COMPOSITIONS FOR THE TREATMENT OF MALARIA

FIELD OF THE INVENTION

This invention relates to compositions and methods of preparing compositions for use as anti-malarials

BACKGROUND OF THE INVENTION

The group of oxygenated tetracycline triterpenes known as the cucurbitacins are known to have certain pharmaceutical properties and have been reported to exhibit anti-malarial properties (Merck Index 1996 , item 2681)

As the group include some 12 compounds (cucurbitacin A to L) it was decided to investigate which of the twelve was the most efficacious and it was surprisingly found that cucurbitacins B and E, and particularly curcurbitacin B had infinitely greater activity than any of the others.

THE INVENTION

In its widest sense the invention provides an anti-malarial composition containing cucurbitacin B or cucubitacin B and E in an effective and non-toxic amount to cause destruction of the parasite in the liver causing malaria.

In a preferred embodiment, the composition is, or is derived from an extract of a plant of the cucumber family which contains cucurbitacin B or curcurbitacin B and E in an effective and non-toxic amount to cause destruction of the parasite in the liver causing malaria.

In one embodiment, a process is provided for the preparation of a composition for antimalarial use including the formulation of cucurbitacin B or cucurbitacin B and E into a pharmaceutically acceptable form in which the cucurbitacin B is present in an amount of from 1 to 3,5 mcg per unit dosage form. In the preferred form , an amount of about 1,5 mcg/unit dosage form is provided, this amount being well below the toxic dose for an average human (5 mcg/ml is the LD)

The invention also provides a use of the composition as defined above in the manufacture of a medicament for the treatment of malaria.

An effective daily dose of the composition is two tablets, liquid formulation capsule, a porous bag or the like having between 1 mcg and 1,5 mcg per unit dosage form.

The plant chosen for the extract is preferably the African wild cucumber but good results have also be obtained from other members of the cucumber family including melons such as cucumis melo.

It has also been surprisingly found that an extract of a plant of the cucurbitaceae family also contain sterols and sterolins which tend to enhance the activity of cucurbitacin B.

Methanol extracts of C. *Africanus* were serially diluted in complete medium and labelled B and D. There were used to perform dose response experiments on a chloroquine sensitive strain of *Plasmodium falciparum* (D10). The 50% inhibitory concentrations (IC_{50}) were determined from the dose response curves using the graphed Prism V.2.01 package.

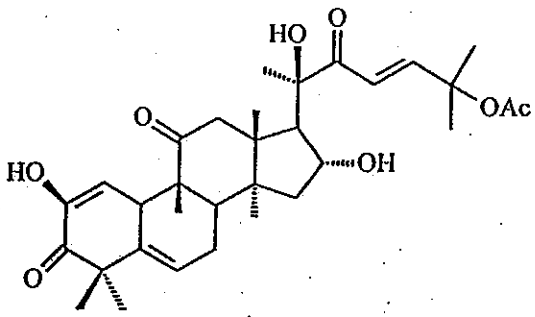
Dose responses using chloroquine (CQ) and artemisinin (ART) were also carried out on the same strain for comparative purposes.

The IC_{50} values obtained for the various samples can be found in Table 1 and the corresponding dose response curves in Figure 1

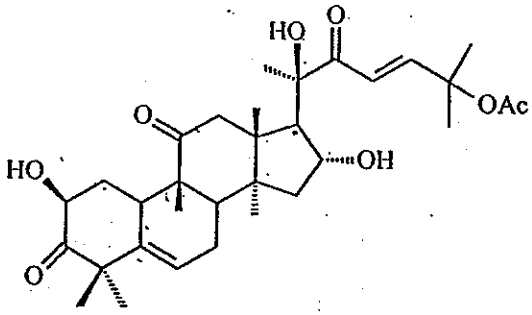
Table 1 : *In vitro* antimalarial activity of the samples B and D, and CQ and ART

SAMPLE	MEAN IC_{50} (*ug*/ml)
B	O.822
D2	29.65
ART	4.28×10^3
CQ	7.93×10^3

Extractives from *Cucumis africanus*



Cucurbitacin E
mass 1g from 200g plant material
0.5%



Cucurbitacin B
mass 2g from 200g plant material
1%

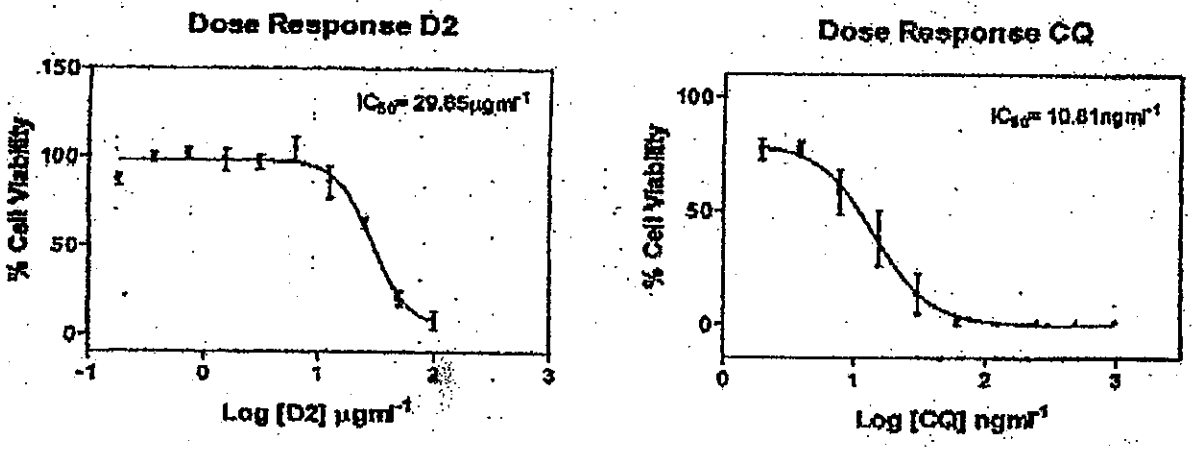


Fig 1. Dose Response Curves for D2 and CQ on a *P. falciparum*

The IC_{50} value obtained for D2 is approximately $30\mu gml^{-1}$.

Antimalarial Activity of Cucurbitacin E Extract

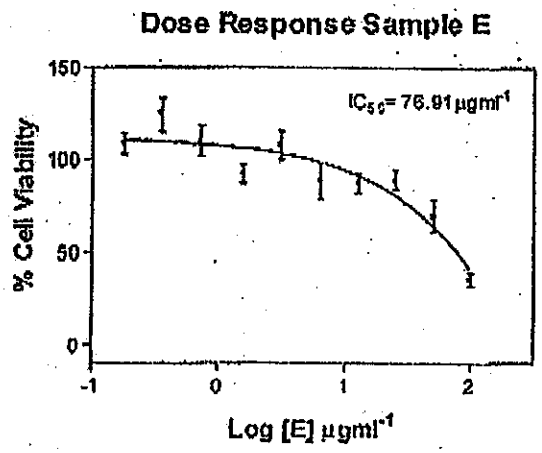
Sample E was used to perform dose response experiments on a chloroquine sensitive strain of *Plasmodium falciparum* (D10). The sample was relatively insoluble in water, and was initially dissolved in methanol and serially diluted in complete medium. Despite dissolving sample E in the highest concentration of methanol that the parasites could be exposed to, it still did not dissolve completely. Therefore, the 50% inhibitory concentration (IC_{50}) value obtained may not be an accurate representation of its *in vitro* antimalarial activity.

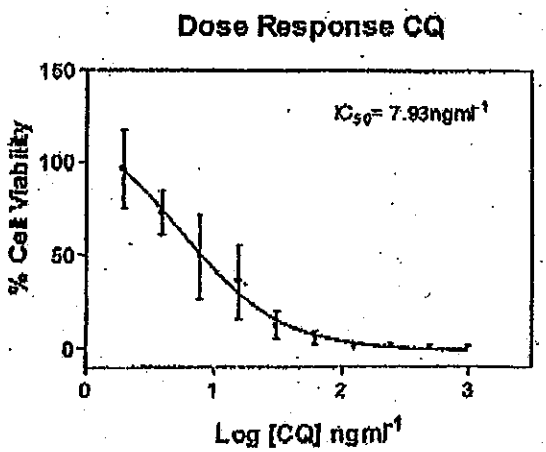
Dose responses using chloroquine (CQ) were also carried out on the same strain for comparative purposes.

The IC_{50} values obtained for sample E and CQ can be found in Table 1 and the corresponding dose response curves in Fig. 1.

Table 1. ***In vitro*** **antimalarial activity of the sample E and CQ**

SAMPLE	MEAN IC_{50} (µg/ml)
E	76.91
CQ	7.93×10^{-3}





CLAIMS

1.

An anti-malarial composition containing cucurbitacin B or cucubitacin B and E in an effective and non-toxic amount to cause destruction of the parasite in the liver causing malaria.

2.

The composition according to claim 1 in which the composition is, or is derived from an extract of a plant of the cucumber family which contains cucurbitacin B or curcurbitacin B and E in an effective and non-toxic amount.

3.

A process for the preparation of a composition for antimalarial use including the formulation of cucurbitacin B or cucurbitacin B and E into a pharmaceutically acceptable form.

4.

The process according to claim 3 in which the cucurbitacin B is present in an amount of from 1 to 3,5 mcg per unit dosage form.

5.

The process according to claim 4 in which an amount of about 1,5 mcg/unit dosage form is provided.

6.

Use of a composition of claims 1 or 2 in the manufacture of a medicament for treatment of malaria.

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ABSTRACT

The present invention provides an anti-malarial composition containing cucurbitacin B or cucubitacin B and E in an effective and non-toxic amount to cause destruction of the parasite in the liver casing malaria. The present invention also provides a process for the preparation of a composition for anti-malarial use and also a use of the anti-malarial composition for treatment of malaria.