[0005] The formulations comprising two or more of an extract of *Ganoderma lucidum*, an extract of *Salvia miltiorrhiza* and an extract of *Scutellaria barbata* are known to have several beneficial effects such as anti-proliferative, antioxidant, immune-boosting, anti-inflammatory, cell cycle modulatory, anti-viral and other activities, while having low toxicity and side effects typically associated with .

[0006] Therefore, there is a need for formulations that allow more efficient formulations that allow delivery of increased amounts of these extracts.

SUMMARY OF THE INVENTION

[0007] The present ~~invention~~ disclosure relates to compositions and methods of preparation of oral formulations with enhanced bioavailability of botanical extracts comprising synergistically active amounts of extracts of *Ganoderma lucidum*, *Salvia miltiorrhiza, Scutellaria baicalensis* and *Scutellaria barbata*. In some embodiments the extracts are organic extracts. In a preferred embodiment, the extract is an ester (ethyl acetate) extract.

[0008] ~~The invention discloses~~In one aspect, there is provided an anti-proliferative formulation comprising: two or more of an extract of *Ganoderma lucidum*, an extract of *Salvia miltiorrhiza*, an extract of *Scutellaria barbata*, and an extract of *Scutellaria baicalensis* wherein each extract comprises about 1 to about 90 percent by weight; and at least one emulsifying agent. In some embodiments the emulsifying agent is selected from Cremophor EL, oleic acid and labrasol.

[0009] The formulation may further comprising an antioxidant. In some embodiments the antioxidant is selected from ascorbic acid and alpha tocopherol.

[0010] The formulation may further comprising a diluent. In some embodiments the diluent is soya oil.

[0011] In some embodiments the extracts are made in a non-alcoholic organic solvent. In some embodiments the non-alcoholic organic solvent is an ester. In preferred embodiments, the ester is ethyl acetate.

[0012] The formulation disclosed exhibits increased bioavailability compared to a formulation without an emulsifying agent and exhibits increased maximum tolerated dose (MTD) compared to a formulation without an emulsifying agent.

[0013] The preferred formulation is disclosed, comprising: an ethyl acetate extract of *Ganoderma lucidum*, an ethyl acetate extract of *Salvia miltiorrhiza*, and an ethyl acetate extract of *Scutellaria barbata* wherein each extract comprises about 1 to about 90 percent by

weight; at least one emulsifying agent selected from Cremophor EL, oleic acid and labrasol; an antioxidant selected from ascorbic acid and alpha tocopherol; and a diluent selected from soya oil.

[0014] The disclosed formulations may further comprise a chemotherapeutic agent. In some embodiments the chemotherapeutic agent is selected from carboplatin, navelbine® (vinorelbine), anthracycline (Doxil), lapatinib (GW57016), Herceptin, gemcitabine (Gemzar®), capecitabine (Xeloda®), alimta, cisplatin, 5-fluorouracil, epirubicin, cyclophosphamide, avastin, velcade®, paclitaxel and docetaxel.

[0015] In some embodiments the chemotherapeutic agent is selected from the group consisting of antimetabolites, nucleoside analogs, platinum-based agents, alkylating agents, tyrosine kinase inhibitors, anthracycline antibiotics, vinca alkloids, proteasome inhibitors, macrolides, and topoisomerase inhibitors.

[0016] In another aspect, there is provided a use of the formulation as disclosed herein in the manufacture of a medicament for alleviating a symptom of cancer or a related disease in a subject suspected of having cancer or the related disease. A method is disclosed for treating a subject suspected of having cancer or a related disease, the method comprising: administering an amount of the formulation according to any of claims 1-15, sufficient for alleviating a symptom of cancer or a related disease.

[0017] In some embodiments the method comprises administration of a formulation comprising 0.1 to 100 mg of an active ingredient consisting of two or more of an extract of *Ganoderma lucidum*, an extract of *Salvia miltiorrhiza*, an extract of *Scutellaria barbata*, and an extract of *Scutellaria baicalensis*.

[0018] In some embodiments of the method 1, 1.5, 2. 2.5, 3, 4, or 5 g of the active ingredient is administered daily.

[0019] In some embodiments of the method, the formulation is administered in 7, 14 or 28 day cycles of 1, 2, 3, 4, 5, or 6 cycles.

[0020] In some embodiments the method further comprises administering a chemotherapeutic agent either in the same formulation or separately administered as part of a therapeutic regimen.

[0021] In some embodiments the chemotherapeutic agent is selected from carboplatin, navelbine® (vinorelbine), anthracycline (Doxil), lapatinib (GW57016), Herceptin®, gemcitabine (Gemzar®), capecitabine (Xeloda®), Alimta®, cisplatin, 5-fluorouracil, epirubicin, cyclophosphamide, Avastin®, Velcade®, paclitaxel and docetaxel.

[0022] In some embodiments the chemotherapeutic agent is selected from the group consisting of antimetabolites, nucleoside analogs, platinum-based agents, alkylating agents, tyrosine kinase inhibitors, anthracycline antibiotics, vinca alkloids, proteasome inhibitors, macrolides, and topoisomerase inhibitors.

[0023] The present ~~invention~~ disclosure and other objects, features, and advantages of the present ~~invention~~ disclosure will become further apparent in the following Detailed Description of the Invention and the accompanying Figures and embodiments.

BRIEF DESCRIPTION OF THE FIGURES

[0024] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present disclosure, the inventions of which can be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein. The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0025] Figure 1 shows an extraction platform for botanical extracts of *Ganoderma lucidum* (#9), *Scutellaria barbata* (#15), and *Salvia miltiorrhiza* (#14).

[0026] Figure 2 shows a schematic of the extraction and first stage concentration for the manufacture of the botanical extracts.

[0027] Figure 3 shows photographs of seven different formulations dispersed in water at a dilution of 10X according to Table 3.

DETAILED DESCRIPTION OF THE INVENTION

[0028] The present invention provides novel methods and botanical compositions for use as multifunctional and multitargeted prophylactics and treatments for human diseases, preferably chronic human diseases. The compositions of the invention have one more of the following properties; anti-inflammatory, anti-oxidant, immune modulating, antiviral, antibacterial, antiproliferative, anticarcinogenic and analgesic. The present invention relates to a novel discovery that botanical extract-based compositions can effectively inhibit numerous response pathways and be substantially less toxic and have less side-effects when administered to an individual.

12. The formulation according to any of claims 1-10, wherein the formulation exhibits increased maximum tolerated dose (MTD) compared to a formulation without an emulsifying agent.

13. The formulation according to claim 1, comprising:

an ethyl acetate extract of *Ganoderma lucidum*, an ethyl acetate extract of *Salvia miltiorrhiza*, and an ethyl acetate extract of *Scutellaria barbata* wherein each extract comprises about 1 to about 90 percent by weight;

at least one emulsifying agent selected from Cremophor EL, oleic acid and labrasol;

an antioxidant selected from ascorbic acid and alpha tocopherol; and

a diluent selected from soya oil.

14. The formulation according to any of claims 1 through 13, further comprising a chemotherapeutic agent.

15. The formulation of claim 14, wherein the chemotherapeutic agent is selected from carboplatin, navelbine® (vinorelbine), anthracycline (Doxil), lapatinib (GW57016), Herceptin®, gemcitabine (Gemzar®), capecitabine (Xeloda®), Alimta®, cisplatin, 5-fluorouracil, epirubicin, cyclophosphamide, Avastin®, Velcade®, paclitaxel and docetaxel.

16. The formulation of claim 14, wherein the chemotherapeutic agent is selected from the group consisting of antimetabolites, nucleoside analogs, platinum-based agents, alkylating agents, tyrosine kinase inhibitors, anthracycline antibiotics, vinca alkloids, proteasome inhibitors, macrolides, and topoisomerase inhibitors.

17. Use of the formulation according to any one of claims 1-15 in the manufacture of a medicament ~~A method~~ for alleviating a symptom of cancer or a related disease ~~treating~~ in a subject suspected of having cancer or ~~a~~ the related disease~~, the method comprising: administering an amount of the formulation according to any of claims 1-15, sufficient for alleviating a symptom of cancer or a related disease~~.

18. The ~~method of~~use according to claim 17, wherein the formulation comprises 0.1 to 100 mg of an active ingredient consisting of two or more of an extract of *Ganoderma lucidum*, an extract of *Salvia miltiorrhiza*, an extract of *Scutellaria barbata*, and an extract of *Scutellaria baicalensis*.

19. The ~~method of~~use according to claim 18 wherein 1, 1.5, 2. 2.5, 3, 4, or 5 g of the active ingredient is to be administered daily.

20. The ~~method of~~use according to claim 18, wherein the formulation is to be administered in 7, 14 or 28 day cycles of 1, 2, 3, 4, 5, or 6 cycles.

21. The ~~method of~~use according to claim 17, ~~further comprising administering~~ wherein a chemotherapeutic agent is to be administered either in the same formulation or separately ~~administered~~ as part of a therapeutic regimen.

22. The ~~method of~~use according to claim 21, wherein the chemotherapeutic agent is selected from carboplatin, navelbine® (vinorelbine), anthracycline (Doxil), lapatinib (GW57016), Herceptin®, gemcitabine (Gemzar®), capecitabine (Xeloda®), Alimta®, cisplatin, 5-fluorouracil, epirubicin, cyclophosphamide, Avastin®, velcade®, paclitaxel and docetaxel.

23. The ~~method of~~use according to claim 21, wherein the chemotherapeutic agent is selected from the group consisting of antimetabolites, nucleoside analogs, platinum-based agents, alkylating agents, tyrosine kinase inhibitors, anthracycline antibiotics, vinca alkloids, proteasome inhibitors, macrolides, and topoisomerase inhibitors.