(21) International Application Number: PCT/US99/17932
(22) International Filing Date: 10 August 1999 (10.08.99)
(30) Priority Data: 09/132,983 12 August 1998 (12.08.98) US

Published
With international search report.

(54) Title: PRODUCTS CONTAINING UNPLEASANT TASTING BIO-AFFECTING AGENTS AND METHODS OF MAKING THEM

(57) Abstract

New fast-dissolving consumable units, e.g., tablets, are made from compositions containing unpleasant-tasting, water-soluble agents, along with saccharide-based shearform floss particles and excipients.
FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL  Albania          ES  Spain          LS  Lesotho
AM  Armenia        FI  Finland        LT  Lithuania
AT  Austria        FR  France        LU  Luxembourg
AU  Australia      GA  Gabon         LV  Latvia
AZ  Azerbaijan     GB  United Kingdom MC  Monaco
BA  Bosnia and Herzegovina GE  Georgia      MD  Republic of Moldova
BB  Barbados       GH  Ghana         MG  Madagascar
BE  Belgium        GN  Guinea        MK  The former Yugoslav Republic of Macedonia
BF  Burkina Faso   GR  Greece        ML  Mali
BG  Bulgaria       HU  Hungary       MN  Mongolia
BJ  Benin          IE  Ireland       MR  Mauritania
BR  Brazil         IL  Israel        MW  Malawi
BY  Belarus        IS  Iceland       MX  Mexico
CA  Canada         IT  Italy         NE  Niger
CF  Central African Republic JP  Japan       NL  Netherlands
CG  Congo          KE  Kenya         NO  Norway
CH  Switzerland    KG  Kyrgyzstan    NZ  New Zealand
CI  Côte d’Ivoire  KP  Democratic People’s Republic of Korea PL  Poland
CM  Cameroon       KR  Republic of Korea PT  Portugal
CN  China          KZ  Kazakhstan     RO  Romania
CU  Cuba           LC  Saint Lucia    RU  Russian Federation
CZ  Czech Republic LC  Liechtenstein  SD  Sudan
DE  Germany        LI  Sri Lanka      SE  Sweden
DK  Denmark        LR  Liberia        SG  Singapore
SI  Slovenia       SK  Slovakia       SN  Senegal
SZ  South Africa   TD  Chad          TG  Togo
TJ  Tajikistan     TM  Turkmenistan   TR  Turkey
TT  Trinidad and Tobago UA  Ukraine
UG  Uganda         US  United States of America
VU  Vietnam        YU  Yugoslavia
ZW  Zimbabwe
PRODUCTS CONTAINING UNPLEASANT TASTING BIO-AFFECTING AGENTS AND METHODS OF MAKING THEM

This application is a continuation-in-part of U.S. Patent 5,869,098, issued February 9, 1999.

FIELD OF THE INVENTION:

The invention deals with fast-dissolving or easily chewable oral products containing unpleasant tasting, water-soluble bio-affecting agents, such as ascorbic acid (Vitamin C). The products are comestible units made from compositions containing a blend of microparticles of the bio-affecting agents along with shearform floss particles. Methods of making the products are also described.

BACKGROUND OF THE INVENTION:

Ascorbic acid is exemplary of the generally water-soluble unpleasant-tasting, bio-affecting agents used herein.

Ascorbic acid, a water-soluble vitamin, is used in the prevention or treatment of scurvy, anemia, gum infections, dental caries, and other ailments. As a dietary supplement, doses of 30 mg to 60 mg per day for children and 60 mg per day for adults are recommended.

Ascorbic acid is readily absorbed into the body. However, oral products for administering ascorbic acid have drawbacks. Among these drawbacks is the acid's astringent taste, which tends to lower patient compliance with recommended dosage levels.

Most products on the market do not dissolve quickly in the mouth's saliva, requiring vigorous chewing or taking the products with water. Such products can stay in the mouth for significant periods of time, resulting in exposure to the undesirable taste of any unpleasant tasting bio-affecting agents therein for significant periods of time.

There is a need for oral products of unpleasant tasting bio-affecting agents, e.g., ascorbic acid, which dissolve quickly in the mouth with or without chewing and minimize the patient's perception of the agent's unpleasant taste.

SUMMARY OF THE INVENTION:

Comestible units for the oral delivery of water-soluble, unpleasant-tasting active
agents are made from a composition containing the following components:

(a) optionally coated microparticles containing one or more unpleasant-tasting agents;
(b) saccharide-based shearform floss particles; and
(c) suitable excipients selected from lubricants, flavor enhancers, glidants, fillers and colorants.

The method of making these units comprises combining and shaping components (a)-(c), as follows:

(1) preparing saccharide-based shearform floss particles,
(2) contacting them with a crystallization enhancer,
(3) blending the product of step (2) with microparticles containing unpleasant tasting bio-affecting agent(s) and excipients, and
(4) shaping to form comestible units.

Applicants believe that in preferred embodiments, the combination of (I) the taste-masking/improved stability coating on the microparticles of unpleasant tasting active agent with (II) the pleasing taste, or sweetness, of the floss particles renders the bio-affecting agents' unpleasant taste almost undetectable, so that tablets containing them have an acceptable taste.

ADVANTAGES:

Comestible units made using the compositions and methods of the invention generally dissolve in the consumer's mouth instantaneously, i.e., in 10 seconds or less, based on organoleptic testing, without the need for chewing or drinking water. The saliva in the mouth provides sufficient liquid to cause quick dissolution. The use of fast-dissolving units assures that the water-soluble vitamin or other unpleasant tasting bio-affecting agent(s) spend a minimal amount of time in the mouth, so that their unpleasant taste is barely detected and patient compliance improves.

In another embodiment, the comestible units made using the compositions and methods of the invention generally dissolve in the consumer's mouth upon gentle chewing, (i.e., in 10 seconds or less, based on organoleptic testing, without the need for drinking water).
Also, the optional presence of one or more coatings on the microparticles of agent(s) and the pleasant flavor of the floss and other excipients tends to make any unpleasant taste less noticeable.

**DETAILED DESCRIPTION OF THE INVENTION:**

The invention relates to novel comestible units and the method of making them. Unless otherwise noted, all parts and percentages recited are weight percentages, based on total composition weight.

**THE COMPOSITIONS:**

Compositions from which the units are made have three principal components:

(a) coated or uncoated microparticles of bio-affecting agents,

(b) saccharide-based shearform matrix particles, and

(c) one or more excipients.

When present, the coatings on the microparticles provide improved stability, taste-masking, or both.

**A. Microparticles of Bio-affecting Agents**

The bio-affecting agents used in the invention include unpleasant tasting watersoluble vitamins or other water-soluble active agents, *i.e.*, agents having biological activity. Suitable agents include: ascorbic acid, ferrous fumarate, folic acid, niacinamide, pyridoxine hydrochloride, riboflavin, thiamine mononitrate, Vitamin A acetate, Vitamin B₁₂, Vitamin D (e.g., Vitamin D₃) and Vitamin E and its acetate. Ascorbic acid and Vitamin D, along with pharmaceutically acceptable derivatives of same and combinations with other bio-affecting agents, e.g., Vitamin D with calcium carbonate, are preferred.

The microparticles used in the invention are generally particles of about 0.1 to about 600 microns in size. They need not be coated.

The microparticles preferably have one or more coating layers, with each layer containing one or more materials selected from: mono- and diglycerides; starch; or cellulose derivatives, *e.g.*, ethyl cellulose. Other coating materials which impart taste-masking, improved stability, or other properties can be used.

Coated microparticles generally contain from about 50% to about 100%, preferably about 60%, of active agent(s), with the remainder being one or more coating(s).
Preferred coated ascorbic acid particles include "DESCOTE ASCORBIC ACID
60%" sold by Particle Dynamics of St. Louis, MO.

Useful ascorbic acid particles may have no coatings, i.e., be 100% acid. These
include "Ascorbic Acid USP 100%" from BASF, Mt. Olive, NJ.

The particles may have low coating levels, such as those bearing about 2% to 4%,
preferably 2.5%, ethyl cellulose coatings. The product sold as Ascorbic Acid 97.5% by
Roche Vitamins of Paramus, NJ is useful.

The particles may be granulated with starch and lactose. The product sold as
Ascorbic acid 90% C-90 by Roche Vitamins of Paramus, NJ is useful.

Spherical microparticles, e.g., microspheres, are useful in the invention. However,
they are not required. Accordingly, suitably sized microparticles having irregular and/or
non-spherical shapes can be used.

While "ascorbic acid" is referred to herein, other bio-affecting agents, as well as
mixtures containing same, may be used.

B. Shearform Floss Particles

Useful shearform floss particles are particles described in U. S. Applications SN
08/915,067 and SN 08/915,068, both filed August 20, 1997, and assigned to Fuisz
Technologies Ltd.

Preferred flosses are termed "unifloss" particles. They contain one or more
saccharides and two or more sugar alcohols. Suitable particles are made from
compositions containing about 80% to 85% sucrose, about 5% to 20% sorbitol, about 5%
to 25% xylitol, and about 0 to 10% polyoxyethylene sorbitan fatty acid esters (e.g.,
TWEEN 80).

Other ingredients, such as one or more of the excipients discussed at section C,
infra, may be used as floss constituents. The floss particles dissolve very quickly in the
mouth, releasing the sweeteners therein almost instantaneously.

The flosses are made by subjecting blends of sugar(s) and sugar alcohol(s) to flash
flow processing in a suitable spinning device, such as that described in U. S. Patent
Application Serial No. 08/854,344, filed May 12, 1997.

The spun floss is chopped for about 0.5 to about 5 minutes, preferably about 1 to 2
minutes, in the presence of 0% to about 2%, preferably about 2%, lactose, using a Littleford Mixer or other suitable mixing/grinding device. The chopped floss particles generally range in size from about 1 to about 1,000 microns.

Thereafter, the floss is contacted with about 0.1% to about 10% ethanol or other suitable crystallization enhancer(s). Preferably, ethanol is used in amounts ranging from about 0.5% to about 5.0%. The floss is then treated to remove excess ethanol.

Other useful crystallization enhancers include surfactants, such as Tween 80, which are used at concentration levels of about 0.001% to about 1.00%.

The amount of floss must be such that the fast dissolving properties and pleasant taste associated with its use are realized in the final comestible units.

C. Excipients

A wide variety of excipients conventionally used in comestible units, especially those employed in food and pharmaceutical formulations, can be employed in the invention. They include lubricants, flavors, flavor enhancers (e.g., sweeteners), glidants, fillers, colorants, perfumes and the like.

Lubricants are generally employed in amounts of about 0.05% to about 5.0%, with 0.3% to about 0.8% preferred. Adipic acid, a preferred lubricant, also functions as a flavor enhancer and a salivation enhancer. Another preferred lubricant is sodium stearyl fumarate. Magnesium stearate is a preferred lubricant for the chewable comestible units.

It is preferred that the lubricant particles be milled to #200 mesh size before they are added.

Flavor enhancers are present in amounts of about 1% to about 10%. Typical flavor enhancers include sweeteners, e.g., mannitol, monoammonium glycyrrhizinate (MAGNASWEET 100 of Mafco Worldwide Corp., Camden, NJ) and the like. Mixtures can be used.

Flavors include those that are perceived as orange, lemon, fruit punch, or whipped cream flavors and the like. Mixtures can be used.

Conventional colorants for foods and pharmaceuticals, e.g., FD&C Yellow #6 Lake and others can be used. Mixtures are operable.

Glidants, such as fumed silica (e.g., SYLOID 244FP) or talc, are generally used at

-5-
levels of about 0.05% to about 2.0%.

The following table gives quantities for the ingredients typically used in the invention.

<table>
<thead>
<tr>
<th></th>
<th>Parts by Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Broad</td>
</tr>
<tr>
<td>Range</td>
<td>Range</td>
</tr>
<tr>
<td>A. Microparticles of Active Agents</td>
<td>10-70 30-60</td>
</tr>
<tr>
<td>B. Shearform Floss Particles</td>
<td>30-90 40-70</td>
</tr>
<tr>
<td>C. Excipients</td>
<td>0-20  20-10</td>
</tr>
</tbody>
</table>

THE PROCESS:

The comestible units of the invention are made by mixing the microparticles, the floss, and the excipients, then shaping the mix, e.g., via compression, into comestible units, preferably tablets.

The overall process involves:

1. preparation of the floss particles;
2. mixing microparticles of active agent(s) and excipient(s) therewith; and
3. shaping.

Optionally, the microparticles are coated, using conventional coating techniques prior to step (2).

(1) Preparation of the Floss Particles

The floss particles are prepared using procedures described in U. S. Patent Application Serial No. 08/915,068, filed August 20, 1997.

One highly useful type of floss is made as follows:

A mixture of sucrose, sugar alcohols and TWEEN 80 is prepared and spun into a floss at about 3,500 to 4,000 rpm (50 to 60 Hz) using a suitable spinning device. The floss was chopped in a higher shear mixer/chopper for about 0.5 to 2.0 minutes.

About 0.5% to 5.0% of ethanol, or another crystallization enhancer, is then contacted with the surfaces of the floss particles via spraying or other suitable methods to initiate crystallization. After contacting with the crystallization enhancer, the floss is
treated to remove excess enhancer and is optionally milled or screened. It is then used in making tablets or other comestible units.

(2) Mixing the Bio-Affecting Agent Particles and Excipients with the Floss Particles

In general, any mixing technique can be used which provides a uniform blend of the ingredients while maintaining the structural integrity of the optionally coated microparticle component and the floss component.

The ingredients are typically blended in a Littleford Mixer. They are mixed at speeds of about 60 to about 140 rpm for about 5 to about 15 minutes.

Alternatively, the ingredients may be mixed with a V-blender or other suitable mixing device.

(3) Tableting

The blends are tableted using a standard pharmaceutical tablet press, e.g., a Kilian T-200 tablet press.

Tablets are made to thicknesses of about 3 to about 8 millimeters, with 4.5 to 5.5 millimeters preferred.

The fast dissolving tablets are compressed to hardnesses of about 0.5 to about 6.0 pounds, with about 1.0 to about 3.0 pounds preferred. The chewable tablets are compressed to hardnesses of about 6.0 pounds to 20.0 pounds, with about 10.0 to about 12.0 pounds preferred.

The preparation of tablets is described above. However, the compositions and methods of the invention can also be used to make other comestible units. It is preferred that the units be orally ingestible, e.g., tablets, lozenges, and the like.

EXAMPLES:

The following examples illustrate the invention.

Example 1

A floss containing 78.25% sucrose, 11.00% sorbitol, 10.0% xylitol and 0.75% Tween 80 was prepared as follows:

The mix of ingredients (2 kg) was spun into floss at 3600 rpm (60Hz) using a 5" spinning head in the device described in U. S. Serial No. 08/854,344, filed May 12, 1997.
The floss was chopped in a high shear mixer/chopper for 2 minutes. The chopped floss was treated with 0.5% ethanol and allowed to dry for 90 minutes.

The ethanol-treated floss particles were then used in the following formulation:

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESCOTE 60% Ascorbic Acid</td>
<td>30.77</td>
</tr>
<tr>
<td>Floss</td>
<td>63.00</td>
</tr>
<tr>
<td>Milled Adipic Acid</td>
<td>2.00</td>
</tr>
<tr>
<td>Mannitol</td>
<td>3.00</td>
</tr>
<tr>
<td>Natural Orange Flavor</td>
<td>1.00</td>
</tr>
<tr>
<td>SYLOID FP244</td>
<td>0.10</td>
</tr>
<tr>
<td>FD &amp; C Yellow #6 Lake</td>
<td>0.10</td>
</tr>
<tr>
<td>MAGNASWEET 100</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

The ingredients were mixed in a Littleford Mixer for 10 to 15 minutes. The mix was tableted on a Kilian T-200 press to yield 0.65g tablets of 2 pounds hardness, and 3.06% moisture content, having thicknesses of 4.5mm to 5.5mm.

**Example 2**

Using the floss particles and the general procedure of Example 1, 250mg tablets of ascorbic acid, weighing 1 gram each, were made from the following formulation:

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESCOTE 60% Ascorbic Acid</td>
<td>43.75</td>
</tr>
<tr>
<td>Floss</td>
<td>50.20</td>
</tr>
<tr>
<td>Citric Acid</td>
<td>0.70</td>
</tr>
<tr>
<td>Mannitol</td>
<td>3.00</td>
</tr>
<tr>
<td>Natural Orange Flavor</td>
<td>1.50</td>
</tr>
<tr>
<td>SYLOID FP244</td>
<td>0.25</td>
</tr>
<tr>
<td>FD &amp; C Yellow #6 Lake</td>
<td>0.10</td>
</tr>
<tr>
<td>Sodium stearyl fumarate</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>
Organoleptic tests, used to indicate dissolution, showed that the tablets of Examples 1 and 2 dissolved in the mouth, without chewing or drinking water, in 5 to 10 seconds.

**Example 3**

For a 500mg chewable tablet of ascorbic acid, the floss was prepared and chopped using the general procedure of Example 1. The chopped floss was treated with 4.0% ethanol and allowed to dry for 90 minutes. The 4.0% ethanol-treated floss particles were then used in the following formulation.

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descote 60% Ascorbic Acid</td>
<td>50%</td>
</tr>
<tr>
<td>Floss (4% ethanol-treated)</td>
<td>44.15</td>
</tr>
<tr>
<td>Mannitol</td>
<td>3.00</td>
</tr>
<tr>
<td>Natural Orange Flavor</td>
<td>1.50</td>
</tr>
<tr>
<td>Syloid 244 FP</td>
<td>0.25</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>1.00</td>
</tr>
<tr>
<td>FD&amp;C Yellow No. 6 Aluminum Lake</td>
<td>0.10</td>
</tr>
</tbody>
</table>

The ingredients were mixed in a Littleford Mixer for 10 to 20 minutes. The mix was tableted on a Kilian T-200 press to yield 1.75g tablets of 11 pounds hardness, having a thickness of 6.5 to 7.5 mm.

**Example 4**

A chewable calcium carbonate/vitamin D combination product was made as follows:

<table>
<thead>
<tr>
<th>Floss Formulation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucrose</td>
<td>78.25%</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>11%</td>
</tr>
<tr>
<td>Xylitol</td>
<td>10%</td>
</tr>
<tr>
<td>Polysorbate 80</td>
<td>0.75%</td>
</tr>
</tbody>
</table>

The sucrose, sorbitol, xylitol, and Polysorbate 80 were blended in a Littleford FKM600 mixer for 10 minutes. The blend was then subjected to Shearform processes at
60Hz and 250°C temperature using the 5” Pharma processing head. The floss manufactured was chopped in the Littleford FKM600 mixer with 2% lactose and treated with ethanol (7% of the floss). The floss was dried at 45°C for 150 minutes. The floss was then milled/sieved through a 20mesh screen using a Fitzmill or Apexmill.

Tablet Formulation

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Carbonate Destab SE 95%</td>
<td>47.85%</td>
</tr>
<tr>
<td>Vitamin D₃</td>
<td>0.16%</td>
</tr>
<tr>
<td>Floss</td>
<td>48.48%</td>
</tr>
<tr>
<td>N&amp;A Lemon Flavor</td>
<td>1.00%</td>
</tr>
<tr>
<td>Citric Acid</td>
<td>1.00%</td>
</tr>
<tr>
<td>Syloid 244FP</td>
<td>0.50%</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>1.00%</td>
</tr>
</tbody>
</table>

The calcium carbonate was blended with vitamin D₃ for 15 minutes at speed 1 in a Diosna 600. The milled floss was added and blended further for 10 minutes. The flavors and flow agent were added and blend for additional 7 minutes. The blend was compressed on a rotary tablet press at 85N hardness, 2.75g tablet weight, 19mm concave round or 19mm flat-faced radial edge tooling.

Example 5

Vitamin C EZ Chew 500mg Tablet

The floss was prepared and chopped using the general procedure of Example 1. The chopped floss was treated 7.0% ethanol and allowed to dry for 150 minutes at 45°C. The 7.0% ethanol treated floss was then used in the following formulation.

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coated Ascorbic acid (97.5%)</td>
<td>37.61%</td>
</tr>
<tr>
<td>UniFloss (7% ethanol)</td>
<td>53.54%</td>
</tr>
<tr>
<td>Orange flavor</td>
<td>2.00%</td>
</tr>
<tr>
<td>Mannitol Powder</td>
<td>5.00%</td>
</tr>
<tr>
<td>Acesulfame potassium</td>
<td>0.10%</td>
</tr>
<tr>
<td>Syloid 244 FP</td>
<td>0.50%</td>
</tr>
</tbody>
</table>
Magnesium Stearate 1.00%
Color 0.25%

100%

The ingredients were mixed in a Littleford Mixer for 10-20 minutes. The mix was compressed on a Kilian T-200 press to yield 1.5g tablets at 80N-100N hardness using 16.5 flat faced tooling. Tablet includes 10% excess ascorbic acid of label claim.

Reasonable variations, such as those which would occur to a skilled artisan, can be made herein without departing from the scope of the invention.
WE CLAIM:

1. A comestible unit for orally administering one or more unpleasant tasting bio-affecting agents comprising:
   (a) optionally coated microparticles containing ascorbic acid;
   (b) saccharide-based shearform floss particles; and
   (c) one or more excipients selected from lubricant(s), flavor(s), flavor enhancer(s), glidant(s), filler(s), and colorant(s).

2. The comestible unit of claim 1 wherein (a) contains microparticles of ascorbic acid coated with one or more coatings comprising at least one material selected from: mixtures of mono- and diglycerides; starch; and cellulose derivatives.

3. The comestible unit of claim 2 wherein (b) comprises floss particles made from compositions containing sucrose, sorbitol, xylitol, and polyoxyethylene sorbitan fatty acid esters.

4. The comestible unit of claim 3 containing:
   (a) about 30 to about 50 parts of ascorbic acid particles coated with mono- and diglycerides,
   (b) about 45 to about 65 parts floss particles, and
   (c) about 4 to about 10 parts of a mixture of: adipic acid, mannitol, flavorant, glidant, colorant and sweetener.

5. The comestible unit of claim 4 which is a tablet.

6. A comestible unit made from a composition comprising:
   30.77% glyceride coated ascorbic acid;
   63% of a floss made from a composition containing: 78.25% sucrose,
11.00% sorbitol, 10.0% xylitol and 0.75% polyoxyethylene sorbitan fatty acid ester;
2.0 % milled adipic acid;
3.0 % mannitol;
1.0 % natural orange flavor;
0.1 % fumed silica;
0.10 % FD & C Yellow #6 Lake; and
0.30 % monoammonium glycyrrhizinate

7. A comestible unit made from a composition comprising:
43.75 % glyceride coated ascorbic acid;
50.20% of a floss made from a composition containing:
78.25% sucrose, 11.00% sorbitol, 10.0% xylitol and
0.75% polyoxyethylene sorbitan fatty acid ester;
0.70 % citric acid;
3.00 % mannitol;
1.50 % natural orange flavor;
0.25 % fumed silica;
0.10 % FD & C Yellow #6 Lake; and
0.50 % sodium stearyl fumarate.

8. A comestible unit made from a composition comprising:
50% Descote 60% Ascorbic Acid
44.15% Floss (4% ethanol-treated)
3.0% Mannitol
1.5% Natural Orange Flavor
0.25% Syloid 244 FP
1.0% Magnesium Stearate
0.10% FD&C Yellow No. 6 Aluminum Lake

wherein the floss component contains 78.25% sucrose, 11.00% sorbitol, 10.0% xylitol
9. A comestible unit made from a composition comprising:

- Calcium Carbonate Destab SE 95% 47.85%
- Vitamin D₃ 0.16%
- Floss 48.48%
- N&A Lemon Flavor 1.00%
- Citric Acid 1.00%
- Syloid 244FP 0.50%
- Magnesium Stearate 1.00%

wherein the floss component contains 78.25% sucrose, 11% sorbitol, 10% xylitol, and 0.75% polyoxyethylene sorbitan fatty acid ester.

10. A comestible unit made from a composition comprising:

- Coated Ascorbic acid (97.5%) 38.61%
- Floss (7% ethanol) 53.24%
- Orange flavor 2.00%
- Mannitol Powder 5.00%
- Acesulfame potassium 0.10%
- Syloid 244 FP 0.50%
- Magnesium Stearate 1.00%
- Color 0.25%

wherein the floss component contains 28.25% sucrose, 11% sorbitol, 10% xylitol and 0.75% polyoxyethylene sorbitan fatty acid ester.
A. CLASSIFICATION OF SUBJECT MATTER

IPC 7  A61K9/20

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7  A61K

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents:

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

E* earlier document but published on or after the international filing date

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

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

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

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

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

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

F* document member of the same patent family

Date of the actual completion of the international search

26 November 1999

Date of mailing of the international search report

03/12/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5618 Patentlaan 2 NL - 2280 HV Rijswijk

Tel. (+31-70) 340-2040, Tx. 31 651 epi nl, Fax (+31-70) 340-3016

Authorized officer

Benz, K

Form PCT/ISA/210 (second sheet) (July 1992)
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AU 8698398 A</td>
<td>08-03-1999</td>
</tr>
</tbody>
</table>