive, chloroquine at the usual dose of 5 mg/kg was only 1.2 to 1.3 times more potent. Translating this into an index of comparison in antimalarial studies, the chloroquine-equivalent of the freeze-dried extractive at 6.25 mg/kg is 0.77 while at 12.5 mg/kg, the chloroquine-equivalent is 0.82.

The results of the novelty-induced behaviors with MAMA Syrup showed that the acute administration produced significant \((p<0.05)\) effect only on locomotor activity at the highest dose (600 mg/kg) administered while there was no significant effect at doses of 150 and 300 mg/kg. Both rearing and grooming behaviors were not affected by MAMA Syrup, thus, suggesting a possible central excitatory effect on the animal. The sub-chronic administration of MAMA Syrup at doses administered caused significant central effects in rats with significant effects on locomotion at the dose of 600 mg/kg and increase in rearing behavior at the dose of 150 mg/kg, further supporting possible central excitatory effects. Grooming behavior was significantly decreased dose-dependently due to sub-chronic administration of MAMA Syrup to rats. This suggested a possible relaxation effect since grooming is known to increase due to anxiety in rats. Grooming is a behavior through which the animals care for their body surface. Throughout the 30 days of administration of MAMA Syrup, there was no significant manifestation of any unexpected reaction. None of the animals administered with the drug died. For the percentage change in body weight, ANOVA indicated no significant variation among the various groups of vehicle-treated and MAMA Syrup-treated rats. This shows that MAMA Syrup does not cause any significant change in the body weight. For the biochemical assay, the plasma concentration of
triglycerides, cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) showed no significant variation between the *MAMA Syrup*-treated groups and the vehicle-treated group. In addition, the liver concentration of triglycerides, cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) indicated no significant difference among the various groups of rats administered with *MAMA Syrup*. Damage to the essential internal organs such as liver, kidney, testes, spleen, brain and lungs often results in the elevation of biochemical parameters such as plasma and liver enzymes namely: AST, ALT and ALP [22]. Thus, the results clearly indicated that *MAMA Syrup* has no significant deleterious effects on the essential organs biochemically and that the absence of any significant increase in the biochemical parameters (cholesterol, triglyceride, alkaline phosphatase, AST and ALP) showed that *MAMA Syrup* did not have any sub-chronic toxicity.

5.0 CONCLUSION
The results obtained in this study showed that the decoction of *P. nitida* seed and *A. boonei* stem-bark mixture in ratio 1:1 possessed considerable antiplasmodial activities, thereby confirming the ethnomedical claims. *MAMA Syrup*, prepared from the same plant combination possessed significant central excitatory effects when administered sub-chronically but showed no significant toxicity potential biochemically on the essential organs of rats. Indeed, *MAMA Syrup*, as an antimalarial remedy is not used chronically but for only 4 to 5 days in any malaria episode. Nevertheless, we have planned to examine other combination ratios of the two plants as well as the chronic toxicity in order to maximize the safety documentation and to optimize the potency of *MAMA Syrup*.

REFERENCES


