malaria, the compound of Formula (III) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, comprised in the pharmaceutical composition is released from the pharmaceutical composition at a rate providing an average concentration of trans-2-[4-(4-chlorophenyl)cyclohexyl]-3-hydroxy-1,4-naphthalenedione in the blood plasma of said subject of at least about 1000 nM over about 13 weeks. In the method for the treatment or prevention of malaria, the method may further comprise administering an additional antimalarial agent. In the method for the treatment or prevention of malaria, the additional antimalarial agent is selected from artemisinin, artemisinin derivatives, atovaquone, proguanil, quinine, chloroquine, amodiaquine, pyrimethamine, doxycycline, clindamycin, mefloquine, primaquine, pyronaridine, halofantrine, or ELQ-300.

[0012a] Described herein is the use of a compound described herein or a pharmaceutical composition described herein for the preparation of a medicament for treatment or prevention of malaria, wherein the medicament is to be administered to the subject.

[0013] Described herein are methods of killing or inhibiting the growth of a Plasmodium species comprising contacting the species with an effective amount of a compound of Formula (IV). In the method of killing or inhibiting the growth of a Plasmodium species, the Plasmodium species is Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, or Plasmodium knowlesi.

[0013a] Described herein is a method of killing or inhibiting the growth of a Plasmodium species such as Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, or Plasmodium knowlesi comprising contacting the species with an effective amount of a compound described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] **FIG. 1** depicts the exposure of ELQ-300 following PO or IM dosing with Compound 2.

[0015] **FIG. 2A** depicts the percent protection following a sporozoite challenge at day 14 following IM administration of Compound 2 (3, 10, and 30 mg/kg).

[0016] **FIG. 2B** depicts the exposure of ELQ-300 in mouse following IM administration of Compound 2 (3, 10, and 30 mg/kg).

[0017] **FIG. 3A** depicts the exposure of ELQ-300 in rat following IM administration of Compound 2 (3.72 mg/kg in sesame oil).

[0018] **FIG. 3B** depicts the plasma exposure of ELQ-300 and Compound 2 in dog following IM administration of Compound 2 (20 mg/mL, 3% TPGS, 1% HPMC E5 suspension).

[0019] **FIG. 4A** depicts the exposure of ELQ-300 in mouse following IM administration of Compound 2, 4, 8, 9, and 10 (3 mg/kg, 1.5 mg/mL in sesame oil).

[0020] **FIG. 4B** depicts the exposure of ELQ-300 in mouse following IM administration of Compound 12, 13, 14, 16, 17, and 18 (3 mg/kg, 1.5 mg/mL in sesame oil).

[0021] **FIG. 5** depicts the characteristic X-ray diffraction pattern of the crystalline ELQ-300-Form IA.

[0022] **FIG. 6** depicts the characteristic X-ray diffraction pattern of the crystalline ELQ-300-Form IB.

[0023] **FIG. 7** depicts the characteristic X-ray diffraction pattern of the crystalline ELQ-300-Form II (first preparation).

[0024] **FIG. 8** depicts the DSC of the crystalline ELQ-300-Form II (first preparation).

[0025] **FIG. 9** depicts the characteristic X-ray diffraction pattern of the scaled up crystalline ELQ-300-Form II (1st scale up batch).

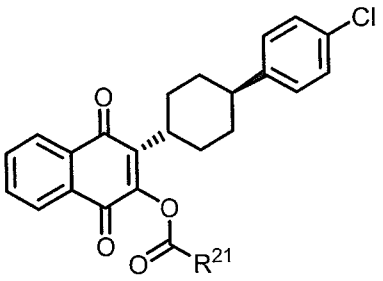
[0026] **FIG. 10** depicts the characteristic X-ray diffraction pattern of the 2nd scale up batch of crystalline ELQ-300-Form II (2nd scale up batch).

[0027] **FIG. 11** depicts the DSC of crystalline ELQ-300-Form II (2nd scale up batch).

CLAIMS

We Claim:

1. A compound of Formula (IV) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof:



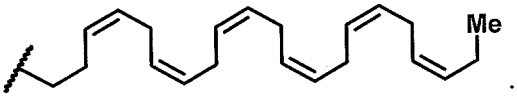
wherein R^{21} is optionally substituted C_3-C_{30}alkenyl or optionally substituted C_2-C_{30}alkynyl.

2. The compound of claim 1, wherein R^{21} is C_3-C_{30}alkenyl.

3. The compound of claim 1, wherein R^{21} is C_6-C_{30}alkenyl.

4. The compound of claim 1, wherein R^{21} is C_6-C_{25}alkenyl.

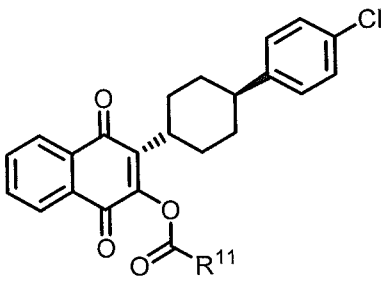
5. The compound of claim 1, wherein R^{21} is C_{15}-C_{25}alkenyl.

6. The compound of claim 1, wherein R^{21} is .

7. A pharmaceutical composition comprising:

(i) an oil; and

(ii) a compound of Formula (III) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof:



Formula (III)

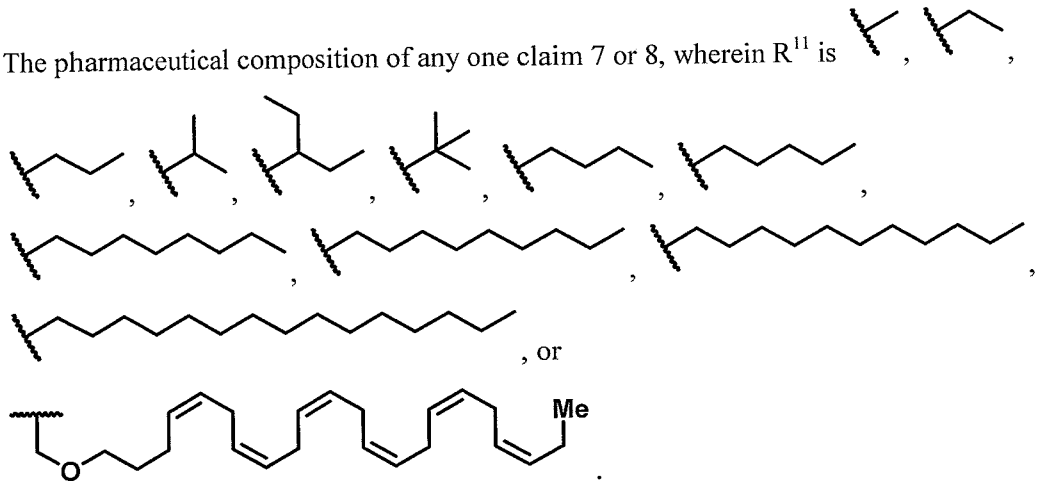
wherein:

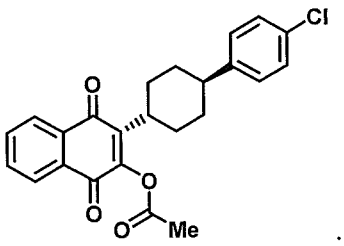
R^{11} is a lipophilic moiety.

8. The pharmaceutical composition of claim 7, wherein R^{11} is optionally substituted C_1-C_{30}alkyl, optionally substituted C_2-C_{30}alkenyl, or optionally substituted C_2-C_{30}alkynyl.

9. The pharmaceutical composition of claim 7 or 8, wherein R^{11} is optionally substituted C_1-C_{20}alkyl, optionally substituted C_2-C_{20}alkenyl, or optionally substituted C_2-C_{20}alkynyl.

10. The pharmaceutical composition of claim 7 or 8, wherein R^{11} is C_1-C_6alkyl.

11. The pharmaceutical composition of any one claim 7 or 8, wherein R^{11} is 

12. The pharmaceutical composition of claim 7, wherein the compound of Formula (III) is 

13. The pharmaceutical composition of any one of claims 7-12, wherein the oil is a vegetable oil.

14. The pharmaceutical composition of any one of claims 7-13, wherein the oil is selected from corn oil, peanut oil, sesame oil, olive oil, palm oil, safflower oil, soybean oil, cottonseed oil, rapeseed oil, sunflower oil and mixtures thereof.

15. The pharmaceutical composition of any one of claims 7-14, wherein the oil is sesame oil.

16. The pharmaceutical composition of any one of claims 7-15, wherein the concentration of the compound of Formula (III) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof is greater than about 50 mg/mL.

17. The pharmaceutical composition of any one of claims 7-16, wherein the concentration of the compound of Formula (III) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof is greater than about 100 mg/mL, in particular greater than about 200 mg/mL.

18. Use of a compound of any one of claims 1-6 or a pharmaceutical composition of any one of claims 7-17 for the preparation of a medicament for treatment or prevention of malaria, wherein the medicament is to be administered to the subject.

19. The use of claim 18, wherein the medicament is to be administered by subcutaneous or intramuscular injection.

20. The use of claim 18 or 19, wherein the medicament is effective for sustained or controlled release.

21. The use of any one of claims 18-20, wherein the compound of Formula (III) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, comprised in the pharmaceutical composition of any one of claims 7-17 is to be administered at a dose of about 5 to about 20 mg/day.

22. The use of any one of claims 18-21, wherein the compound of Formula (III) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, comprised in the pharmaceutical composition of any one of claims 7-17 is released from the pharmaceutical composition over a period of a minimum of about 30 days after administration.

23. The use of any one of claims 18-22, wherein the compound of Formula (III) or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, comprised in the pharmaceutical composition of any one of claim 7-17 is released from the pharmaceutical composition at a rate providing an average concentration of trans-2-[4-(4-chlorophenyl)cyclohexyl]-3-hydroxy-1,4-naphthalenedione in the blood plasma of said subject of at least about 1000 nM over about 13 weeks.

24. The use of any one of claims 18-23, said medicament is to be used in combination with an additional antimalarial agent.

25. The use of claim 24, wherein the additional antimalarial agent is selected from artemisinin, artemisinin derivatives, atovaquone, proguanil, quinine, chloroquine, amodiaquine,

pyrimethamine, doxycycline, clindamycin, mefloquine, primaquine, pyronaridine, halofantrine, or ELQ-300.

26. A method of killing or inhibiting the growth of a Plasmodium species such as Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, or Plasmodium knowlesi comprising contacting the species with an effective amount of a compound of any one of claims 1-6.