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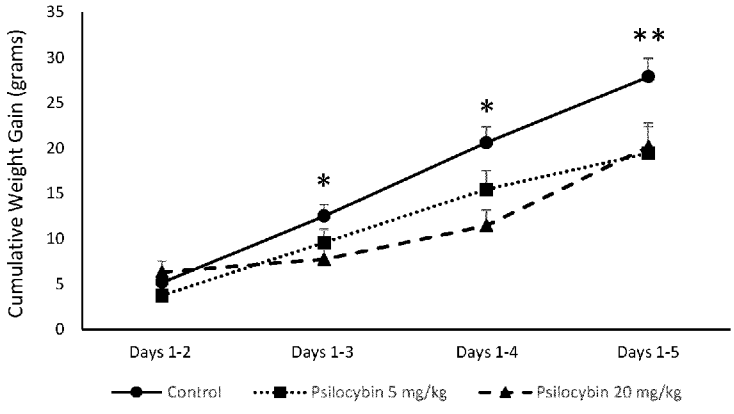
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(54) Title: USE OF LSD, ESA, OR DMT FOR WEIGHT LOSS.

Figure 1



* = significantly different versus 20 mg/kg psilocybin group, $p < 0.05$
** = significantly different versus both psilocybin groups, $p < 0.05$

(57) Abstract: Disclosed is a method of aiding in weight loss, treating compulsive eating disorder, treating obesity or a complication thereof, and/or altering the diet of an individual comprising administering DMT, LSD, LSA, or an analog thereof.

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[Continued on next page]

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Field of Invention

The invention relates to methods of using broad 5-HT agonists and in particular 5-HT_{2A} agonists, such as serotonergic psychadelics such as DMT or LSD, for weight loss.

Background

Obesity

Obesity has been formally recognized by the World Health Organization as a global epidemic. Over 35% of adults in the United States, and more than 500 million adults on the planet are categorized as obese. Obesity is expected to cause or contribute to hundreds of thousands of deaths a year in the United States alone. Obesity reduces life expectancy, increases susceptibility to other disease states such as cardiovascular disease, high blood pressure, diabetes mellitus, hypertension, multiple sclerosis, erectile dysfunction, urinary incontinence, chronic renal failure, sleep apnea, asthma, and many forms of cancer. In addition to the clinically defined obese (those with a Body Mass Index (in kg/m^2) of greater than 30), a large percentage of the population, while not obese, are overweight, which is undesired in many cultures. Obesity, and overweightness, is a leading preventable cause of death worldwide.

In most cases, obesity and overweightness is caused by a food energy intake that exceeds energy use. This is typically due to a combination of excessive eating and a lack of physical activity, though insufficient sleep, endocrine disruptors, a natural genetic disposition, and atypical antipsychotic use may also contribute. In almost all cases, obesity and overweightness can be treated by either or a combination of decreased caloric intake and increased exercise.

Unfortunately, decreasing caloric intake can be a very difficult task for many people. The Dieting industry is enormous, with some estimates showing that Americans spend over $60 billion annually on diet and weight loss products. Unfortunately, many of these diets do not work; much of this is thought to be because it is not enough to change food

intake, an individual's behavior needs to change for long term success.

Many diet disorders exist, including binge eating disorder, also called compulsive eating disorder, where an individual will eat even when uncomfortably full or not hungry, often eating much faster than normal with a loss of control over how much or what is eaten. Compulsive overeating may also be ironically caused by a restrictive diet. Many people also overeat simply because they are hungry. Quality of diet also has a significant impact on obesity and overweightness, with low caloric content foods such as green vegetables contributing less to obesity than calorie dense foods which have high calories for their volume, such as refined carbohydrates. Interestingly, human food preferences (such as preferences for certain types of food) have been linked with a 5-HT_{2A} serotonergic receptor polymorphism (Prado-Lima et al, Mol Psychiatry 2006 Oct). Other 5-HT_{2A} receptors have been associated with anorexia nervosa and bulimia nervosa.

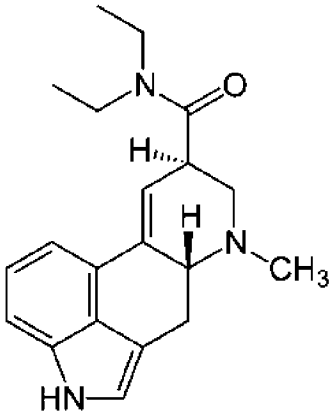
Obesity, over-eating, and an individual's relationship with food (including food choices) is an extremely complex, multi-factorial problem, which includes psychological issues, biochemical issues, as well as other issues such as social, cultural, and class issues. There is some evidence that the mesolimbic dopamine reward system is heavily implicated in the addictive role of both food and drugs of abuse (e.g. alcohol and nicotine). There has also recently been a line of evidence that suggests that specific kinds of foods that are high in sugars and fats may also induce behaviours that are hallmarks of addiction. For example, it has been suggested that rats will drink sugar-laced water in a binge-like manner, which will also subsequently release dopamine in the nucleus accumbens (Avena et al., . Neuroscience, 139(3), 813-820 (2006); Rada et al., Neuroscience, 134(3), 737-744 (2005)). Thus, it has been suggested that obesity and disorders of addiction may have a similar neurobiological aetiology. Also, in healthy individuals with a BMI in the 'normal' range, there is similar functional activity associated with the consumption of foodstuff high in sugar and fats. Certain foods stimulate release of dopamine in the ventral striatum at a rate which is proportional to the rating of the pleasantness of the food. Food cravings have been found to be a predictor of treatment outcomes in relation to obesity; thus reduction of food cravings may be a useful focus in treatment of obesity and

obesity-caused diseases/disorders or diseases/disorders to which obesity is a contributing factor.

Drugs that modify the serotonergic (5-hydroxytryptophan [5-HTP]) system have historically represented the most common and effective compounds for weight loss (Halford JC et al., Drugs 2007; 67(1):27-55). These include compounds such as sibutramine and the combination of fenfluramine/phentermine (known as "fen-phen"). Serotonin plays a key role in meal satiety, as increased serotonin levels in the brain result in decreased appetite, with subsequent weight loss. This is posited to occur through selective stimulation of the 5-HT1B, 5-HT2A and 5-HT2C serotonin receptors (Voigt JP and H. Fink, Behav Brain Res. 2015; 277:14-31; Currie PJ and DV Coscina, Brain Res. 1998; 803(1-2):212-217). However, drugs such as fenfluramine/phentermine work by causing a general increase in serotonin levels. As there are at least 14 different types of serotonin receptors (Green, Br. J. Pharmacol. 2006; 147 Suppl 1 (Suppl 1): S145-52), this results in many "off target" serotonin receptors being stimulated, which in turn causes a host of unwanted side-effects (such as cardiac valvulopathies with fenfluramine/phentermine).

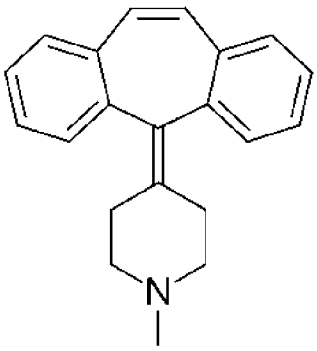
LSD

LSD, or lysergic acid diethylamide, is a hallucinogenic drug. It currently has no approved medical use, though it has been studied for use as treatment of alcoholism, depression, anxiety, and drug dependence, with positive preliminary results. The predominant use of LSD is as a recreational hallucinogenic; it is widely known for the visual hallucinations and illusions, including anything from subtle changes in perception to dramatic cognitive shifts, with changes in auditory and visual perception commonly occurring. Sense of time, memories, emotions, senses, and general awareness are typically altered, sometimes dramatically. Stationary objects may appear to move and/or talk; distortion of time and sound are also seed with commonly used dosages. LSD has been known to trigger anxiety, panic, and/or paranoia, sometimes very strongly, while under its influence, in a phenomena known colloquially as a "bad trip". CIA research suggests that individuals may be more suggestible or succeptible to influence while under its effects.

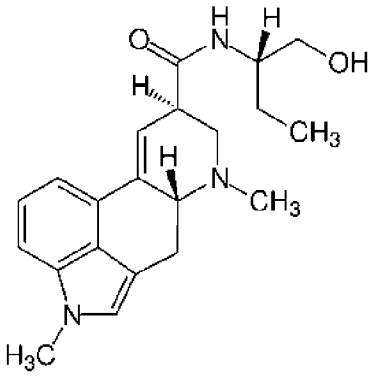


LSD

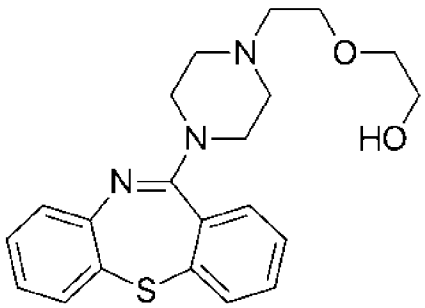
LSD is known to bind primarily to 5-HT_{1A}, 5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_{5A} and 5-HT_{6} receptors. Its psychedelic effects are attributed to cross-activation of 5-HT_{2A} receptor heteromers. Interestingly, antagonists specific to 5-HT_{2A} are known to block the psychedelic effects of LSD, while leaving it able to bind with other 5HT2 receptors. 5-HT_{2A} specific antagonists include cyproheptadine (periactin), methysergide (1-methyl-D-lysergic acid butanolamide or methysergide maleate), and quetiapine.



Cyproheptadine



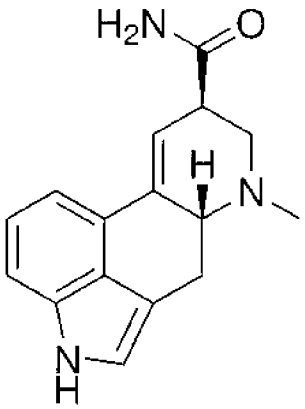
Methysergide



Quetiapine

LSD has also been shown to activate DARPP-32 related pathways, and enhance dopamine D2 receptor protomer recognition and signaling of D2-5HT2A receptor complexes.

A related drug, d-lysergamide, or d-lysergic acid amide (LSA), is believed to work on similar receptors, but has significantly lower hallucinatory or psychedelic effects.



LSA

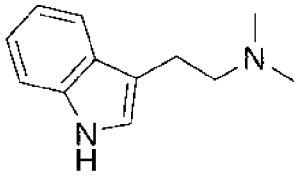
Recreational (psychoactive) doses of LSD may be between 20 and 500 micrograms, and may be administered sublingually, through buccal administration, internasal administration (snorting powder), intramuscularly, subcutaneously, or intravenously. Typically, it is taken by putting a tab of blotting paper, containing the drug, under the tongue.

So-called "microdosing" of LSD is also known, for use as a "cognitive enhancer" (Rose, S "Do Microdoses of LSD Change Your Mind?" Scientific American, April 16, 2019). Microdosing means taking less than a traditional psychoactive dose, at a repeated frequency. For example, taking roughly 1/10th of a trip-inducing dose (10 micrograms of LSD), every three or four days (Fadiman, J, "The Psychadelic Explorer's Guide", 2011). Anecedotal reports of the benefits of microdosing include decreased anxiety and depression, increased feelings of determination and self-resolve. Microdosed individuals reportedly do not feel the typical effects of the drug but over-reproduced temporal intervals of 2000 ms and longer (Yanakieva S et al, "The effects of microdose LSD on time perception: a randomized, double-blind, placebo-controlled trial", Psychopharmacology 236, 1159-1170).

DMT

DMT, or *N,N*-Dimethyltryptamine, is a derivative and structural analog of tryptamine. It is known as a hallucinogenic drug. It currently has no approved medical use, though DMT-containing plants are commonly used in indigenous Amazonian shamanic practice, and is sometimes found in the drink ayahuasca. DMT is found naturally in several

plants including *Mimosa tenuiflora, Diplopterys cabrerana*, and *Psychotria viridis.* It is structurally similar to psilocin and its precursor psilocybin, a chemical found in so-called "magic mushrooms". The predominant use of DMT is as a recreational hallucinogenic. It can be inhaled, ingested, or injected, and, can be orally ingested in combination with a monoamine oxidase inhibitor to increase the duration of its effect.



DMT

DMT may be extracted or purified from a variety of plants and trees that contain it; synthetic synthesis is also well elucidated in the art.

DMT effects may include profound time-dilation, visual, auditory, tactile and proprioceptive distortions and hallucinations, and even experiences that may defy verbal or visual description, including perception of hyperbolic geometry, impossible objects, or even aliens, higher beings, non-human gnomes, angels, or demons, sometimes colloquially referred to as "fractal elves" or "machine elves".

The metabolic pathway that causes the DMT effects is largely unknown, though it is believed to have non-selective binding to 5-HT_{1A}, 5-HT_{1B}, 5-HT_{1D}, 5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_{6}, 5-HT_{7}, with an agonist activity at 5-HT_{1A}, 5-HT_{2A} and 5-HT_{2C}. It has also been shown to have affinity for dopamine D1, alpha1 and alpha2-adrenergic, sigma1, and imidazoline-1 receptors. Its psychedelic effects are typically attributed to its 5-HT_{2A} agonist activity, where it acts as a functionally selective activator of the 5-HT_{2A} receptor, though 5-HT_{1A} and 5-HT_{2C} activity may also be a factor.

Recreational (psychoactive) doses of DMT differ dramatically depending on route of administration. Intravenous doses of 0.2 – 0.4 mg/kg of body weight have been known to cause hallucinogenic effects, where lower doses, such as 0.01 to 0.05 mg/kg have been shown to produce somaesthetic and emotional responses but not hallucinations. Vaporized,

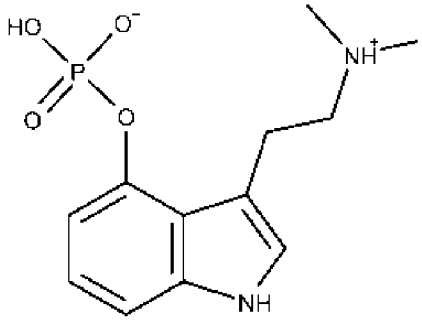
inhaled DMT is typically taken at a dose of 20-60 milligrams, in one or more successive breaths, and typically has extremely fast onset of action (less than a minute) with peak effects reached within a minute and effects lasting 5-15 minutes. Oral administration is usually combined with a monoamine oxidase inhibitor such as a reversible inhibitor of monoamine oxidase A (RIMAs); this decreases metabolizing of the DMT and prolongs the effect time of the drug. natural source RIMAs, such as curcumin, harmaline, and harmine, may be utilized, as may a commercially - available RIMA such as brofaromine, caroxazone, eprobemide, minaprine, metralindole, methylene blue, moclobemide, pirlindole, or toloxatone.

Functional and structural analogs of DMT are known, such as *O*-acetylpsilocin (4-AcO-DMT), 5-MeO-DMT, bufotenin (5-HO-DMT), psilocybin (4-PO-DMT) and psilocin (4-HO-DMT).

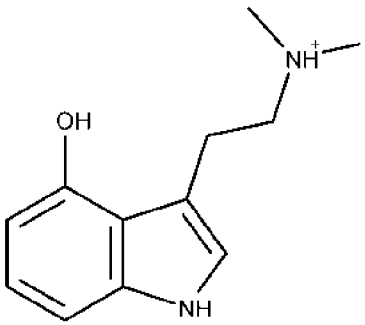
So-called "microdosing" of DMT is not known, since the only known use of DMT is as a hallucinatory recreational drug. Microdosing means taking less than a traditional psychoactive dose, at a repeated frequency. For example, taking roughly 1/10th of a trip-inducing dose (2 milligrams by inhalation, for example), daily.

Psilocin/Psilocybin

Psilocin, or 4-hydroxy-N,N-dimethyltryptamine, and its phosphorylated prodrug, psilocybin, were first isolated from *Psilocybe Mexicana* in 1958. They have both since been synthetically produced. Structural analogs of psilocin, many having higher stability, are also known, such as 4-SH-dimethyltryptamine, 1-methylpsilocin, 4-fluoro-N,N-dimethyltryptamine, O-acetylpsilocin, 4-hydroxy-N-methyl-N-isopropyltryptamine, and 4-hydroxy-N-methyl-N-ethyltryptamine.



Psilocybin



Psilocin

Psilocin/psilocybin and its analogs are most commonly used as a psychoactive recreational drug, with a half-life of 1-3 hours when orally administered. Interestingly, they are known as 5-HT_{2A}, 5-HT_{2C} and 5-HT_{1A} agonists or partial agonists. Psilocybin is present in most psychedelic mushrooms, and at "normal" dosages creates mind-altering effects including euphoria, visual and mental hallucinations, changes in perception, a distorted sense of time, spiritual experiences, nausea, and panic attacks.

Psilocybin/psilocin, is a direct agonist at select serotonin receptors.

Like DMT and LSD, Psilocin and psilocybin are also used recreationally, both in small amounts (microdosing) and in larger amounts that induce hallucinatory effects.

"Creative" doses of psilocin/psilocybin have been used recreationally for decades, and are also commonly referred to as "recreational", "hallucinatory" "psychedelic" or "hypnagogic" doses. These doses are typically over 250 mg of dried *psilocybin cubensis* mushroom in a single dose, more typically about 1 to about 3.5 g, equivalent, broadly speaking, to about 1.5 to 22 mg of psilocybin, for example, 6 - 13 mg of psilocybin. Doses of as high as 5 g (equivalent to about 32 mg of psilocybin) are known and commonly used. Creative doses are well documented, and create what is often referred to as a "trip", the effects of which include increased intensity of emotional experiences, increased introspection, and altered psychological functioning in the form of "hypnagogic experiences" thought of as a transitory state between wakefulness and sleep. Many people on such creative doses report perceptual changes, such as a distorted sense of time and hallucinations, with changes in visual perception, such as halos around lights and objects, and images or patterns appearing even when eyes are closed. "Creative" doses are sometimes referred to as minidoses (for doses at the low end of the creative range – about 250-750 mg of dried *psilocybin cubensis* or equivalent active); medium doses (for doses in the middle of the creative range – about 500-1500 mg of dried *psilocybin cubensis* or equivalent active) and moderate doses (for doses at the high end of the creative range – 1500 – 3500 mg of dried *psilocybin cubensis* or equivalent active) (http://thethirdwave.co/psychedelics/shrooms/, incorporated herein by reference). As would be understood, these denotations of "mini", "medium" and "moderate" may overlap and are subjective in nature, with different dosing having different effects on different people with different weights, metabolisms, and sensitivity to psilocybin. As well, being largely an illegal, recreational drug, dosing has varied widely, as has "recommended dosing", which is part of why different references list overlapping dosing protocols. Dosing protocols are also often provided based on "dried mushroom fruiting bodies", which may vary in their concentration of active ingredient.

Early trials of psilocybin have suggested that when given under supportive, controlled conditions, many participants reported lasting beneficial changes in personality, behavior, values and attitudes. These have included greater

appreciation of music and nature, increased creativity, and the like.

Psychotherapeutic arts are well established and highly useful in treatment of many physical illnesses and disorders by treating the psychological aspects of such illnesses and disorders. Psychotherapy is often utilized in the treatment or management of compulsive diseases as well as eating disorders. It can help with self-worth and self-esteem, recognition of hidden trauma from family genetics or childhood, an understanding of pain and pleasure dynamics, and more. Less traditional psychotherapeutic arts which have become increasingly utilized include Chi Yoga, Cartharsis meditation, mindfulness, Chakra, and sound and colour visualization therapy.

Summary of the Invention

According to one aspect of the invention is provided a method of treating compulsive eating disorder in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

According to a further aspect of the invention is provided a method of aiding in weight loss in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

According to a further aspect of the invention is provided a method of treating obesity in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

According to a further aspect of the invention is provided a method of treating a complication associated with obesity in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

According to a further aspect of the invention is provided a method of altering a diet of an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

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In certain embodiments, the method further comprises administration of a 5-HT2A specific antagonist, for example, cyproheptadine, methysergide, or quetiapine.

In certain embodiments, the effective amount of LSD, LSA, DMT or analog thereof is a microdose amount, insufficient to induce psychedelic effects.

In certain embodiments, the effective amount of LSD, LSA, DMT or analog thereof imparts a psychedelic effect.

In certain embodiments, the method further comprises a therapy session concurrent with the psychedelic effect.

In certain embodiments, the therapy session is initiated about one hour after the administering of the compound.

In certain embodiments, the method further comprises a therapy session prior to the psychedelic effect.

In certain embodiments, the therapy session comprises one or more of a psychotherapy, a Chi yoga session, a catharsis treatment, and a mindfulness program.

In certain embodiments, the mindfulness program comprises one or more of a guided mindful chakra and a Sanskrit mantra sound and colour visualization therapy.

In certain embodiments, the effective amount is 5 to 400 micrograms of LSD, LSA or an analog thereof, once to seven times per week.

In certain embodiments, the effective amount is 5, 10, 20, 25, 30, 40, 50, 80, 100, 150, 200, 250, 300, 350, or 400 micrograms of LSD, LSA or an analog thereof, once to seven times per week.

In certain embodiments, the effective amount is administered once per week, 2-3 times per week, 4-5 times per week, 6 times per week, or 7 times per week.

In certain embodiments, the effective amount results in a peak DMT concentration of 0.7 to 150 micrograms of DMT per litre of whole blood, once to thirty times per month.

In certain embodiments, the effective amount is 0.05-1 mg/kg of DMT, administered intramuscularly, once to thirty times per month.

In certain embodiments, the effective amount is 0.1 to 0.4 mg/kg of DMT, administered intramuscularly, once to four times per month.

In certain embodiments, the effective amount is administered once per week, 2-3 times per week, 4-5 times per week, 6 times per week, or 7 times per week.

In certain embodiments, the complication associated with obesity is selected from the group consisting of sleep apnea, abnormal regulation of blood glucose, diabetes mellitus, cardiovascular disease, high blood pressure, hypertension, multiple sclerosis, erectile dysfunction, urinary incontinence, chronic renal failure, asthma, and cancer.

In certain embodiments, the administering is of DMT and is a intramuscular administration.

In certain embodiments, the administering is of LSD or LSA and is a sublingual administration.

In certain embodiments, the administering is of DMT and is via inhalation.

In certain embodiments, the administering is an oral administration.

In certain embodiments, the oral administration is in combination with a MOA-I.

In certain embodiments, the oral administration is in combination with a RIMA.

Brief Description of Figures

The present invention will be further understood from the following description with reference to the Figures, in which:

Figure 1 shows cumulative weight gain per day in untreated and psilocybin-administered rats.

Figure 2 shows total weight gain over a 5 day period in untreated and psilocybin-administered rats.

Figure 3 shows cumulative weight gain, as a percentage of body weight, in untreated and psilocybin administered rats.

Figure 4 shows total weight gain over 5 days, as a percentage of body weight, in untreated and psilocybin administered rats.

Detailed Description

Unless otherwise explained, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Patent applications, patents, and publications referred to herein to assist in the understanding of the aspects described are herewith incorporated by reference in their entirety.

In understanding the scope of the present application, the articles "a", "an", "the", and "said" are intended to mean that there are one or more of the elements. Additionally, the term "comprising" and its derivatives, as used herein, are intended to be open-ended terms that specify the presence of the stated features, elements, components, groups, integers, and/or steps, but do not exclude the presence of other unstated features, elements, components, groups, integers and/or steps. The foregoing also applies to words having similar meanings such as the terms "including", "having" and their derivatives.

It will be understood that any aspects describing as "comprising" certain components may also "consist of" or "consist essentially of", wherein "consisting of" has a closed-ended or restrictive meaning and "consisting essentially of" means including the components specified but excluding other components except for materials present as impurities, unavoidable materials present as a result of processes used to provide the components, and components added for a purpose other than achieving the technical effect of the invention.

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All ranges given herein include the end of the ranges and also any intermediate range points, whether explicitly stated or not.

Terms of degree such as "substantially", "about" and "approximately" as used herein mean a reasonable amount of deviation of the modified term such that the end result is not significantly changed. These terms of degree should be construed as including a deviation of at least +/- 5% of the modified term if the deviation would not negate the meaning of the word it modifies.

Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of this disclosure, suitable methods and materials are described below. The abbreviation "e.g." is used herein to indicate a non-limiting example. The word "or" is intended to include "and" unless the context clearly indicates otherwise.

We have found that administration of LSD, LSA, DMT or analogs thereof, both in psychedelic and, even more surprisingly, in non-psychedelic, microdose amounts, results in an overall weight loss in individuals. Regular psychedelic or microdose administration of LSA, LSD, DMT (or analogs thereof) can reduce food cravings, counteract compulsive overeating, and may even aid in improving quality of diet, by altering food choices. Recreational or microdose administration of LSA, LSD, DMT (or analogs thereof) may have the additional weight loss effect of increasing metabolism, which, combined with a decrease in food cravings or compulsive overeating, or altering food choices to less calorie dense foods, can result in substantial and beneficial weight loss. We have also found that, even a single "creative" or psychedelic dose, preferably but not necessarily combined with a supportive therapeutic treatment as detailed further below while the person is experiencing the effects of the dose, can provide significant, long term, weight loss benefits, often lasting many months.

These weight loss effects may be a result of reducing food cravings, counteracting compulsive overeating, and in some cases an improvement in quality of diet and an alteration of food choices to more "positive", less fattening, foods. A single dose of LSA, LSD, DMT, or analogs thereof may have the additional, long term, weight loss effect of increasing metabolism, which, combined with a decrease in food cravings

or compulsive overeating, or altering food choices to less calorie dense foods, can result in substantial and beneficial weight loss.

We believe that, unlike conventional weight loss medications, the administration of even a single dose (or two) of DMT, LSD, LSA or analogs thereof, optionally but preferably combined with therapy as detailed further below, can have a durability of effect of up to or even greater than 6 months, avoiding the "plateau" or "rebound" effect found with conventional weight loss medications. Re-treatment approximately every six months should provide a steady weight loss without such a plateau or rebound effect.

It is generally understood that obesity and overweightness is well correlated to an increased probability of diabetes and pre-diabetes conditions, and that these conditions can be ameliorated or sometimes even prevented through weight loss. Weight loss, and a decrease in compulsive overeating, can also aid in regulation of blood glucose in overweight/obese individuals with diabetes. Accordingly, recreational or microdose administration of LSD, LSA, DMT (or analogs thereof) may be useful in treatment or regulation of diabetes, and regulation of blood glucose, particularly in overweight or obese individuals. A recreational or microdose administration of DMT (or analogs thereof) may also reduce susceptibility to cardiovascular disease, high blood pressure, diabetes mellitus, hypertension, multiple sclerosis, erectile dysfunction, urinary incontinence, chronic renal failure, sleep apnea, asthma, and many forms of cancer, to an overweight or obese individual. LSD/LSA/DMT/analogs may also be used by non-overweight individuals, either to maintain a healthy weight, or to aid with compulsive eating.

Combination Treatments

Interestingly, and possibly paradoxically, LSD, LSA or DMT may be used in combination with a 5-HT_{2A} – specific or an 5-HT_{2A}-selective or weighted antagonist to provide similar results, but while decreasing or even eliminating hallucinatory or psychedelic effect. Without being limited to theory, it is believed this may be because the weight-loss effects of LSD, LSA and DMT are due to a complex interaction between these compounds and a variety of 5-HT receptors, but

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that the hallucinatory or psychedelic effects of the LSD/LSA/DMT are primarily caused by its agonist activity on cross-activation of 5-HT_{2A} heteromers, such activity being blocked, at least in part, by the 5-HT_{2A} specific antagonist. Accordingly, a larger dose of LSD, LSA or DMT may be given, for improved weight loss effects without hallucinatory effects, or the same amount of LSD/LSA/DMT may be given while reducing its hallucinatory effects, by combining with a dose of 5-HT_{2A} specific antagonist. 5-HT_{2A} specific antagonists that may be combined with LSD for such improved effect include cyproheptadine, methysergide, and quetiapine.

Dosing regimens can vary widely. For example, doses resulting in a blood concentration at peak of about 15 to 150 micrograms of DMT per litre of whole blood (or about 30-200 micrograms of DMT per litre of plasma) typically result in hallucinatory dosing; doses resulting in a blood concentration of 5-50% of this amount will typically be considered "microdose" administrations. Accordingly, doses resulting in a peak blood concentration of about 0.7 to 150 micrograms of DMT per litre of whole blood may be used. For example, 20-60 milligrams of vaporized DMT may be administered through vapour inhalation, or even 1 to 10 milligrams of vaporized DMT may be administered for a microdose effect. DMT may be administered via intramuscular injection at a dose of about 0.05 - 0.35 mg/kg (drug/body weight) for microdose effect, or larger doses, up to about 1mg/kg for hallucination-inducing effect. DMT may also be taken orally, for example, in a gel cap, either alone or in combination with a MAO-I such as a RIMA.

For LSD and LSA, dosages may also vary widely, for example, 5 micrograms to 400 micrograms, for instance, 10, 20, 25, 30, 40, 50, 80, 100, 150, 200, 250, 300, 350, or 400 micrograms of LSD, with one or multiple doses taken per week. A typical dosage regime may be 50 micrograms of LSD, administered sublingually, per day, taken about 2-3 times per week. Dosing may be for a specified length of time (for example, for two months) or may be for an indefinite duration. Dosing may also be "as needed" or as desired by the user.

When combined with a 5-HT_{2A} antagonist, the 5-HT_{2A} antagonist may be taken at a dosage similar to the suggested dosage for its primary indication, or it may be taken at a much lower dosage. It may be taken daily, or taken at the

same time as the LSD/LSA/DMT. It may be taken orally or as it is administered for its primary indication.

While a patient is under the influence of the LSD/LSA/DMT/analog thereof, especially at psychedelic dosages, it has been found that they are in a particularly suggestive state. Surprisingly, it has been found that suggestions made within that state may have long-acting effects, long after the "trip" i.e. after the known psychoactive effects of the drug have worn off.

Thus, to be particularly effective, while the psychoactive effects of the drug are felt by the user, the user should be administered a treatment therapy protocol. The treatment therapy protocol may be one or more of a psychotherapy, a psychological support session, a Chi yoga session, a Cartharsis treatment, a Mindfulness program for example a guided mindful chakra, and a Sanskrit Mantra sound and colour visualization therapy.

The treatment therapy protocol should preferably take place directly before the effects of the psychoactive drug are felt, and may be taken the same day, or, for example, the same week as administration of the LSD/LSA/DMT/analog. In preferable embodiments, the therapy treatment protocol may take place during the administration of the drug. The therapy helps prepare the patient for a deeper understanding of their emotional states, and helps prevent "bad trips". The therapy may also continue after the psychoactive effects of the LSD/DMT/LSA/analog has worn off.

Psychotherapy Treatment Therapy

Psychotherapy may be utilized as described in WO2020/212951A1, for example, the entirety of the disclosure of which is hereby incorporated by reference. Psychotherapy treatment therapy may include self discovery exploration of the emotional relationship to the person's physical image; a discussion of the need for a change in perspective, to one free of self-judgement, condemnation and self loathing; and an exploration of self love. The psychotherapy treatment may include an exploration of unresolved issues in the patient's life that are embedded in their subconscious, including a discussion/acknowledgement/examination of pain, abuse and/or humiliation from early childhood. It may also include building self-esteem, the patient taking responsibility for

their own condition, self empowerment, and acknowledging or releasing the patient's unhealthy self defence mechanism of overeating. Such psychotherapy treatment therapies may differ between patients, but follow well-established and documented known psychotherapy protocols.

Psychological Support Session

A psychological support session typically includes supervision during the psychedelic experience, by one or more trained therapists. Preferably, the supervision may be in person, though optionally (though less preferably) the supervision may be done remotely, by video conference or audio conference. The psychological support session may be or include one or more pre-administration psychological support sessions.

Pre-administration psychological support sessions may be held for example about two weeks prior to the DMT/LSD/LSA/analog administration, or 1 week prior, or 3 days prior, or 1 day prior, or immediately prior to the administration. In some embodiments, the pre-administration psychological support session may be held immediately after the administration of the drug, but before the patient feels psychedelic effects.

In some embodiments, the patient may participate in one, two, three, four, of more, pre-administration psychological support sessions, for example, once a week for a month.

The pre-administration psychological support sessions may be individual sessions, where a subject meets with one or more therapist, or may be group sessions, where the subject meets with other subjects and one or more therapists in a group setting. In some embodiments, one or more of the patient's family members, friends, or other third party support may be present at the pre-administration psychological support session.

The goals of the pre-administration psychological support session may include (i) establishing therapeutic alliance or trust between the subject and the therapist; (ii) answering the subject's questions and addressing or quelling concerns; (iii) reducing subject anxiety about the psychedelic experience; and/or (iv) practicing self-directed inquiry and/or experiential processing. The pre-administration

psychological support sessions may include discussion and/or preparation for the psychedelic effects of the drug, practicing relevant therapeutic techniques used during the psychedelic treatment to reduce avoidance and anxiety, eliciting relevant therapeutic goals, building rapport, building trust, or establishing therapeutic alliance.

The pre-administration psychological support session may include practicing and/or learning breathing exercises meant to promote calm and/or ease anxiety. These breathing exercises may include instructing the subject to focus on breath and/or sensations associated with the breath throughout the body. For example, the subject may be instructed to breathe in for a count of four, to hold their breath for a moment, then to breathe out for a count of eight. In some embodiments, the pre-administration psychological support session may include guided mindful chakra, colour therapy, or chi yoga as described further below. In some embodiments, the pre-administration psychological support sessions can establish a therapeutic goal for the LSA/DMT/LSD/analog administration. The therapeutic goal can be directed by the therapist, or suggested by the subject. The pre-administration psychological support session may include counselling.

The pre-administration psychological support session may be administered by a person with mental health training, for example, a clinical psychologist, a psychiatrist, a psychedelic experience guru, a social worker, a doctor, or a nurse. It may be administered by a therapist having, for example, independent clinical experience with direct subject care in areas that require counselling and psychotherapeutic skills; a person holding a professional license and good professional standing; a person who themselves have gone through similar therapy.

The Psychological support during the LSD/LSA/DMT/analog session may comprise supervision by one or more trained therapists. It may be the same therapist as the pre-administration psychological support session, or it may be a different therapist. The psychological support may include any measure taken by the therapist during the subject's LSD/LSA/DMT/analog session to ensure the safety of the subject, the comfort of the subject, or to maximize the clinical effectiveness of the DMT/LSA/LSD/analog session. For example, the psychological support may help ensure the

psychological safety of the subject, it may allow the subject's experience to unfold naturally within the boundaries of the therapeutic intention set at the preparation, it may help to maintain the participant's attention and awareness of the experience, to increase exposure or processing of the subject to the emotional states and/or personal memories triggered, it may aid the subject generate insights and solutions for the resolution of challenging personal situations, conflicts and traumatic experiences. Support may be in the form of therapeutic touch, verbal reassurance, guided imagery, relaxation exercises, breathing exercises, or the chi yoga/carthartic meditation/guided mindful chakra/colour therapy described below, or other forms of therapy. The support may include verbal reminders, encouragement, or active guiding.

In some embodiments, the main therapeutic goals of the therapist during the DMT/LSD/LSA/analog session are to (i) minimize extreme anxiety and (ii) provide appropriate support that enables the skills and processes of self-directed inquiry and experiential processing. In some embodiments, the therapist demonstrates genuine presence, patience, curiosity and/or openness during the LSD/LSA/DMT/analog session, exuding calmness and inquisitiveness. The therapist should be interested and willing to understand the subject's experience, and avoid making assumptions, allowing the participant to take their time to explore their experience without necessarily directing or controlling the experience.

In some embodiments, the psychological support may comprise curious questioning, for example, using brief, detailed questioning of subjects to help the subject shift and sustain their attention towards different levels of cognition and emotions.

In some embodiments, the level of psychological support will vary during the various stages of the subject's psychedelic experience (initial, early, peak, and late stages, for example). The type and intensity of psychological support may vary during these stages.

In some embodiments, a subject may experience a compromised sense of self during the subject's psychedelic experience, this may in some instances be interpreted from a psychoanalytic perspective as a disruption of ego-boundaries, which results in a blurring of the distinction between self-

representation and object-representation, and may preclude the synthesis of self-representations into a coherent whole. In some embodiments, non-dual, ego-dissolution, or "unitive" experiences may be achieved, referring to an altered state of consciousness in which there is a reduction in the self-referential awareness that defines normal waking consciousness, resulting in a compromised sense of "self" and instead only an undevided background awareness, often characterized by a sense of unity of "oneness" that exceeds sensory or cognitive apprehension. In some embodiments a non-dual experience is experienced - a state of consciousness in which the subject-object dichotomy in normal waking consciousness is substituted for a unified background awareness that is centerless and undivided. In some embodiments, an ego dissolution experience is experienced - a spontaneously occurring state of consciousness where there is a reduction in the self-referential awareness that defines normal waking consciousness, resulting in a compromised sense of "self". In some embodiments, a unitive experience is experienced – an experience characterized by a sense of unity or "oneness" that exceeds sensory or cognitive apprehension.

At the initial and early stage of the LSD/LSA/DMT/analog session, psychological support may be used to reduce severe and/or prolonged anxiety. Anxiety prior to or during the onset of psychoactive effects is not uncommon, and the therapist may be specially trained to recognize and actively manage subjects through such periods of anxiety until the subject is comfortable enough to continue on their own. In some embodiments, therapists validate the subject's feelings of anxiety without providing interpretations of perceptual disturbances or guiding subjects towards a particular image or memory, other than encouraging them to stay relaxed and open to the emergent experiences. In some embodiments, the therapist may help alleviate anxiety using a grounding exercise, for example, encouraging subjects to pay attention to the sounds around them, or the sensations on their skin when touching objects.

At the initial and early stage of the LSD/LSA/DMT/analog session, the therapist may encourage the subject to lie down, practice relaxation and breathing exercises, and/or listen to calming music. In some embodiments, the therapist may remind the subject of the intention for the treatment session. For example, the therapist may ask the subject "What does it feel like to be lighter and spritelier?" or any number of similar

questions. Such reminders prior to the onset of or at the onset of psilocybin effects may provide an implicit direction for the subjective experience during the LSD/LSA/DMT/analog session. In some embodiments, the therapist may remind the subject that their primary task during this session is to simply collect new and interesting experiences which can then be discussed with the therapist after the session. The therapist may remind the participant of the purpose of the drug therapy and the role of experiential processing, namely allowing the participant to be open and curious to whatever arises and encountering thoughts and feelings previously unknown to them. In some embodiments, the therapist emphasizes that this process inherently requires letting go and a willing passivity to the psychedelic experience.

During the acute onset of action, the subject may experience perceptual changes in visual, auditory or olfactory modes, and a range of unusual physical sensations. These experiences could be anxiety-provoking. In some embodiments, the therapist may practice reassuring "arm holding". This is where, upon the subject's request, a therapist will place his or her hand on the subject's wrist, arm, hand, or shoulder, as a way of helping the subject feel secure during this phase. This exercise may have been previously practiced during the pre-administration psychological support session.

In some embodiments, the therapist may encourage the subject to put on an eye mask. In some embodiments, the therapist encourages the subject to put on the eye mask before, during, or after the onset of the drug's psychoactive effects.

In some embodiments, the therapist may encourage the subject to put on headphones and listen to music. In some embodiments, the headphones reduce outside noise (e.g., "noise cancelling" headphones). In some embodiments, the music is calming music such as instrumental (e.g., classical) music. In some embodiments, the music comprises nature sounds and/or the sound of moving water (e.g., ocean sounds). In some embodiments, the music comprises isochronic tones. In some embodiments, the music comprises moments of silence. In some embodiments, the music is emotionally evocative. In some embodiments, the music comprises a playlist which mirrors the pharmacodynamics of a typical high-dose LSD/LSA/DMT session: the initial stage, the early stage, the peak stage, and the late stage. In some embodiments, listening to music helps the

subject to focus on their internal experience. In some embodiments, the music may include diurnal beats.

During the peak and late stages of the LSD/LSA/DMT/analog session, the therapist may encourage subjects to face and explore their experience, including the challenging ones. Therapists may direct subjects to participate self-directed inquiry and experiential processing to develop a different perspective on their personal challenges and conflicts, and to generate their own solutions. Such self-generated insights are not only therapeutic because of the emotional resolution, but also empowering to subjects.

In some embodiments, the therapist will employ a transdiagnostic therapy. In some embodiments, the transdiagnostic therapy is a Method of Levels (MOL) therapy. In still further embodiments, the MOL therapy comprises Self-Directed Enquiry and Experiential Processing. Typically, MOL uses brief, but detailed, curious questioning to help subjects shift and sustain their attention towards different levels of cognition and emotions (Carey, 2006; Carey, Mansell & Tai, 2015). The emphasis within MOL is on identifying and working with a subject's underlying distress as opposed to just their symptoms. Such MOL related methods and techniques can include: (1) Self-directed enquiry - directing attention to internal states. Participants are encouraged to be curious about experiences in the present moment, including foreground and background thoughts, emotions, and physical sensations; during the preparation and integration stages, such enquiry can mean asking specific and detailed questions to help direct attention to internal states, although for some embodiments, during the period of drug action, enquiry can refer to an attitude of openness to inner experiences; and (2) Experiential processing - sustained focus on the experience; refers to a participant's ability to maintain full attention on the experiences that come into awareness through self-directed enquiry. This includes a willingness and ability to be with and/or move 'in and through' even uncomfortable or challenging thoughts, feelings, sensations or emotions, until discomfort is diminished or resolved.

In some embodiments, the psychological support comprises mindfulness-based therapy or CBT cognitive behavioral therapy (CBT). In some embodiments, the psychological support is informed by a functional theory of human behavior called Perceptual Control Theory.

Occasionally, the subject will try to avoid emerging experiences or distract him/herself while trying to regain cognitive control over the unusual state of their mind. Such distractions may take different forms. For example, the subject might want to engage in a conversation or prematurely describe in detail their experience, visions or insights. When this occurs, the therapist may aim to remain as silent as possible, thereby enabling the subject and his/her inner experience to direct the course of the LSD/LSA/DMT session. In some embodiments, the therapist may use active listening skills paired with prompts to encourage the subject to continue focusing attention on present experiences, particularly if the participant engages the therapist in conversation. In another example, a subject might ask to go to the bathroom or have a drink of water. The sudden and urgent character of such requests might suggest that they are really trying to avoid emerging material. In such cases, the therapist may encourage the subject to stay with the experience by simply redirecting their attention. For example, the therapist may say something like, "We will take a bathroom break at the end of this piece of music" or "I will get you water in a little while. Why don't you put the eye shades back on and relax for a few minutes?" If the subject is trying to avoid a difficult experience, they might listen to the suggestion and relax.

In some embodiments, spontaneous movement such as shaking, stretching or dancing while engaging with the experience is accepted and often encouraged, unless the movement seems to be a way to distract oneself from the experience. In some embodiments, reminders to periodically return to a lying down position and to actively focus inwards may be provided.

The therapist is not required to understand, support or even have an opinion about the nature or content of the subject's experiences, but the therapist may validate them and convey openness toward the subject's own view of them without dismissing or pathologizing any experience based on its unusual content. These experiences may provide the subject with a perspective that goes beyond identification with their personal narrative. In some embodiments, the therapist will validate one or more of the subject's experiences. In some embodiments, validation of the experiences simply means acknowledging the courage of opening up to the experience and

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the possibility that any experience will serve the intention of the session.

In some embodiments, a therapist provides psychological support for approximately 4-8 hours immediately after administration of the LSD/LSA/DMT. In some embodiments, the therapist uses guided imagery and/or breathing exercises to calm the subject and/or focus the subject's attention. In some embodiments, the therapist holds the hand, arm, or shoulder of the subject. In some embodiments, the therapist counsels the subject to do one or more of the following: (1) to accept feelings of anxiety, (2) to allow the experience to unfold naturally, (3) to avoid psychologically resisting the experience, (4) to relax, and/or (5) to explore the subject's own mental space.

In some embodiments, the therapist avoids initiating conversation with the subject, but responds if the subject initiates conversation. Typically, active intervention is kept to a minimum during the treatment experience. In some embodiments, the subject is encouraged to explore their own mental space, and simple guided imagery may be used to assist relaxation."Guided imagery" refers to an exercise wherein the subject is asked to imagine a scene (e.g.,"Invite a scene, perhaps a landscape, and tell me where you find yourself';"Imagine a place that feels safe to you.")

In some embodiments, the subject may participate in a Post-Administration Psychological Support Session. This is a process that involves processing, or embodying, a psychedelic experience within a therapeutic context. The process initially begins by the subject verbalising and reflecting upon any experience from the LSD/LSA/DMT session, and discussing it openly with their therapist. Successful integration of a LSD/LSA/DMT experience accommodates for emotional changes and comprises of translating experiences into new insights, perspectives, and subsequently new behaviors that can be used to benefit the subject's quality of life. New perspectives might in turn influence the participant's current knowledge or values and lead to new ways of relating to cognitions, emotions, behaviors and physical experiences. In some embodiments, the goals and supportive methods used by the therapist throughout integration sessions should remain consistent, regardless of the intensity or content of the subjective experience explored by the subject. That said, the

methods of support used by the therapist should accommodate for the full range of experiences a subject might have faced.

The post-administration process is not one that should be limited to the sessions with the therapist, and is a process that will likely continue to unfold beyond the visits in clinic. The therapist might encourage the participant to use methods such as spending time in nature, exercise, or creative expression to help facilitate the process further. The subject might also be encouraged to discuss experiences with their friends, family, and/or support network. The role of the integration sessions is not to cover and work on every experience, but to empower the participant by building their capacity to experientially process information safely. This enables the participant to continue self- directed integration, even outside of study visits.

In some embodiments, the subject participates in at least one psychological support session after administration of the drug ("post-administration psychological support session"). In some embodiments, a post-administration psychological support session may be held on the same day as the LSD/LSA/DMT session, after the effects of the drug have substantially worn off. In some embodiments, a post-administration psychological support session may be held the day after the LSD/LSA/DMT session. In some embodiments, a post administration psychological support session may be held two days after the LSD/LSA/DMT session. In some embodiments, a post-administration psychological support session may be held three days after the LSD/LSA/DMT session. In some embodiments, a post-administration psychological support session may be held about one week after the LSD/LSA/DMT session. In some embodiments, a post-administration psychological support session may be held about two weeks after the LSD/LSA/DMT session. In some embodiments, a post-administration psychological support session may be held about one month after the LSD/LSA/DMT session. In some embodiments, a post administration psychological support session may be held about three months after the LSD/LSA/DMT session. In some embodiments, a post-administration psychological support session may be held about six months after the LSD/LSA/DMT session. In some embodiments, a post-administration psychological support session may be held about twelve months after the LSD/LSA/DMT session.

In some embodiments, the subject may participate in one, two, three, four, five, six, seven, or eight post-administration psychological support sessions. In some embodiments, the subject may participate in at least two, or at least three post-administration psychological support sessions.

The post-administration psychological support sessions may be individual sessions, wherein a subject meets one-on-one with a therapist. In some embodiments, the psychological support sessions may be group sessions, wherein more than one subject meets with a single therapist, or more than one therapist. In some embodiments, one or more of the subject's family members or friends may be present at the post-administration psychological support session(s).

In some embodiments, the post-administration psychological support session may focus on integration of the psychedelic experience. Integration may involve processing a psychedelic experience in a therapeutic context. Integration may comprise psychological and somatic processing of the experience and a successful assimilation of insights into the subject's life for the purpose of growth, healing and/or well-being. During an integration session, a subject may be encouraged to talk about and reflect upon their experiences during the LSD/LSA/DMT session. In some embodiments, integration may comprise an external expression of the psychedelic experience, such as choice of words, tone of voice, gestures, and/or particular physical activities (yoga, exercise, bodywork, etc.) In some embodiments, integration comprises creatively expressing any insights or experiences gained during a LSD/LSA/DMT experience, for example through poetry, art, music/singing, dance, writing or drawing.

In some embodiments, the subject may be encouraged to reflect on both the thoughts and the feelings that he or she underwent during the LSD/LSA/DMT session, as well as to express those ideas and emotions into a concrete form that can serve as a tool for continuing to remember and integrate those lessons into the future. In some embodiments, the subject may be encouraged to acknowledge and connect with the range of the emotional cognitive and physical experiences of the LSD/LSA/DMT session, and relate them to current experiences in their life situation. This may be accomplished, for example, by discussing them initially with their therapist, and perhaps later with their family, friends, and support circle.

Integration helps accommodate changes in emotional states as new insights are generated and integrated. When further explored through oscillating attention between foreground and background thoughts and emotions, such insights may lead to natural and effortless changes in perspectives or behaviors. In some embodiments, the integration process is not limited to initial integration meetings with the therapist, but continues to unfold spontaneously through a participant's own processing and actions in everyday life.

In the case of a low-intensity experience, the integration process might focus on the mental content that emerged during the hours of relaxation and introspection. This might also include reactions to what might have been an unremarkable experience, such as feeling of disappointment, anger, relief etc.

In some embodiments, the LSD/LSA/DMT is administered in a facility specifically designed for psychedelic drug administration. Administration of the LSD/LSA/DMT to the subject in a facility where the subject feels safe and comfortable may help ease anxiety in the subject, and may facilitate maximum clinical benefit. LSD/LSA/DMT may be administered to a subject, for example, in the subject's home or at a clinical facility. In some embodiments, the LSD/LSA/DMT is administered to the subject in a facility (e.g., a room) with a substantially non-clinical appearance. For example, the LSD/LSA/DMT can be administered in a room that comprises soft furniture (e.g., plush couches, chairs, or pillows) and/or plants. In some embodiments, the room may be decorated using muted colors (e.g., greyed, dulled, or desaturated colors). In some embodiments, the light in the room is dimmed and/or light levels are kept or adjust to be relatively low. In some embodiments, the room lighting is adjusted for intensity and/or color. In some embodiments, a virtual reality or augmented reality system (e.g., computer with visual/graphical and auditory outputs) is used. In some embodiments, the room comprises a sound system, for example a high-resolution sound system. In some embodiments, the sound system can allow for simultaneous ambient and earphone listening. In some embodiments, the subject may bring meaningful photographs or objects into the administration room.

In some embodiments, each subject is supervised by one therapist during the LSD/LSA/DMT session. In some embodiments,

each subject is supervised by more than one therapist during the LSD/LSA/DMT session, such as two therapists, three therapists, four therapists, or five therapists. In some embodiments, one therapist multiple subjects, wherein each subject is participating in a LSD/LSA/DMT session. For example, one therapist may supervise two, three, four, five, six, seven, eight, nine, or ten subjects.

Chi yoga

Chi yoga is a known art that blends the elements of Chinese body energy clock with prana yoga and zen breathing for self psychotherapy, and has been reported to create a benefit of mind, body, and soul. Chi yoga is a rhythmic, flowing blend of stretching and breathing, using the body energy clock and what is known in the art as zen breathing, using three breaths for each movement.

First stage: recognition of the pain and trauma
Second stage: Visualization and release
Third stage: Letting go.

Typically, a chi yoga session will be between half an hour and two hours, preferably about an hour long, and focuses on core strength, flexibility, dynamic movement of breath through the limbs from head to toe, and emotional release. Without being limited to theory, it is believed that core stabilization, which is improved with chi yoga, helps release tension.

Cathartic meditation using sounds and movement

Cathartic meditation is a known art that is an intense methodology used to break old ingrained patterns and to experience freedom of mind, body and soul. Typically, it uses a combination of breath work, sound, and movement.

In one exemplification, cathartic meditation comprises three steps, each typically about 15 minutes long, followed by about 15 minutes of silence, for a total of about an hour.

In the first step, the patient utilizes chaotic breath work to release energy and emotion. In the second step, the patient expresses emotions that surface, including sadness, anger, frustration, and/or happiness. In the third step, the

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patient uses sound and tapping movements on the patient's throat, head and face, to release tension and relax the patient. Typically, the execution of the three steps transition the patient to a calm collected state. The three steps are followed by 15 minutes of silence, to aid the patient in self communication and a transformation process.

Guided Mindful Chakra, followed by Sanskrit Mantra Sound and Colour Visualization Therapy

Mindfulness therapy, including guided mindful chakra, is a known art. In one exemplification of guided mindful chakra, the therapy is performed in total silence, and the patient is guided to use breath to be in touch with their own experiences. The patient starts by laying down with their back straight, visualizing connecting their spine with the earth until they find a comfortable position.

The patient is instructed to breathe in deeply through their nose, down to their stomach. They are guided to breathe out through their mouth, focusing on letting go of any physical tension, recognizing the trauma associated with pain until they start to feel relaxed for a deeper connection. The patient is now more aware of their breath "from head to toe", the weight of their body, the heaviness of their limbs, and are fully focused on relaxing.

The patient is then instructed to visualize or imagine pure white light entering the center of their body, and to feel the light expanding as they breathe in, allowing the body to fill up with the pure light.

Once the patient is fully calm and relaxed, the Sanskrit Mantra Sound and Colour Visualization Therapy can be initiated. Sanskrit Mantra Sound and Colour visualization therapy is a known art. The patient is instructed to inhale while visualizing drawing up the "energy of the earth through their roots and up into their body".

Step 1 – the patient is instructed to visualize this energy at the base of the spine, pouring into their root chakra.

Focus: The root chakra governs physical health, vitality, thoughts, beliefs and feelings.

Colour for visualization: Red

Sound used: Lam

Musical Note: C

Step 2 – sacral chakra – focus on the sacral below the navel. Sacral chakra is related to the sense of taste, feeling of relativity, harmonious relationships and balanced sexual energy.
Colour for visualization: Orange
Sound: VAL
Musical Note: D

Step 3 – solar plexus is located above the navel and below the chest. The focus is on feelings of personal power and sel-control.
Colour for visualization: Yellow
Sound: RAM
Musical Note: E

Step 4 – Heart chakra, located right in the center of the chest. The focus is the sense of touch, feelings of compassion, and love.
Colour for visualization: Green
Sound: Yam
Musical Note: F

Step 5 – Throat chakra is in the center of the throat. The focus relates to sound, speech and communication.
Colour for visualization: Blue
Sound: AUM
Musical Note: G

Step 6 – Third eye, located in the center of the forehead. The focus is on opening the mind, understanding the discriminating between thoughts motivated by strength fear and illusion.
Colour for visualization: Indigo
Sound: AUM
Musical Note: A

Step 7 – Crown chakra, located on top of the head. The focus relates to thoughts, knowledge and intuition.
Colour: Violet
Sound PRANAV OM
Musical Note: B

As would be understood, this is but one sequence of many known sequences in Sanskrit mantra sound and colour

visualization therapy, and many variations are possible and within the scope of the invention.

Once the patient has gone through the therapy, they are instructed to embrace the psychedelic experience, and to focus on breathing and awareness.

The treatment therapy protocol is preferably administered by a live individual present in the same room as the patient. Though a physical presence is desirable, it is, however, not necessary. The treatment therapy protocol may be administered via video or audio, and may even be pre-recorded.

Without being limited by theory, it is believed that the beneficial diet and obesity treatment effects of LSD, LSA, DMT, and/or analog may be due to their HT-1A agonist activity.

In some embodiments, the treatment described herein is combined with a known weight loss drug, diet, and/or exercise regimen.

The above disclosure generally describes the present invention. A more complete understanding can be obtained by reference to the following specific examples. These examples are provided for purposes of illustration only and are not intended to be limiting unless otherwise specified. Thus the invention should in no way be construed as being limited to the following examples, but rather, should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

The following examples do not include detailed descriptions of conventional methods, which are well known to those or ordinary skill in the art and are described in numerous publications.

Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the compounds of the present invention and practice the claimed uses and methods. The following working examples therefore, specifically point out the typical aspects of the present invention and are not to be construed as limiting in any way the remainder of the disclosure.

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Example 1: Effects on Compulsive Eating Disorder (Microdose)

Individuals diagnosed with compulsive eating disorder are asked to self-report instances of compulsive eating over a two month period. They are then put on one of four treatment protocols over a two month period, and asked to self-report instances of compulsive eating: A) placebo treatment, once a day; B) 0.1 mg/kg of DMT, administered intramuscularly, once a day; C) 40 microgram blotter tab of LSD, once a day, sublingually; D) 40 microgram blotter tab of LSD, once a day, sublingually, combined with 4 mg oral dose of cyproheptadine, three times a day. Individuals in group B, C, and D report a decrease in compulsive eating as compared to the first two months where they received no treatment. Individuals in group A report generally similar amounts of compulsive eating as compared to the first two months. Individuals in Group C report greater reduction in compulsive eating than individuals in Group B. The microdose of 0.1 mg/kg of DMT did not induce any hallucinatory effects.

Example 2: Effects on Compulsive Eating Disorder (Psychedelic dose)

Individuals diagnosed with compulsive eating disorder are asked to self-report instances of compulsive eating over a two month period. They are then put on one of five treatment protocols over a two month period, and asked to self-report instances of compulsive eating: A) placebo treatment B) placebo treatment with psychotherapy session; C) a single, psychedelic dose of 1mg/kg of DMT, administered intramuscularly; C) a single, psychedelic dose of 1mg/kg of DMT, administered intramuscularly, combined with psychologic therapy treatment concurrent with the psychedelic effects of the drug; D) a psychedelic dose, 400 microgram blotter tab of LSD, sublingually; E) a psychedelic dose, 400 microgram blotter tab of LSD, sublingually, combined with psychologic therapy treatment, concurrent with the psychedelic effects of the drug. Two months after the single treatment, individuals in group B, C, D, and E self- report a decrease in compulsive eating as compared to the first two months where they received no treatment. Individuals in group A report generally similar amounts of compulsive eating as compared to the first two months. Individuals in Group C and E report greater reduction in compulsive eating than individuals in Group B and D.

Example 3: Weight Loss

Males all weighing between 250 and 275 lbs and all having BMI indexes between 30 and 35 kg/m^2 are split into four groups. The first is provided with placebo; the second was injected with a single intramuscular administration of 0.7 mg/kg total body weight of DMT. The third group was administered blotter tabs containing 200 micrograms of LSD. The fourth and fifth group were replicates of the second and third group, respectively, however, these patients received a guided mindful chakra, followed by a Sanskrit mantra sound and colour visualization therapy, 1 hour after administration of the drug. A sixth group was administered blotter tabs containing 20 micrograms of LSD, and were instructed to take one blotter tab daily, 4 days out of 7, for two months. At the end of two months, the first (placebo) group is found to have a similar weight as before the treatment, whereas each patient in the second, third and sixth group is found to lose an average of 12 lbs each. The patients in the fourth and fifth group are found to lose an average of 16 lbs each.

Example 4: Sleep Apnea

30 females all suffering from sleep apnea, weighing between 225 and 250 lbs, and having BMI indexes above 30 kg/m^2 are split into five groups. The first is provided with placebo "puffers", the second with "puffers" providing a metered dosage of 2.5 milligrams of DMT per inhalation. The third is provided with placebo blotter tabs, the fourth is provided with blotter tabs containing 100 micrograms of LSA. The fifth group is provided with the same LSA blotter tabs, as well as a psychotherapy treatment once a week, focusing on anxiety. The first two groups are instructed to inhale 1-2 breaths from the puffer every morning immediately upon waking up, for two months. The third, fourth and fifth group are instructed to place the blotter tab sublingually every evening before going to sleep, every second night, for two months. All subjects are given a nocturnal polysomnography test before, and after, the two months of treatment. Females in the second, fourth and fifth group present with a decreased diagnosis of sleep apnea after treatment, as compared to before treatment. Females in the placebo groups present with similar amounts of sleep apnea before and after treatment. The group in the fifth group presents with even less sleep apnea than the second and fourth groups.

Example 5: Food selection

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30 females are split into five groups. The first is provided with placebo "puffers", the second with "puffers" containing 20 milligrams of DMT per inhalation. The third is provided with placebo blotter tabs, the fourth with blotter tabs containing 30 micrograms of LSD. The fifth is provided with the LSD blotter tabs containing 30 micrograms of LSD as well as 25 mg oral dosage of quetiapine, twice daily. The first two groups are instructed to inhale once from the inhaler, once a week, while in a stable, comforting environment. The third, fourth and fifth group are instructed to take one blotter tab sublingually, twice per week; the fifth group also takes two 25mg dosages of quetiapine every day. Subjects are asked to log their food intake for two months before, then two months during, treatment. Females in the second, fourth and fifth group record less carbohydrate-rich food intake, as compared to before treatment. Females in the placebo groups do not have altered food intake. Females in the fifth group record even less carbohydrate-rich food, as compared to either of the third or fourth group.

Example 6: Pre-clinical study of weight-loss properties of psilocybin with a high calorie diet

Like DMT, psilocin is a recreational psychedelic drug known to have 5-HT2A agonist activity. As such, experiments with psilocin may be useful in understanding DMT and its effects.

In order to determine whether psilocybin has anorectic – and therefore weight loss – properties, a preclinical study of the drug was conducted, using a well-validated animal model. Rodent models of food consumption and weight gain have a strong homology with humans, as rodents are omnivores with a very similar metabolic physiology. Prior art rodent studies that have tested drugs with known weight-loss benefits in humans have demonstrated similar effects in the animals (Hansen HH et al., Eur J. Pharmacol. 2010; 636(1-3):88-95; Vickers SP et al., Br J Pharmacol 2011; 164(4):1248-62). The goal of the present study was to cause accelerated weight gain with a high calorie diet, consisting of a highly palatable food with a large proportion of fat and carbohydrate, compared to standard animal food, which is designed to maintain a healthy weight. We evaluated whether treatment with two different doses of psilocybin could reduce the accelerated weight gain caused by this diet.

Adult, male Sprague-Dawley rats were purchased from the animal supplier, and then housed in pairs in polycarbonate cages, with access to water and standard rat food *ad libitum*. Rats were given a period of time to acclimate to the animal colony. They were then all given unlimited access to a highly palatable diet that is very high in carbohydrate and fat (consisting predominantly of a hazelnut-flavored chocolate spread combined with peanut butter) that has been used routinely in multiple published studies with rats to study rapid weight gain (Hansen et al., Acta pharmacologica Sinica. 2012; 33(2):194-200). Animals were randomly assigned to one of three treatment groups, which consisted of once daily administration of either a lower dose (5 mg/kg; n = 7 animals) of psilocybin, a higher dose (20 mg/kg; n = 7 animals) of psilocybin, or no psilocybin (n = 12 animals). The psilocybin was supplied by the Katz Group at the University of Alberta, and was legally approved by an exemption from Health Canada.

Rats were administered the drug approximately two hours before the lights went off in the animal colony, which is when feeding typically commences. Animals were free to consume as much of the regular rat food or high calorie diet as they wished. They were weighed each day prior to drug treatment, to determine how much weight had been gained in the previous 24 hours. The study administered the drug over five consecutive days. Data were statistically analyzed by (SPSS Version 24 software package) using a one-way Analysis of Variance (ANOVA) with a LSD-post hoc test to detect between-group differences.

Animals quickly learned to eat the high calorie diet food. The control group, which did not receive treatment with psilocybin, exhibited a large and constant increase in body weight, of 5-8 grams per day (Figure 1). In contrast, both of the psilocybin-treated groups showed a reduced amount of weight gain, between 1-8 grams per day. When the total weight gain was measured over the 5 day period (Figure 2), the control group on average gained 27.8 grams, while the 5 mg/kg psilocybin group gained on average only 19.4 grams and the 20 mg/kg gained on average only 20.1 grams. This represents a 31% and 28% reduction in weight gain with psilocybin treatment. The formal analysis indicated that these effects were statistically significant. The ANOVA indicated that the two psilocybin treated groups showed less total weight gain than controls [$F(2,25) = 3.99$, $p < 0.05$]. When the data were analyzed on a day-by-day basis, comparing the cumulative

weight gain for each day, the 20 mg/kg dose of psilocybin demonstrated a significantly reduced weight gain compared to controls by Day 3. By Day 5, both psilocybin-treated groups exhibited significantly decreased weight gain compared to controls.

As the control group of rats were slightly lighter than the other groups on the first day of treatment (which would underestimate the effects of drug treatment, because larger rats gain more weight daily, in absolute terms), we also analyzed the weight gain relative to their baseline weight. We determined their daily weight gain in proportion to their weight prior to drug treatment. Results were expectedly similar to measures of absolute weight gain, but statistically more significant. A similar pattern of cumulative weight gain over the 5 days was evident (Figure 3). Total relative weight gain was 8.4% in controls, and 5.7% in both of the psilocybin groups (Figure 4) – a 32% decrease in relative weight gain in the latter two groups, which was statistically significant [$F(2,25) = 5.24$, $p = 0.01$]. On a day-by-day basis, the 20 mg/kg psilocybin group gained statistically less relative weight by day 3 compared to controls, and both psilocybin groups gained less relative weight by day 4 ($p < 0.05$).

Controls rats readily consumed the high calorie, palatable diet and therefore gained weight quickly. This was significantly reduced by both doses of psilocybin, whereby weight gain was strongly decreased, by approximately one third. The effect of psilocybin was rapid, as it happened within days. The observation can only represent an effect on food consumption, as the animals had no opportunity to exercise in their cage, and so calorie expenditure was unaltered. These overall findings indicate that in a well-validated preclinical model, psilocybin is strongly able to reduce consumption of “junk” foods and maintain body weight at healthier levels. As these rodent models are highly predictive of similar effects in humans, clinical trials in overweight individuals are expected to yield similar results.

The above disclosure generally describes the present invention. Although specific terms have been used herein, such terms are intended in a descriptive sense and not for purposes of limitation.

All publications, patents and patent applications cited above are herein incorporated by reference in their entirety

to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference in its entirety.

Although preferable embodiments of the invention have been described herein in detail, it will be understood to those skilled in the art that variations may be made thereto without departing from the spirit of the invention or the scope of the appended claims.

Claims:

1. A method of treating compulsive eating disorder in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

2. A method of aiding in weight loss in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

3. A method of treating obesity in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

4. A method of treating a complication associated with obesity in an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

5. A method of altering a diet of an individual in need thereof, comprising administering an effective amount of DMT, LSD, LSA, or an analog thereof.

6. The method of any one of claims 1-5 further comprising administration of a 5-HT2A specific antagonist.

7. The method of claim 6 wherein the 5-HT2A specific antagonist is selected from the group consisting of cyproheptadine, methysergide, and quetiapine.

8. The method of any one of claims 1-7 wherein the effective amount of LSD, LSA, DMT or analog thereof is a microdose amount, insufficient to induce psychedelic effects.

9. The method of any one of claims 1-7 wherein the effective amount of LSD, LSA, DMT or analog thereof imparts a psychedelic effect.

10. The method of claim 9 further comprising a therapy session concurrent with the psychedelic effect.

11. The method of claim 10 wherein the therapy session is initiated about one hour after the administering of the compound.

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12. The method of claim 9 further comprising a therapy session prior to the psychedelic effect.

13. The method of any one of claims 10 - 12 wherein the therapy session comprises one or more of a psychotherapy, a Chi yoga session, a catharsis treatment, and a mindfulness program.

14. The method of claim 13 wherein the mindfulness program comprises one or more of a guided mindful chakra and a Sanskrit mantra sound and colour visualization therapy.

15. The method of claim 8 wherein the effective amount is 5 to 400 micrograms of LSD, LSA or an analog thereof, once to seven times per week.

16. The method of claim 9 wherein the effective amount is 5, 10, 20, 25, 30, 40, 50, 80, 100, 150, 200, 250, 300, 350, or 400 micrograms of LSD, LSA or an analog thereof, once to seven times per week.

17. The method of claim 15 or 16 wherein the effective amount is administered once per week, 2-3 times per week, 4-5 times per week, 6 times per week, or 7 times per week.

18. The method of claim 8 wherein the effective amount results in a peak DMT concentration of 0.7 to 150 micrograms of DMT per litre of whole blood, once to thirty times per month.

19. The method of claim 9 wherein the effective amount is 0.05-1 mg/kg of DMT, administered intramuscularly, once to thirty times per month.

20. The method of claim 19 wherein the effective amount is 0.1 to 0.4 mg/kg of DMT, administered intramuscularly, once to four times per month.

21. The method of claim 19 wherein the effective amount is administered once per week, 2-3 times per week, 4-5 times per week, 6 times per week, or 7 times per week.

22. The method of claim 4 wherein the complication associated with obesity is selected from the group

consisting of sleep apnea, abnormal regulation of blood glucose, diabetes mellitus, cardiovascular disease, high blood pressure, hypertension, multiple sclerosis, erectile dysfunction, urinary incontinence, chronic renal failure, asthma, and cancer.

23. The method of any one of the preceding claims wherein the administering is of DMT and is a intramuscular administration.

24. The method of any one of the preceding claims wherein the administering is of LSD or LSA and is a sublingual administration.

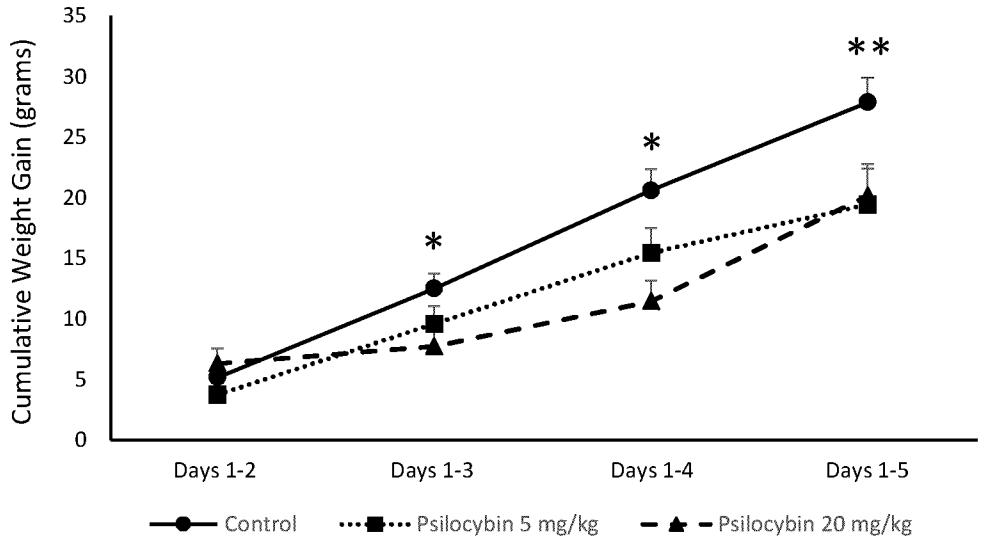
25. The method of any one of the preceding claims wherein the administering is of DMT and is via inhalation.

26. The method of any one of the preceding claims wherein the administering is oral.

27. The method of claim 15 wherein the oral administration is in combination with a MOA-I

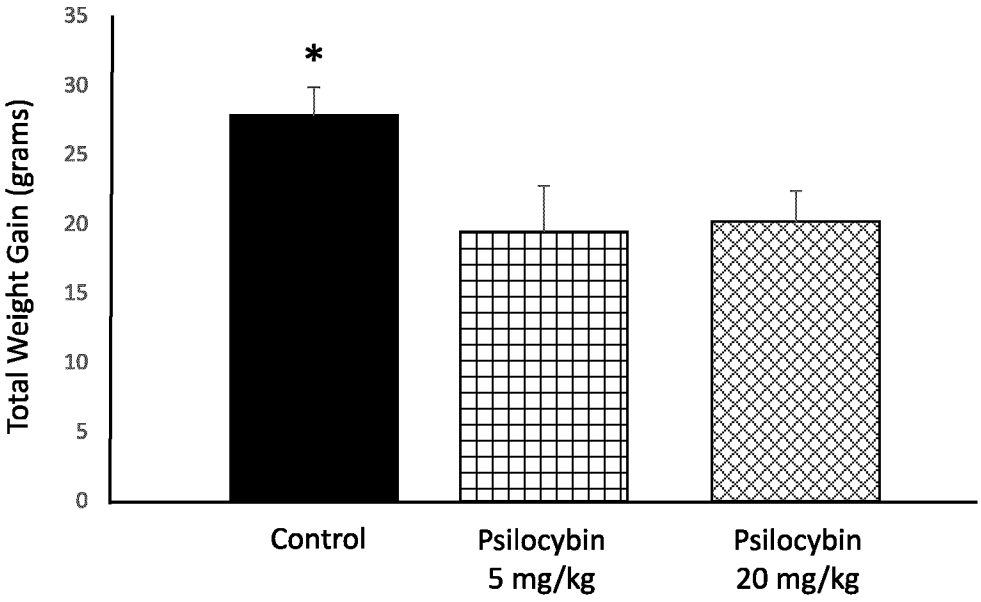
28. The method of claim 16 wherein the oral administration is in combination with a RIMA.

Figure 1



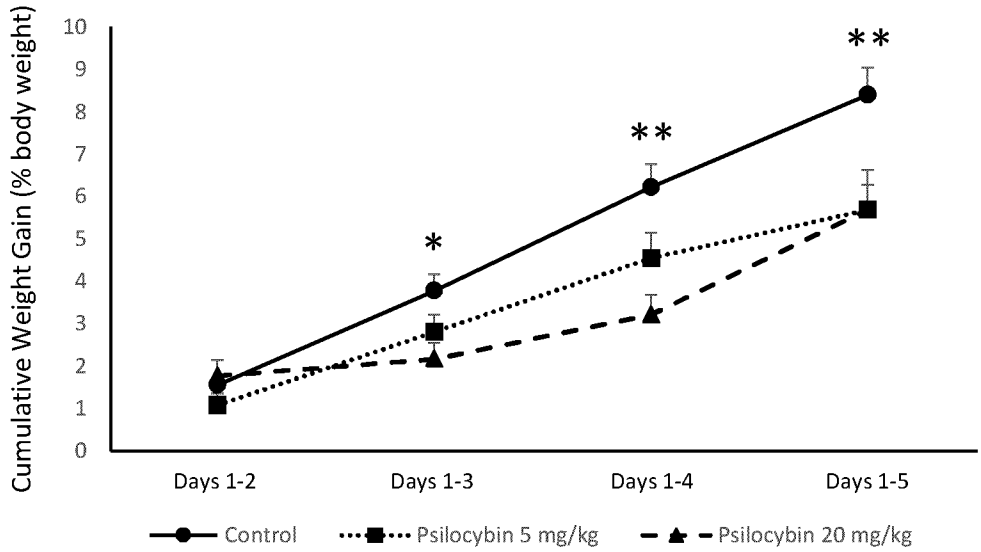
* = significantly different versus 20 mg/kg psilocybin group, $p < 0.05$
** = significantly different versus both psilocybin groups, $p < 0.05$

Figure 2



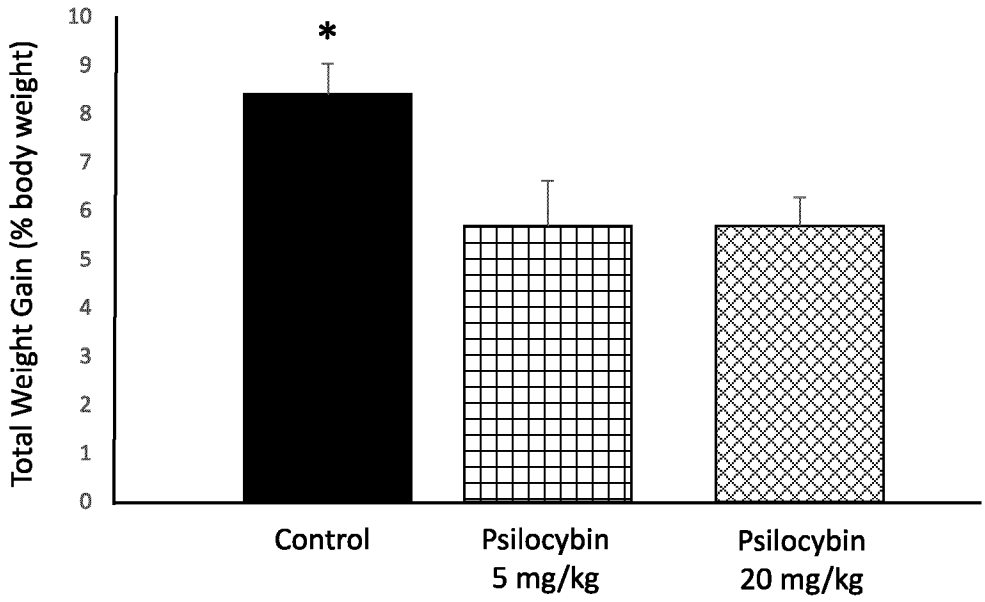
* = significantly different from psilocybin groups, $p < 0.05$

Figure 3



* = significantly different versus 20 mg/kg psilocybin group, $p < 0.05$
** = significantly different versus both psilocybin groups, $p < 0.05$

Figure 4



* = significantly different from psilocybin groups, $p < 0.05$

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2021/050757

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **A61K 31/48** (2006.01), ***A61K 31/4045*** (2006.01), ***A61K 31/451*** (2006.01), ***A61K 31/554*** (2006.01), ***A61P 25/30*** (2006.01), ***A61P 3/04*** (2006.01), ***C07D 209/46*** (2006.01), ***C07D 211/70*** (2006.01), ***C07D 281/16*** (2006.01), ***C07D 457/06*** (2006.01).

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 31/48 (2006.01), A61K 31/4045 (2006.01), A61K 31/451 (2006.01), A61K 31/554 (2006.01), A61P 25/30 (2006.01), A61P 3/04 (2006.01), C07D 209/46 (2006.01), C07D 211/70 (2006.01), C07D 281/16 (2006.01), C07D 457/06 (2006.01).

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

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
QUESTEL (FAMPAT)/ STN (SCIFINDER)/ SCOPUS: DMT OR DIMETHYLTRYPTAMINE OR (LYSERGIC ACID DIETHYLAMIDE) OR LSD OR LYSERGIDE OR LYSERGAMIDE OR LSA) AND (OBESITY OR "WEIGHT LOSS" OR "EATING DISORDER")

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2020/0147038 A1 RUSS et al. 14 May 2020 (14-05-2020) **D1**: paragraphs 0003-0004; 0013-0014; 0016-0017; 0031; 0040; 0043; 0058; 0084; 0139; 0323; 0353; claims 3 &122.	1-6, 9-14, 22-26 27-28
X Y	VAUPEL et al., "The inhibition of food intake in the dog by LDS, mescaline, psilocin, d-amphetamine and phenylisopropylamine derivatives." Life sciences, 24(26), pp. 2427-2431. 25 June 1979 (25-06-1979) [DOI: 10.1016/0024-3205(79)90451-x] [ISSN: 0024-3205] https://doi.org/10.1016/0024-3205(79)90451-X **D2:** pages 2427-2428.	1-6, 8-9, 15-17 27-28

☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

*	Special categories of cited documents:	"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"D"	document cited by the applicant in the international application	"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
"E"	earlier application or patent but published on or after the international filing date	"&"	document member of the same patent family
"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		

Date of the actual completion of the international search 15 September 2021 (15-09-2021)	Date of mailing of the international search report 15 September 2021 (15-09-2021)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 819-953-2476	Authorized officer Christine Bourque (819) 576-2951

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	DAVIS, K., "The effects and Hazards of LSD." Medical News Today, 22 June 2017 (22-06-2017) **D3**: section Other short-term effects. https://www.medicalnewstoday.com/articles/295966	1-6 and 9 27-28
X Y	WELTMAN et al., "Effect of Lysergic Acid Diethylamide (LSD-25) on Growth Metabolism and the Resistance of Male Rats to Histamine Stress." Journal of Pharmaceutical Sciences, 54(9), pp. 1382-1384. September 1965 (09-1965). [ISSN: 0022-3549] https://doi.org/10.1002/jps.2600540935 **D4**: Abstract; Results and Discussion	1-6, 9, and 16-17 27-28
X	US20180318298 A1 STEINBERG et al. 8 November 2018 (08-11-2018) **D5**: paragraphs 0071-0072; claim 5.	1-6, 8-9, 18, 22-23, and 25
Y	PASSIE et al., "The Pharmacology of Lysergic Acid Diethylamide: A Review." CNS Neuroscience & Therapeutics, 14(4), pp. 295-314. December 2008 (12-2008)[ISSN:1755-5949] [DOI: 10.1111/j.1755-5949.2008.00059.x] https://onlinelibrary.wiley.com/doi/10.1111/j.1755-5949.2008.00059.x **D6**: page 306; Table 9.	27-28
P,X	WO2020/212951 A1 LONDESBROUGH et al. 22 October 2020 (22-10-2020) Page 2, lines 1-6; page 16, lines 1-15; claims 22-23; 44-55.	
P,X	WO2020/181194 A1 MANFREDI et al. 10 September 2020 (10-09-2020) Paragraphs 00111; 00132-00133; 00140-00141.	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2021/050757

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claim Nos.: 27
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claim 27 is not fully supported by the description. Specifically, "MOA-I" is not present in the description. The claim has been searched and examined as it the aforesaid element is "MAO-I" which finds support on page 17, line 30 of the description.

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2021/050757

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US2020147038A1	14 May 2020 (14-05-2020)	WO2018195455A1	25 October 2018 (25-10-2018)
US2018318298A1	08 November 2018 (08-11-2018)	CA2900413A1	21 August 2014 (21-08-2014)
		EP2956139A1	23 December 2015 (23-12-2015)
		JP2016509017A	24 March 2016 (24-03-2016)
		US2015366865A1	24 December 2015 (24-12-2015)
		US9937173B2	10 April 2018 (10-04-2018)
		WO2014124523A1	21 August 2014 (21-08-2014)
WO2020212951A1	22 October 2020 (22-10-2020)	TW202103699A	01 February 2021 (01-02-2021)
		WO2020212948A1	22 October 2020 (22-10-2020)
		WO2020212952A1	22 October 2020 (22-10-2020)
WO2020181194A1	10 September 2020 (10-09-2020)	None	