diabetes, treating inflammation and its associated diseases, and/or lowering blood cholesterol.

Summary

[0006] The present disclosure has identified a composition comprising *Pinus pinaster* stem bark extract, papain, and *Aloe vera* extract that exerts a number of health benefits, for example, the ability to improve organ function, reduce inflammation, and regulate blood sugar levels.

[0007] Accordingly, the present disclosure provides a composition comprising *Pinus pinaster* stem bark extract, papain, and *Aloe vera* extract.

[0007a] In one aspect, the present disclosure provides an aqueous composition comprising *Pinus pinaster* stem bark extract, papain, *Aloe vera* extract, and an acid, wherein the *Pinus pinaster* stem bark extract is present at a concentration of from 2 mg/mL to l0 mg/mL, the papain is present at a concentration of from 1 mg/mL to 5 mg/mL, and the *Aloe vera* extract is present at a concentration of from 0.5 mg/mL to 4 mg/mL, and wherein the composition has a pH of between 3.2 and 4.2.

[0008] The present disclosure provides a composition comprising a therapeutically effective amount of *Pinus pinaster* stem bark extract, papain, and *Aloe vera* extract.

[0009] The present disclosure provides an aqueous composition comprising about 2.6 mg/mL *Pinus pinaster* stem bark extract, about 2.4 mg/mL papain, and about 1.75 mg/mL *Aloe vera* extract.

[0009a] In another aspect, the present disclosure provides an aqueous composition comprising 2.6 mg/mL *Pinus pinaster* stem bark extract, 2.4 mg/mL papain, and 1.75 mg/mL *Aloe vera* extract, and 2 mg/mL glacial acetic acid.

[0010] The following options may be used in conjunction with the aspects as defined above either individually or in any suitable combination.

[0011] The *Aloe vera* extract may be *Aloe vera* leaf extract.

[0012] The therapeutically effective amount of *Pinus pinaster* stem bark extract may correspond to a daily adult human dosage of from about 60 mg to about 1500 mg *Pinus pinaster* stem bark extract; the therapeutically effective amount of papain may correspond to a daily adult human dosage of from about 30 mg to about 1200 mg papain; and the therapeutically effective amount of *Aloe vera* extract may correspond to a daily adult human dosage of from about 15 mg to about 600 mg *Aloe vera* extract.

family *Papilionaceae* such as *Glycyrrhiza uralensis* Fish., or from the family *Asclepiadaceae*, such as *Gongronema latifolium* Benth., or *Gymnema montanum* Hook, or from the family *Sterculiaceae* such as *Helicteres isora* L., As., or from the *Rubiaceae* family such as *Hintonia standleyana*, or from the *Gramineae* family such as *Hordeum vulgare* L. (Barley), or from the *Convolvulaceae* family such as *Ipomoea aquatic* Forsk., or *Ipomea batata* Linn (Sweet potato), or from the *Loranthaceae* family such as *Loranthus micranthus* Linn, or from the *Moraceae* family such as *Morus indica*. L., or from the *Musaceae* family such as *Musa sapientum* Kuntz (Banana), or from the *Euphorbiaceae* family such as *Phyllanthus amarus* Schum. Thonn, or *Phyllanthus niruri* L., or *Phyllanthus sellowianus* Mull. Arg., or from the *Piperacea* family such as *Piper longum*, or from the *Myrtaceae* family such as *Psidium guajava* L., or *Syzygium alternifolium* (Wt) Walp, or from the *Lythraceae* family such as *Punica granatum* L. (pomegranate), or from the *Papilionaceae* family such as *Retama raetam (RR)* (Forssk) Webb., or from the *Adoxaceae* family such as *Sambucus nigra* L., or from the Apocynaceae family such as *Sanguis draxonis*, or from the *Anacardiaceae* family such as *Sclerocarya birea* (A. Rich), or from the *Scrophariaceae* family such as *Scoparia dulcis* L., or from the *Caryophyllaceae* family such as *Spergularia purpurea*, or from the *Chenopodiaceae* family such as *Suaeda fruticosa* (SF) Euras, or from the *Combretaceae* family such as *Terminalia chebula* Retz., or *Terminalia bellirica* (Gaertn), or from the *Menispermaceae* family such as *Tinospora cordifolia* Miers., or from the *Urticaceae* family such as *Urtica pilulifera* L., or from the *Astereaceae* family such as *Vernonia amygdalina* Del., or from the *Solanaceae* family such as *Withania soimifera* (L) Dunal, or from the *Zygophyllaceae* family such as *Zygophyllum gaetulum* Emb and Maire and combinations thereof.

[0035] In another aspect, the present disclosure provides an aqueous composition comprising: 2.40 mg/mL papain; 2.60 mg/mL dry *Pinus pinaster* stem bark extract; 1.75 mg/mL dry *Aloe vera* inner leaf juice; 100.00 mg/mL honey; 2.00 mg/mL glacial acetic acid; 3.00 mg/mL sodium chloride; 400 µg/mL potassium sorbate; 400 µg/mL sodium benzoate; 10.00 mg/mL wildberry flavour UA71225; and 800 µg/mL anthocyanin extract.

[0036] ~~In another aspect, t~~The present disclosure provides an aqueous composition comprising papain, *Pinus pinaster* stem bark extract, and *Aloe vera* inner leaf juice in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice of 2.40 : 2.60 : 1.75 by weight.

[0037] In one embodiment, there is provided an aqueous composition comprising papain, *Pinus pinaster* stem bark extract, *Aloe vera* inner leaf juice, and honey in a ratio of papain : dry *Pinus*

pinaster stem bark extract : dry *Aloe vera* inner leaf juice : honey of 2.40 : 2.60 : 1.75 : 100 by weight.

[0038] In another embodiment, there is provided an aqueous composition comprising papain, *Pinus pinaster* stem bark extract, *Aloe vera* inner leaf juice, and glacial acetic acid in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : glacial acetic acid of 2.40 : 2.60 : 1.75 : 2.00 by weight.

[0039] In another embodiment, there is provided an aqueous composition comprising papain, *Pinus pinaster* stem bark extract, *Aloe vera* inner leaf juice, honey, and glacial acetic acid in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : honey : glacial acetic acid of 2.40 : 2.60 : 1.75 : 100 : 2.00 by weight.

[0040] In yet another embodiment, there is provided an aqueous composition comprising papain, *Pinus pinaster* stem bark extract, *Aloe vera* inner leaf juice, honey, glacial acetic acid, and sodium chloride in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : honey : glacial acetic acid : sodium chloride of 2.40 : 2.60 : 1.75 : 100 : 2.00 : 3.00 by weight.

[0040a] In another aspect, the present disclosure provides an aqueous composition comprising papain, dry *Pinus pinaster* stem bark extract, dry *Aloe vera* inner leaf juice, honey, glacial acetic acid, and sodium chloride in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : honey : glacial acetic acid : sodium chloride of 2.40 : 2.60 : 1.75 : 100 : 2.00 : 3.00 by weight.

[0040b] In another aspect, the present disclosure provides an aqueous composition comprising papain, *Pinus pinaster* stem bark extract, ~~and~~ *Aloe vera* inner leaf juice~~:~~ and glacial acetic acid in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : glacial acetic acid of 2.40 : 2.60 : 1.75 : 2.00 by weight.

[0041] There is provided an aqueous composition comprising papain, dry *Pinus pinaster* stem bark extract, dry *Aloe vera* inner leaf juice, honey, glacial acetic acid, sodium chloride, potassium sorbate, sodium benzoate, wildberry flavour UA71225 and anthocyanin extract in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : honey : glacial acetic acid : sodium chloride : potassium sorbate : sodium benzoate : wildberry flavour UA71225 : anthocyanin extract of 2.40 : 2.60 : 1.75 : 100 : 2.00 : 3.00 : 0.40 : 0.40 : 10.00 : 0.80 by weight.

[0041a] In another aspect, the present disclosure provides an aqueous composition comprising papain, *Pinus pinaster* stem bark extract, *Aloe vera* inner leaf juice, honey, glacial acetic acid, sodium chloride, potassium sorbate, sodium benzoate, wildberry flavour UA71225 and anthocyanin extract in a ratio of papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : honey : glacial acetic acid : sodium chloride : potassium sorbate : sodium benzoate : wildberry flavour UA71225 : anthocyanin extract of 2.40 : 2.60 : 1.75 : 100 : 2.00 : 3.00 : 0.40 : 0.40 : 10.00 : 0.80 by weight.

[0042] The present disclosure provides a method of treating or preventing elevated blood glucose, comprising administering to a subject in need thereof an effective amount of a composition as defined above.

[0042a] There is provided the use of an effective amount of a composition as defined above in the manufacture of a medicament for treating or preventing elevated blood glucose in a subject.

[0043] The present disclosure provides a method of preventing or delaying the onset of type 2 diabetes mellitus (T2DM), comprising administering to a subject in need thereof an effective amount of a composition as defined above.

[0044] The present disclosure provides a method of treating or preventing pre-diabetes, comprising administering to a subject in need thereof an effective amount of a

composition as defined above.

[0045] The present disclosure provides a method of reducing inflammation, comprising administering to a subject in need thereof an effective amount of a composition as defined above.

[0046] The present disclosure provides a method of decreasing cytokine-induced inflammation comprising administering to a subject in need thereof an effective amount of a composition as defined above.

[0047] The present disclosure provides a method of decreasing an oxidative stress response comprising administering to a subject in need thereof an effective amount of a composition as defined above.

~~[0047a] There is provided the use of an effective amount of a composition as defined above in the manufacture of a medicament for decreasing an oxidative stress response in a subject.~~

[0048] The present disclosure provides a method of treating or preventing a disease characterised by elevated levels of cytokine-induced inflammation, comprising administering to a subject in need thereof an effective amount of a composition as defined above.

thereof an effective amount of a composition as defined above. The dysfunction may be selected from the group consisting of: increased thirst and hunger, frequent urination, fatigue/lethargy, blurry vision, sleepiness, and muscle weakness.

[0053] In one embodiment, the composition is administered in combination with metformin or another blood glucose lowering medication.

[0054] The present disclosure provides a method of improving organ function comprising administering to a subject in need thereof an effective amount of a composition as defined above.

~~[0054a] There is provided a use of an effective amount of a composition as defined above in the manufacture of a medicament for improving organ function in a subject.~~

[0055] The present disclosure provides a method of lowering blood cholesterol, comprising administering to a subject in need thereof an effective amount of a composition as defined above. The blood cholesterol may be selected from the group consisting of: low density lipoproteins (LDL), high density lipoproteins (HDL), trigylcerides and total cholesterol. In one embodiment, the present disclosure provides a method of lowering low density lipoprotein (LDL) blood cholesterol levels, comprising administering to a subject in need thereof an effective amount of a composition as defined above. In another embodiment, the present disclosure provides a method of increasing high density lipoprotein (HDL) blood cholesterol levels, comprising administering to a subject in need thereof an effective amount of a composition as defined above. In yet another embodiment, the present disclosure provides a method of decreasing the ratio of Total Cholesterol to HDL, comprising administering to a subject in need thereof an effective amount of a composition as defined above. In yet another embodiment, the present disclosure provides a method of decreasing blood triglyceride levels, comprising administering to a subject in need thereof an effective amount of a composition as defined above.

~~[0055a] There is provided the use of an effective amount of a composition as defined above in the manufacture of a medicament for lowering blood cholesterol in a subject.~~

[0056] The effective amount of the composition may correspond to: a daily adult human dosage of from about 60 mg to about 1500 mg *Pinus pinaster* stem bark extract; a daily adult human dosage of from about 30 mg to about 1200 mg papain; and a daily adult human dosage of from about 15 mg to about 600 mg *Aloe vera* extract. For example, the effective amount of the composition may correspond to: a daily adult human dosage of about 260 mg *Pinus pinaster* stem bark extract; a daily adult human dosage of about 240 mg papain; and a daily adult human dosage of about 175 mg *Aloe vera* extract. The daily adult human dosage of *Pinus pinaster* stem

as defined above for the manufacture of a medicament for increasing general wellbeing, e.g., increasing energy levels, improving vitality, improving sleep, improving breathing ability, improving levels of physical activity, improving mental functioning, and/or improving physical functioning in a subject.

[0078a] In another aspect, there is provided a method of manufacturing the aqueous composition as defined above, said method comprising: combining *Pinus pinaster* stem bark extract, papain, *Aloe vera* extract~~-~~, and an ~~glacial acetic~~ acid in water.

[0078b] In another aspect, there is provided a method of manufacturing the aqueous composition of any one of claims 21 to 24, said method comprising: combining *Pinus pinaster* stem bark extract, papain, *Aloe vera* inner leaf juice, and glacial acetic acid in water.

Brief Description of the Drawings

[0079] Embodiments of the present invention will now be described, by way of example only with reference to the accompanying figures wherein:

[0080] **Figure 1** shows that a composition according to Example 1 decreases inflammatory markers (a) TNF-alpha-induced VCAM-1, (b) TNF-alpha-induced ICAM-1 and (c) TNF-alpha-induced ELAM in human coronary artery endothelial cells. HCAECs were exposed to the indicated amounts (µL/mL) of the composition of Example 1 for 3 hours prior to exposure to TNF-alpha.

[0081] **Figure 2** shows that a composition according to Example 1 decreases protein levels of (a) TNF-alpha-induced VCAM-1 and (b) TNF-alpha-induced ICAM-1 in human coronary artery endothelial cells. HCAECs were exposed to the indicated amounts (µL/mL) of the composition of Example 1 for 3 hours prior to exposure to TNF-alpha.

[0082] **Figure 3** shows that a composition according to Example 1 decreases activation of the key mediator of inflammation, NFkB. HCAECs were exposed to the indicated amounts (µL/mL) of the composition of Example 1 prior to exposure to TNF-alpha.

[0083] **Figure 4** shows that a composition according to Example 1 decreases cytokine-induced ROS levels in TNF-alpha-induced HCAECs. HCAECs were exposed to the indicated amounts (µL/mL) of the composition of Example 1 for 3 hours prior to exposure to TNF-alpha.

[0084] **Figure 5** shows that a composition according to Example 1 decreases (a) NOX-4 and increases (b) SOD-1 levels in TNF-alpha-induced HCAECs. HCAECs were exposed to the indicated amounts (µL/mL) of the composition of Example 1 prior to exposure to TNF-alpha.

[0085] **Figure 6** shows that a composition according to Example 1 ingested by athletes pre-training decreases CRP levels in their blood post-training (dark grey = runners, light grey = cyclists).

[0086] **Figure 7** shows that a composition according to Example 1 blocks VCAM-1 levels from

CLAIMS:

1. An aqueous composition comprising *Pinus pinaster* stem bark extract, papain, *Aloe vera* extract, and an acid, wherein
   the *Pinus pinaster* stem bark extract is present at a concentration of from 2 mg/mL to l0 mg/mL,
   the papain is present at a concentration of from 1 mg/mL to 5 mg/mL, and
   the *Aloe vera* extract is present at a concentration of from 0.5 mg/mL to 4 mg/mL, and
   wherein the composition has a pH of between 3.2 and 4.2.

2. The aqueous composition according to claim 1, wherein the *Aloe vera* extract is *Aloe vera* leaf extract.

3. The aqueous composition according to claim 1 or claim 2, wherein the acid is acetic acid.

4. The aqueous composition according to any one of claims 1 to 3, wherein the composition further comprises honey.

5. The aqueous composition according to any one of claims 1 to 4, wherein the composition comprises one or more additives selected from the group consisting of: a preservative, a flavouring agent, a salt, and a pigment.

6. The aqueous composition according to any one of claims 1 to 5, wherein the composition comprises a salt, and wherein the salt is sodium chloride.

7. The aqueous composition according to any one of claims 1 to 6, further comprising an additional component selected from the group consisting of: an omega-3 fatty acid, a phytonutrient, a source of protein, an amino acid, an antioxidant, a vitamin, a mineral, a plant extract, and mixtures thereof.

8. The aqueous composition according to any one of claims 1 to 7, wherein the composition is synergistic.

9. The aqueous composition according to any one of claims 1 to 8, wherein the

composition is adapted for oral administration.

10. The aqueous composition according to claim 9, wherein the composition is in a form selected from the group consisting of: ~~a tablet,~~ a capsule, ~~a chewable tablet,~~ a soft gel capsule, ~~a sachet, a powder, granules,~~ a liquid, a syrup, a liquid suspension, an emulsion, and a solution~~, and combinations thereof~~.

~~11. The composition according to any one of claims 1 to 10, wherein the composition is an aqueous composition.~~

~~12~~11. The aqueous composition according to any one of claims 1 to ~~11~~10, wherein the composition has a pH of 3.7.

~~13~~12. The aqueous composition according to any one of claims 1 to ~~12~~11, wherein the *Pinus pinaster* stem bark extract is present at a concentration of 2.6 mg/mL.

~~14~~13. The aqueous composition according to any one of claims 1 to ~~13~~12, wherein the papain is present at a concentration of 2.4 mg/mL.

~~15~~14. The aqueous composition according to any one of claims 1 to ~~14~~13, wherein the *Aloe vera* extract is present at a concentration of 1.75 mg/mL.

~~16~~15. The aqueous composition according to any one of claims 1 to ~~15~~14, wherein the composition comprises glacial acetic acid at a concentration of from 1 mg/mL to 8 mg/mL.

~~17~~16. The aqueous composition according to claim ~~16~~15, wherein the glacial acetic acid is present at a concentration of 2 mg/mL.

~~18~~17. The aqueous composition according to any one of claims 1 to ~~17~~16, wherein the composition further comprises honey at a concentration of from 50 mg/mL to 200 mg/mL.

~~19~~18. The aqueous composition according to claim ~~18~~17, wherein the honey is present at a concentration of 100 mg/mL.

~~20~~19. An aqueous composition comprising 2.6 mg/mL *Pinus pinaster* stem bark extract, 2.4 mg/mL papain, 1.75 mg/mL *Aloe vera* extract, and 2 mg/mL glacial acetic acid.

~~21~~20. The aqueous composition according to claim ~~20~~19, further comprising 100 mg/mL honey.

~~22~~21. An aqueous composition comprising:

2.40 mg/mL papain;

2.60 mg/mL *Pinus pinaster* stem bark extract;

1.75 mg/mL *Aloe vera* inner leaf juice;

100.00 mg/mL honey;

2.00 mg/mL glacial acetic acid;

3.00 mg/mL sodium chloride;

400 µg/mL potassium sorbate;

400 µg/mL sodium benzoate;

10.00 mg/mL wildberry flavour UA71225; and

800 µg/mL anthocyanin extract.

~~23~~22. An aqueous composition comprising papain, *Pinus pinaster* stem bark extract, *Aloe vera* inner leaf juice, honey, glacial acetic acid, sodium chloride, potassium sorbate, sodium benzoate, wildberry flavour UA71225 and anthocyanin extract

in a ratio of

papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : honey : glacial acetic acid : sodium chloride : potassium sorbate : sodium benzoate : wildberry flavour UA71225 : anthocyanin extract

of 2.40 : 2.60 : 1.75 : 100 : 2.00 : 3.00 : 0.40 : 0.40 : 10.00 : 0.80 by weight.

~~24~~23. An aqueous composition comprising papain, dry *Pinus pinaster* stem bark extract, dry *Aloe vera* inner leaf juice, honey, glacial acetic acid, and sodium chloride

in a ratio of

papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : honey : glacial acetic acid : sodium chloride

of 2.40 : 2.60 : 1.75 : 100 : 2.00 : 3.00 by weight.

~~25~~24. An aqueous composition comprising papain, *Pinus pinaster* stem bark extract, ~~and~~ *Aloe vera* inner leaf juice~~:~~ and glacial acetic acid in a ratio of

papain : dry *Pinus pinaster* stem bark extract : dry *Aloe vera* inner leaf juice : glacial acetic acid

of 2.40 : 2.60 : 1.75 : 2.00 by weight.

~~26~~25. A method of manufacturing the aqueous composition of any one of claims 1 to ~~24~~20, said method comprising:

combining *Pinus pinaster* stem bark extract, papain, *Aloe vera* extract, and ~~glacial acetic~~ an acid in water.

26. A method of manufacturing the aqueous composition of any one of claims 21 to 24, said method comprising:

combining *Pinus pinaster* stem bark extract, papain, *Aloe vera* inner leaf juice, and glacial acetic acid in water.

27. The method of claim 25 or 26, further comprising:

adding honey.