Antiplasmodial activity of extract and compounds from *Vachellia xanthophloea* (Benth.) P.J.H. Hurter (African fever tree)

Nasir Tajuddeen¹, Dustin Laming², Heinrich Hoppe², Fanie R. Van Heerden¹

¹School of Chemistry and Physics, University of KwaZulu-Natal, Private Bag X01, Scottsville 3209, Pietermaritzburg.
²Department of Biochemistry & Microbiology, Rhodes University, PO Box 94, Grahamstown, 6140

**INTRODUCTION**

Malaria is an infectious disease that is caused by *Plasmodium* parasites and is spread by mosquitoes. Before 2010, malaria was responsible for the death of over one million people annually. However, malaria-related mortality consistently declined from 2010 to just over 430 000 deaths in 2015 and 2016, mainly due to early detection and treatment using antimalarial drugs. Alarmingly, there appears to be a reversal (in some regions) or levelling off of this decline as recorded in the World Malaria Report for 2019 due to delayed drug response and resistance development to the most effective antimalarial drugs (ACTs). Therefore, there is an urgent need to discover new antimalarial agents in order to sustain the battle against the disease. Incidentally, the most successful drugs against malaria (quinine, chloroquine, and artemisinin) were inspired by or originated from plants that were traditionally used to treat malaria/fever. South Africa has an active traditional medicine system that takes advantage of its huge biodiversity to treat diseases such as malaria. Therefore, the aim of this project was to investigate the compounds responsible for the antiplasmodial activity of *Vachellia xanthophloea* (Benth.) (previously named *Acacia xanthophloea*), one of the widely used antimalarial remedies in Zulu folk medicine.³

**Extraction of plant leaves**

- Powdered leaves
- Macerated in solvent
- Concentrated in vacuo
- Crude extract

**Fractionation scheme for antimalarial assay**

- crude extract in 90% MeOH
- partition with hexane
- 90% MeOH
- concentrate and reconstitute in H₂O
- hexane fraction
- partition with EtOAc
- residual aqueous fraction
- EtOAc fraction
- partition with 1% NaCl
- tannin free EtOAc fraction

**In vitro antiplasmodial and cytotoxic activity of *V. xanthophloea* leaf extract and compounds**

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC₅₀, P. falciparum 3D7</th>
<th>IC₅₀, Vero</th>
<th>IC₅₀, HeLa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µg/mL</td>
<td>µM</td>
<td>µM</td>
</tr>
<tr>
<td>V. xanthophloea</td>
<td>10.6</td>
<td>894.2 µg/mL</td>
<td>98%</td>
</tr>
<tr>
<td>Methyl gallate (12)</td>
<td>1.2 ± 0.07</td>
<td>6.52</td>
<td>n.d.</td>
</tr>
<tr>
<td>Mixture (1:1) of 3-O-methylquercetin (4) and methyl gallate (12)</td>
<td>4.6</td>
<td>97.7</td>
<td>n.d.</td>
</tr>
<tr>
<td>Kaempferol (8)</td>
<td>25.0</td>
<td>87.3</td>
<td>n.d.</td>
</tr>
<tr>
<td>Dihydroquercetin (7)</td>
<td>27.6</td>
<td>90.71</td>
<td>89.1</td>
</tr>
<tr>
<td>3-O-methylquercetin (4)</td>
<td><em>82.9 ± 1.5</em></td>
<td>n.d.</td>
<td><em>57.9 ± 5.2</em></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>n.d.</td>
<td>0.017</td>
<td>n.d.</td>
</tr>
<tr>
<td>Etmetine</td>
<td>n.d.</td>
<td>n.d.</td>
<td>0.015</td>
</tr>
<tr>
<td>Dorsurolchin chloride</td>
<td>n.d.</td>
<td>n.d.</td>
<td>6.75</td>
</tr>
</tbody>
</table>

*IC₅₀* % viability at 33 µg/mL, % viability at 10 µg/mL, n.d. = not done

**Conclusions**

- The prolonged and widespread use of *V. xanthophloea* for malaria treatment suggests that it might be efficacious.
- The leaf extract showed antimalarial activity against the 3D7 strain of *P. falciparum*.
- Two new flavonoids, including a new polymethylated 5,7-dioxyflavonol, and eight other compounds were isolated from the active leaf extract.
- Methyl gallate displayed the best antimalarial activity with minimal cytotoxicity.
- Methyl gallate was previously reported to possess potent antimalarial activity.²
- Methyl gallate has the potential to be developed into a potent antimalarial agent.
- Similarly, a standardised phenolics-rich fraction could be developed from the plant leaves and used as an antimalarial herbal remedy.

**Acknowledgements**

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