[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 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] 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 a combination of emulsifying agentscomprising Cremophor EL, oleic acid and labrasol, and wherein the extracts are made in a non-alcoholic organic solvent.

[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 treating cancer in a subject suspected of having cancer. A method is disclosed for treating a subject suspected of having cancer or a related disease, the method comprising: administering an amount of the formulationdisclosed herein, 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.

What is claimed is:

1. A 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 a combination of emulsifying agents comprising: Cremophor EL, oleic acid and labrasol, and wherein the extracts are made in a non-alcoholic organic solvent.

2. The formulation of claim 1, wherein an additional emulsifying agent is added, said additional emulsifying agent selected from the group consisting of: a fatty acid, oleic acid, polyoxyethylene glycerol ester of fatty acids, Tagats, polooxylated castor oil, ethylene glycol esters, glycol stearate, glycol distearate, propylene glycol ester, propylene glycol myristate; glyceryl ester of fatty acids, glyceryl stearates, glyceryl monostearate, sorbitan ester, Span, Tween; polyglyceryl esters, polyglyceryl 4-oleate, fatty alcohol ethoxylates, Brij type emulsifiers, ethoxylated propoxylated block copolymers, poloxamers, polyethylene glycol esters of fatty acids, Labrafils, Labrafacs, and Labrasols, cremophores, glycerol monocaprylate/caprate, Campmul CM 10, Gelucire, Capryol, Captex, Acconon, transcutol, and triacetin.

3. The formulation of claim 1 further comprising an antioxidant.

4. The formulation of claim 3 wherein the antioxidant is selected from ascorbic acid and alpha tocopherol.

5. The formulation of claim 1 further comprising a diluent.

6. The formulation of claim 5 wherein the diluent is soya oil.

7. The formulation of claim 1 wherein the non-alcoholic organic solvent is an ester.

8. The formulation of claim 7 wherein the ester is ethyl acetate.

9. The formulation according to any of claims 1-8, wherein the formulation exhibits increased bioavailability compared to a formulation without an emulsifying agent.

10. The formulation according to any of claims 1-8, wherein the formulation exhibits increased maximum tolerated dose (MTD) compared to a formulation without an emulsifying agent.

11. 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;

a combination of emulsifying agents comprising Cremophor EL, oleic acid and labrasol;

an antioxidant selected from ascorbic acid and alpha tocopherol; and

a diluent selected from soya oil.

12. The formulation according to any of claims 1 through 11, further comprising a chemotherapeutic agent.

13. The formulation of claim 12, 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.

14. The formulation of claim 12, 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.

15. Use of the formulation according to any one of claims 1-13 in the manufacture of a medicament for the treatment of cancer in a subject suspected of having cancer.

16. The use according to claim 15, 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*.

17. The use according to claim 16, wherein 1, 1.5, 2. 2.5, 3, 4, or 5 g of the active ingredient is to be administered daily.

18. The use according to claim 16, wherein the formulation is to be administered in 7, 14 or 28 day cycles of 1, 2, 3, 4, 5, or 6 cycles.

19. The use according to claim 15, wherein a chemotherapeutic agent is to be administered either in the same formulation or separately as part of a therapeutic regimen.

20. The use according to claim 19, 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.

21. The use according to claim 19, 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.