



(51) International Patent Classification:

A61K 31/352 (2006.01) *A61P 21/02* (2006.01)
A61K 31/00 (2006.01) *A61P 25/00* (2006.01)

SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(21) International Application Number:

PCT/GB2024/053151

Published:

— with international search report (Art. 21(3))

(22) International Filing Date:

18 December 2024 (18.12.2024)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

2319656.1 20 December 2023 (20.12.2023) GB

(71) Applicant: **NICOVENTURES TRADING LIMITED**
[GB/GB]; Globe House, 1 Water Street, London WC2R
3LA (GB).

(72) Inventors: **RIVERA, Andrea Domenico**; c/o Nicoven-
tures Trading Limited, Globe House, 1 Water Street, Lon-
don WC2R 3LA (GB). **KHALED, Sara Ben**; c/o Nicoven-
tures Trading Limited, Globe House, 1 Water Street, Lon-
don WC2R 3LA (GB).

(74) Agent: **O'FARRELL, Jennifer**; D Young & Co LLP, 3 No-
ble Street, London EC2V 7BQ (GB).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,
CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG,
KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY,
MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA,
NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO,
RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS,
ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, CV,
GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST,
SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ,
RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ,
DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT,
LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE,

(54) Title: COMBINATION OF QUERCETIN AND ONE OR MORE ADDITIONAL ACTIVE SUBSTANCES FOR USE IN MOOD
MODULATION AND/OR REDUCTION OF MUSCLE AND MENTAL FATIGUE

(57) Abstract: The present disclosure relates to non-therapeutic uses of a bioactive substance in combination with one or more addi-
tional active substance(s); a composition comprising the bioactive substance in combination with one or more additional active sub-
stance(s); non-therapeutic methods comprising administering the bioactive substance in combination with one or more additional ac-
tive substance(s) or the composition to a subject; a consumable comprising the bioactive substance in combination with one or more
additional active substance(s) or the composition; and a delivery system comprising the consumable.



COMBINATION OF QUERCETIN AND ONE OR MORE ADDITIONAL ACTIVE SUBSTANCES
FOR USE IN MOOD MODULATION AND/OR REDUCTION OF MUSCLE AND MENTAL FATIGUE

FIELD OF THE INVENTION

5 The present disclosure relates to non-therapeutic uses of a bioactive substance in combination with one or more additional active substance(s); a composition comprising the bioactive substance in combination with one or more additional active substance(s); non-therapeutic methods comprising administering the bioactive substance in combination with one or more additional active substance(s) or the composition to a subject; a consumable comprising the
10 bioactive substance in combination with one or more additional active substance(s) or the composition; and a delivery system comprising the consumable.

BACKGROUND OF THE INVENTION

15 The present disclosure relates to bioactive substances or biologically active ingredients in combination with one or more additional active substance(s) intended for human use and compositions comprising bioactive substances or biologically active ingredients in combination with one or more additional active substance(s).

20 The wellness industry is growing, with consumers increasingly interested in their overall physical and mental wellbeing and/or performance. Therefore, products that can provide a beneficial effect such as enhancing the wellbeing of an individual, be that through improved health, better sleep, increased mindfulness or other measures of 'wellness', have become popular and are of increased commercial importance. Such products may include bioactive
25 ingredients that are delivered to the user in order to cause a biological response in the user that may enhance physical or mental wellbeing and/or performance of the user.

Therefore, it would be desirable to provide consumers with non-therapeutic products to modulate mood, enhance performance and/or provide other health benefits such as providing
30 an anti-fatigue effect, restoring balance and increasing adaptability to overcome daily physical and mental challenges.

SUMMARY OF THE INVENTION

35 In accordance with some embodiments described herein, there is provided a non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s) for mood modulation of a subject, wherein the bioactive substance is quercetin.

The additional active substance may be cannabidiol (CBD) or a derivative thereof.

The additional active substance may be CBD.

5

Suitably, the bioactive substance in combination with one or more additional active substance(s) may improve mood of the subject.

10

The bioactive substance in combination with one or more additional active substance(s) may modulate (e.g. improve) mood by activating the serotonin pathway.

The bioactive substance in combination with one or more additional active substance(s) may modulate the mood of the subject by providing the subject with a calming effect.

15

The bioactive substance in combination with one or more additional active substance(s) may modulate the mood of the subject by providing the subject with a stimulating effect.

20

In accordance with some embodiments described herein, there is provided a non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s), pre-exercise, to reduce muscle and/or mental fatigue in a subject, wherein the bioactive substance is quercetin and the additional active substance comprises CBD or a derivative thereof.

25

The additional active substance may be CBD.

The use of the bioactive substance may be before exercise.

30

In accordance with some embodiments described herein, there is provided a composition comprising the bioactive substance in combination with one or more additional active substance(s) for use in non-therapeutic mood modulation of a subject as described herein, or for use to reduce muscle and/or mental fatigue in a subject as described herein.

35

The additional active substance in the composition may be CBD or a derivative thereof. The additional active substance in the composition may be CBD.

The composition may additionally comprise one or more flavour(s).

The one or more flavour(s) may comprise an aroma.

In accordance with some embodiments described herein, there is provided a non-therapeutic method of modulating mood in a subject, wherein said method comprises administering the
5 bioactive substance in combination with one or more additional active substance(s) as described herein or the composition as described herein, to the subject.

In accordance with some embodiments described herein, there is provided a non-therapeutic method of reducing muscle and/or mental fatigue of a subject, during or after exercise,
10 comprising administering the bioactive substance in combination with one or more additional active substance(s) as described herein or the composition as described herein.

Suitably, the bioactive substance in combination with one or more additional active substance(s) as described herein or the composition as described herein may be administered
15 to the subject before the exercise commences.

In accordance with some embodiments described herein, there is provided a consumable comprising the bioactive substance in combination with one or more additional active substance(s) as described herein or the composition as described herein.
20

In accordance with some embodiments described herein, there is provided a delivery system comprising the consumable as described herein.

The delivery system may be a non-combustible aerosol provision system, or an aerosol-free
25 delivery system.

The delivery system may be a vaping device, home diffuser, car diffuser, wax melt or an inhaler.

30 The delivery system may be an aerosol-free delivery system.

The aerosol-free delivery system may be one or more of an edible, a lozenge, a gum, a patch, an inhalable powder, a beverage, a shot, an oil, an ointment, a supplement or an oral product.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of the invention will now be described by way of example only, with reference to accompanying drawings, in which:

5

Figure 1: shows a dose response curve demonstrating the synergistic effect of quercetin in combination with different concentrations of CBD (200 nM and 1 μ M).

DEFINITIONS

10

This disclosure is not limited by the exemplary methods and materials disclosed herein, and any methods and materials similar or equivalent to those described herein can be used in the practice or testing of embodiments of this disclosure.

15

The headings provided herein are not limitations of the various aspects or embodiments of this disclosure which can be had by reference to the specification as a whole. Accordingly, the terms defined immediately below are more fully defined by reference to the specification as a whole.

20

As used herein, “bioactive substance” refers to one or more compounds that has an effect on a living organism, tissue or cell. The “bioactive substance” may be derived from plants, animals, or animal products. The “bioactive substance” may also be synthetic.

25

As used herein, “synthetic” refers to ‘man-made’ compounds, e.g. those synthesised by *in vitro* methods. However, “synthetic” compounds may also include “biosynthetic” compounds, for example compounds that are produced in a living organism, or a laboratory process modelled after the synthesis pathway in a living organism. “Biosynthetic” compounds may include those compounds that are produced by or in, for example, a plant, bacteria, fungi, etc., e.g. following genetic engineering to insert the relevant gene(s) to result in the expression of the desired synthetic compound.

30

35

As used herein, “subject” refers to the recipient of the bioactive substance. The “subject” may be human or animal. In some embodiments, the subject is human. In some embodiments, the subject is an animal. Where the subject is an animal, the animal may be mammalian, avian, reptilian, amphibian, invertebrate or aquatic (fish). Where the animal is a mammalian animal, the mammalian animal may be a monotreme (such as a platypus or echidna), marsupial (such as a kangaroo, wallaby, wombat, etc.), or a placental mammal

(such as a primate – monkeys, apes; canine – dogs, wolves, foxes, etc.; feline – domestic cats, lions, tigers, etc.)

As used herein, “calming” refers to the state of being soothed, pacified, placated, sedate, tranquil, content, satisfied, comfortable, serene, composed, unwound, relaxed, rejuvenated, or other similar terms. The feeling of “calm” is unique to each subject. Thus, a subject is considered to have achieved a feeling of “calm” if they feel any reduction in tension, agitation, nervousness, frustration, anger, anxiousness, upset, distress, worry, unrest, apprehension, vexation, fear, stress, or similar negative moods or emotions.

As used herein, “stimulating” refers to the state of being revitalised, revived, refreshed, uplifted, invigorated, boosted, aroused, elevated or other similar terms. The feeling of “stimulation” is unique to each subject. Thus, a subject is considered to have achieved a feeling of “stimulation” if they feel any increase in energy, motivation, drive, enthusiasm, or similar positive moods or emotions or a decrease in apathy, lethargy, or similar negative moods or emotions.

As used herein, “fatigue” refers to muscle and/or mental fatigue. The state of “muscle fatigue” refers to the feeling of weakness in the muscle following exertion. Other symptoms of muscle fatigue may include soreness, localised pain, muscle twitching, trembling, a weak grip and muscle cramps. The state of “mental fatigue” refers to exhaustion, burnout, feeling drained, tiredness, reduction in concentration, or other similar terms. The feeling of “muscle fatigue” and “mental fatigue” is unique to each subject. Thus, a subject is considered to have achieved a reduction in “muscle fatigue” and/or mental fatigue, if they feel a reduction in any of the listed symptoms compared to how they would feel following exercise without having taken the bioactive substance. For example, the subject may experience a feeling of being restored, refilled, energised, rebalanced, refreshed, recovered or recharged, or other similar terms.

As used herein, “anxiolytic active” refers to an active which has the general effect of reducing anxiety and/or stress.

As used herein, “ergogenic active” refers to an active which enhances performance, especially physical performance and athleticism i.e. is energy-giving.

As used herein, “nootropic active” refers to an active which improves cognitive function such as memory, creativity and attention, i.e. is cognitive-enhancing.

As used herein, "relaxant active" refers to an active which has a calming or relaxing but not sedative effect.

As used herein, "synergy" and "synergistic" refers to an effect produced by a combination of two or more compounds, wherein the combined effect is greater than could be predicted by the individual potencies of each compound.

As used herein, the terms "flavour" and "flavourant" refer to materials which, where local regulations permit, may be used to create a desired taste, aroma or other somatosensorial sensation in a product for adult consumers. They may include naturally occurring flavour materials, botanicals, extracts of botanicals, synthetically obtained materials, or combinations thereof (e.g., tobacco, cannabis, licorice (liquorice), hydrangea, eugenol, Japanese white bark magnolia leaf, chamomile, fenugreek, clove, maple, matcha, menthol, Japanese mint, aniseed (anise), cinnamon, turmeric, Indian spices, Asian spices, herb, wintergreen, cherry, berry, red berry, cranberry, peach, apple, orange, mango, clementine, lemon, lime, tropical fruit, papaya, rhubarb, grape, durian, dragon fruit, cucumber, blueberry, mulberry, citrus fruits, Drambuie, bourbon, scotch, whiskey, gin, tequila, rum, spearmint, peppermint, lavender, aloe vera, cardamom, celery, cascarilla, nutmeg, sandalwood, bergamot, geranium, khat, naswar, betel, shisha, pine, honey essence, rose oil, vanilla, lemon oil, orange oil, orange blossom, cherry blossom, cassia, caraway, cognac, jasmine, ylang-ylang, sage, fennel, wasabi, piment, ginger, coriander, coffee, hemp, a mint oil from any species of the genus *Mentha*, eucalyptus, star anise, cocoa, lemongrass, rooibos, flax, ginkgo biloba, hazel, hibiscus, laurel, mate, orange skin, rose, tea such as green tea or black tea, thyme, juniper, elderflower, basil, bay leaves, cumin, oregano, paprika, rosemary, saffron, lemon peel, mint, beefsteak plant, curcuma, cilantro, myrtle, cassis, valerian, pimento, mace, damien, marjoram, olive, lemon balm, lemon basil, chive, carvi, verben, tarragon, limonene, thymol, camphene), flavour enhancers, bitterness receptor site blockers, sensorial receptor site activators or stimulators, sugars and/or sugar substitutes (e.g., sucralose, acesulfame potassium, aspartame, saccharine, cyclamates, lactose, sucrose, glucose, fructose, sorbitol, or mannitol), and other additives such as charcoal, chlorophyll, minerals, botanicals, or breath freshening agents. They may be imitation, synthetic or natural ingredients or blends thereof. They may be in any suitable form, for example, liquid such as an oil, solid such as a powder, or gas.

Other definitions of terms may appear throughout the specification. Before the exemplary aspects and embodiments are described in more detail, it is important to understand that this disclosure is not limited to particular aspects or embodiments described, which as such may,

of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular aspects or embodiments only, and is not intended to be limiting, since the scope of the present disclosure will be limited only by the appended claims.

5

It must be noted that as used herein and in the appended claims, the singular forms “a”, “an”, and “the” include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to “a bioactive substance” or “a flavour” includes a plurality of such candidate agents and equivalents thereof known to those skilled in the art, and so forth.

10

DETAILED DESCRIPTION OF THE INVENTION

In one aspect, there is provided a non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s) for mood modulation of a subject, wherein the bioactive substance is quercetin.

15

In an embodiment, the bioactive substance modulates mood by activating the serotonin pathway.

20 In an embodiment, the mood modulation of the subject is calming or stimulating.

In an embodiment, the mood modulation of the subject is calming.

In an embodiment, the mood modulation of the subject is stimulating.

25

In one embodiment the bioactive substance is an anxiolytic active.

In one embodiment the bioactive substance is an ergogenic active.

30 In one embodiment the bioactive substance is a nootropic active.

In one embodiment the bioactive substance is a relaxant active.

In one aspect, there is provided a non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s) to reduce exercise induced muscle and/or mental fatigue in a subject, wherein the bioactive substance is quercetin.

35

In an embodiment, there is provided a non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s) to reduce exercise induced muscle fatigue in a subject, wherein the bioactive substance is quercetin.

- 5 In an embodiment, there is provided a non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s) to reduce exercise induced mental fatigue in a subject, wherein the bioactive substance is quercetin.

10 In an embodiment, the non-therapeutic use of the bioactive substance in combination with one or more additional active substance(s) is before exercise.

The additional active substance

15 In an embodiment, the bioactive substance described herein is provided in combination with one or more additional active substance(s).

In an embodiment, the bioactive substance described herein is provided in combination with two or more additional active substance(s).

20 In an embodiment, the bioactive substance described herein is provided in combination with three or more additional active substance(s).

In an embodiment, the bioactive substance described herein is provided in combination with four or more additional active substance(s).

25

In an embodiment, the bioactive substance described herein is provided in combination with five, six, seven, eight, nine, ten or more additional active substance(s).

30 The additional active substance may be any substance that elicits a desired effect on the subject.

The bioactive substance and the additional active substance may work synergistically to potentiate the desired effect.

35 The desired effect produced by the bioactive substance in combination with one or more additional active substance(s) may be calming, stimulating, or reducing muscle and/or mental fatigue.

The bioactive substance in combination with one or more additional active substance(s) provides a calming effect.

- 5 The bioactive substance in combination with one or more additional active substance(s) provides a stimulating effect.

The bioactive substance in combination with one or more additional active substance(s) reduces muscle fatigue.

10

The bioactive substance in combination with one or more additional active substance(s) reduces mental fatigue.

- 15 Alternatively, the additional active substance may produce an additional desired effect that is different to the desired effect produced by the bioactive substance. The additional desired effect may be complementary to the desired effect produced by the bioactive substance.

- 20 In some instances, the additional active substance may work both synergistically with the bioactive substance and produce an additional desired effect, such that the desired effect is greater than when the bioactive substance is used alone and an additional desired effect is also experienced.

- 25 In instances where multiple additional active substances are provided, multiple different additional desired effects may be achieved and/or one or more of the additional active substances may work synergistically with the bioactive substance. These effects may be complimentary to the desired effect produced by the bioactive substance.

- 30 In a further embodiment, the additional active substance potentiates the effect of the bioactive substance.

- In a further embodiment, the additional active substance potentiates the effect of the bioactive substance and produces an additional effect to the effect produced by the bioactive substance.

- 35 In a further embodiment, the additional active substance produces an additional effect to the effect produced by the bioactive substance.

In a further embodiment, the combination of the bioactive substance and the one or more additional active substance(s) is synergistic.

5 In an embodiment, the one or more additional active substance comprises CBD or a derivative thereof.

In an embodiment, the one or more additional active substance comprises CBD.

10 In an embodiment, the one or more additional active substance is CBD.

Composition

15 In one aspect, there is provided a composition comprising the bioactive substance in combination with one or more additional active substance(s) for use in non-therapeutic mood modulation of a subject as described herein, or for use to reduce exercise induced muscle and/or mental fatigue in a subject as described herein.

In one embodiment, the bioactive substance is quercetin.

20 In one embodiment the additional active substance comprises CBD or a derivative thereof.

In one embodiment the additional active substance comprises or is CBD.

25 In an embodiment, the composition additionally comprises one or more flavours.

In an embodiment, the flavour comprises menthol, spearmint and/or peppermint.

In an embodiment, the flavour comprises flavour components of cucumber, blueberry, citrus fruits and/or redberry.

30 In an embodiment, the flavour comprises eugenol.

In an embodiment, the flavour comprises flavour components extracted from tobacco.

35 In an embodiment, the flavour comprises flavour components extracted from cannabis.

In an embodiment, the flavour may comprise a sensate, which is intended to achieve a somatosensorial sensation which are usually chemically induced and perceived by the stimulation of the fifth cranial nerve (trigeminal nerve), in addition to or in place of aroma or taste nerves, and these may include agents providing heating, cooling, tingling, numbing
5 effect. A suitable heat effect agent may be, but is not limited to, vanillyl ethyl ether and a suitable cooling agent may be, but not limited to eucalyptol, WS-3.

In a further embodiment, the one or more flavours comprises an aroma.

10 In an embodiment, the composition comprises:

- i) a bioactive substance, wherein the bioactive substance is quercetin;
- ii) one or more additional active substance(s); and optionally
- iii) one or more flavours as disclosed herein.

15 In a further embodiment, the one or more additional active substance(s) is CBD.

Method

In one aspect, there is provided a non-therapeutic method of modulating mood in a subject,
20 wherein said method comprises administering the bioactive substance in combination with one or more additional active substance(s) as described herein or the composition as described herein, to the subject.

In one aspect, there is provided a non-therapeutic method of reducing muscle and/or mental
25 fatigue of a subject, during or after exercise, comprising administering the bioactive substance in combination with one or more additional active substance(s) as disclosed herein or the composition as disclosed herein, to the subject before the exercise commences.

The subject is a healthy individual. For example the subject has not been diagnosed with any
30 disease, medical condition, or deficiency.

Consumable

In one aspect, there is provided a consumable comprising the bioactive substance in
35 combination with one or more additional active substance(s) as described herein or the composition as described herein.

A consumable is an article comprising or consisting of aerosol-generating material, part or all of which is intended to be consumed during use by a user. A consumable may comprise one or more other components, such as an aerosol-generating material storage area, an aerosol-generating material transfer component, an aerosol generation area, a housing, a wrapper, a mouthpiece, a filter and/or an aerosol-modifying agent. A consumable may also comprise an aerosol generator, such as a heater, that emits heat to cause the aerosol-generating material to generate aerosol in use. The heater may, for example, comprise combustible material, a material heatable by electrical conduction, or a susceptor.

A consumable may also be an article that does not comprise an aerosol-generating material. Instead, the consumable comprises an article, part or all of which is intended to be consumed during use by a user, such as gums, patches, or inhalable powders.

Delivery system

In one aspect, there is provided a delivery system comprising the consumable as disclosed herein.

As used herein, the term “delivery system” is intended to encompass systems that deliver at least one substance to a user, and includes:

non-combustible aerosol provision systems that release compounds from an aerosol-generating material without combusting the aerosol-generating material, such as electronic cigarettes, tobacco heating products, and hybrid systems to generate aerosol using a combination of aerosol-generating materials; and

aerosol-free delivery systems that deliver the at least one substance to a user orally, nasally, transdermally or in another way without forming an aerosol, including but not limited to, lozenges, gums, patches, articles comprising inhalable powders, and oral products such as snus or moist snuff.

In an embodiment, the delivery system is a non-combustible aerosol provision system, or an aerosol-free delivery system.

According to the present disclosure, a “non-combustible” aerosol provision system is one where a constituent aerosol-generating material of the aerosol provision system (or component thereof) is not combusted or burned in order to facilitate delivery of at least one substance to a user.

In an embodiment, the delivery system is a non-combustible aerosol provision system, such as a powered non-combustible aerosol provision system.

In an embodiment, the non-combustible aerosol provision system is an electronic cigarette, also known as a vaping device or electronic nicotine delivery system (END), although it is noted that the presence of nicotine in the aerosol-generating material is not a requirement.

In an embodiment, the non-combustible aerosol provision system is an aerosol-generating material heating system, also known as a heat-not-burn system. An example of such a system is a tobacco heating system, although it is noted that the presence of tobacco in the heat-not-burn system is not a requirement.

In an embodiment, the non-combustible aerosol provision system is a hybrid system to generate aerosol using a combination of aerosol-generating materials, one or a plurality of which may be heated. Each of the aerosol-generating materials may be, for example, in the form of a solid, liquid or gel. In some embodiments, the hybrid system comprises a liquid or gel aerosol-generating material and a solid aerosol-generating material. The solid aerosol-generating material may comprise, for example, tobacco or a non-tobacco product.

Typically, the non-combustible aerosol provision system may comprise a non-combustible aerosol provision device and a consumable for use with the non-combustible aerosol provision device.

In an embodiment, the consumable for use with the non-combustible aerosol provision device is a consumable as disclosed herein.

In an embodiment, the disclosure relates to consumables comprising aerosol-generating material and the composition as disclosed herein, configured to be used with non-combustible aerosol provision devices. These consumables are sometimes referred to as articles throughout the disclosure.

In an embodiment, the non-combustible aerosol provision system, such as a non-combustible aerosol provision device thereof, may comprise a power source and a controller. The power source may, for example, be an electric power source or an exothermic power source. In some embodiments, the exothermic power source comprises

a carbon substrate which may be energised so as to distribute power in the form of heat to an aerosol-generating material or to a heat transfer material in proximity to the exothermic power source.

- 5 In an embodiment, the non-combustible aerosol provision system may comprise an area for receiving the consumable, an aerosol generator, an aerosol generation area, a housing, a mouthpiece, a filter and/or an aerosol-modifying agent.

- 10 In an embodiment, the consumable for use with the non-combustible aerosol provision device may comprise aerosol-generating material and the composition as disclosed herein, an aerosol-generating material storage area, an aerosol-generating material transfer component, an aerosol generator, an aerosol generation area, a housing, a wrapper, a filter, a mouthpiece, and/or an aerosol-modifying agent.

- 15 In an embodiment, the delivery system is a non-combustible aerosol provision system.

In a further embodiment, the non-combustible aerosol provision system is one or more of the group comprising or consisting of a vaping device, home diffuser, car diffuser, wax melt or an inhaler.

20

In yet a further embodiment, the inhaler is a metered dose inhaler, a dry powder inhaler, or a soft mist inhaler.

In an embodiment, the delivery system is an aerosol-free delivery system.

25

In an embodiment, the delivery system is an aerosol-free delivery system that delivers at least one substance to a user orally, nasally, transdermally or in another way without forming an aerosol, including but not limited to, lozenges, gums, patches, articles comprising inhalable powders, and oral products such as snus or moist snuff. Whilst snus or moist snuff are traditionally tobacco products, the contents of the snus pouch or snuff may be something other than tobacco.

30

In a further embodiment, the aerosol-free delivery system is an edible, a lozenge, a gum, a patch, an inhalable powder, a beverage, a shot, an oil, an ointment, a supplement or an oral product.

35

The various embodiments described herein are presented only to assist in understanding

and teaching the claimed features. These embodiments are provided as a representative sample of embodiments only, and are not exhaustive and/or exclusive. It is to be understood that advantages, embodiments, examples, functions, features, structures, and/or other aspects described herein are not to be considered limitations on the scope of the invention as defined by the claims or limitations on equivalents to the claims, and that other embodiments may be utilised and modifications may be made without departing from the scope of the claimed invention. Various embodiments of the invention may suitably comprise, consist of, or consist essentially of, appropriate combinations of the disclosed elements, components, features, parts, steps, means, etc., other than those specifically described herein. In addition, this disclosure may include other inventions not presently claimed, but which may be claimed in future.

The invention will now be described with reference to the following non-limiting examples.

EXAMPLES

Example 1: MAPK signalling pathway activation by the bioactive

MAPK signalling pathway activation is measured by the degree of ERK1/2 phosphorylation. The heterologous expression system consists of HEK-293T cells expressing the human version of the G protein-coupled receptors (GPCRs) that are tested.

To avoid reliability issues due to the use of Western blot for measuring pERK versus total ERK phosphorylation, a Perkin Elmer proprietary method is used. It consists of the AlphaScreen®SureFire® kit (Perkin Elmer, Wellesley, USA).

Cultured cells are placed in 96-well plates in non-supplemented medium two hours before starting the incubation with the different compounds. For the agonistic assay type, compounds were added 7 minutes before agonist removal and cell lysis (see below for details when assaying allosteric potential). Cells were washed twice with cold PBS before the addition of 30 µl/well "Ultra lysis buffer" -PerkinElmer- (15 min treatment). Afterwards, 10 µl of each supernatant were placed in white ProxiPlate 384-well plates and ERK1/2 phosphorylation was determined using an AlphaScreen®SureFire® kit (PerkinElmer), following the instructions of the supplier, and using an EnSpire® Multimode Plate Reader (PerkinElmer, Waltham, MA, USA). The reference value (100%) was the value achieved in the absence of any treatment (basal). Agonist effects were given in percentage with respect to the basal value.

Allosteric potential

Allosteric potential was assayed using 100 nM of the compound 15 minutes before adding a selective agonist of the tested receptor.

5 EC50 calculation

Dose response curves were obtained using compounds in concentrations ranging from 10 nM to 10 µM. Values are given in percentage considering that 100% was the basal level of phosphorylation. IC50 values were obtained by non-linear regression using the following equation

10
$$Y = Min + \frac{Max - Min}{1 + (X/EC50)^{Hill\ coefficient}}$$

Concentration is in the X axis and the effect (percentage) is in the Y axis. The percentage of ERK1/2 phosphorylation is given respect to the basal value in the absence of any compound (100), therefore, MIN=100. Calculated MAX is the maximal degree of phosphorylation, i.e. the
15 maximal effect of a given compound. Hill coefficient value is fixed to 1.

The effect of quercetin with or without the addition of CBD was screened against human receptors 5HT-1A (Serotonin 1A), expressed in the HEK cell line.

20 It is clear that the combination of quercetin and CBD is synergistic. Figure 3 demonstrates that both the tested concentrations of CBD (200 nM and 1 µM) provide more than an additive effect when combined with increasing concentrations of quercetin.

For example, quercetin alone generates no increase in ERK 1/2 phosphorylation and the
25 response to 200 nM CBD is also negligible. However, when combined, the entire dose response curve is shifted upwards, demonstrating that the combination of quercetin and CBD results in activity that could not be predicted from the response to quercetin or CBD alone. An even greater increase in the response is seen with the addition of 1 µM CBD in combination with quercetin. It is therefore plausible that the concentrations of CBD and quercetin may be
30 adjusted to tailor the level of response seen at the 5HT-1A receptor.

Results of the analysis are displayed in Figure1.

Example 2: ADMET prediction data for quercetin and CBD

Absorption, Distribution, Metabolism, Excretion and Toxicity predictions were analysed for quercetin, and CBD. Results of the predicted pharmacokinetics are summarised in Table 1 below.

		Quercetin	CBD
Solubility class	ESOL	Soluble	Moderate
	Ali	Soluble	Poor
	Silicos- IT	Soluble	Moderate
GI absorption		High	High
BBB permeant		No	Yes
Pgp substrate		No	No
CYP1A2 inhibitor		Yes	No
CYP2C19 inhibitor		No	Yes
CYP2C9 inhibitor		No	Yes
CYP2D6 inhibitor		Yes	Yes
CYP3A4 inhibitor		Yes	Yes
Log Kp [cm/s]		-7.05	-3.59

Table 1: ADMET predictions

CLAIMS

1. Non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s) for mood modulation of a subject, wherein the bioactive substance is quercetin and the one or more additional active substance(s) comprises cannabidiol (CBD) or a derivative thereof.

2. The bioactive substance in combination with one or more additional active substance(s) according to claim 1, wherein the bioactive substance modulates mood by activating the serotonin pathway.

3. The bioactive substance in combination with one or more additional active substance(s) according to claim 1 or claim 2, wherein the mood modulation of the subject is calming or stimulating.

4. Non-therapeutic use of a bioactive substance in combination with one or more additional active substance(s) to reduce exercise induced muscle and/or mental fatigue in a subject, wherein the bioactive substance is quercetin and the one or more additional active substance(s) comprises CBD or a derivative thereof.

5. The non-therapeutic use according to claim 4, wherein the use of the bioactive substance in combination with one or more additional active substance(s) is before exercise.

6. The bioactive substance in combination with one or more additional active substance(s) according to any one of claims 1-5, wherein the one or more additional active substance(s) is CBD.

7. The bioactive substance in combination with one or more additional active substance(s) according to any one of claims 1-6, wherein the combination of the bioactive substance and the one or more additional active substance(s) is synergistic.

8. A composition comprising the bioactive substance in combination with one or more additional active substance(s), wherein the one or more additional active substance(s) comprises CBD or a derivative thereof, for use in non-therapeutic mood modulation of a subject according to any one of claims 1-3, 6, and 7, or for use to reduce exercise induced muscle and/or mental fatigue in a subject according to any one of claims 4-7.

9. The composition according to claim 8, wherein the one or more additional active substance(s) is CBD.

10. The composition according to claim 8 or claim 9, wherein the composition additionally
5 comprises one or more flavours.

11. The composition according to claim 10, wherein the one or more flavours comprises an aroma.

10 12. A non-therapeutic method of modulating mood in a subject, wherein said method comprises administering the bioactive substance in combination with one or more additional active substance(s) according to any one of claims 1-3, 6, and 7 or the composition according to any one of claims 8-11, to the subject.

15 13. A non-therapeutic method of reducing muscle and/or mental fatigue of a subject, during or after exercise, comprising administering the bioactive substance in combination with one or more additional active substance(s) according to any one of claims 4-7 or the composition according to any one of claims 8-11, to the subject.

20 14. The non-therapeutic method according to claim 13, wherein said bioactive substance in combination with one or more additional active substance(s) or composition is administered to the subject before the exercise commences.

25 15. A consumable comprising the bioactive substance in combination with one or more additional active substance(s) according to any one of claims 1-7 or the composition according to any one of claims 8-11.

16. A delivery system comprising the consumable according to claim 15.

30 17. The delivery system according to claim 16, wherein the delivery system is a non-combustible aerosol provision system, or an aerosol-free delivery system.

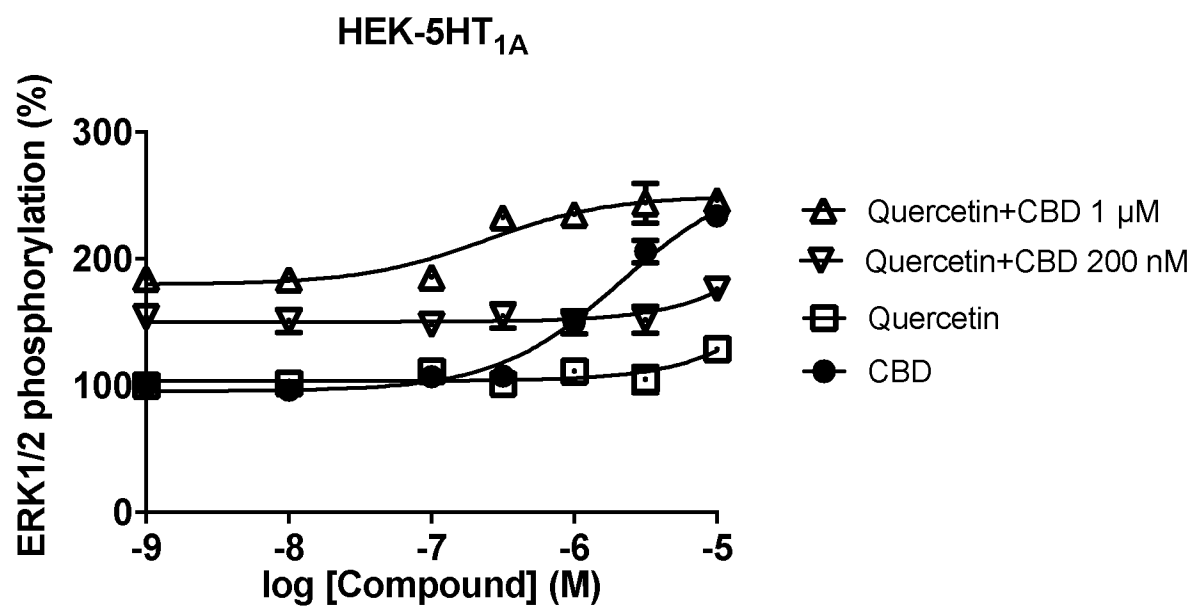
18. The delivery system according to claim 16 or claim 17, wherein the delivery system is a vaping device, home diffuser, car diffuser, wax melt or an inhaler.

35

19. The delivery system according to claim 17, wherein the delivery system is an aerosol-free delivery system.

20. The delivery system according to claim 19, wherein the aerosol-free delivery system is one or more of an edible, a lozenge, a gum, a patch, an inhalable powder, a beverage, a shot, an oil, an ointment, a supplement or an oral product.

Figure 1



INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2024/053151

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/352 A61K31/00 A61P21/02 A61P25/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2023/270764 A1 (YIRMIYA RAZ [IL]) 31 August 2023 (2023-08-31) claims; examples -----	1-20
X	US 2020/281890 A1 (MACNAIR LAURA [CA] ET AL) 10 September 2020 (2020-09-10) example 1 -----	1-20
X	US 2022/401406 A1 (MAIDA VINCENZO [CA]) 22 December 2022 (2022-12-22) examples -----	1-20
X	CN 112 472 661 A (YUNNAN SUWANGRUN BIO PHARMACY CO LTD) 12 March 2021 (2021-03-12) claim 19 paragraph [0001] examples -----	1-20
	- / - -	



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

20 March 2025

Date of mailing of the international search report

28/03/2025

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Moutafidou, Nikoleta

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2024/053151

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PINZONE ANTHONY G. ET AL: "Cannabis use for exercise recovery in trained individuals: a survey study", JOURNAL OF CANNABIS RESEARCH, vol. 5, no. 1, 5 August 2023 (2023-08-05), XP093261455, ISSN: 2522-5782, DOI: 10.1186/s42238-023-00198-5 Retrieved from the Internet: URL:https://link.springer.com/article/10.1186/s42238-023-00198-5/fulltext.html> results; discussion; the whole document -----	1-20
X	ROJANO-ORTEGA DANIEL ET AL: "Quercetin supplementation promotes recovery after exercise-induced muscle damage: a systematic review and meta-analysis of randomized controlled trials", BIOLOGY OF SPORT, vol. 40, no. 3, 1 January 2023 (2023-01-01), pages 813-825, XP093261466, ISSN: 0860-021X, DOI: 10.5114/biolsport.2023.121320 the whole document -----	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2024/053151

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2023270764 A1	31-08-2023	US 2023270764 A1 WO 2022013874 A1	31-08-2023 20-01-2022
US 2020281890 A1	10-09-2020	CA 3076929 A1 EP 3687527 A1 US 2020281890 A1 WO 2019056128 A1 WO 2019056129 A2	28-03-2019 05-08-2020 10-09-2020 28-03-2019 28-03-2019
US 2022401406 A1	22-12-2022	AU 2020358148 A1 BR 112022004703 A2 CA 3057647 A1 CA 3153176 A1 CN 114502156 A EP 4037675 A1 IL 291416 A JP 2022551845 A KR 20220079894 A US 2022401406 A1 WO 2021062555 A1	07-04-2022 14-06-2022 03-04-2021 08-04-2021 13-05-2022 10-08-2022 01-05-2022 14-12-2022 14-06-2022 22-12-2022 08-04-2021
CN 112472661 A	12-03-2021	NONE	