6 months, and the liposuction site may become uneven. Therefore, statistical analyses revealed that even though many people have considered liposuction to reduce the accumulation of localized subcutaneous fat or improve body curves, less than 40 percent of them actually went through liposuction. It shows that the customers who want to improve body curves or reduce localized fat are deterred from the problems of side effects of liposuction, pain after liposuction, or risks of liposuction.

[0004] Although some non-surgical localized fat-reducing pharmaceutical compositions or equipments can partially lower the side effects, they are usually not effective and come with other side effects, such as necrosis of surrounding normal cells, inflammation of surrounding tissues, and sharp pain. Additionally, their administration sites are limited. Therefore, the market is eagerly demanding for an effective localized fat-reducing pharmaceutical composition that has less side effects, a better safety profile, and a shorter recovery period.

[0005] In case of the customers and doctors have significant high demand, the pressing concern is to develop a localized fat-reducing pharmaceutical composition that breaks through the limits of current technologies.

SUMMARY

[0006] In view of the deficiency of prior arts, the present disclosure provides a pharmaceutical composition for reducing localized fat, comprising drug-containing micelles made of surfactants, and curcumin encapsulated in said drug-containing micelles. The pharmaceutical composition for reducing localized fat can reduce the fat at the administration site, and has the advantages of high stability, high fat tissue bioavailability, few side effects, and sustained release.

[0006a] In one aspect, the present invention refers to a pharmaceutical composition to be administered at a local site of a subject, comprising:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, said drug-containing micelles are a microstructure formed by a pharmaceutically acceptable polyoxyethylene castor oil derivative, and the hydrophilic-lipophilic balance value (HLB value) of the polyoxyethylene castor oil derivative is greater than 10.

[0006b] In another aspect, the present invention refers to an aesthetic method of reducing the subcutaneous fat at a local site of a subject, comprising a step of administering a pharmaceutical composition to the local site of the subject, wherein, the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, the drug-containing micelle is a microstructure formed by a pharmaceutically acceptable non-ionic surfactant, and the hydrophilic-lipophilic balance value (HLB value) of the non-ionic surfactant is greater than 10.

[0006c] In another aspect, the present invention refers to an aesthetic method of reducing body weight of a subject, comprising a step of administering a pharmaceutical composition to the subject, wherein, the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, the drug-containing micelle is a microstructure formed by a pharmaceutically acceptable non-ionic surfactant, and the hydrophilic-lipophilic balance value (HLB value) of the non-ionic surfactant is greater than 10.

[0007] The present disclosure can promote apoptosis of the local adipocytes at the administration sites, thereby achieving the goal of reducing localized fat. The present disclosure drastically improves the adverse reactions and side effects of the prior arts such as necrosis of the surrounding cells and inflammation reactions. The present disclosure is suitable for direct injection, subcutaneous implantation, intravenous injection, implanted infusion, cream, patch, and other skin absorption systemic delivery methods to administer at the sites requiring fat reduction without the need or assistance of any surgery or equipment. Preferably, it is administered locally at the subcutaneous fat layer via subcutaneous injection. Preferably, the injection formulation of the present pharmaceutical composition includes but is not limited to powder for injection, or powder for solution for injection. The localized fat mentioned herein includes but is not limited to the fat at the waist, the legs, the arms, the chin, and the face.

[0008] In the present disclosure, the term "turmeric extract" refers to the curcumin ingredient mixture extracted by any solvent and any extraction method, commercially available turmeric extract, any mixture containing at least 75% (wt%) of curcumin, any mixture containing at least 75% (wt%) of curcuminoid, or commercially available curcumin.

[0009] Wherein, curcuminoid is a collective term for curcumin, demethoxycurcumin, and bisdemethoxycurcumin.

[0010] In the present disclosure, the term "resveratrol" refers to the resveratrol extracted from natural plants or commercially available resveratrol. Preferably, the purity of resveratrol is 90% to 100% (wt%).

[0011] In the present disclosure, the term "green tea extract" refers to the green tea ingredient mixture extracted by any solvent and any extraction method, commercially available green tea extract, any mixture containing at least 45% of epigallocatechin gallate (EGCG), or commercially available epigallocatechin gallate (EGCG).

[0012] In the present disclosure, the term "micelle" refers to a microstructure formed by surfactants, wherein each of the surfactants has a hydrophilic end and a hydrophobic (lipophilic) end, and the surfactants are arranged in a way that the hydrophilic ends face outward and the hydrophobic (lipophilic) ends face inward to form the microstructure. Preferably, the microstructure is a spherical structure, a spheroidal structure, or other microstructural structures.

[0013] In the present disclosure, the term "drug-containing micelles" refer to the micelles containing curcuminoid. Preferably, drug-containing micelles refer to the micelles containing curcumin; that is, drug-containing micelles refer to the micelles encapsulating or containing curcuminoid. Preferably, drug-containing micelles refer to the micelles encapsulating or containing curcumin.

[0014] In the present disclosure, the term "second lipophilic drug-containing micelles" refer to the micelles containing any lipophilic drug except curcuminoid. That is, the second lipophilic drug-containing micelles refer to the micelles encapsulating or containing the second lipophilic drug.

[0015] Wherein, the term "other lipophilic drug (or the second lipophilic drug)" refers to at least one of quercetin, synephrine, puerarin, resveratrol, and any lipophilic drug except curcuminoid, or combination thereof. Or, the other lipophilic drug refers to any lipophilic drug except curcumin.

[0016] In the present disclosure, the term "hydrophilic drug" refers to at least one of green tea extract, epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, gallocatechin gallate, gallocatechin, catechin gallate, catechin, epigallocatechin gallate (EGCG), caffeine, carnitine, L-carnitine, synephrine, chlorogenic acid, and other hydrophilic drugs, or combination thereof.

[0017] In the present disclosure, the term "state without precipitation", as used herein, refers to a state wherein no precipitation can be observed with the naked eye, that is,

without the need by the assistance of artificial instruments.

[0018] In the present disclosure, the term "localized subcutaneous fat" refers to the subcutaneous fat at the site administered with the pharmaceutical composition, subcutaneous injection formulation, or subcutaneous fat layer injection formulation of the present disclosure.

[0019] In the present disclosure, the term "pharmaceutically acceptable solution" is at least one of water for injection, aqueous solution for injection, and normal saline, or combination thereof.

[0020] In the present disclosure, the term "local anesthetic" is at least one of amides, para-aminobenzoic acid esters, amino ethers, and other local anesthetic, or combination thereof. Preferably, the amides are at least one of dibucaine, lidocaine, mepivacaine HCl, bupivacine HCl, pyrrocaine HCl, prilocaine HCl, digammacaine, and oxethazaine, or combination thereof. Preferably, the para-aminobenzoic acid esters are at least one of butacaine, dimethocaine, and tutocaine, or combination thereof. Preferably, the amino ethers are at least one of quinisocaine and pramocaine, or combination thereof.

[0021] In the present disclosure, the term "antioxidant" is at least one of beta-carotene, lutein, lycopene, bilirubin, vitamin A, vitamin C (ascorbic acid), vitamin E, uric acid, nitric oxide, nitroxide, pyruvate, catalase, superoxide dismutase, glutathione peroxidases, N-acetyl cysteine, naringenin, and other antioxidant, or combination thereof.

[0022] In the present disclosure, the pharmaceutical composition maintains at a state without precipitation for at least 24 hours when it is subjected to accelerated stability test at 25°C ± 2°C, relative humidity 60% ± 5%, and in the absence of direct light.

[0023] Or, the pharmaceutical composition maintains at a state without precipitation for at least 6 months when it is subjected to accelerated stability test at 25°C ± 2°C, relative humidity 60% ± 5%, and in the absence of direct light.

[0024] The present disclosure provides a pharmaceutical composition to be

[0055] The present disclosure further provides a use of the pharmaceutical composition in preparing a subcutaneous injection formulation, a subcutaneous fat layer injection formulation, a subcutaneous implanted device, a subcutaneous implant, an intravenous injection formulation, a solution for implanted infusion, a cream, a patch, or other skin-absorption delivery systems.

[0056] Preferably, the pharmaceutical composition further comprises second lipophilic drug-containing micelles, and the second lipophilic drug-containing micelles are evenly distributed in the pharmaceutically acceptable aqueous solution; wherein, the second lipophilic drug-containing micelle is a second microstructure formed by a second non-ionic surfactant, and a second lipophilic drug is encapsulated in said second lipophilic drug-containing micelles.

[0057] Preferably, the second non-ionic surfactant is at least one of polysorbate 80 (tween 80), 2-hydroxyethyl 12-hydroxyoctadecanoate (solutol HS 15), polyoxyethylene castor oil derivatives, and other non-ionic surfactants, or combination thereof.

[0058] Preferably, the polyoxyethylene castor oil derivative is at least one of Kolliphor ELP (also known as Cremophor ELP), cremophor RH 40, and other polyoxyethylene castor oil derivatives, or combination thereof.

[0059] Preferably, the pharmaceutically acceptable aqueous solution further comprises a hydrophilic drug.

[0060] The present disclosure further provides a use of the pharmaceutical composition in preparing a drug or a subcutaneous injection formulation for reducing localized subcutaneous fat; the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, the drug-containing micelle is a microstructure formed by a pharmaceutically acceptable non-ionic surfactant, and the hydrophilic-lipophilic balance value (HLB value)

[0080] Preferably, the formulation of the drug is subcutaneous injection formulation or subcutaneous fat layer injection formulation, and the administered dosage of the drug to be injected at the local site is 0.02 ~ 20 mg/cm^2. 。

[0081] The formulation of the drug is subcutaneous injection formulation or subcutaneous fat layer injection formulation, and the administered dosage of the drug to be injected is 0.04 ~ 16 mg/cm^2.

[0082] Preferably, the formulation of the drug is subcutaneous injection formulation or subcutaneous fat layer injection formulation, and the administered dosage of the drug to be injected is 0.01 ~ 40 mg/kg. 。

[0083] Preferably, the formulation of the drug is subcutaneous injection formulation or subcutaneous fat layer injection formulation, and the administered dosage of the drug to be injected is 0.1 ~ 20 mg/kg.

[0084] Preferably, the dosing frequency of the drug to be administered at the administration site is 1~12 times every other day to every 30 days.

[0085] Preferably, the dosing frequency of the drug to be administered at the administration site is 1~6 times every other day to every 30 days.

[0086] Preferably, the curcuminoid is curcumin.

[0087] Preferably, the pharmaceutical composition further comprises at least one of a cosolvent, a suspending agent, and an oil phase excipient, or combination thereof.

[0088] Preferably, the microstructure is co-formed by the non-ionic surfactant and at least one of the oil phase excipient and cosolvent.

[0089] The present disclosure further provides a use of a pharmaceutical composition in preparing a drug or a subcutaneous injection formulation for reducing weight; the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

the administered dosage of the drug to be injected is 0.4 ~ 8 mg/cm^2. 。

[0096] Preferably, the formulation of the drug is subcutaneous injection formulation, intravenous injection formulation, or subcutaneous fat layer injection formulation, and the administered dosage of the drug to be administered is 0.4 ~ 40 mg/kg. 。

[0097] Preferably, the formulation of the drug is subcutaneous injection formulation, intravenous injection formulation, or subcutaneous fat layer injection formulation, and the administered dosage of the drug to be injected is 0.8 ~ 20 mg/kg. 。

[0098] Preferably, the dosing frequency of the drug to be administered at the administered site is 3~60 times every other day to every 20 days.

[0099] Preferably, the dosing frequency of the drug to be administered at the administered site is 6~42 times every other day to every 14 days.

[0100] Preferably, the pharmaceutical composition further comprises at least one of a cosolvent, a suspending agent, and an oil phase excipient, or combination thereof.

[0101] Preferably, the microstructure is co-formed by the non-ionic surfactant and at least one of the oil phase excipient and cosolvent..

[0102] The present disclosure provides a method for reducing subcutaneous fat at a local site of a subject, comprising a step of administering a pharmaceutical composition at the local site of the subject, wherein, the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, the drug-containing micelle is a microstructure formed by a pharmaceutically acceptable non-ionic surfactant, and the hydrophilic-lipophilic balance value (HLB value) of the non-ionic surfactant is greater than 10.

[0103] Preferably, the step is to administer the pharmaceutical composition at the local site of the subject with a subcutaneous injection formulation, a subcutaneous fat layer injection formulation, a solution for implanted infusion, cream formulation, a patch

formulation, or other skin-absorption delivery systems.

[0104] Preferably, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.02 ~ 20 mg/cm^2 。

[0105] Preferably, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.01 ~ 40 mg/kg 。

[0106] Preferably, the dosing frequency of the pharmaceutical composition to be administered at the local site of the subject is 1~12 times every other day to every 30 days.

[0107] The present disclosure provides a method for reducing body weight of a subject, comprising a step of administering a pharmaceutical composition to the subject, wherein, the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, the drug-containing micelle is a microstructure formed by a pharmaceutically acceptable non-ionic surfactant, and the hydrophilic-lipophilic balance value (HLB value) of the non-ionic surfactant is greater than 10.

[0108] Preferably, the step is to administer the pharmaceutical composition at the local site of the subject with a subcutaneous injection formulation, an intravenous injection formulation, or a subcutaneous fat layer injection formulation.

[0109] Preferably, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.2 ~ 16 mg/cm^2.

[0110] Preferably, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.4 ~ 40 mg/kg.

[0111] Preferably, the dosing frequency of the pharmaceutical composition to be administered at the local site of the subject is 3~60 times every other day to every 20 days.

least one of green tea extract, epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, gallocatechin gallate, gallocatechin, catechin gallate, catechin, epigallocatechin gallate (EGCG), caffeine, carnitine, L-carnitine, synephrine, chlorogenic acid, and other hydrophilic drugs, or combination thereof.

18. The pharmaceutical composition of claim 16, the weight ratio of the curcuminoid to the hydrophilic drug is 30:1 to 1:10.

19. An aesthetic method of reducing the subcutaneous fat at a local site of a subject, comprising a step of administering a pharmaceutical composition to the local site of the subject, wherein, the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, the drug-containing micelle is a microstructure formed by a pharmaceutically acceptable non-ionic surfactant, and the hydrophilic-lipophilic balance value (HLB value) of the non-ionic surfactant is greater than 10.

20. The aesthetic method of claim 19, the non-ionic surfactant is at least one of polysorbate 80 (Tween 80), 2-hydroxyethyl 12-hydroxyoctadecanoate (solutol HS 15), polyoxyethylene castor oil derivatives, and other non-ionic surfactants, or combination thereof.

21. The aesthetic method of claim 20, the polyoxyethylene castor oil derivative is at least one of Kolliphor ELP (also known as. Cremophor ELP), cremophor RH 40, and other polyoxyethylene castor oil derivatives, or combination thereof.

22. The aesthetic method of claim 19, the weight ratio of the curcuminoid to the

non-ionic surfactant is 1:5 to 1:500.

23. The aesthetic method of claim 19, the concentration of curcuminoid in the pharmaceutical composition is 0.3 ~ 120 mg/g.

24. The aesthetic method of claim 19, the diameter of the drug-containing micelles is 3 ~ 50 nm.

25. The aesthetic method of claim 19, the pharmaceutical composition further comprises a pharmaceutically acceptable aqueous solution.

26. The aesthetic method of claim 19 or 25, the pharmaceutical composition further comprises a second lipophilic drug-containing micelles; wherein, the second lipophilic drug-containing micelle is a second microstructure formed by a second non-ionic surfactant, and a second lipophilic drug is encapsulated in said second lipophilic drug-containing micelles.

27. The aesthetic method of claim 26, the hydrophilic-lipophilic balance value (HLB value) of the second non-ionic surfactant is greater than 10.

28. The aesthetic method of claim 26, the second non-ionic surfactant is at least one of polysorbate 80 (tween 80), 2-hydroxyethyl 12-hydroxyoctadecanoate (solutol HS 15), polyoxyethylene castor oil derivatives, and other non-ionic surfactants, or combination thereof.

29. The aesthetic method of claim 28, the second non-ionic surfactant is at least one of Kolliphor ELP (Cremophor ELP), cremophor RH 40, and other polyoxyethylene castor oil derivatives, or combination thereof.

30. The aesthetic method of claim 26, the second lipophilic drug is at least one of quercetin, synephrin, puerarin, resveratrol, and any lipophilic drug except curcuminoid, or combination thereof.

31. The aesthetic method of claim 26, the weight ratio of the curcuminoid to the second lipophilic drug is 30:1 ~ 1:10.

32. The aesthetic method of claim 19 or 25, the pharmaceutical composition further comprises a hydrophilic drug.

33. The aesthetic method of claim 32, the hydrophilic drug is at least one of green tea extract, epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, gallocatechin gallate, gallocatechin, catechin gallate, catechin, epigallocatechin gallate (EGCG), caffeine, carnitine, L-carnitine, synephrine, chlorogenic acid, and other hydrophilic drugs, or combination thereof.

34. The aesthetic method of claim 19, the weight ratio of the curcuminoid to the hydrophilic drug is 30:1 to 1:10.

35. The aesthetic method of claim 19, the step is to administer the pharmaceutical composition to the local site of the subject with a subcutaneous injection formulation, a subcutaneous fat layer injection formulation, a solution for implanted infusion, a cream formulation, a patch formulation, or other skin-absorption delivery systems.

36. The aesthetic method of claim 19, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.02 ~ 20 mg/cm^2 ◦

37. The aesthetic method of claim 19, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.01 ~ 40 mg/kg ◦

38. The aesthetic method of claim 19, the dosing frequency of the pharmaceutical composition to be administered at the local site of the subject is 1~12 times every other day to every 30 days.

39. The aesthetic method of claim 19, the curcuminoid is curcumin.

40. The aesthetic method of claim 19, the pharmaceutical composition further comprises at least one of a cosolvent, a suspending agent, and an oil phase excipient, or combination thereof.

41. The aesthetic method of claim 40, the microstructure is co-formed by the non-ionic surfactant and at least one of the oil phase excipient and cosolvent.

42. An aesthetic method of reducing body weight of a subject, comprising a step of administering a pharmaceutical composition to the subject, wherein, the pharmaceutical composition comprises:

drug-containing micelles; and

curcuminoid encapsulated in said drug-containing micelles;

wherein, the drug-containing micelle is a microstructure formed by a pharmaceutically acceptable non-ionic surfactant, and the hydrophilic-lipophilic balance value (HLB value) of the non-ionic surfactant is greater than 10.

43. The aesthetic method of claim 42, the curcuminoid is curcumin.

44. The aesthetic method of claim 42, the pharmaceutical composition further comprises a pharmaceutically acceptable aqueous solution.

45. The aesthetic method of claim 42 or 44, the pharmaceutical composition further comprises a second lipophilic drug-containing micelles; wherein, the second lipophilic drug-containing micelle is a second microstructure formed by a second non-ionic surfactant, a second lipophilic drug is encapsulated in said second lipophilic drug-containing micelles, and the second lipophilic drug is at least one of quercetin, synephrin, puerarin, resveratrol, and any lipophilic drug except curcuminoid, or combination thereof.

46. The aesthetic method of claim 42 or 44, the pharmaceutical composition further

comprises a hydrophilic drug, and the hydrophilic drug is at least one of green tea extract, epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, gallocatechin gallate, gallocatechin, catechin gallate, catechin, epigallocatechin gallate (EGCG), caffeine, carnitine, L-carnitine, synephrine, chlorogenic acid, and other hydrophilic drugs, or combination thereof.

47. The aesthetic method of claim 42, the step is to administer the pharmaceutical composition to a local site of the subject with a subcutaneous injection formulation, an intravenous injection formulation, or a subcutaneous fat layer injection formulation.

48. The aesthetic method of claim 47, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.2 ~ 16 mg/cm^2.

49. The aesthetic method of claim 47, the administered dosage of the pharmaceutical composition to be injected at the local site of the subject is 0.4 ~ 40 mg/kg.

50. The aesthetic method of claim 47, the dosing frequency of the pharmaceutical composition to be administered at the local site of the subject is 3~60 times every other day to every 20 days.

51. The aesthetic method of claim 42, the pharmaceutical composition further comprises at least one of a cosolvent, a suspending agent, and an oil phase excipient, or combination thereof.

52. The aesthetic method of claim 51, the microstructure is co-formed by the non-ionic surfactant and at least one of the oil phase excipient and cosolvent.

53. The aesthetic method of claim 42, the step is to administer the pharmaceutical composition to the local site of the subject with a subcutaneous injection

formulation, a subcutaneous fat layer injection formulation, an intravenous injection formulation, a solution for implanted infusion, a cream, a patch, or other skin-absorption delivery systems.