INTRODUCTION

There has been a rapid expansion of allopathic system of medical treatment in many countries during the past century. However, some of these drugs have adverse effect and people are going back to nature with hope of safety. On the other hand, herbs are safe, cheaper, easily available and with no fear of any side effects. A number of interesting outcomes have been found with the use of a mixture of natural products or plant extracts to treat diseases. It is evident that many valuable herbal drugs have been discovered by knowing that particular plant was used by the ancient folk healers for the treatment of some kind of ailment. Moreover, the medicinal plant wealth is our national heritage and it seems to be the first and foremost line of defense for the treatment of various diseases mostly in tribal and rural communities. The study of natural products has had a number of rewards. It has led to the discovery of a variety of useful drugs for the treatment of diverse diseases and contributed to the development of separation of science and technology, spectroscopic methods of structure elucidation and synthetic methodologies that is now the basis of analytical organic chemistry. In recent years, traditional medicine has received renewed interest from scientists because of the advent of multidrug resistant microorganisms, serious side-effects obtained with a number of synthetic drugs, and because of the incurable nature of a number of diseases, where modern medicine seems to have failed to make any positive impact. The demand for herbal medicines is increasing rapidly due to their fewer of side effects. Further as health care costs continue to escalate, the attraction for low-cost remedies has stimulated consumers to re-evaluate the potential of alternatives.

Literature has shown that some plants have found application in medicine. In Africa, particularly in Nigeria, herbal medicine has become a part of peoples culture though this form of medicine is not well organize as in China and India. The Nigerian flora has made and would continue to make great contributions to health care of Nigerians. In fact the indigenous medicinal plants form an important component of the natural wealth and culture of Nigeria. Natural plant products have been used in Nigeria especially in the tropical rain forest zone of Southern Nigeria in local medicinal practice but very little of such substance has been subjected to scientific verification. Vitex doniana Sweet, a plant commonly known black plum, in English, Prunier noir in French, dinyo in Hausa , ucha koro in Igbo, ooori-mla in yoruba and ngarmi in Kanuri is a medium-sized deciduous tree, 8-18m high, with a heavy rounded crown and a clear bole up to 5m. V. doniana is from Verbenaceae family and abundantly occurring in savannah regions. Vitex specie has a lot of medicinal importance. It has been has been traditionally used to treat a number of ailments, but with particular emphasis on menstrual disorders and related hormonal problems. Vitex possesses anti-inflammatory and antibacterial properties it has been reported that one of the Vitex specie called vitex negundo antihistamine properties. Also there is a reported anti-inflammatory and antipyretic properties of methanolic leaf extracts of Vitex doniana. This study aim at evaluating anti-inflammatory, anticonvulsant and antipyretic activities of stem bark ethanolic extract of V. doniana Sweet.

MATTERIAS AND METHODS

Sample collection and identification

The stem bark of Vitex doniana leaves were collected in Kawuri village of Konduga (11°39'6"N 13°25'10"E) Local Government Area of Borno state of Nigeria. The plant specimen was identified and authenticated by a Plant Taxonomist, Prof. S.S. Sanusi of the Department of...
Biological Sciences, Faculty of Science, and University of Maiduguri. The herbarium specimen with a voucher number 555C was deposited at the Research Laboratory, Department of Chemistry. The stem bark of the *Vitex doniana* was cleaned and air-dried in the laboratory. Two kilogram (2kg) of the stem bark of *Vitex doniana* was pulverized into a coarse powder.

**Extraction of stem bark and Phytochemical analysis**

The weighed powdered air-dried sample (2kg) was macerated with 95% ethanol for five days filtered and evaporated in vacuo at 40°C using a rotary evaporator. The extract concentrate was labeled and the percentage yield was calculated in w/w. The ethanolic extract was subjected to qualitative chemical screening for identification of secondary metabolites such as flavonoids, alkaloids, steroids, triterpenes, saponins, anthracenosides, tannins, polyuronides, emodin\(^{12,13}\).  

**Pharmacological Evaluation**

**Animals**

Eighty (80) Albinio wister rats of both sexes weighing 100-150g and thirty (30) mice of both sexes weighing 20-30g. They were obtained from a colony of rats maintained at the animal house of the Institute of Trypanosomiasis Research Vom, Nigeria. They were housed in clean cages and had access to feeds (ECWA FEEDS) and water *ad libitum*. They were allowed to acclimatize for two (2) weeks in the Veterinary Physiology, Pharmacology and Biochemistry Laboratory before the commencement of the study. All the animals were handled according to the guiding principles of biomedical research involving animals as certified by the ethics committee of Faculty of Veterinary Medicine, University of Maiduguri, Nigeria\(^{14}\).  

**Acute Toxicity studies (LD\(_{50}\))**  
The acute toxicity (LD\(_{50}\)) value of the crude stem bark ethanolic extract of *Vitex doniana* will be determined using standard conventional procedures as described by Lorke\(^{15}\). In this study two different routes of administration will be considered, that is the oral and intra-peritoneal. In phase 1 rats will be divided into 3 groups of three rats for each route (a total of nine rats) and then treated with crude ethanolic extract at doses of 10, 100 and 1000 mg/kg body weight intraperitoneally and orally and observed for 24 hours for mortality. In the phase II, the animals in group for each route will be divided into 4 groups(one animal in group 1, two in group 2, three in group 3 and five in group 4) and the ethanolic extract administered at doses to be determined after the phase one. The final LD\(_{50}\) value will be calculated as the geometric mean of the surviving group and the death group in the second phase.

**Anti-inflammatory Evaluation**

Twenty five male rats weighing between 150-200g was used. They were placed into 5 groups five rats each A, B, C, D, and E. Group A served as the control while groups B, C, and D were treated with various dose levels 100mg/kg, 200mg/kg, 400mg/kg of the stem bark extract. Group E was given 60mg/kg of aspirin. The extract and the drug treatment were intraperitoneally injected 30 minutes prior to the induction of edema. Edema was induced by injecting 0.1ml of egg albumin into right paw of the rats. Using vernier caliper, the diameter of the paws was measured after every hour for 5 hours, with the final reading taken 24 hours after edema induction\(^{16}\). Percentage inhibitions were calculated using the formula of Hernandez-Perez et al\(^{17}\).

**Statistical Analysis**

Data expressed as mean±SD and mean±SEM. Test of Significance between control and treatment means were carried out by Analysis of Variance (ANOVA) using Graph Pad Software\(^{21}\).

**RESULTS AND DISCUSSION**

The extracts concentrate yields of ethanol is 14.8%w/w. Preliminary phytochemical analysis of the ethanolic stem bark extract of *V. doniana* revealed the presence of tannins, phlobatannins, saponins, carbohydrates, cardioactive glycoside, flavonoids, steroids and terpenes. Alkaloids and anthracenosides is absent in the extract (table 1). The phytochemicals found are implicated to have many medicinal importances. The intraperitoneal LD\(_{50}\) in rats was found to be 2154.06mg/kg. On administration of 5000mg/kg dose of the extract via oral route, there was no dead which makes it impossible to estimate LD\(_{50}\) via oral route using the Lorke method\(^{22}\). According the classification of Clarke and Clarke\(^{23}\) substances that have an intraperitoneal LD\(_{50}\) between a
50 and 500mg/kg are considered toxic and Onyeillilli et
al categorized an intraperitoneal LD_{50} of 1400mg/kg under
dilute toxicity.

The result of table 2. shows the effect of different dosages of
the V. doniana stem bark extract and Aspirin (60mg/kg) on
the egg albumen induced edema. The results demonstrate that
the extract reduced the mean paw diameter when compared
with the control which is distilled water. Also, the extract at
doses of 400mg/kg and 300mg/kg conferred the high
percentages inhibitions of 86.45% and 69.32% in laboratory
rats after five (5) hours. The extract produced dose dependant
reduction of increased paw diameter induced by the egg
albumen. The paw mean size diameter (mm) decreases from
6.14± 0.33 on administration of 1000mg/kg to finally
3.45±0.12 on treatment with 400mg/kg of the V. doniana
ethanolic extract when compared to the control which
reduced the paw size by 7.30± 1.33. Aspirin(60mg/kg) has a
percentage inhibitions of 25.40%, 43.20% and 63.45%
respectively after 3, 4, and 5 hours of administration to the
laboratory rats. Thus the V. doniana stem bark ethanolic
extract at 300mg/kg and 400mg/kg has higher percentage of
inhibition when compared to the aspirin (60mg/kg), a
standard anti-inflammatory drugs that inhibit prostaglandin
synthesis^{25}. This result clearly demonstrated the anti-
inflammatory properties of V. doniana stem bark ethanolic
extract. The anti-inflammatory activities of the extract may
be due to its content of tannins, and tannins apart from acting
as astringent are known to inactivate enzymes^{25} and these
may be responsible for anti-inflammatory activities. This
observation is an indication of possible usage of the plant for
treatment of inflammatory conditions

In the anticonvulsant studies the rats that received the
600mg/kg of stem bark ethanol extract had 80% protection
against PTZ induced convulsion while those that received
300mg/kg dose of the extract had 60% protection as shown in
table 3. The mean onset of convulsion for 600mg/kg was
13.60±011 (min) and the mean onset of death was 27.40±023
(min), and only one rats convulsed in this group. Convulsion
is a symptom of dysfunction in the gray matter of the brain
rather than disease itself^{26}. PTZ act by stimulation of the
medulla^{27}. The ability of the V. doniana extract to protect
against rats stimulated with PTZ may be an indication of
depressant effect on the spinal cord and brain stem. The
ability of the extract to protect animals from induced seizures
shows that it contains some chemical components that are
able of antagonizing chemically induced seizures. This
depressant activities may be due to presence of phytochemical like saponins, flavones tannins glycosides
which may have singly or in combination brought about the
anticonvulsant activities This is accordance with the works of
Abdurahaman et al.,^{28} who use this method to study this
anticonvulsant properties of different plant extracts.

The stem bark extract of V.doniana also possess antipyretic
properties as shown in table 4. High dose of 400mg/kg
significantly reduced rectal temperature from 40.12±0.05 ^{\circ}C
after 18 hours of induction of fever by Brewers yeast to 39.30
±0.13^{\circ}C after one hour on administration of the extract. Four
hours later the rectal temperature reduce to 37.81±0.67 ^{\circ}C.
Also Aspirin (60mg/kg) reduced the rectal temperature from
39.90±0.25^{\circ}C on 18 hours of fever induction to 38.14±0.2^{\circ}C
after just one hour and subsequently to 37.50 ±0.01 after 5
hours. The effects of the aspirin (60mg/kg) are high as

compared to the extract as seen in table 4. Thus the stem bark
extract demonstrated an antipyretic properties. This
observation supports the claim of local people in folkloric
treatment of fever. Fever may a result of infection or one of
the consequence of tissue damage inflammation or other
diseases state^{29}. Antipyretic drug reduces elevated body
temperature and this activity may be due to presence of
flavonoid compounds as some flavonoidal compound are
predominant inhibitors of cyclooxygenase and
lipoxygenase^{30}. This antipyretic properties of the extract due
to brewer yeast induced pyrexia is in accordance with the
similar work on Terminalia avicennoides Morinda Lucinda
and Khaya senegalensis^{29}

CONCLUSION
This research shows that the ethanolic extract of V. doniana
possesses significant antipyretic, anti-inflammatory, anti-
convulsant properties on laboratory rats. The phytochemicals
found such as flavonoid, tannins, steroids, saponins,
carbohydrates, terpenes and cardio-active glycosides are
implicated in having the pharmacological actions that was
observed This finding collaborate the use of Vitex doniana
stem bark in folkloric medicine and demonstrates its
possible neurologol effect as observed in the dose
dependant reduction of Inflammation, anticonvulsant
activity and reduction of induced pyrexia.

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Maiduguri, Nigeria

REFERENCES
1. Gibbons S. An overview of plant extracts as potential therapeutics.
2. Sheffall K. and Dwivedi Sumeet. Indigenous ayurvedic knowledge of
   some species in thetreatment of human disease and disorders. International
   journal of pharmacy and life sciences. Explorer Research
   Article.2010. 1(1):44-4
   D.A., Croom, E.M., Pharmacy and herbal medicine in the US.
5. Gibile Z.O. and Adesina, S.K. Nigerian Solanum species of Economic
   862-865.
6. Maduka, H.C. The theoretical Mechanist Concept of Sacogollotis
   Gabonensis. A Nigerian Alchoholic Beverage Additive as an Antioxidant
   protection against Hepotoxicity. The international journal of
7. Loch E., Selle H., Boblitz A. Treatment of Pre-mensural syndrome with
   phytopharmaceutical formulations containing Vetix agnus cactus.
   A systematic review of adverse events. Drug safety. 2005. 28. 319
9. Kapoor S.L. and Kapoor L.D., Medicinal Plants wealth of the
   Karimnagar district of Andra Pradesh. Bulletin of Medicinal
   Ethnobotanical Research 1980. 1. 120-144
10. Dharmasiri M.G., Jayakody J.R., Galhena G., Liyanage S.S., and
    Ratnasooriya W.D. -Anti-inflammatory and analgesic activities of
    mature fresh leaves of vetix negundo. Journal of Ethnopharmacology
    2003. 87,199-206
11. Abdurahaman F.I., Tijjani M.A. and Sandabe U.K. Antipyretic and
    Anti-inflammatory Properties of the methanolic leaf extract of Vitex
12. Sofowora, A. Medicinal Plants and Traditional Medicine in Africa.
    Published in Association with Spectrum Books Ltd. Ibadan by John
Table 1. Phytochemical analysis of stem bark ethanolic extract of V. doniana

<table>
<thead>
<tr>
<th>S/N</th>
<th>Class of Chemical Components</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Terpenoid test</td>
<td>+</td>
</tr>
<tr>
<td>2.</td>
<td>Test for soluble starch</td>
<td>-</td>
</tr>
<tr>
<td>3.</td>
<td>Test for phlobatannins</td>
<td>+</td>
</tr>
<tr>
<td>4.</td>
<td>Test of Alkaloids</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Dragendorf reagent</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Meyers reagent</td>
<td>-</td>
</tr>
<tr>
<td>5.</td>
<td>Test for Flavonoid</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Shinoda Test</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Lea acetate test</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Sodiuhydroxide test</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Ferric Chlorides test</td>
<td>++</td>
</tr>
<tr>
<td>6.</td>
<td>Test for carbohydate</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>General Test (Molish test)</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Test of monosaccharide</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Test for reducing sugar (Fehling test)</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Combine reducing sugar test</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Test for ketoses</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Test for pentose</td>
<td>-</td>
</tr>
<tr>
<td>7.</td>
<td>Test for tannins</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Ferric chloride</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Lead acetate</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Hydrochloric acid test</td>
<td>-</td>
</tr>
<tr>
<td>8.</td>
<td>Test for free Anthraquinones (Boutrase)</td>
<td>-</td>
</tr>
<tr>
<td>9.</td>
<td>Test for combined anthraquinone</td>
<td>-</td>
</tr>
<tr>
<td>10.</td>
<td>Test for cardio active glycoside</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Salkowski test</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Liebermann Burchard test</td>
<td>++</td>
</tr>
</tbody>
</table>

Key: + = Present, ++ = Present in Moderate Concentration, - = Absent

Table 2. Effect of ethanolic extract of V. doniana stem bark on egg albumen induced oedema in laboratory rats

<table>
<thead>
<tr>
<th>Extract dose (mg/kg)</th>
<th>Mean paw size diameter (mm±SEM)</th>
<th>Percentage Inhibitions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3hrs</td>
<td>4hrs</td>
</tr>
<tr>
<td>Control (DW)</td>
<td>7.30±0.33</td>
<td>1.30</td>
</tr>
<tr>
<td>100</td>
<td>6.14±0.33</td>
<td>19.10</td>
</tr>
<tr>
<td>200</td>
<td>5.58±0.45</td>
<td>23.50</td>
</tr>
<tr>
<td>300</td>
<td>4.23±0.23</td>
<td>26.70</td>
</tr>
<tr>
<td>400</td>
<td>3.45±0.12*</td>
<td>38.30</td>
</tr>
<tr>
<td>Aspirin 60</td>
<td>5.04±0.35 *</td>
<td>25.40</td>
</tr>
</tbody>
</table>

P< 0.05 significantly different from the control

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Table 3: Effect of ethanolic stem bark extract of *V. doniana* on Pentylenetetrazole (PTZ) induced convulsion

<table>
<thead>
<tr>
<th>Extract pre-treatment (mg/kg)</th>
<th>Mean ± SD onset of convulsion (min)</th>
<th>Mean±SD onset death (min)</th>
<th>Quantal death</th>
<th>Survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control + 50mg/kg of PTZ</td>
<td>3.40±0.55</td>
<td>10.5±0.57</td>
<td>5/5</td>
<td>0</td>
</tr>
<tr>
<td>100mg/kg of extract + 50mg/kg of PTZ</td>
<td>6.23±0.67</td>
<td>16.21±0.93</td>
<td>3/5</td>
<td>40</td>
</tr>
<tr>
<td>300mg/kg of extract + 50mg/kg of PTZ</td>
<td>9.36±0.33</td>
<td>21.90±0.11</td>
<td>2/5</td>
<td>60</td>
</tr>
<tr>
<td>600mg/kg of extract + 50mg/kg of PTZ</td>
<td>13.60±0.11</td>
<td>27.40±0.23</td>
<td>1/5</td>
<td>80</td>
</tr>
</tbody>
</table>

Table 4: Effect of ethanolic stem bark extract of *Vitex doniana* on Brewer’s yeast induced hyperpyrexia in rats

<table>
<thead>
<tr>
<th>Treatment groups (mg/kg)</th>
<th>Rectal Temperature °C</th>
<th>Mean ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>After yeast injection</td>
<td>After drugs Administration</td>
<td></td>
</tr>
<tr>
<td>0(min)</td>
<td>18(hrs)</td>
<td>120(min)</td>
</tr>
<tr>
<td>Control (DW)</td>
<td>37.0</td>
<td>39.7±0.22</td>
</tr>
<tr>
<td>100</td>
<td>37.1</td>
<td>40.63±0.34*</td>
</tr>
<tr>
<td>200</td>
<td>37.4</td>
<td>40.47±0.22</td>
</tr>
<tr>
<td>300</td>
<td>37.3</td>
<td>39.01±0.49*</td>
</tr>
<tr>
<td>400</td>
<td>37.8</td>
<td>40.12±0.05*</td>
</tr>
<tr>
<td>Aspirin (60mg/kg)</td>
<td>37.5</td>
<td>39.90±0.25*</td>
</tr>
</tbody>
</table>

*P<0.0001 significant compared to control

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