

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

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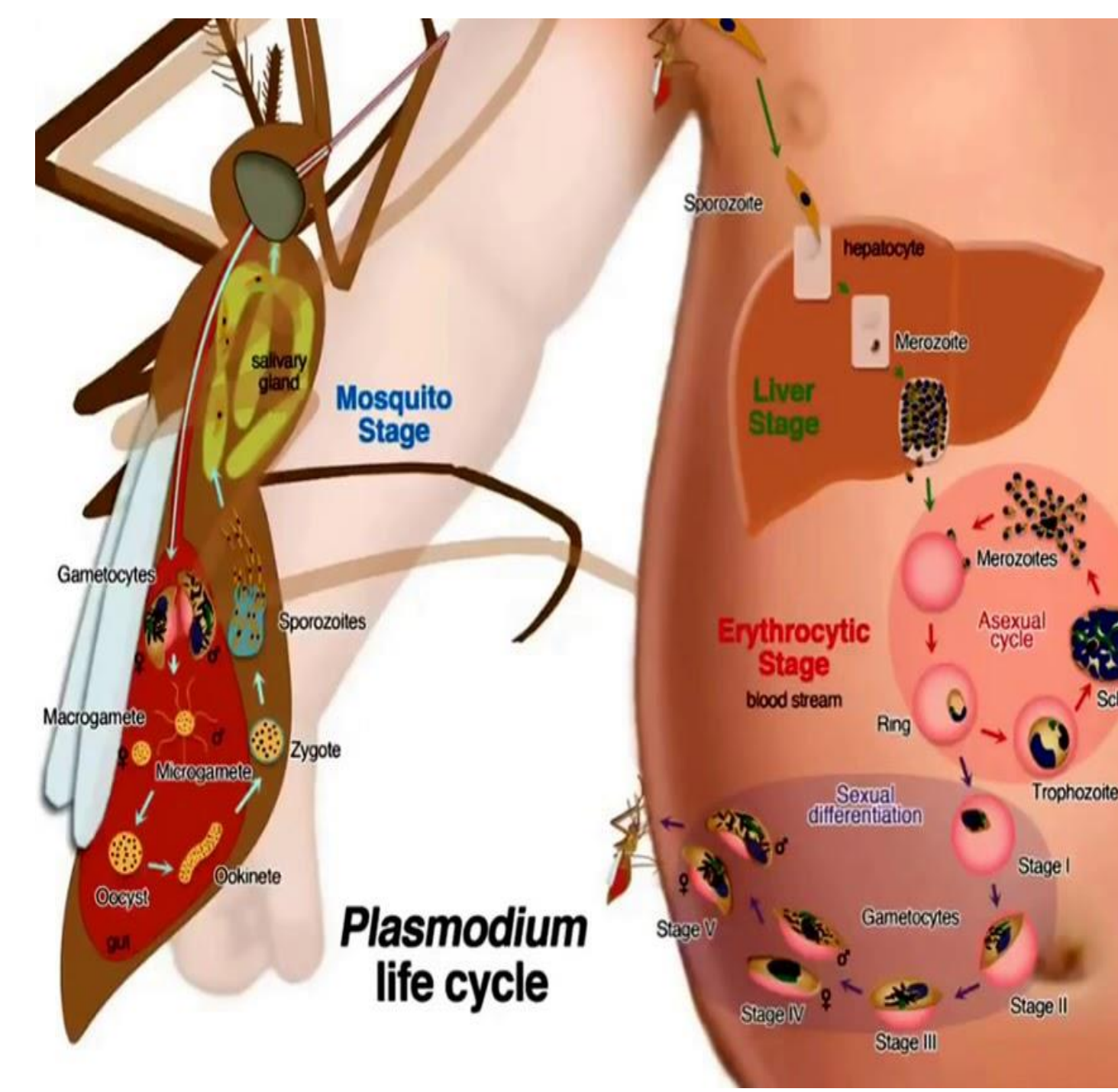
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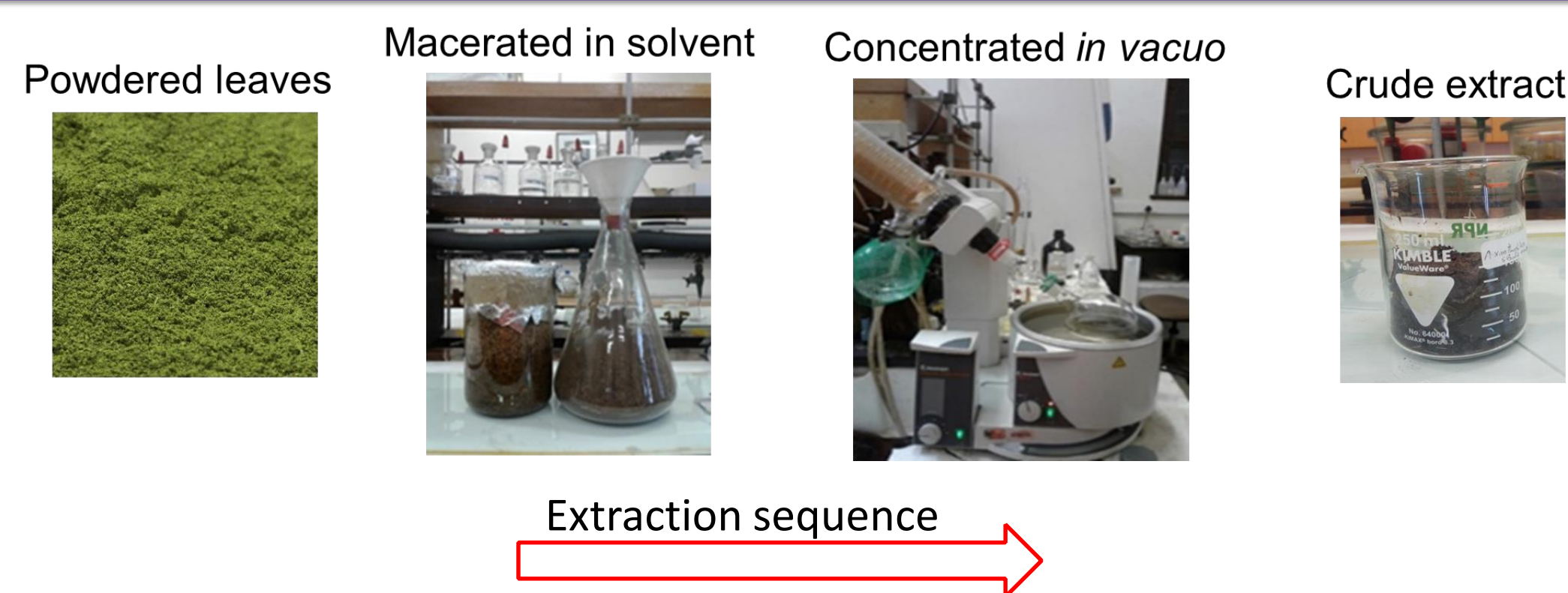
INTRODUCTION



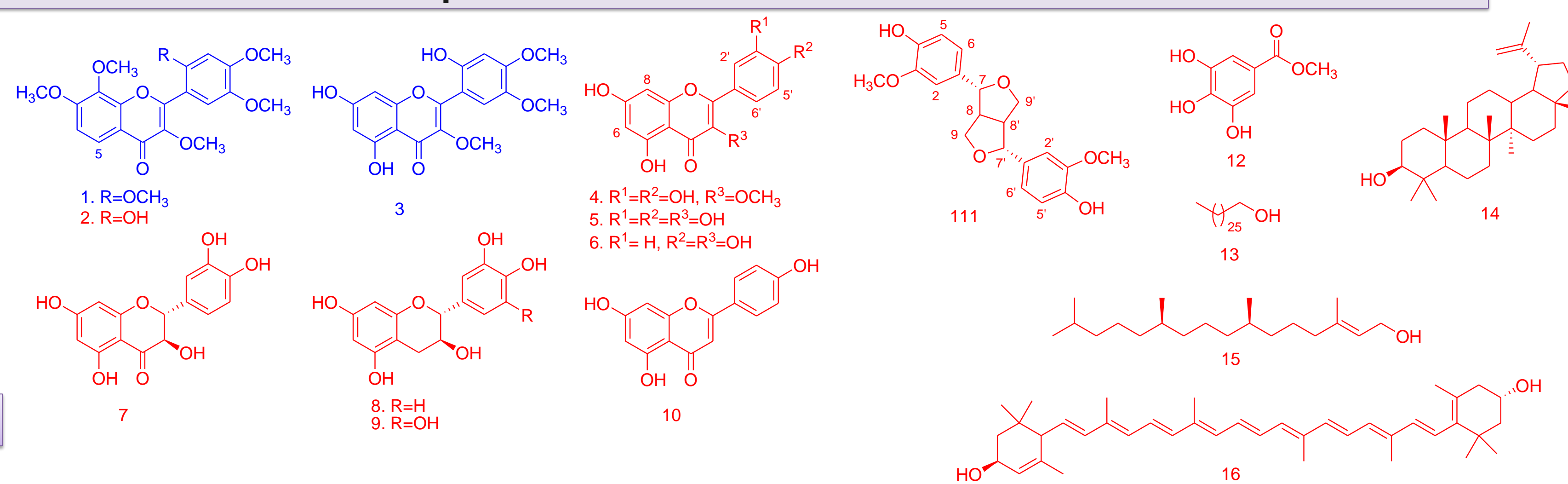
Malaria is an infectious disease that is caused by *Plasmodium* parasites and is spread by mosquitoes. Before 2010, malaria was responsible for the death of over one million people annually. However, malaria-related mortality consistently declined from 2010 to just over 430 000 deaths in 2015 and 2016,^[1] mainly due to early detection and treatment using antimalarial drugs. Alarming, there appears to be a reversal (in some regions) or levelling off of this decline as recorded in the World Malaria Report for 2019^[2] 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]



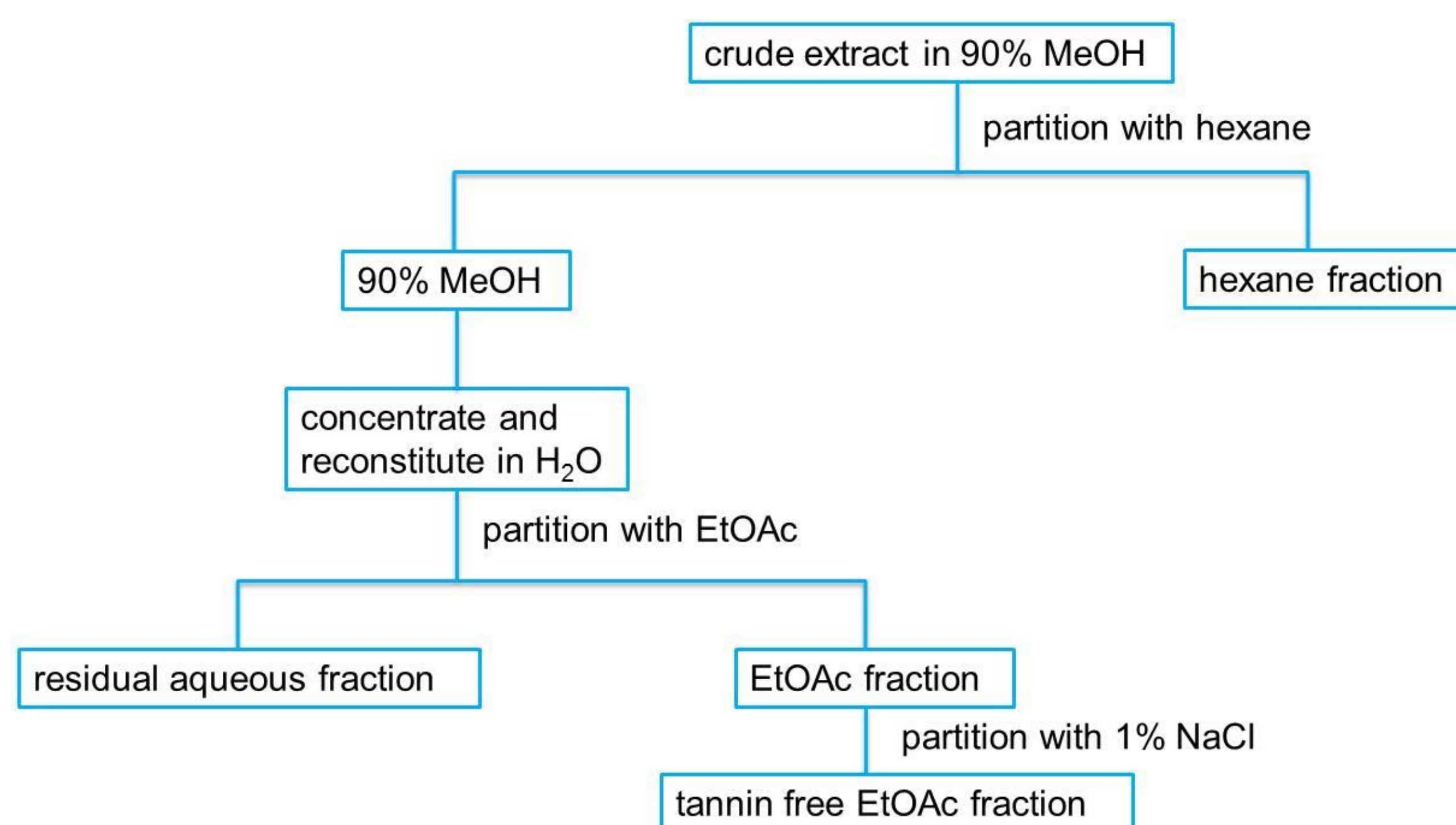
Extraction of plant leaves



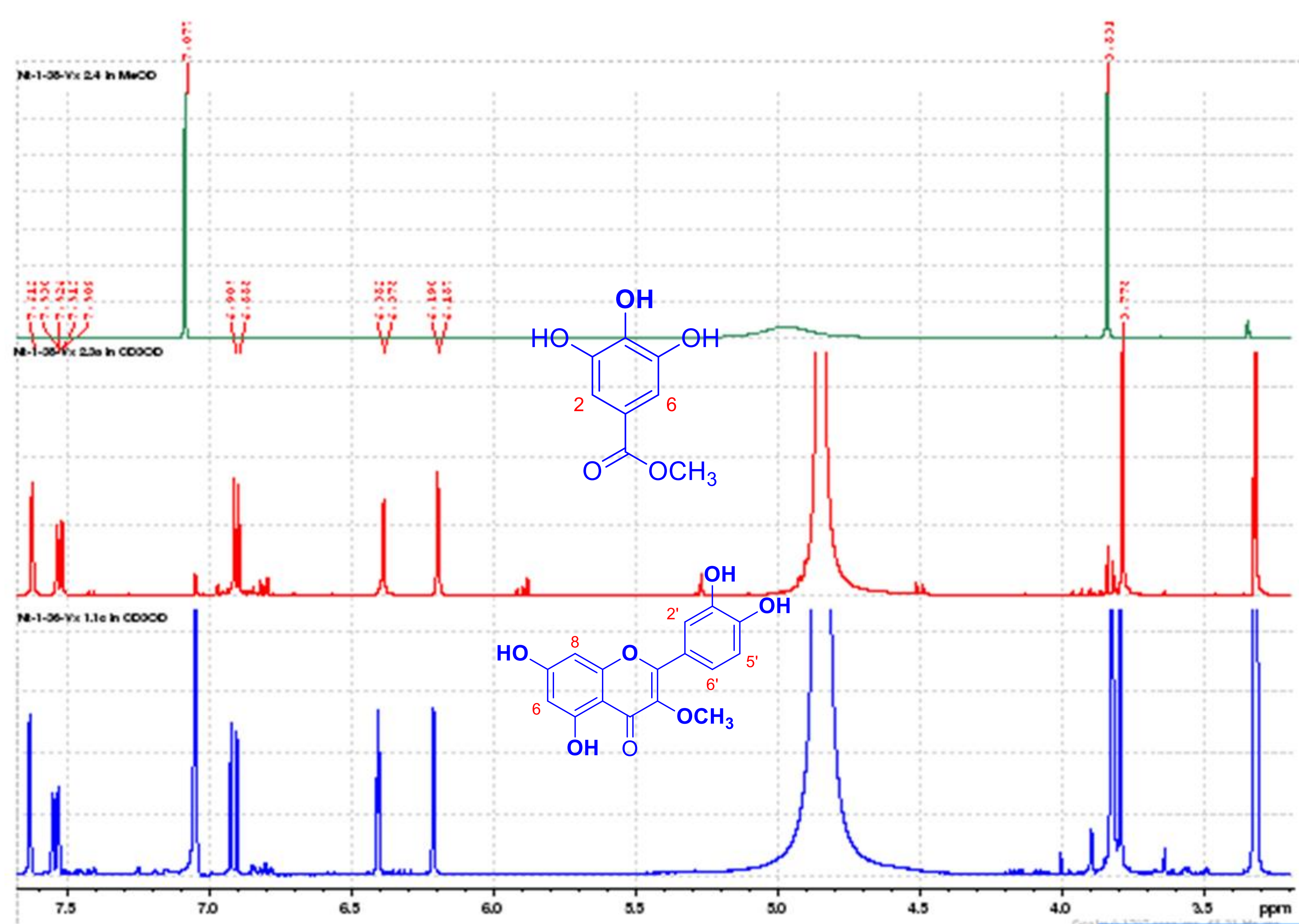
Compounds isolated from the active extract



Fractionation scheme for antimalarial assay



Representative ¹H NMR spectrum



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

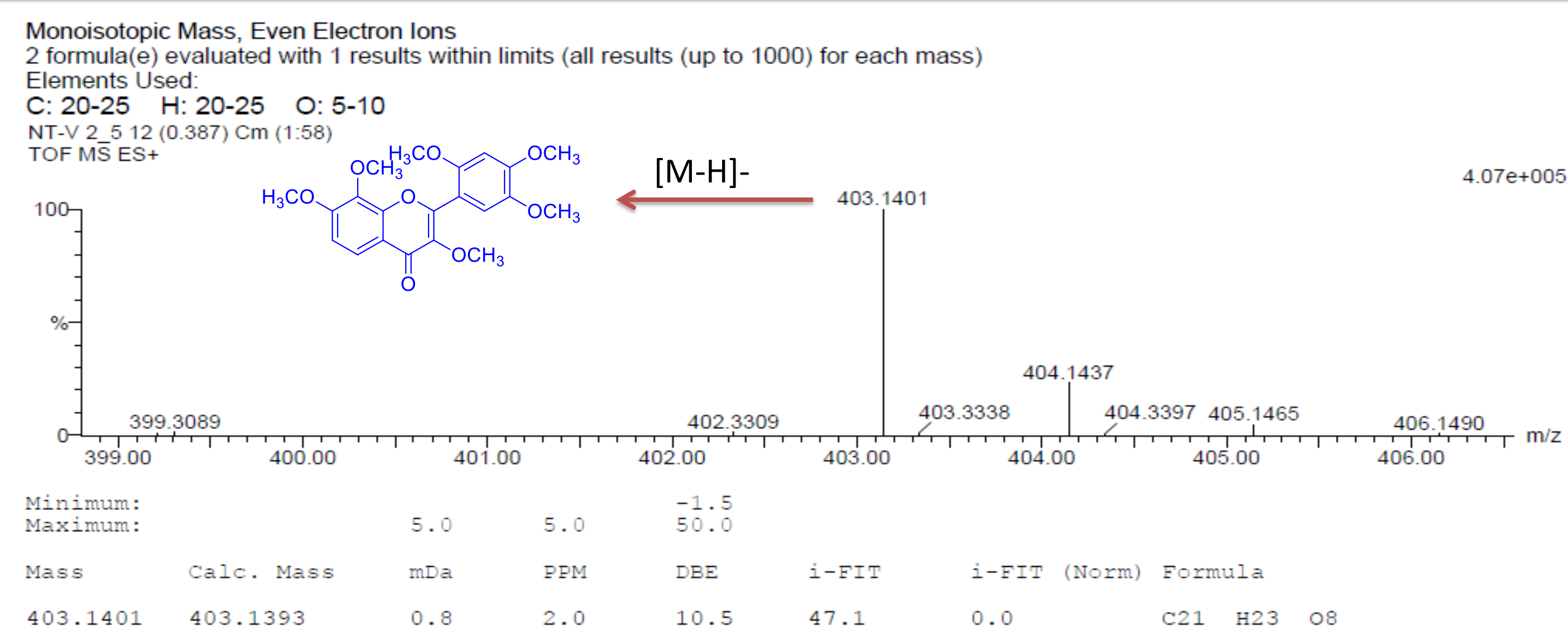
| Compound | IC ₅₀ | | | |
|--|-----------------------------------|--------------------------------|---------------|-------------|
| | <i>P. falciparum</i> 3D7 μg/mL | <i>P. falciparum</i> 3D7 μM | Vero μg/mL | HeLa μM |
| <i>V. xanthophloea</i> | 10.6 | - | 894.2 μg/mL | #98% |
| Methyl gallate (12) | 1.2 ± 0.07 | 6.52 | n.d. | *68.6 ± 2.0 |
| Mixture (1:1) of 3-O-methylquercetin (4) and methyl gallate (12) | 4.6 | - | 97.7 | n.d. |
| Kaempferol (6) | 25.0 | 87.3 | n.d. | n.d. |
| Dihydroquercetin (7) | 27.6 | 90.71 | 89.1 | n.d. |
| 3-O-methylquercetin (4) | *82.9 ± 1.5 | - | n.d. | *57.9 ± 5.2 |
| Chloroquine | - | 0.017 | n.d. | n.d. |
| Emetine | n.d. | n.d. | n.d. | 0.015 |
| Doxorubicin chloride | n.d. | n.d. | 6.75 | n.d. |

#% 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 antiplasmodial activity against the 3D7 strain of *P. falciparum*
- Two new flavonoids, including a new polymethoxylated 5-deoxyflavonol, and eight other ones, a furofuranlignan and a phenolic ester were isolated from the active leaf extract
- Methyl gallate displayed the best antiplasmodial activity with minimal cytotoxicity
- Methyl gallate was previously reported to possess potent antiplasmodial activity^[4]
- Methyl gallate has the potential to be developed into a potent antiplasmodial agent
- Similarly, a standardised phenolics-rich fraction could be developed from the plant leaves and used as an antimalarial herbal remedy

Representative mass spectrum



REFERENCES

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