

NOVEL EFFERVESCENT FORMULATION COMPRISING VITAMIN C AND GLUTATHIONE

Field of Invention

The present invention relates to the field of dietary supplements. In particular, the present invention relates to an effervescent formulation comprising vitamin C and glutathione.

Background of Invention

In the field of dietary supplements, vitamin C is used for growth, development and repair of body tissues, which include skin tissue. Vitamin C has been proven to be a key ingredient in maintenance of skin health¹. It has been further discovered that a combination of vitamin C and glutathione is able to improve skin complexion².

Vitamin C is a water-soluble vitamin, which is an essential micronutrient required for normal metabolic functioning of the body as humans have lost the ability to naturally synthesize vitamin C^{3,4}. This would require vitamin C to be consumed as a dietary supplement to obtain sufficient vitamin C necessary for growth, development and repair of body tissues, which includes skin tissue.

When used in skin products for example, vitamin C is used to promote the synthesis of collagen. According to Boyera et al., Vitamin C serves as a co-factor of essential enzymes in the synthesis of collagen, which is a main component of skin tissue⁵.

Glutathione on the other hand plays an important role in liver detoxification and skin whitening. Matsuki et al., for example cites that Glutathione is a scavenger of free radicals and is able to promote skin whitening by inhibiting tyrosinase, which skews melanogenesis from darker eumelanin to lighter phaeomelanin².

The effervescent formulation according to the present invention provides for an intended dosage of vitamin C and glutathione to be evenly dispersed in water to form a beverage. The formulation allows faster absorption of these active ingredients compared to other oral solid dosage forms of dietary supplements. The effervescent formulation is stable during storage and is able to resist moisture without triggering an effervescent reaction.

It is therefore an object of the present invention to provide a dietary supplement capable of delivering vitamin C and glutathione to a consumer orally in an effective means. A dietary supplement can be provided orally via powders, coated tablets, gummies or effervescent formulations among others.

- 5 An efficient way to deliver active ingredients to a consumer is via effervescent formulations. Effervescence (which is the mechanism of an effervescent formulation) is the evolution of gas bubbles from a liquid, as the result of a chemical reaction between an edible organic acid and an alkali carbonate or alkali bicarbonate in the presence of water to produce carbon dioxide, alkali salts, and water.
- 10 Effervescent formulations are orally administered formulations containing a mixture of active ingredients in a dosage form that dissolves in liquids, releasing gas bubbles as they disintegrate. Effervescent formulations in a tablet, pill or caplet form for example have a major advantage over other orally administered formulations in that an intended dosage of active ingredients can be evenly dispersed in water to form a beverage.
- 15 Further, effervescent formulations provide for faster absorption when compared to other conventional oral solid dosage formulations such as tablets, capsules or powders. The active ingredients are administered as a beverage that is easily absorbed by the human body. Effervescent formulations are also beneficial for humans who have difficulty swallowing or dislike swallowing tablets.
- 20 Effervescent formulations are considered sensitive to moisture or “moisture sensitive”. In order to produce and store such a formulation that is moisture sensitive, processes involved in manufacturing and storage should be done in a method such that contact of the product with water is minimized. If an effervescent formulation comes into contact with water, an effervescent reaction will begin and it will be difficult to stop this
- 25 reaction, as water is a product of this reaction, which would create a cascading effect, causing further reactions to occur.

Conventionally, effervescent formulations are made using a combination of acids and alkali bicarbonates to achieve an effervescent effect. However, it is discovered that the usage of alkali bicarbonate alone is unfavorable as it is highly sensitive to moisture

30 and easily starts an effervescent reaction during storage making the product unusable if not stored in appropriate conditions.

There is therefore a need to be able to deliver vitamin C and glutathione via a stable effervescent formulation to enable fast absorption of a desired dosage of said active ingredients by the human body while at the same time providing the formulation with a stable structure which is able to resist higher levels of moisture without triggering an effervescent reaction compared to existing effervescent formulations.

An orally ingestible formulation comprising the combination of vitamin C and glutathione is disclosed in Chinese patent application CN102499371A for example. The application however discloses that the formulation is in the form of a powder, which is mixable in liquid to be administered to a consumer. There is a limitation to this formulation such that it may not be able to provide an intended dosage of active ingredients consistently and efficiently compared to an effervescent formulation. This is because powders usually involve scooping using spoons or other scooping means, which leave room for error in measurement.

Besides that, European patent application EP1082957A1 discloses in an embodiment of the invention, effervescent granules are able to provide effective delivery of active agents such as vitamins and minerals such that the effervescent granules are formed by an effervescent agent comprising alkali carbonate. This allows the formulation to achieve some stability towards moisture. However, the formulation does not provide as much resistance to moisture as that which could be attained by an effervescent agent comprising a combination of both alkali carbonates and alkali bicarbonates.

Despite the studies and innovations in the field of effervescent preparation which have been published, there is no disclosure of an effervescent formulation comprising the reaction between an acid and base of both alkali carbonate and alkali bicarbonate in combination to allow the formulation to have a high level of stability against reaction and ability to resist moisture during storage without triggering an effervescent reaction.

Therefore, it is an object of this invention to provide an effervescent formulation, which is able to deliver an intended dosage of vitamin C and glutathione, which is able to resist moisture during storage without triggering an effervescent reaction. In particular, the invention is aimed at providing an effervescent formulation comprising vitamin C and glutathione as active ingredients and an effervescent agent comprising acid and base components whereby the base component comprise both alkali carbonates and alkali bicarbonates.

Summary of Invention

According to the present invention, the effervescent formulation is formulated to allow a dosage of vitamin C and glutathione to be sufficiently consumed by humans as a beverage in a convenient form. The formulation is easily absorbed by the body and stable during storage.

In an embodiment of the present invention, the effervescent agent used in the effervescent formulation is an acid and base, whereby the base is a combination of alkali carbonate and alkali bicarbonate in the ratio, which enables the formulation to achieve stability during storage. A significantly lower amount of carbonates used in proportion to an amount of bicarbonates enables the formulation to achieve stability as alkali carbonate has an additional reaction step in effervescent reaction enabling the combination of the alkali carbonates and bicarbonates to withstand certain levels of moisture during storage.

A preferred embodiment of the present disclosure provides an effervescent formulation comprising an effervescent agent and vitamin C in combination with glutathione and vitamin E wherein the effervescent agent is an acid and base, whereby the base is a combination of alkali carbonate and alkali bicarbonate in the ratio, which enables the formulation to achieve stability during storage. A significantly lower amount of carbonates used in proportion to an amount of bicarbonates enables the formulation to achieve stability as alkali carbonate has an additional reaction step in effervescent reaction enabling the combination of the alkali carbonates and bicarbonates to withstand certain levels of moisture during storage.

A preferred embodiment of the present disclosure provides an effervescent formulation comprising an effervescent agent and vitamin C in combination with glutathione, vitamin E and flavoring agents wherein the effervescent agent is an acid and base, whereby the base is a combination of alkali carbonate and alkali bicarbonate in the ratio, which enables the formulation to achieve stability during storage. A significantly lower amount of carbonates used in proportion to an amount of bicarbonates enables the formulation to achieve stability as alkali carbonate has an additional reaction step in effervescent reaction enabling the combination of the alkali carbonates and bicarbonates to withstand certain levels of moisture during storage.

Detailed Description of the Invention

It is to be understood that the embodiments disclosed herein are illustrative of the principles of the claims. Other modifications that may be employed are within the scope of the claims. Thus, by way of example, but not of limitation, alternative embodiments may be utilized in accordance with the disclosure herein.

5 Accordingly, the claims are not limited to embodiments precisely as shown and described. Throughout this specification and the claims, which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group
10 of integers or steps.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or
15 information derived from it) or known matter forms part of the common general knowledge in the field of endeavor to which this disclosure relates.

As used herein, the following terms have the following meanings.

"Effervescent" or "effervescence" refers to emitting small bubbles of gas continuously produced for a period of time.

The present invention relates to an effervescent formulation comprising active
20 ingredients and an effervescent agent. The effervescent formulation preferably comprises an effervescent agent comprising an acid and a base wherein the base comprises an alkali carbonate and alkali bicarbonate in combination. The alkali carbonate can be selected from alkali metal carbonate or alkaline earth metal carbonate where else the alkali bicarbonate can be selected from alkali metal
25 bicarbonate or alkaline earth metal bicarbonate.

The effervescent formulation is water-soluble and is able to dissolve quickly. The effervescent formulation is able to dissolve completely without leaving scum or residue into a solution when placed in water in less than 5 minutes. The formulation when fully dissolved is easily swallowed. This solution provides active ingredients in a form,
30 which is easily absorbed by the human body when compared to other forms of delivery such as coated tablets, coated pills, capsules or gummies.

In order to produce effervescence, the effervescent agent enables a reaction between an acid and a base counterpart with the reaction taking place when the effervescent agent comes into contact with moisture (in a preferred situation, the effervescent formulation is placed in water).

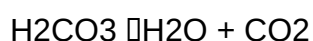
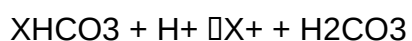
- 5 The effervescent agent comprising an alkali carbonate or alkali bicarbonate in combination is reacted with an organic acid. When the effervescent formulation (such as in the form of an effervescent tablet) is placed in liquid (such as water), the water molecules liberate the acid and base, enabling the acid and base to react with each other to produce carbon dioxide gas, which in turn causes carbonation to the aqueous
10 mixture of effervescent formulation and liquid.

In order to stabilize the effervescent formulation during storage, a combination of alkali carbonates and bicarbonates at an appropriate ratio is vital, as the effervescent formulation is sensitive to moisture. The addition of alkali carbonate to alkali bicarbonate will introduce an additional reaction step during the effervescent reaction.

- 15 This additional step reduces the sensitivity of the effervescent formulation to moisture thus enhancing the stability of the formulation during storage. Typically, alkali carbonates are used in combination with alkali bicarbonates in the ratio of 1:1 to 1:10. Preferably, in the ratio of 1:1 to 1:6.

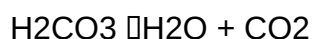
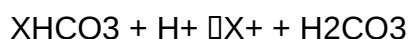
- Alkali carbonates have an additional reaction step during the effervescent reaction,
20 which allows it to be able to absorb more moisture without triggering an effervescent reaction when compared to alkali bicarbonate. Thus, a combination of alkali carbonates and alkali bicarbonates produce a significant stabilization effect when compared with formulations only using alkali carbonates or alkali bicarbonates alone. The alkali carbonate or bicarbonate will react with the acid to start an effervescent
25 reaction.

The alkali bicarbonate reaction is as follows:



The alkali carbonate reaction is as follows:

- 30 $\text{X}_2\text{CO}_3 + \text{H}^+ \rightarrow \text{XHCO}_3 + \text{X}^+$



Examples of suitable organic acids include but are not limited to citric acid, malic acid, tartaric acid, adipic acid, succinic acid and fumaric acid, preferably the effervescent formulation comprises citric acid. The organic acids also play a role in giving a unique taste profile. Preferably, the use of citric acid gives off a unique, citrusy sourness profile. The acid used is preferably in the amount of 15% by weight to about 50% by weight.

Examples of suitable bases include a combination of alkali carbonate and bicarbonate combinations preferably a combination selected from but not limited to alkali metal carbonates, alkali earth metal carbonates, alkali metal bicarbonates and alkali earth metal bicarbonates; more preferably calcium carbonate, sodium carbonate, magnesium carbonate, potassium carbonate, sodium bicarbonate, and potassium bicarbonate. The effervescent formulation preferably includes base in the amount of about 10% by weight to about 60% by weight.

In a preferred embodiment of the present invention, the present invention relates to an effervescent formulation comprising of vitamin C in combination with at least another active ingredient, which is used to promote general health maintenance. Vitamin C in combination with vitamin E and glutathione for example is used to improve skin complexion due to their antioxidant properties to fight against free radicals, which cause aging.

Vitamin C is a water-soluble vitamin, which has various biological functions for example to promote the synthesis of collagen. Boyera et al has cited that Vitamin C serves as a co-factor of two essential enzymes in the synthesis of collagen helps to maintain the collagen structure by stabilizing its triple helical structure. (*Boyera et al. (1998)*).

The effervescent formulation comprises vitamin C preferably in an amount of at least 25 mg to around 2000 mg. The effervescent formulation comprises vitamin C preferably in the amount of about 0.5% by weight to about 58% by weight.

The vitamin C can be in various forms. Vitamin C can be sourced from but not limited to sodium ascorbate, calcium ascorbate, esters, other salt forms of ascorbic acids and ascorbic acid.

5 The effervescent formulation may also comprise various additional active ingredients combined with vitamin C such as but not limited to vitamins, minerals and dietary supplements including vitamin E and glutathione.

In a preferred embodiment of the present invention, the application relates to an effervescent formulation comprising an effervescent agent and vitamin C in combination with glutathione.

10 The effervescent formulation may comprise glutathione in an amount sufficient to improve skin whitening by scavenges free radicals and inhibits tyrosinase which skews melanogenesis from the darker eumelanin to the lighter phaeomelanin.

15 Tyrosinase is an enzyme present in human tissues that catalyses the production of melanin and other pigments from tyrosine by oxidation. Free radicals on the other hand are unstable molecules that are produced during normal cell metabolism, which build up in cells, damaging other molecules in the body. The glutathione absorbed by the body through the ingestion of the effervescent formulation is formulated such that the composition of the glutathione component is in an amount, which promotes inhibition of tyrosinase and concurrently scavenges free radicals in the body. Through these
20 processes, the effervescent formulation is able to skews melagonesis to favor production of lighter phaeomelanin from darker eumelanin.

Preferably, the glutathione in the formulation is in an amount of at least 20 mg to 500mg, preferably in an amount of at least 50 mg to around 400 mg. The glutathione can be in the amount of about 0.5% by weight to about 15% by weight.

25 Glutathione, which forms part of the formulation, can be in various forms such as but not limited to reduced and oxidized forms, other salt forms of glutathione and/or its conjugates thereof.

In a preferred embodiment of the present invention, the application relates to an effervescent formulation comprising an effervescent agent and vitamin C in
30 combination with glutathione and vitamin E.

The effervescent formulation may comprise vitamin E in an amount sufficient to nourish and protect the skin, as it is a lipid-soluble antioxidant that protects the skin from the adverse effects of oxidative stress caused by various conditions such as UV ray exposure or consumption of an unbalanced diet.

- 5 Preferably, the vitamin E in the formulation is in an amount of at least 5 IU to 25 IU, preferably in an amount of at least 10 IU to 15 IU. The vitamin E can be in the amount of about 0.2% by weight to about 1.5% by weight.

Vitamin E, which forms part of the formulation, can be in various forms such as but not limited to alpha- (or α -) tocopherol, esters or other pharmaceutically acceptable forms
10 of vitamin E and/or its conjugates thereof.

The effervescent formulation may also include flavoring agents comprising sugar alcohol and sweetener. Suitable sugar alcohols include but not limited to mannitol, sorbitol, xylitol, and erythritol. Suitable sweeteners such as artificial sweeteners include but not limited to aspartame, acesulfame potassium, saccharin, stevia,
15 sucralose, advantame, monk fruit extract and combinations thereof. The sugar alcohol used is in an amount from about 10% by weight to about 35% by weight, while the sweetener used is in an amount of about 0.1% by weight to about 2.0% by weight.

The effervescent formulation may also include other ingredients such as food, drug and cosmetic (FD&C) coloring (e.g. dyes and lakes).

- 20 The effervescent formulation may be in the form of a tablet. When in the form of a tablet, the composition may include a binder. Examples of suitable binders include but not limited to, polyvinylpyrrolidone, glucose, sucrose, starch, cellulose derivatives and mixtures thereof. Where present, the composition includes a sufficient amount of binder to assist in holding the components of the composition together in the form of
25 a tablet. When present, the effervescent formulation preferably includes binder in an amount from about 0.5% by weight to about 15% by weight. It is preferred that the effervescent formulation is in the form of a tablet, which is round with flat upper and lower surfaces.

For example, an effervescent formulation in accordance with the invention was
30 prepared by mixing citric acid anhydrous, l-glutathione, dl-alpha tocopherol acetate, sodium chloride, sugar alcohol, calcium carbonate, ascorbic acid in a mixer. Then, an

optionally pre-prepared binder solution and color solution were mixed and poured into the mixer for mixing. Granules were formed and were transferred to a blender. Sodium bicarbonate and sweeteners were then added into the blender and blended. The granules were then compressed into tablets.

- 5 For storage of the effervescent formulation, the effervescent formulation is stored in a moisture resistant packaging such as but not limited to metal foil pouches, blister packs, tubes with caps pre-inserted with silica gel, strip packing and sachets among others.

Administration of the effervescent formulation is done by adding the effervescent
10 formulation to liquid such as water. The mixture of effervescent composition and water can be stirred to speed up the dispersion of the effervescent solution in the liquid.

For example, an effervescent formulation in tablet form was added to 150mL of water and was observed to completely dissolve . The color of the resulting composition was dark orange to light orange. There were no visible sediments in the mixture once the
15 effervescent reaction was completed.

The tablet manufacturing and initial packing operations are preferably performed in a controlled environment in which the temperature and humidity are controlled to be relatively low.

References

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CLAIMS

1. An effervescent formulation comprising:

an effervescent agent having a combination of alkali carbonate and alkali bicarbonate as a base in a ratio of 1:1 to 1:6;

5 vitamin C and glutathione.

2. The effervescent formulation according to claim 1 wherein the effervescent formulation further comprises vitamin E.

- 10 3. The effervescent formulation according to any one of the preceding claims wherein the formulation further comprises a flavoring agent.

4. The effervescent formulation according to claim 3 wherein the flavoring agent comprises sugar alcohol, sweeteners or a combination thereof.

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5. The effervescent formulation according to any one of the preceding claims wherein vitamin C is 25 mg to 2000 mg by weight.

- 20 6. The effervescent formulation according to any one of the preceding claims wherein vitamin C in an amount of 0.5% by weight to 58% by weight.

7. An effervescent formulation according to any of the preceding claims wherein vitamin C is in the form of ascorbic acid or a pharmaceutically acceptable form thereof.

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