Antimalarial properties of South African medicinal plants

**INTRODUCTION**

Malaria continues to be one of the major health problems facing Sub-Saharan Africa. One of the contributing factors to the increased prevalence and distribution of the disease is the emergence and spread of drug-resistant malaria parasites, highlighting the need for new chemically diverse, effective drugs. Historically, one of the major sources of antimalarial agents is the world's 50 000 medicinal plant species, as well as a long tradition of medicinal plant use. A national multidisciplinary-camptus was established to scientifically investigate South African medicinal plants for the treatment of malaria. The results arising from the study of one of the plants, Vernonia staehelinoides Harv. (Asteraceae), are discussed.

**METHODOLOGY**

- Plant taxa, native to or naturalised in South Africa with reported medicinal use related to malaria and/or fever, were selected semi-quantitatively using weighted criteria. Plant material, collected from various locations around the country, was dried, ground and extracted sequentially with dichloromethane, dichloromethane/methanol (1:1), methanol and water.
- Extracts of 134 taxa, representing 54 families, were tested for in vitro antiplasmodial activity against the D10 strain (chloroquine-sensitive) using the parasite lactate dehydrogenase (pLDH) assay. Active extracts (IC$_{50}$ ≤ 10 µg/ml) were evaluated against the chloroquine-resistant K1 strain (Table 1).
- The organic extracts of V. staehelinoides, collected in the Magaliesburg region of the Gauteng province in South Africa, were subjected to bioassay-guided fractionation using silica gel chromatography and in vitro antiplasmodial activity against the D10 strain as the biological indicator.
- In order to determine the specificity of the antimalarial activity, the active compounds were tested for cytotoxicity against a Chinese Hamster Ovarian (CHO) cell line using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay.
- Compounds were characterised by NMR spectroscopy and mass spectrometry.

**RESULTS AND DISCUSSION**

Of the 134 plant taxa assayed, 66 species (49%) showed promising antiplasmodial activity with IC$_{50}$ values of ≤ 10 µg/ml and 23 species (17%) were found to be highly active with IC$_{50}$ values of ≤ 5 µg/ml (Clarkson et al, 2004). Several plant species were shown for the first time to possess in vitro antiplasmodial activity, of which V. staehelinoides was promising (Clarkson et al, 2004).

<table>
<thead>
<tr>
<th>Compound</th>
<th>D10 IC$_{50}$ (µg/ml)</th>
<th>K1 IC$_{50}$ (µg/ml)</th>
<th>CHO IC$_{50}$ (µg/ml)</th>
<th>SI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td>12</td>
<td>182</td>
<td>18.5</td>
<td>1542</td>
</tr>
<tr>
<td>1</td>
<td>240</td>
<td>1800</td>
<td>2.9</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>246</td>
<td>2600</td>
<td>0.9</td>
<td>4</td>
</tr>
<tr>
<td>Mucochloric acid</td>
<td>152</td>
<td>137</td>
<td>4.8</td>
<td>32</td>
</tr>
<tr>
<td>Mucobromic acid</td>
<td>422</td>
<td>359</td>
<td>6.3</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 2: In vitro antimalarial activity, cytotoxicity and SI values for chloroquine, compounds 1 and 2, mucochloric acid and mucobromic acid.

Two main privileged substructures, a 2(SH)-furanoane unit and a dihydrofurano-4-one unit, were identified as potential pharmacophores (Figure 1). In order to verify this, mucochloric and mucobromic acids were selected as appropriate 2(SH)-furanoane substructures and were found to display superior activity against the K1 strain and improved selectivity to the malaria parasites relative to the hirsutinoline natural product (Table 2). The antimalarial data obtained in respect of mucochloric and mucobromic suggests that the 2(SH)-furanoane is at least one of the key pharmacophores responsible for the observed antimalarial activity and the synthesis of structure-activity derivatives around these simplified structures is currently under way.

**CONCLUSIONS**

The study identified a number of promising South African medicinal plants for further investigation as plant-based antimalarial agents. The overall screening results, coupled with the identification of potential pharmacophores from the further investigation of the antimalarial properties of V. staehelinoides, support a rational rather than random approach to the selection of screening candidates as potential sources of antimalarial lead compounds.

**REFERENCES**