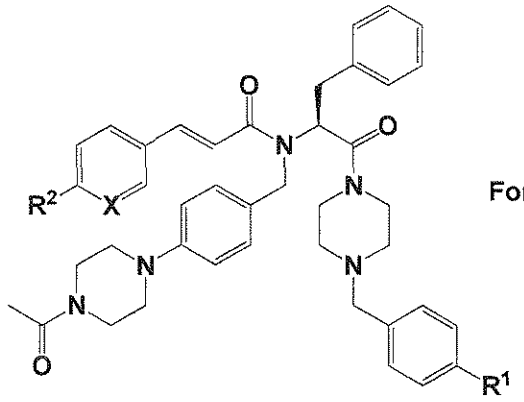
novel low molecular weight, non-peptidic, non-quinoline compounds of formula I which are useful in the treatment and/or prevention of protozoal infections, especially in the treatment and/or prevention of malaria, in particular plasmodium falciparum malaria.

WO 2007/046075 also discloses piperazine derivatives as antimalarial agents. The compound of WO 2007/046075 which comes closest to some of the presently claimed compounds is the compound of Example 54 which corresponds to reference Example 1 herein. However, the presently claimed compounds which come structurally closest to the compound of Example 54 of WO 2007/046075 exhibit an *in vitro* activity against erythrocytic stages of the P. falciparum strain NF54 in the presence of 50% serum which is significantly higher compared to the compound of Example 54 of WO 2007/046075 (see Table 1 below).

Summary

In one aspect, there is provided a compound of the **formula I:**



Formula I

wherein

- **X** is CH or N;
  R^1 represents -NO_2, -$N(CH_3)_2$, or -$NCH_3(CH_2CH_2OH)$; and
  R^2 represents hydrogen, methyl, ethyl, n-propyl, isopropyl, tert-butyl, cyano, halogen, methoxy, ethoxy, n-propoxy, isopropoxy, trifluoromethyl, difluoromethoxy, methylsulfonyl, acetyl, or acetylamino; or
- **X** is CH, **R**^{1} is hydrogen, and **R**^{2} is ethyl, isopropyl, tert-butyl, ethoxy, n-propoxy, isopropoxy, methylsulfonyl, acetylamino, or methoxycarbonyl; or

- **X** is CH, R^1 is cyano, and R^2 is ethyl, isopropyl, tert-butyl, ethoxy, n-propoxy, isopropoxy, trifluoromethyl, difluoromethoxy, trifluoromethoxy, methylsulfonyl, or acetylamino; or
- **X** is CH, R^1 is chloro, and R^2 is ethyl, isopropyl, tert-butyl, ethoxy, n-propoxy, isopropoxy, difluoromethoxy, methylsulfonyl, or acetylamino; or
- **X** is CH, R^1 is methoxy or isopropoxy, and R^2 is trifluoromethyl; or
- **X** is CH, R^1 is methylsulfonyl or ethylsulfonyl, and R^2 is trifluoromethyl, ethyl, isopropyl, tert-butyl, ethoxy, n-propoxy, isopropoxy, or difluoromethoxy;

or a salt of such a compound.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier material.

In yet another aspect, there is provided a compound as defined above, or a pharmaceutically acceptable salt thereof, or a composition as defined above, for use as a medicament.

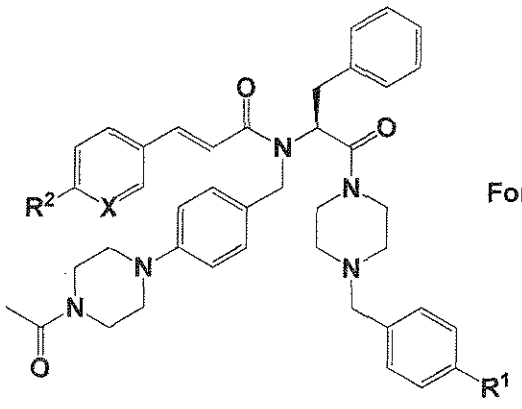
In still another aspect, there is provided a compound as defined above, or a pharmaceutically acceptable salt thereof, for use in the treatment and/or prevention of protozoal infections.

In another aspect, there is provided a compound as defined above, or a pharmaceutically acceptable salt thereof, for use in the treatment and/or prevention of malaria.

In yet another aspect, there is provided the use of a compound as defined above, or a pharmaceutically acceptable salt thereof, for the preparation of a pharmaceutical composition for the treatment and/or prevention of protozoal infections.

Detailed description of the invention:

i) The present invention relates to novel compounds of the **formula I:**



Formula I

wherein

- **X** is CH or N;
  R^1 represents $-NO_2$, $-N(CH_3)_2$, or $-NCH_3(CH_2CH_2OH)$; and
  R^2 represents hydrogen, methyl, ethyl, n-propyl, isopropyl, tert-butyl, cyano, halogen, methoxy, ethoxy, n-propoxy, isopropoxy, trifluoromethyl, difluoromethoxy, methylsulfonyl, acetyl, or acetylamino; or
- **X** is CH, R^1 is hydrogen, and R^2 is ethyl, isopropyl, tert-butyl, ethoxy, n-propoxy, isopropoxy, methylsulfonyl, acetylamino, or methoxycarbonyl; or
- **X** is CH, R^1 is cyano, and R^2 is ethyl, isopropyl, tert-butyl, ethoxy, n-propoxy, isopropoxy, trifluoromethyl, difluoromethoxy, trifluoromethoxy, methylsulfonyl, or acetylamino; or