The results are summarized in Table 1. While *Piper umbellatum* and *Mellotus appositifolius* extracts had moderate activity against the parasite with 40 µg/ml of each giving 70% and 57% inhibition, respectively, extracts from *Cymbopogon citratus*, *Mangifera indicus* and *Annona muricata* were found to possess greater effects on the growth with 20 µg/ml of each giving 57.9%, 50.4% and 67% inhibition, respectively. *Achromanes difformis* and *Cleome rutidosperma* extracts showed the least antiplasmodial activity even with 40 µg/ml of each resulting in 32.4% and 31.6% inhibition, respectively (Table 1).

It is not known whether the *in vitro* effect of these extracts against *F32 P. falciparum* is due to the concerted activity of their components. This issue could be addressed after chemical fractionation and isolation of the principles. Toxicology studies in animals may provide additional information on the feasibility of their use in humans.

Acknowledgement

We acknowledge the advice of the late Prof. Johnson Ayafor on the plant extraction procedure, and of Mr. Nahou Ndam in identifying the plant extracts. This investigation received financial support from the University of Buea, Cameroon and the International Program in Chemical Sciences (IPiCS) Uppsala University, Sweden.


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References


### Table 1

<table>
<thead>
<tr>
<th>Concentrations</th>
<th>0.08</th>
<th>0.16</th>
<th>0.32</th>
<th>0.64</th>
<th>2.5</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>40</th>
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<tbody>
<tr>
<td>Drug/Extract</td>
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<tr>
<td>1. Achromanes difformis</td>
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<td>2. Cleome rutidosperma</td>
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<td>3. Cymbopogon citratus</td>
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<td>4. Piper umbellatum</td>
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<td>5. Mellotus appositifolius</td>
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<td>6. Mangifera indicus</td>
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<td>7. Annona muricata</td>
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<td>8. Chloroquine</td>
<td>5</td>
<td>47</td>
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<td>89</td>
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</tr>
</tbody>
</table>

*Concentration of chloroquine (0.08-0.64) is in µM and those of plant extracts (2.5-40) are in µg/ml. Values are mean percentage inhibition at the concentration of extract given in the top row. *More than 50% inhibition of parasite growth at 20 µg/ml of extract. ‘-’ = Not determined.

Piracetam attenuates minoxidil-induced antinociception in mice

Sir,

Piracetam is a nootropic agent and has been used to treat various dementias for several years as it enhances or facilitates various learning and other cognitive functions. Piracetam has been shown to attenuate the opioid antinociception. Besides, piracetam increases the intracellular ATP concentration in the nerve cell which may have an inhibitory effect over the ATP-gated potassium channels (K<sub>ATP</sub> channels). Therefore, the present study has been designed to investigate the effect of piracetam on the K<sub>ATP</sub> channel opener-induced antinociception. Minoxidil is a selective K<sub>ATP</sub> channel opener and produces antinociception in mice when administered centrally.

Six to eight-weeks-old healthy inbred BALB/c mice (25±3 g) of either sex were used in the study. They were housed in an animal house provided with a 12 h light/dark cycle and had free access to food and water. Minoxidil (Dr. Reddy’s Laboratories Ltd., Hyderabad, India) and piracetam (Micro Labs Ltd., Pondicherry, India) were dissolved in normal saline immediately before use. The institutional ethical committee approved all experimental procedures.

Minoxidil was injected i.c.v. in conscious mice in a volume of 10 µl with Hamilton syringe as described by Haley and McCormick. Time course studies were used to ascertain peak antinociception as tested by the tail flick test. Peak time for minoxidil was 10 min after injection.

nociceptive threshold was measured by the tail flick test in mice. The tail flick latency was considered as the time between tail exposure to radiant heat and tail withdrawal. An electrically heated nichrome wire was used as a source of radiant heat in the analgesiometer. The intensity of radiant heat was regulated in order to obtain pretreatment latency between 2 to 3 s. A cut-off latency time was fixed at 10 s. Tail flick latency was expressed as a percentage of the maximum pos-
sible effect (MPE):

\[
\text{MPE} (\%) = \frac{(\text{Post-treatment latency} - \text{Pretreatment latency}) \times 100}{\text{Pretreatment latency}}
\]

Mice were divided into 6 groups of 5 each. Group I was administered 10 µl of vehicle i.c.v. and served as vehicle control. Group II was administered minoxidil, 25 µg/mouse, i.c.v. and served as a control for piracetam-treated groups. Groups III, IV, V and VI were administered minoxidil, 25 µg/mouse, i.c.v. 30 min after the administration of 125, 250, 500 and 1000 mg/kg, i.p. of piracetam respectively. Tail flick latency was observed before and 10 min after minoxidil administration. One-way ANOVA and Student’s t’ test were used to determine the significance of the difference between the values of the various groups. P values <0.05 were considered significant.

Minoxidil (25 µg/mouse, i.c.v.) produced significant increase in % MPE as compared to vehicle-treated controls. Piracetam significantly attenuated minoxidil-induced antinociception. The attenuation was found to be dependent on the dose of piracetam (Table 1).

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Percent MPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control (10 µl/mouse, i.c.v.)</td>
<td>4.34 ± 2.12</td>
</tr>
<tr>
<td>Minoxidil (25 µg/mouse, i.c.v.)</td>
<td>57.21 ± 6.53*</td>
</tr>
<tr>
<td>Piracetam (125 mg/kg, i.p.) + Minoxidil (25 µg/mouse, i.c.v.)</td>
<td>40.12 ± 5.20**</td>
</tr>
<tr>
<td>Piracetam (250 mg/kg, i.p.) + Minoxidil (25 µg/mouse, i.c.v.)</td>
<td>27.92 ± 4.72**</td>
</tr>
<tr>
<td>Piracetam (500 mg/kg, i.p.) + Minoxidil (25 µg/mouse, i.c.v.)</td>
<td>15.62 ± 3.10**</td>
</tr>
<tr>
<td>Piracetam (1000 mg/kg, i.p.) + Minoxidil (25 µg/mouse, i.c.v.)</td>
<td>9.10 ± 2.95**</td>
</tr>
</tbody>
</table>

Values are expressed as mean (n=5) of percent maximum possible effect (MPE) ±SEM, *P<0.05 Vs vehicle control, **P<0.05 Vs minoxidil control

The results of the present study demonstrate that minoxidil-induced antinociception was dose-dependently attenuated by piracetam. It has been demonstrated that minoxidil-induced antinociception is attenuated by K<sub>ATP</sub> channel blockers, glyburide and opioid antagonists, thus indicating the possible role of K<sub>ATP</sub> channels and released endogenous opioids. K<sub>ATP</sub> channel openers have also been shown to potentiate opioid analgesia whereas naloxone and antisense to block the K<sub>ATP</sub> channel opener-induced antinociception. Piracetam has also been shown to attenuate opioid analgesia. Moreover, at higher concentrations piracetam has shown to have an affinity to bind to opioid receptors. Besides, piracetam also increases the intracellular ATP concentration in the nerve cell which may have an inhibitory effect over the K<sub>ATP</sub> channels. Thus, it may be suggested that piracetam attenuates minoxidil-induced antinociception by a mechanism related to the antagonism of endogenous opioids, possibly through a K<sub>ATP</sub> channel-linked mechanism. Further study is however required to elucidate this effect of piracetam.

### Acknowledgements

The authors are grateful to Dr. N. K. Talwar, Punjab Veterinary Vaccine Institute, Punjab Agriculture University, Ludhiana for technical help and animal house and laboratory facilities.

### References


Hepatotoxicity of isoniazid: A study on the activity of marker enzymes of liver toxicity in serum and liver tissue of rabbits

Sir,

Isoniazid (INH) is used as a first-line drug in the treatment and chemoprophylaxis of tuberculosis. It can cause moderate abnormalities in serum transaminases leading to hepatotoxicity, hence the measurement of serum transaminases is often advocated during INH administration, to assess the extent of INH-induced hepatotoxicity. Though a study conducted in rabbits substantiates the hepatotoxic potential of INH or its metabolites as indicated by elevated serum transaminases, conclusive evidence is not available in the literature to demonstrate such alterations in the liver tissue. Since evaluation

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**Research Letter**

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