

COMPOSITIONS FOR RELIEVING PAIN OR IRRITATION ASSOCIATED WITH MUCOSAL-IRRITATING COMPOUNDS

BACKGROUND OF THE INVENTION

[001] Many people enjoy eating food products that contain hot peppers and/or garlic and/or onions. Hot peppers, garlic and onions contain different concentrations of *capsaicinoids* and allium, which are the natural occurring in these food products that cause irritation, pain and/or burning sensation within the mouth, causing the eyes to water and the nose to run.

[002] This sensitivity to *capsaicinoids* is due to the human's neural receptors that respond to warm stimuli which have a peak sensitivity above normal body temperature. These receptors can be found inside the mouth and when exposed to the heat stimuli from the hot peppers will respond to the heat stimuli as long as they are in contact with the hot pepper. The heat level of these hot peppers is measured in Scoville units and can range from 100 for Bell peppers to 300,000 for Habanero peppers.

[003] There are several types of *capsaicinoids* that exist in hot peppers. The minor capsaicinoids that exist include nordihydrocapsaicin, homocapsaicin, and homodihydrocapsaicin and are illustrated by their chemical structures below.

[004] The most common and the most pungent *capsaicinoid* is capsaicin, also known as N-Nanillyl-8-methyl-6-E)-noneamide. Capsaicin is synthesized in the placenta of the pepper on which the seeds grow. The capsaicin then slowly permeates through the remainder of the pepper depositing more or less of the compound in the remaining parts. The heat sensation of pure capsaicin is approximately 16,000,000 Scoville units and is so hot that in its pure form diluted one hundred thousand-fold it can cause blistering of the tongue. Capsaicin and the compound dihydro-capsaicin together make up about 80-90% of

the capsaicinoids found in peppers and can be present in a 1:1 or 2:1 ratio. The capsaicinoid content in any varieties of hot peppers can range from 0.1 to 1.0%.

[005] For a typical individual to enjoy the taste of hot peppers with such a concentration of capsaicin it becomes prudent for a composition to exist that can quickly neutralize the capsaicin heat on the oral cavity, tongue, and esophagus.

SUMMARY OF THE INVENTION

[006] The invention provides a topical composition comprising at least one casein protein or any salt (or derivative) thereof and tiger nut (*Cyperus esculentus*) for use in the treatment of local pain or irritation caused by capsaicin or allium on the skin or mucosal membrane of a subject suffering therefrom.

[007] When referring to a “*topical composition*” it should be understood to encompass a locally applied composition comprising the agent(s) disclosed herein, to a particular place on or in the body surfaces such as the skin or mucous membranes to treat ailments via a large range of classes including creams, foams, gels, lotions, and ointments. In some embodiments, a topical composition of the invention is epicutaneous, meaning that it is applied directly to the skin. In other embodiments, said a topical composition of the invention is inhalational. In other embodiments, said a topical composition of the invention is in the form of a nose plug. In other embodiments, said topical composition of the invention is in the form of eye drops applied to the conjunctiva, or ear drops placed in the ear. In other embodiments, said topical composition of the invention is applied to the oral cavity mucosal membrane, such as for example the gingival tissue, interior lip/cheek tissue, palate tissue, tongue, lingual frenum, lingual papillae and so forth. In other embodiments, said topical composition of the invention is applied to the anal cavity mucosal membrane.

[008] The invention further provides a composition comprising at least one casein protein or any salt (or derivative) thereof and tiger nut for use in the treatment of local pain or irritation caused by pharmaceutical compositions comprising capsaicin or allium on the skin or mucosal membrane of a subject suffering therefrom.

[009] In some embodiments, said composition of the invention further treats and/or alleviates any digestive and gastrointestinal (GI) symptoms caused by capsaicin or allium.

[0010] The invention further provides a composition comprising at least one casein protein or any salt thereof and tiger nut for use in the treatment of digestive and gastrointestinal (GI) symptoms caused by capsaicin or allium. In some embodiments, said composition is a topical composition.

[0011] When referring to “*digestive and gastrointestinal (GI) symptoms*” it should be understood to include symptoms such as burning sensation in any part of the GI tract (for example mouth, tongue, esophagus and stomach), nausea, cramps, vomiting, heartburn, diarrhea, pain, and other symptoms. When referring to the gastrointestinal tract (GI tract, digestive tract, alimentary canal) it should be understood to include the tract or passageway of the digestive system that leads from the mouth to the anus. GI tract includes both the upper (mouth, pharynx, esophagus, stomach, duodenum) and lower GI (the small intestine including the duodenum, jejunum, and ileum; the large intestine including cecum, ascending, transverse, descending, and sigmoid colon, rectum, and anal canal). Without being bound by theory, studies have shown that consumption of capsaicin may inhibit gastric acid production, damage the GI mucosa by inducing gastric inflammation, cause structural changes of the intestinal barrier, and further result in other GI symptoms.

[0012] In some embodiments, said topical composition is selected from a topical solution, a lotion, a shake lotion, a cream, an ointment, a gel, a foam, a patch, a powder, a solid, a

sponge, a tape, a vapor, an aerosol, a spray, a dissolving powder, an effervescent strip or powder, a paste, a tincture, a strip, a chewing gum, a candy (including hard candy, gummy candy, chewable candy, dissolvable candy, effervescent candy, sugar-less or no-sugar candy or any type of confectionary product or a combinations thereof) and so forth.

[0013] In some embodiments, said topical composition further comprises at least one hydrophobic carrier. In other embodiments, a composition of the invention further comprises at least one water soluble polymer. In another embodiment, a composition of the invention further comprising at least one of plasticizer, surfactant, saliva stimulating agent, filler, vegetable oil, coloring agent, flavoring agent and any combination thereof.

[0014] When referring to “*at least one casein protein*” it should be understood to encompass at least one of a family of related phosphoproteins (α S1, α S2, β , κ) that are commonly found in mammalian milk, (including cow, sheep, goat, human and so forth).

[0015] In some embodiments, said at least one casein protein provides at least 3% wt of the composition. In other embodiments, said casein protein provides 3% to 70% wt of the composition. In other embodiments, said casein protein provides 3%wt, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70% of the composition.

[0016] In some embodiments, said tiger nut is in the form of oil. In some embodiments, said tiger nut is in the form of a powder. In some embodiments, said tiger nut is in the form of a liquid (tiger nut milk). In some embodiments, said tiger nut is in a raw form. In some embodiments, said tiger nut is in a roasted form. In some embodiments, said tiger nut is in a baked form. In other embodiments, said tiger nut is in the form of powder. In further embodiments, said tiger nut provides at least 0.5% of the composition. In further embodiments, said tiger nut provides 0.5%, 1%, 1.5%, 2%, 2.5%, 3%, 3.5%, 4%, 4.5%, 5%,

5.5%, 6%, 6.5%, 7%, 7.5%, 8%, 8.5%, 9%, 9.5%, 10% of the composition. In further embodiments, said tiger nut provides between about 0.5% to about 10% of the composition.

[0017] In some other embodiments, a composition of the invention further comprises at least one of breath fresheners, taste additives, essential oils, pain relieving agent, vitamins, anti-acid agent, and any combinations thereof.

[0018] In some embodiments, a composition of the invention is formulated into a chewing confectionary product.

[0019] In some embodiments, the composition of the invention is an orally dissolvable film. In other embodiments, said film is a multi-layered film. In further embodiments, said film dissolves at a rate of at least 1% per 1h.

[0020] In further embodiments, said composition is a lingual papillae dermatological composition.

[0021] When referring to “*casein protein*” it should be understood to include at least one of a family of related phosphoproteins (α S1, α S2, β , κ) commonly found typically in mammalian milk. In some embodiments, said at least one casein protein is from a mammalian source (dairy) is selected from cow, sheep, buffalo, human, camel, goat and any combinations thereof. In some embodiments, said at least one casein protein is from a non-dairy source (for example synthetic or semi-synthetic source). In some embodiments, said at least one casein protein is a plant-based equivalent of casein protein.

[0022] *Capsaicin* (8-methyl-N-vanillyl-6-nonenamide) is an active component of chili peppers, which are plants belonging to the genus *Capsicum*. It is an irritant for mammals, including humans, and produces a sensation of burning in any tissue with which it comes into contact. *Allium* is a genus of monocotyledonous flowering plants that include hundreds of species, including the cultivated onion, garlic, scallion, shallot, leek, and chives.

[0023] When referring to “*skin or mucosal membrane*” it should be understood to encompass any tissue membrane exposed to said capsaicin or allium including, but not limited to gingival tissue, interior lip/cheek tissue, palate tissue, tongue, lingual frenum, lingual papillae, conjunctiva tissue, inner ear tissue, skin tissue (including hands, feet, lips, nose, fingernails, scalp, neck, nipple, armpit), and any combinations thereof. In other embodiments mucosal membrane includes any GI tract mucosal membrane (including both the upper (mouth, pharynx, esophagus, stomach, duodenum) and lower GI (the small intestine including the duodenum, jejunum, and ileum; the large intestine including cecum, ascending, transverse, descending, and sigmoid colon, rectum, and anal canal).

[0024] The invention further provides a composition comprising casein protein or any salt thereof for use in the prevention of local pain caused by capsaicin.

[0025] The invention provides a product comprising at least one composition of the invention.

[0026] The invention further provides a method of treating a subject suffering from local pain caused by capsaicin, said method comprising administering to said patient a composition comprising casein protein or any salt or derivative or derivative thereof.

[0027] The invention further provides a method of preventing a subject from suffering from local pain or irritation on the skin or mucosal membrane caused by capsaicin, said method comprising administering to said patient a composition comprising casein protein or any salt or derivative thereof.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

[0028] In the following detailed description, numerous specific details are set forth in order to provide a thorough understanding of the invention. However, it will be understood by those skilled in the art that the present invention may be practiced without these specific

details. In other instances, well-known methods, procedures, and components have not been described in detail so as not to obscure the present invention.

[0029] **Example 1 - Components of a product of the invention**

[0030] Table 1 below provides a list of optional ingredients of an embodiment of a composition of the invention.

Table 1

Ingredients	Amount	Examples
Compound	5-30% w/w	Casein
Compound	1 – 8%	Tiger nut
Water Soluble polymer	45%w/w	HPMC E3, E5 and E15 and K-3, Methyl cellulose A-3 and A1-5, Pullulan, carboxmethylcellulose cekol 30, polyvinylpyrrolidone PVP k-90, pectin, gelatin, sodium, alginate, hydroxypropylcellulose, polyvinyl alcohol, maltodextrins,
Plasticizer	0-20%w/w	glycerol, dibutyl phthalate, polyethylene glycol
Surfactants	q.s.	Sodium lauryl sulfate, benzalkonium chloride, tween
Sweetening agents	3-6%w/w	Saccharin, cyclamate, and aspartame
Saliva stimulating agents	2-6%w/w	Citric acid, maleic acid, lactic, and Ascorbic acid
Filters, colors, flavors	q.s.	FD and C colors, US FDA approved flavors, salt, vegetable oil

[0031] **Example 2 - Preparation of a product of the invention (an aerosol/spray)**

Table 2

Ingredient	Amount %
water	63.9
ethanol	21
Tiger nut	8
Sodium caseinate	5
Chickpea protein	0.5
Citric Acid	0.2
Spearmint flavor	0.1
Lime flavor	0.1

Glycerol	1
Methyl cellulose	0.2

[0032] **Example 3 - Comparative Example #1**

[0033] Products that are examined: (Group 1) a spray of the invention; (Group 2) a casein spray (cow milk origin); (Group 3) a tiger nut oil spray; (Group 4) placebo (water spray).

[0034] Subjects tested: 12 volunteers of ages between 20 to 70, healthy with no relevant diseases. Subjects are divided into the above groups and are using the provided spray after consuming 5gr of mayonnaise comprising 0.1 – 2 gr of tabasco (increasing quantities). Each subject is rating the hot taste (pain) before and after spraying 1 – 5 doses of the spray provided.

[0035] **Example 4 - Comparative Example #2**

[0036] Each participant between the ages of 20 to 70 performs the experiment, with each test being conducted at intervals of at least one day. Each day, each participant is introduced with only one product of the same type. A total of 180 – 360 subjects.

[0037] Product composition tested: A - Formula of the Invention Spray (Example 1); B- Formula of the Invention Spray (different concentration of tiger nut); C- Formula of the Invention Spray (different concentration of casein); D - Milk/Casein Spray; E - Tiger Nut Spray; F - Placebo Water Spray.

[0038] The course of the research: In each group, each participant is asked to eat a measured amount of spicy mayonnaise in a spoon in 2 stages: Stage 1 - Each participant is asked to consume a spoonful of spicy mayonnaise (5 grams) containing a variable amount of Tabasco (starting from 1 gram and increasing by 0.5 grams in each measurement) in the following order: 0.5 grams of Tabasco, 1.5 grams of Tabasco, 1 gram Tabasco, 2 grams of Tabasco. The participant is asked to consume the spoonful of spicy mayonnaise slowly

when the whole compound is placed on the tongue. Stage 2 – Each participant is asked to spray 3 times from the spray into the mouth 5 seconds after consumption - the spray must be sprayed into the oral cavity just above the tongue and immediately rate the level of spiciness on a scale of 1 to 10. The participant is asked to rate the intensity of the spiciness again at the following times from consuming the spicy mayonnaise: a. T0- 00:00:00, b. T1- 00:00:30, c. T2- 00:01:30, d. T3- 00:03:30, e. T4- 00:05:30.

CLAIMS

[0039] What is claimed is:

1. A composition comprising at least one casein protein or any salt thereof and tiger nut; for use in the treatment of local pain or irritation caused by capsaicin or allium on the skin or mucosal membrane of a subject suffering therefrom; wherein said composition is a topical composition.
2. A composition according to claim 1, further comprising at least one hydrophobic carrier.
3. A composition according to claim 1, further comprising at least one water soluble polymer.
4. A composition according to claim 1, further comprising at least one of plasticizer, surfactant, saliva stimulating agent, filler, vegetable oil, coloring agent, flavoring agent and any combination thereof.
5. A composition according to any one of the preceding claims, wherein said at least one casein protein provides at least 3% of the composition.
6. A composition according to any one of the preceding claims, wherein said tiger nut is in the form of oil.
7. A composition according to any one of the preceding claims, wherein said tiger nut is in the form of powder.
8. A composition according to any one of the preceding claims, wherein said tiger nut provides at least 0.5% of the composition.
9. A composition according to any one of the preceding claims, further comprising at least one of breath fresheners, taste additives, essential oils, pain relieving agent, vitamins, anti-acid agent, and any combinations thereof.
10. A composition according to any one of the preceding claims, being formulated into a chewing confectionary product.
11. A composition according to any one of the preceding claims, being a liquid formulation.
12. A composition according to any one of the preceding claims, being a dermatological lotion, cream or ointment.

13. A composition according to any one of the preceding claims, being an orally dissolvable film.
14. A composition according to claim 13, wherein said film is multi-layered film.
15. A composition according to claims 13 or 14, wherein said film dissolves at a rate of at least 1% per 1h.
16. A composition comprising casein protein or any salt thereof for use in the prevention of local pain caused by capsaicin.
17. A composition according to any one of the preceding claims wherein said composition is used in the treatment of digestive and gastrointestinal (GI) symptoms caused by capsaicin or allium.
18. A product comprising at least one composition according to any one of the preceding claims.
19. A method of treating a subject suffering from local pain caused by capsaicin, said method comprising administering to said patient a composition comprising casein protein or any salt or derivative or derivative thereof.
20. A method of preventing a subject from suffering from local pain or irritation on the skin or mucosal membrane caused by capsaicin, said method comprising administering to said patient a composition comprising at least one casein protein or any salt or derivative or derivative thereof.
21. A composition comprising at least one casein protein or any salt or derivative thereof, wherein said composition is a lingual papillae dermatological composition.
22. A composition comprising at least one casein protein or any salt thereof and tiger nut for use in the treatment of digestive and gastrointestinal (GI) symptoms caused by capsaicin or allium.