**Antiplasmodial activity of polyphenolic derivatives.**

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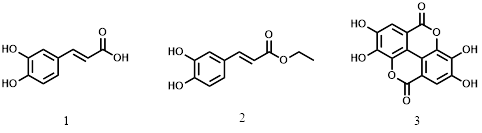
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Despite the progress in the struggle against malaria, this parasitic disease remains a major public health problem with 216 million cases in 2016. The last advance was the development of artemisinin and its derivatives, near 15 years ago. These compounds are employed with success in combination with other antimalarial drugs and are now the recommended treatment by the *World Health Organization*. However, resistance of *Plasmodium* to these molecules appears and spreads over in Asia and Africa. Thus, the design of new antiplasmodial derivatives is imperative to hope the eradication of this infection.

Polyphenolics compounds are well known to have multiple pharmacological activities such as antioxidant2, antitumor3, antimicrobial4 and antiplasmodial5. Regarding this last effect, the screening of caffeic acid (**1**) and its derivatives was performed *in vitro* and *in vivo*. These evaluations permitted to select ethyl caffeate (**2**) as the most potent derivatives against a 3D7 strain in culture. More interestingly, this ester was found active in mice with a stage specificity on the young trophozoites. The major interest of this molecule is that caffeic acid is widely distributed in plants and is considered non-toxic.



**Figure 1** . Structures of caffeic acid (1), ethyl caffeate (2) and ellagic acid (3)

Considering the results obtained with this first series of polyphenolic analogs and based on the known antimalarial activity of ellagic acid (**3**) *in vitro* and *in vivo*6, we currently investigate this widely distributed polyphenol as a scaffold for further pharmacomodulation. The new structures will be screened to determine their antiplasmodial effect.

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