Bioprospection of Brazilian Flora as Source for New Antimalarial Agents: In vitro and In vivo Investigation of *Qualea grandiflora*

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Abstract

Malaria is one of the most prevalent parasitic diseases in the world, an increasing global importance occurs due to the spread of drug-resistance. Treatment remains the main strategy for disease control, thus the development of new drugs is of paramount importance. In this sense, the aim of this work was the bioprospection of Brazilian flora for the discovery of new antimalarial candidates. The in vitro antimalarial activity against *Plasmodium falciparum* cultures of six actives extracts from *Qualea grandiflora* showed IC_{50} values ranging from 3 to 6 µg/mL. The extracts cytotoxic evaluation indicated selectivity index (SI) > 60. Additionally, the antimalarial activity from fruit ethanolic extract was confirmed in vivo, showing a *P. berghei* parasitemia reduction of 83%.

Introduction

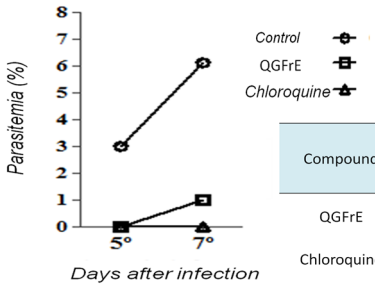
Malaria, caused by *Plasmodium* protozoa, is one of the main public health problems in the worldwide[1]. The emergence of drug resistance parasites makes urgent the search for new chemotherapeutic agents against the disease. Natural products remain as the main source of new antimalarial agents, boosted by the fact that quinine (*Cinchona* sp) and artemisinin (*Artemisia annua*) are the most important antimalarial drugs discovered so far.[2,3] In this work, we evaluated the in vitro and in vivo activity of *Qualea grandiflora* extracts against *P. falciparum* cultures and *P. berghei* infected mice, respectively. The results indicated promising activity both in vitro and in vivo.

Results and discussion

The activity of *Qualea grandiflora* extracts was evaluated *in vitro* against *Plasmodium falciparum (*3D7 sensitive and W2 resistant strains) by SYBR green method. The selectivity index (SI) was calculated using the data from extracts toxicity against human hepatoma cells (HepG2) by Neutral red colorimetric assay. Thein vivo activity was evaluated in *P. berghei* infected mice model. The in vitro assays indicated six *Qualea grandiflora* extracts as active, with IC_{50} values ranging from 3 to 6 µg/mL against both *P. falciparum* strains (Table 1). The extracts showed no toxic effect on hepatic cells (SI > 60) (Table 1). In light of this, the most potent and safe extract, the fruit ethanolic extract (QGFrE), was evaluated in vivo. The data indicated a parasitemia reduction of 100 and 83% after five and seven days of infection, respectively (Figure 1).

Table 1. In vitro and cytotoxic activity of *Qualea grandiflora* extracts against *P. falciparum*.

Extracts	*P. falciparum* IC_{50} (µg/mL)		MDL_{50} (µg/mL)	SI***
	3d7*	W2*	BGM**	
QGFE	6,0± 3,0	2,9 ± 1,4	> 400	137
QGFrE	6 ,0± 0,4	3,5 ± 1,4	> 400	144
QGFrEA	7 ,0± 0,1	5,8 ± 1,0	370 ± 19	97
QGFrEHi	6,0± 1,0	6,6 ± 3,0	> 400	60
QGCcE	5,0 ± 0,3	5,7 ± 1,0	> 400	70
QGCcEA	3,0 ± 2,0	5,3 ± 1,8	> 400	75



Compound	Dose (mg/kg)	% Reduction 5º	% Reduction 8º
QGFrE	100	100	83
Chloroquine	20	100	100

Figure 1. In vivo activity of fruit ethanolic extract (QGFrE) from *Qualea grandiflora* against *P. berghei*.

Conclusions

The in vitro activity of *Qualea grandiflora* extracts was assessed against *P. falciparum* cultures. Additionally, cytotoxicity investigation indicated non-toxic effects. In total, six extracts were active in vitro. The in vivo investigation conducted on the most potent and safe extract indicated a significant reduction in parasitemia. The results suggest *Qualea grandiflora* extracts as promising source of new antimalarials agents.

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