

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 09-134515- -00005-0000

Fecha: 2011-07-15 15:53:52 Dep. 2020 DIR.NUEVASCR
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Act. 329 CTOINFORMACION Folios: 27

SEÑOR

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

E.

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REF: EXPEDIENTE 09-134-515

TÍTULO SOLICITADO: CAPSULAS QUE COMPRENDEN UNO O MÁS
POLIMEROS Y USOS DE LAS MISMAS.PUBLICACIÓN: Gaceta 624 de 20/01/2011, número de publicación
1093.

SOLICITANTE: COLGATE - PALMOLIVE COMPANY.

APODERADO: JUAN PABLO CADENA SARMIENTO.

TRÁMITE: SUSTENTACION DE OPOSICIÓN

JOSÉ LUIS REYES VILLAMIZAR, mayor de edad, identificado como aparece al pie de mi firma, abogado en ejercicio, titular de la tarjeta profesional número 44655 del Consejo Superior de la Judicatura, obrando en calidad de apoderado de la sociedad **TECNOQUÍMICAS S.A.**, dentro del trámite de la referencia, en ejercicio de lo dispuesto por el artículo 42 inciso 2º de la Decisión 486 de 2000, por medio del presente escrito, procedo a sustentar y complementar la oposición presentada el 27 de Septiembre de 2007, en los siguientes términos:

I. RATIFICACIÓN

En primer lugar, cualquier persona medianamente versada en la formulación de productos farmacéuticos debe reconocer que el parámetro de solubilidad de Hildebrand (δ) proporciona una estimación numérica del grado de interacción entre los materiales, y puede ser un buen indicador de la solubilidad, en particular para las materias no polares como muchos polímeros, en donde los compuestos con los mismos valores de δ es probable que sean miscibles. Así mismo dicha persona medianamente versada en la formulación de productos farmacéuticos debe

reconocer que su principal utilidad es proporcionar predicciones simples de equilibrio de fases sobre la base de un único parámetro que se obtiene fácilmente en la mayoría de los compuestos y que además se ha encontrado un uso particular, en la predicción de la solubilidad y la hinchabilidad de los polímeros en diferentes disolventes¹.

Caracterizar los polímeros tal y como se hace en la solicitud colombiana en trámite, específicamente en sus reivindicaciones 5, 6, 14 y 15, no puede sustentar nivel inventivo alguno, puesto que dichos parámetros de solubilidad hacen parte de los factores y/o características que cualquier persona medianamente versada en la materia debe tener en cuenta durante los ensayos de preformulación y formulación en el desarrollo de formas farmacéuticas de este tipo.

La patente americana US 2007/0032396 publicada el 08 de febrero de 2007; la publicación internacional WO 99/059535 publicada el 25 de Noviembre de 1999; la patente Europea EP 0180287 publicada el 17 de Mayo de 1986; la publicación WO 2007/012981 publicada el 01 de Febrero de 2007 y la publicación internacional WO 98/27151 publicada el 25 de Junio de 1998 revelan la versatilidad de la fabricación de cápsulas del mismo tipo que las reivindicadas en la solicitud en trámite, específicamente se revelan una gran variedad de polímeros combinados en diversas proporciones para la elaboración tanto del núcleo como de la película que rodea todas y cada una de las fórmulas de cápsulas descritas en cada anterioridad. Es relevante también indicar que las formulaciones descritas en las anterioridades también se describen para aplicación bucal localizada.

Las técnicas de formulación y el conjunto de compuestos que se pueden utilizar para desarrollar productos farmacéuticos viables en cualquiera de sus formas, son elementos que son claramente conocidos para una persona medianamente versada en la formulación de productos farmacéuticos, así que de ninguna manera puede ser inventivo escoger uno u otro excipiente para conseguir las características de eficacia, eficiencia, seguridad y estabilidad indispensables para todo medicamento, más aun cuando en el estado de la técnica se encuentra suficiente información técnica que puede servir como una clara guía en la

¹ http://en.wikipedia.org/wiki/Hildebrand_solubility_parameter

elaboración del mismo tipo de formulación como la reivindicada en la solicitud colombiana en cuestión.

II. COMPLEMENTO DE INFORMACION.

En complemento a los argumentos dados en su momento en el respectivo escrito de oposición, la patente europea EP 0332175 publicada el 13 de septiembre de 1989 revela:

Accordingly, the object of the present invention is to eliminate the above-mentioned disadvantages of the prior art and to provide a method of producing a microcapsule capable of providing a high degree of protection of a core substance and of completely blocking the permeability of a core substance in an aqueous solution, especially even in an aqueous solution containing a surfactant.

Other objects and advantages of the present invention will be apparent from the following description.

In accordance with the present invention, there is provided a method of producing microcapsules comprising the steps of:

mixing (i) an aqueous dispersion containing a capsule having a wall membrane containing polyvinyl alcohol, and an aqueous solution containing 8% to 50% by weight of an electrolyte or electrolytes, and (ii) an aldehyde or aldehydes having a solubility in water at 20 °C of not more than 10%; and allowing the mixture to react under an acidic condition.

(...)

Example 1

As a core material, 7 g of l-menthol was dissolved in 20 g of 2-octyl dodecanol. Then 4.0 g of polyvinyl alcohol (average degree of polymerization 550, degree of saponification 88 mole%) and 0.3 g of pectin were dissolved in 95.7 g water, and 27 g of the core material was dispersed to adjust an average particle size thereof to about 500 μm .

To the dispersion obtained above, 100 g of 25% aqueous sodium chloride solution was dropwise added while stirring, at a temperature of 30 °C, and microcapsules comprising the core material coated with a concentrated aqueous polyvinyl alcohol solution were obtained.

Thereafter, a mixture of 10 g of a 5% aqueous pectin solution and 60 g of a 25% aqueous sodium sulfate solution was added, followed by adding 30 g of sodium sulfate. As a result, 327 g of the following aqueous dispersion containing capsules having a wall membrane of polyvinyl alcohol dispersed therein was obtained.

Pectin	0.27%
Sodium chloride	8.40%
Sodium sulfate	15.20%
Water	Balance

To the aqueous dispersion of the capsules obtained above, 10% acetic acid was added to adjust the pH to 2.5, and then 10 g of vanillin was added and the mixture was stirred at 40 °C for 20 hours. Thereafter, the pH was changed to 1.5 and the reaction was carried out for 15 hours.

After the reaction, the capsules were separated by a 42 mesh sieve, followed by washing with water, and about 30 g of the capsules was obtained.

(...)

1. A method of producing microcapsules comprising the steps of:
 mixing (i) an aqueous dispersion containing capsules having a wall membrane containing polyvinyl alcohol and an aqueous solution containing 8% to 50% by weight of an electrolyte or electrolytes and (ii) an aldehyde or aldehydes having a solubility in water at 20 ° C of not more than 10%; and
 allowing the mixture to react under an acidic condition.

Se puede evidenciar claramente que esta anterioridad comprende la elaboración de una membrana impermeable o con una permeabilidad restringida que involucra polímeros reticulados (crosslinked) como lo son el alcohol polivinílico y la pectina para obtener una película hermética que restringe la permeabilidad en las cápsulas formadas por dicha película.

Por su parte la patente Española ES 2148114 publicada el 01 de Octubre 2000 revela:

1. Cápsula botánica de revestimiento duro, que comprende:

76,15-81,04 % de agua purificada;

18-22 % de celulosa botánica (HPMC) con una viscosidad de 4-8 cps a una temperatura de 20°C con una concentración del 2 % como materia prima;

0,8-1,2 % de goma Gellan, que es un estabilizador de la viscosidad;

0,05-01, % de citrato de sodio;

0,01-0,05 % de glicerina, que es un plastificante; y

0,1-0,5 % de éster de ácido graso de sacarosa, que es un emulsionante.

En donde también se obtienen cápsulas impermeables a partir de la combinación de polímeros tales como la HPMC y la goma gelán.

Finalmente la patente europea EP 0622408 publicada el 02 de Noviembre de 1994 revela:

3. A film-forming polymeric composition comprising from 1 to 10 weight percent of a gum-blend composition which comprises a gellan gum:(carrageenan gum/mannan gum) wherein the gellan gum concentration ranges from about 0.1 to 50 weight percent and the ratio of carrageenan/mannan gum ranges from 3:1 to 1:3 and a gelling salt and a sequestrant.

(...)

En donde también es evidente la combinación de polímero tales como la goma galán, el k-carragenano y manano (mannan gum) para obtener películas útiles en la fabricación de cápsulas impermeables.

Con lo anterior se sustenta nuevamente la carencia de nivel inventivo de la solicitud colombiana en trámite, que reivindica la combinación de polímeros reticulados (crosslinked) para la elaboración de cápsulas.

Por todo lo anterior, ruego se analicen los argumentos expuestos con el rigor y detenimiento habituales y que en consecuencia se decrete, además de la negación de la solicitud en comento, el archivo del expediente que la contiene.

II. ANEXOS

- La patente europea EP 0332175 publicada el 13 de septiembre de 1989.
- Capítulos reivindicatorios de la patente Española ES 2148114 publicada el 01 de Octubre 2000 y de la patente europea EP 0622408 publicada el 02 de Noviembre de 1994.

Señor Superintendente,



JOSE LUIS REYES VILLAMIZAR
C.C. 79.152.473 de Usaquén
T.P. 44655 del C. S de la J.

⑫

EUROPEAN PATENT APPLICATION

⑰ Application number: 89104123.8

⑤① Int. Cl. 4: B01J 13/02

⑳ Date of filing: 08.03.89

③① Priority: 10.03.88 JP 57894/88

④③ Date of publication of application:
13.09.89 Bulletin 89/37

⑧④ Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

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⑨④ Method of producing microcapsule.

⑨⑤ A method of producing microcapsules comprising the steps of:
mixing (i) an aqueous dispersion containing a capsule having a wall membrane containing polyvinyl alcohol and
an aqueous solution containing 8% to 50% by weight of an electrolyte or electrolytes and (ii) an aldehyde or
aldehydes having a solubility in water at 20 °C of not more than 10%; and
allowing the mixture to react under an acidic condition.

EP 0 332 175 A2

METHOD OF PRODUCING MICROCAPSULE

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a method of producing a microcapsule capable of protecting a core substance by completely blocking a permeation of foreign materials, and having a high safety factor with respect to a human body.

2. Description of the Related Art

Microcapsules have excellent functions in that liquids and gases can be treated as a solid; substances which react with each other can be isolated; and the bleeding of core substances can be controlled in accordance with changes in an ambient environment.

The following techniques for producing dense capsules having an excellent core substance retentionability have been reported.

(1) Japanese Examined Patent Publication (Kokoku) No. 46-38244 discloses a method of treating a capsule wall membrane such as gelatin with a cross-linking agent such as formaldehyde and glutaraldehyde, followed by drying and heating at a temperature of 120°C to 150°C.

(2) GB Patent No. 1190721 discloses a method of adding a polyhydroxy aromatic substance such as resorcinol, hydroquinone, and catechol to a dispersion containing a capsule having a wall membrane of a hydrophilic polymer, such as polyvinyl alcohol, gelatin, and methyl cellulose, which membrane is swollen with a solvent to effect a reaction of the polyhydroxy aromatic substance with the wall membrane, followed by reacting the polyhydroxy aromatic substance with an aldehyde such as formaldehyde, glyoxal, furfural and glutaraldehyde.

(3) Japanese Unexamined Patent Publication (Kokai) No. 56-100630 discloses a method of treating an aqueous dispersion containing a capsule having a wall membrane of polyvinyl alcohol with, for example, acids and dialdehydes such as glyoxal and glutaraldehyde; or acids and urea and/or melamine and formaldehyde; or alkali and divinylsulfone, methylvinyl ketone; or alkali and an epichlorohydrin compound.

(4) Japanese Unexamined Patent Publication (Kokai) No. 56-100631 discloses a method of treating an aqueous dispersion containing a capsule having a wall membrane of polyvinyl alcohol with an organic titanium compound such as diisopropoxy titanium bisacetyl acetonate and aminoalcohol titanium chelate.

(5) U.S. Patent No. 3630955 discloses a method of hydrophobically treating an aqueous dispersion containing a capsule having a wall membrane of a hydrophilic polymer substance, by a free radical polymerizing of a polymerizable unsaturated monomer having a nitrile group and the wall membrane substance in the presence of, for example, iron, cobalt, nickel, copper, chromium, uranyl, and vanadium.

The above-mentioned methods, however, are used to make a water-soluble polymer substantially water-insoluble, to obtain a wall membrane of a capsule by, for example, a crosslinking or chelating reaction with an ion, and thus a large number of hydrophilic groups is present in the polymer constituting a wall membrane of a capsule. For this reason, although a wall membrane of a capsule exhibits a high impermeability in a system having a low water content, the wall membrane absorbs water and is swollen in an aqueous solution system and, therefore, a core substance having even a slight water-solubility will gradually permeate through the wall membrane. Especially, when a surfactant having a strong permeability is present, the permeability through the wall membrane is remarkably increased and even a water-insoluble core substance is disadvantageously ejected from the capsule. Furthermore, a treatment agent having a strong toxicity is sometimes used as a hardening agent for the impermeable treatment.

On the other hand, when a microcapsule having a wall membrane of polyvinyl alcohol is produced by a simple coacervation method, a uniform coating cannot be obtained and non-coated portions are generated, depending upon the core substance, and an aggregation of the capsules occurs whereby acceptable capsules cannot be obtained. These phenomena occur most often, when hydrophobic substances having a polar group, for example, alcohols such as hexanol linalool, benzyl alcohol, and eugenol; and aldehydes such as trans-2-hexenal, benzaldehyde, and anise aldehyde, are used.

SUMMARY OF THE INVENTION

Accordingly, the object of the present invention is to eliminate the above-mentioned disadvantages of the prior art and to provide a method of producing a microcapsule capable of providing a high degree of protection of a core substance and of completely blocking the permeability of a core substance in an aqueous solution, especially even in an aqueous solution containing a surfactant.

Other objects and advantages of the present invention will be apparent from the following description.

In accordance with the present invention, there is provided a method of producing microcapsules comprising the steps of:

- 10 mixing (i) an aqueous dispersion containing a capsule having a wall membrane containing polyvinyl alcohol, and an aqueous solution containing 8% to 50% by weight of an electrolyte or electrolytes, and (ii) an aldehyde or aldehydes having a solubility in water at 20°C of not more than 10%; and
- allowing the mixture to react under an acidic condition.

15

DESCRIPTION OF THE PREFERRED EMBODIMENTS

As a method of producing a microcapsule having a wall membrane containing polyvinyl alcohol, a salt coacervation method (U.S. Patent Nos. 3574133, 3565818, and 4777089 and Japanese Unexamined Patent Publication No. 62-7440), a phase separation method utilizing a cloud point (U.S. Patent No. 4269729), a spray drying method, and a hardening-in-liquid method can be used. Of these methods, a salt coacervation method (a simple coacervation method) is preferable; in particular, a method in which a substantially water insoluble core substance is dispersed in an aqueous solution containing polyvinyl alcohol, as a wall membrane forming substance, while an electrolyte is added thereto. Furthermore, preferably the pectin is added simultaneously with or after the addition of the electrolyte. The pectin can be added in the form of a powder, but preferably, is added as an aqueous solution. Optionally, the pectin is added by dissolving it in an aqueous electrolyte solution. More preferably, the pectin is previously dissolved at a concentration of 0.05% to 0.5% by weight in water and, after the core substance is dispersed in water, the aqueous pectin solution is added thereto simultaneously with the electrolyte or after the addition of the electrolyte. When a core substance is apt to cause aggregation, preferably the pectin is added simultaneously with the addition, of the electrolyte. If a necessary amount of the pectin is added before the addition of the electrolyte, the wall membrane of a microcapsule will be very thin or the wall membrane will not be formed. Preferably, the pectin is added in an amount of 0.1% to 1.0% by weight, based on the amount of water.

When the above-mentioned method is adopted, an acceptable microcapsule can be produced while preventing the formation of a weak membrane or an aggregation of the microcapsules, even when the above-mentioned hydrophobic core substances having a polar group are used.

The polyvinyl alcohol usable in the present invention preferably contains at least 50% by weight of a vinyl alcohol component in the polymer. In addition to the polymer (homopolymer in which all the polymers consist of vinyl alcohol units, polymers with 50% by weight or more of vinyl alcohol component containing other components such as vinyl acetate, vinyl propionate, vinyl butyrate, etc., and anionically modified products thereof or cationically modified products thereof are also included in the polyvinyl alcohol as mentioned in the present invention.

Polyvinyl alcohols are generally available as hydrolyzates of polyvinyl acetates, preferably having a 70 to 100 mole% hydrolysis ratio. Also, two or more polyvinyl alcohols with different hydrolysis ratios may be used as a mixture. The concentration of the polyvinyl alcohol in an aqueous solution is preferably 0.5 to 15% by weight, more preferably 1 to 10% by weight.

When water-soluble polymers other than polyvinyl alcohol, for example, proteins such as gelatin and casein; polysaccharides such as carboxymethyl cellulose, methyl cellulose, gum arabic, and alginic acid; synthetic polymers such as polyacrylic acid and ethylene-maleic anhydride copolymer, are used, the desired impermeable wall membrane cannot be obtained even when the aldehyde treatment according to the present invention is carried out.

Any core substance of a microcapsule which is substantially water-insoluble can be utilized as the core substance of the present invention. Examples of such substances are perfumes or flavors, animal and vegetable oils and fats, hydrocarbons, halogenated hydrocarbons, alcohols having 5 or more carbon atoms, aldehydes, esters, ethers, fatty acids, silicone oils, vitamins A, D, E, F, K, U and derivatives thereof, pharmacologically active substances such as galenicals and drugs, metal powders, metal oxides, adhesives, catalysts, coloring agents, and plastics.

Pectin is naturally widely present as a cell-constituting component of a plant body such as fruit and

vegetables, and is particularly contained in a large amount in the rind of citrus fruit and apples. Thus, pectin is industrially advantageously obtained from the rind of such citrus fruit and apples. Furthermore, quince seed gum is a pectin contained in the flesh of plants represented by *Cydonia oblonga* belonging to a family of rose, can be used. Especially, the use of lemon pectin and apple pectin is preferable.

5 According to the present invention, an aqueous dispersion containing a microcapsule having a polyvinyl alcohol as a wall substance, and an aqueous solution containing 8% to 50% by weight of an electrolyte, is prepared.

In the present invention, any electrolyte capable of causing a phase separation of the polyvinyl alcohol in an acidic aqueous solution can be utilized. Any conventional inorganic and organic electrolytes may be
10 used alone or in any mixture thereof.

The inorganic salts include acids, alkalis and the salts thereof, for example, water-soluble metal salts and ammonium salts of inorganic acids such as sulfuric acid, sulfurous acid, hydrochloric acid, phosphoric acid, metaphosphoric acid, boric acid, and nitric acid.

The organic salts include, for example, water-soluble metal salts and ammonium salts of organic acids.

15 Preferably, electrolytes having a high ionization degree and a high electric charge are used. More preferably, sulfates such as sodium sulfate, potassium sulfate, magnesium sulfate, aluminum sulfate, ammonium sulfate, and alum; chlorides such as sodium chloride, potassium chloride, calcium chloride, and ammonium chloride; and phosphates such as sodium hydrogen phosphate, potassium hydrogen phosphate, and ammonium phosphates, are used.

20 Preferably, the concentration of the electrolyte is 8% to 50% by weight, more preferably 10% to 40% by weight. When the amount is less than 8% by weight, the capsule membrane is dissolved or deformed in water and acceptable capsules cannot be obtained. Conversely, when the amount is more than 50% by weight, the electrolyte is precipitated and thus wastefully used. The term "concentration of the electrolyte" as used in the present invention denotes a concentration of the electrolyte in the aqueous dispersion.

25 Namely, the concentration of the electrolyte = $[\text{electrolyte}/(\text{water} + \text{electrolyte})] \times 100$.

According to the present invention, the micro-capsule can be obtained by reacting the above-mentioned aqueous dispersion containing capsules with an aldehyde having a solubility in water at 20°C of not more than 10%.

Any aldehyde having a solubility in water at 20°C of 10% or less, preferably 0.001% to 7%, can be
30 used. These aldehydes are specifically reacted with the polyvinyl alcohol, whereby the polyvinyl alcohol is hydrophobically treated without crosslinking.

Examples of such aldehydes are isobutylaldehyde, hexylaldehyde, heptylaldehyde, citral, benzaldehyde, salicylaldehyde, m- and p-hydroxybenzaldehyde, o-, m-, and p-methoxybenzaldehyde, o-, m-, and p-ethoxybenzaldehyde, veratraldehyde, vanillin, phenylpropyl aldehyde, phenylacetaldehyde, cinnamic aldehyde, and o-, m-, and p-methylbenzaldehyde.
35

The above-mentioned aldehydes have a low reactivity to hydrophilic polymers, other than the polyvinyl alcohol, for example, gelatin, carboxymethyl cellulose, gum arabic, alginic acid, and the polyacrylic acid content is low or is not substantially reacted therewith. Even if the reaction occurs, a capsule membrane exhibiting a desired impermeability cannot be obtained.

40 Aldehydes having a solubility in water at 20°C of more than 10%, for example, formaldehyde, glyoxal, and glutaraldehyde, have a high reactivity to polyvinyl alcohol, and although the polyvinyl alcohol is crosslinked to be insolubilized in water, the polyvinyl alcohol molecule itself is not insolubilized in water and a number of hydrophilic groups (OH groups) remains in the molecule. As a result, the resultant capsule is swollen in the aqueous solution and, in particular, a high impermeability against the core substance in the
45 presence of a surfactant cannot be realized. Furthermore, aldehydes having a solubility in water at 20°C of more than 10% are extremely toxic to the human body.

Preferably, the aldehydes are added in an amount of 0.3 to 10 times, more preferably 0.3 to 5 times, of the weight of the polyvinyl alcohol.

The hydrophobic treatment with the aldehyde is carried out under an acidic condition, preferably at a
50 pH of 0.5 to 4.5, more preferably a pH of 1.0 to 3.5. When the pH is too low, the desired hydrophobic wall membrane cannot be obtained, and conversely, when the acidity is too weak, the reaction does not proceed as required. Further, if the pH is on the alkaline side, an unwanted reaction occurs and the formation of the desired impermeable wall membrane becomes difficult.

Although there are no critical limitations to the reaction condition, the hydrophobic treatment is
55 preferably carried out at a reaction temperature of 10°C to 80°C, more preferably 20°C to 60°C. When the reaction temperature is too low, the reaction does not substantially occur. Contrary to this, when the reaction temperature is too high, the capsule membrane is softened and deformed and the desired impermeable wall membrane is not obtained. Although the preferable reaction time depends upon the kind

of aldehyde, the suitable reaction time is 1 to 100 hours, more preferably 3 to 60 hours.

The aldehydes having a solubility in water at 20°C of 10% or less are specifically reacted with polyvinyl alcohol, and thus the polyvinyl alcohol is made hydrophobic without crosslinking. The resultant capsule membrane does not swell in water, and therefore, the desired high impermeability of the core substance through the membrane can be obtained. Furthermore, the degree of hydrophobicity of the capsule membrane and the degree of hydrophilicity (or compatibility) of the membrane and the hydrophobic core substance can be adjusted by varying the kind of aldehyde and the reactivity of the polyvinyl alcohol. Accordingly, the core substance is not permeated, and further, a specific substance can be selectively allowed to permeate through the membrane.

According to the present invention, the micro-capsules with a wall membrane having an improved impermeability in an aqueous solution can be prepared by adding a specific aldehyde to an aqueous dispersion containing a microcapsule having a wall membrane of polyvinyl alcohol, followed by reacting the mixture. The resultant capsule completely blocks permeation by the core substance and has a high safety factor with respect to the human body.

The microcapsules obtained by the present invention can be suitably and widely utilized for aqueous products including a surfactant having a strong permeability, for example, a shampoo, rinse, liquid heavy detergent, kitchen detergent, toilet detergent, bathtub detergent, toothpaste, mouth wash agent, and soap, and further, cosmetics such as a cream, lipstick, and lotion, pharmaceutical preparations such as a blennorrhoea agent and blemish agent, adhesives, catalysts; and the like.

EXAMPLES

The present invention will now be further illustrated by, but is by no means limited to, the following Examples, wherein "%" represents "% by weight" unless otherwise specified.

Example 1

As a core material, 7 g of l-menthol was dissolved in 20 g of 2-octyl dodecanol. Then 4.0 g of polyvinyl alcohol (average degree of polymerization 550, degree of saponification 88 mole%) and 0.3 g of pectin were dissolved in 95.7 g water, and 27 g of the core material was dispersed to adjust an average particle size thereof to about 500 μm .

To the dispersion obtained above, 100 g of 25% aqueous sodium chloride solution was dropwise added while stirring, at a temperature of 30°C, and microcapsules comprising the core material coated with a concentrated aqueous polyvinyl alcohol solution were obtained.

Thereafter, a mixture of 10 g of a 5% aqueous pectin solution and 60 g of a 25% aqueous sodium sulfate solution was added, followed by adding 30 g of sodium sulfate. As a result, 327 g of the following aqueous dispersion containing capsules having a wall membrane of polyvinyl alcohol dispersed therein was obtained.

Pectin	0.27%
Sodium chloride	8.40%
Sodium sulfate	15.20%
Water	Balance

To the aqueous dispersion of the capsules obtained above, 10% acetic acid was added to adjust the pH to 2.5, and then 10 g of vanillin was added and the mixture was stirred at 40°C for 20 hours. Thereafter, the pH was changed to 1.5 and the reaction was carried out for 15 hours.

After the reaction, the capsules were separated by a 42 mesh sieve, followed by washing with water, and about 30 g of the capsules was obtained.

Comparative Example 1

To the aqueous capsule dispersion, 10% acetic acid and an aqueous sodium hydroxide solution were added to adjust the pH to 3.5, and thereafter, 10 g of a 50% aqueous glutaraldehyde was added and a

curing reaction was carried out at 10 ° C for 20 hours. After the reaction, the capsules were separated by a 42 mesh sieve, followed by washing with a 20% aqueous sodium sulfate solution, and about 30 g of the capsules was obtained.

5

Comparative Example 2

As a core material, 7 g of l-menthol was dissolved in 20 g of 2-octyldodecanol. Then 27 g of the core material was dissolved in 56 g of a 10% aqueous solution of gelatin (isoelectric point 8.8, jelly strength 260 bloom), followed by adding 28 g of a 20% aqueous gum arabic solution to adjust the average particle size thereof to about 500 μ m.

Thereafter, 5% acetic acid was dropwise added at 40 ° C to adjust the pH to 4.1, the dispersion was allowed to cool to 15 ° C, and capsules comprising the core material coated with the concentrated aqueous solution of gelatin-gum arabic were obtained.

A 4 g amount of 50% glutaraldehyde was then added, followed by effecting a curing reaction at 10 ° C for 20 hours, and after the curing reaction, the resultant capsules were separated by a 42 mesh sieve followed by washing with water, and about 30 g of the capsules was obtained.

Evaluation Example 1

A 10 g amount each of the capsules obtained in Example 1 and Comparative Examples 1 and 2 was independently dispersed in 1000 g of a 5% aqueous sodium lauryl sulfate solution and stored at 50 ° C in a sealed glass bottle.

The aqueous dispersion was sampled at predetermined intervals, and after filtering through a filter paper, the concentration of l-menthol in the aqueous solution was determined by gas chromatography, and the rate of elution of the l-menthol from the capsule was calculated.

The results are shown in Table 1.

30

Table 1

35

No.	Rate of elution (%) of l-menthol	
	14 days	30 days
Example 1	1%	2%
Comparative Example 1	55%	85%
Comparative Example 2	60%	90%

40

As clear from the results shown in Table 1, the rate of elution of l-menthol from the capsule of Example 1 was remarkably low and very little permeation of the substances through the wall membrane of the capsule occurred.

45

Comparative Example 3

In Comparative Example 2, 5 g of vanillin and 20 g of sodium chloride were added, instead of 50% glutaraldehyde, and after adjusting the pH to 4.0 with 30% sulfuric acid, the mixture was warmed to 40 ° C followed by stirring for 30 hours.

When the resultant capsule was added to water at 80 ° C, the wall membrane of the capsule was dissolved.

Comparative Example 4

The procedures of Comparative Example 3 were repeated, except that the pH was adjusted to 2.5.

When the resultant capsule was added to water at 80 ° C, the wall membrane of the capsule was

12

dissolved.

Comparative Example 5

5 In Comparative Example 4, o-methoxybenzaldehyde was used instead of vanillin, and when the resultant capsule was added to water at 80 °C, the wall membrane of the capsule was dissolved.
As clearly shown in Comparative Examples 3 to 5, the desired water-resistant wall membrane cannot be
10 obtained in capsules having a wall membrane composed mainly of gelatin, even when the capsule is treated with aldehydes having a solubility in water at 20 °C of 10% or less.

Example 2

15 To the aqueous dispersion of Example 1, 30% sulfuric acid was added to adjust the pH to 1.5, the 5 g of o-methoxybenzaldehyde was added and a curing reaction was carried out at 40 °C for 15 hours.
After the reaction, the capsules were separated by a 42 mesh sieve followed by washing with a 20% aqueous sodium sulfate solution, and about 30 g of the capsules was obtained.

Evaluation Example 2

20 The capsules of Example 2 and Comparative Examples 1 and 2 were independently formulated at a concentration of 1% in the following toothpaste compositions. The resultant toothpaste compositions were
25 filled in laminate tubes and stored at 40 °C.

Composition of Toothpaste	
Ingredient	%
Silica anhydride	15.0
Sodium carboxymethyl cellulose	1.0
Propylene glycol	2.0
Sorbitol	45.0
Sodium lauryl sulfate	1.0
Saccharin sodium	0.1
Flavor	0.7
Water	Balance

30 A 2 g amount of the toothpaste was sampled at predetermined intervals and the capsules separated by a 42 mesh sieve after diluting five-fold with water. A 5 g amount of the dispersion permeated through the sieve was taken, and after adding 2 g of n-amyl alcohol thereto, the mixture was shaken and l-menthol eluated into the toothpaste was extracted. The concentration of the l-menthol was determined by gas chromatography and the ratio of l-menthol eluated into the toothpaste from the capsule was calculated.
35 The results are shown in Table 2.

Table 2

No.	Rate of eluation (%) of l-menthol	
	14 days	30 days
Example 2	1%	2%
Comparative Example 1	60%	90%
Comparative Example 2	70%	95%

50 As clear from the results shown in Table 2, the permeability of the wall membrane of the capsules of

Example 2 is remarkably lower than those of the Comparative Examples 2 and 3.

Example 3

As a core material, 2 g of Vitamin C stearate was dispersed in 100 g of linolenic acid. Then 17.5 g of polyvinyl alcohol (average degree of polymerization 1000, degree of saponification 88 mole%) and 1.3 g of pectin were dissolved in 400 g of water, and 100 g of the core material was dispersed to adjust the average particle size thereof to about 100 μm .

To the dispersion obtained above, 400 g of a 25% aqueous sodium sulfate solution was dropwise added, followed by adding 40 g of a 5% aqueous pectin solution, 250 g of a 25% aqueous sodium sulfate solution, and 60 g of a 5% aqueous pectin solution.

Accordingly, an aqueous dispersion containing capsules having a strong wall membrane of polyvinyl alcohol was obtained without agglomeration of the capsules.

To the above-prepared aqueous dispersion containing capsules was added 10% hydrochloric acid, to adjust the pH to 2.0, and thereafter, 30 g of heptylaldehyde was added followed by stirring at 50 °C for 20 hours. The capsules were then separated and washed with water, and then stored in a 15% aqueous sodium sulfate solution. The wall membrane of the capsules thus obtained possessed a high water resistance such that the wall membrane was not dissolved in water at 100 °C.

The capsules obtained above were suitable for use in the formulation of a skin cream as a vitamin C providing agent and emollient agent.

Example 4

As a core material, 4 g of benzyl alcohol, 4 g of linalool, 5 g of eugenol, and 15 g of isostearyl alcohol were mixed. Then 4 g of polyvinyl alcohol (average degree of polymerization 500, degree of saponification 87 - 89 mole%) and 0.3 g of pectin were dissolved in water to a total amount of 100 g, and then 28 g of the above-prepared core material was dispersed therein to adjust an average particle size thereof to about 500 μm .

To the dispersion obtained above, a mixture of 51 g of a 25% aqueous sodium chloride solution and 6.5 g of a 5% aqueous pectin solution was dropwise added while stirring, at a temperature at 30 °C. Then a mixture of 46 g of a 25% aqueous sodium chloride solution and 12.5 g of a 5% aqueous pectin solution was dropwise added, followed by adding 60 g of a 25% aqueous sodium sulfate solution.

Accordingly, acceptable capsules were obtained without agglomeration of the capsules.

The pH of the aqueous dispersion of the capsules was adjusted to 3.5 with 10% sodium hydroxide, and then 7 g of phenylpropyl aldehyde was added thereto, followed by stirring at 40 °C for 15 hours. Thereafter, the pH of the aqueous dispersion was adjusted to 1.5 with 10% sulfuric acid, followed by stirring at 40 °C for 20 hours.

The capsules obtained above were centrifugally separated and washed with water, and it was found that the wall membrane of the resultant capsule was stable and was neither swollen nor dissolved in water at 100 °C. The resultant capsules were suitable for use in the formulation of toothpaste.

Example 5

In Example 4, p-methylbenzaldehyde was used instead of the phenylpropyl aldehyde. The wall membrane of the resultant capsules was stable and was neither swollen nor dissolved in water at 100 °C.

Example 6

In Example 4, cinnamic aldehyde was used instead of the phenylpropyl aldehyde. The wall membrane of the resultant capsules was stable and was neither swollen nor dissolved in water at 100 °C.

Example 7

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As a core material, 100 g of methylphenyl silicone, 100 g of liquid paraffin, and 50 g of squalane were mixed.

Then a 5% aqueous solution of polyvinyl alcohol (degree of polymerization 1500, degree of saponification 98.5%) was charged to an outer cylinder of a concentric double orifice (diameter of inner cylinder 0.5 mm, diameter of outer cylinder 2 mm) and was dropwise added to a 1% aqueous borax solution, and a capsule having a wall membrane of polyvinyl alcohol was prepared. After drying, capsules having a particle size of 3 to 5 mm was obtained.

A 30 g amount of the capsules obtained above was dispersed in 200 g of a 25% aqueous sodium sulfate solution, and then 10 g of 5% pectin was added thereto followed by adjusting the pH with 20% sulfuric acid to 1.5. Thereafter, 5 g of o-methoxybenzaldehyde was added, and after stirring at 40°C for 20 hours, the resultant capsules were separated and washed with water. The resultant capsules were stable and were neither swollen nor dissolved at 100°C in water. The capsules were suitable for use in the formulation of a hair rinse.

Evaluation Example 3

The capsules obtained in Examples 3 to 7 were evaluated in the same manner as in Evaluation Example 1.

The results are shown in Table 3.

Table 3

Example No.	Analyzed core component	Rate of elution (%)	
		14 days	30 days
3	linolenic acid	0.5	1
4	benzyl alcohol	1.5	3
5	"	1	2.5
6	"	2	3.5
7	squalane	0	0.5

Claims

1. A method of producing microcapsules comprising the steps of:
mixing (i) an aqueous dispersion containing capsules having a wall membrane containing polyvinyl alcohol and an aqueous solution containing 8% to 50% by weight of an electrolyte or electrolytes and (ii) an aldehyde or aldehydes having a solubility in water at 20°C of not more than 10%; and
allowing the mixture to react under an acidic condition.

2. A method as claimed in claim 1, wherein the polyvinyl alcohol contains at least 50% by weight of a vinyl alcohol component in the polymer.

3. A method as claimed in claim 1, wherein said electrolyte is at least one member selected from the group consisting of inorganic salts and organic salts.

4. A method as claimed in claim 1, wherein a concentration of the electrolyte in the aqueous solution thereof is 10% to 40% by weight.

5. A method as claimed in claim 1, wherein said aldehyde is at least one member selected from the group consisting of isobutylaldehyde, hexylaldehyde, heptylaldehyde, citral, benzaldehyde, salicylaldehyde, m- and p-hydroxybenzaldehyde, o-, m-, and p-methoxybenzaldehyde, o-, m-, and p-ethoxybenzaldehyde, veratraldehyde, vanillin, phenylpropyl aldehyde, phenylacetaldehyde, cinnamic aldehyde, and o-, m-, and p-methylbenzaldehyde.

6. A method as claimed in claim 1, wherein the amount of the aldehyde added is 0.3 to 10 times of the weight of the polyvinyl alcohol.

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- 7. A method as claimed in claim 1, wherein the acidic condition is a pH of 0.5 to 4.5.
- 8. A method as claimed in claim 1, wherein pectin is added simultaneously with or after mixing of the electrolyte.
- 9. A method as claimed in claim 8, wherein the amount of the pectin is 0.1% to 1.0% by weight based upon the amount of the water.

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OFICINA ESPAÑOLA DE
PATENTES Y MARCAS

ESPAÑA



⑪ Número de publicación: **2 148 114**

⑫ Número de solicitud: 009901395

⑬ Int. Cl.⁷: A61K 9/48

A61J 3/07

⑭

SOLICITUD DE PATENTE

A1

⑮ Fecha de presentación: 15.06.1999

⑯ Prioridad: 25.01.1999 KR 99-2204

⑰ Fecha de publicación de la solicitud: 01.10.2000

⑱ Fecha de publicación del folleto de la solicitud:
01.10.2000

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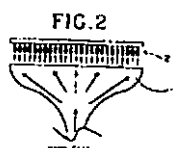
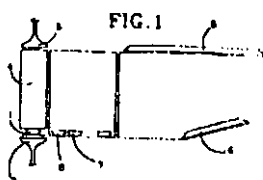
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⑳ Título: Cápsulas botánicas de revestimiento duro y procedimiento para su fabricación.

㉑ Resumen:

Cápsulas botánicas de revestimiento duro y procedimiento para su fabricación.

Las cápsulas se fabrican con celulosa botánica con viscosidad de 4-8 cps a 20°C y una concentración del 2%. En la principal materia prima, con un peso del 18-22%, se mezclan 0,8-1,2% de goma Gellán, 0,05-0,1% de citrato de sodio, 0,01-0,05% de glicerina, 0,1-0,5% de éster de ácido graso de sacarosa, y 76,15-81,04% de agua purificada. Las cápsulas se fabrican manteniendo la temperatura a 55-60°C mientras la cubeta de inmersión (1) de la máquina de moldeo circula a 25-30 rpm; introducir pivotes de moldeo (2) en la disolución durante 10-15 s, transferir los pivotes (2) a un equipo de enfriamiento inferior (3); y enfriar durante 5-10 s; elevar los pivotes (2) hacia el equipo de enfriamiento superior (5), enfriando durante 100-120 s, y controlar el flujo de películas formadas en los pivotes (2) con aire frío; y mover los pivotes (2) que han pasado hacia el túnel de secado (6), y secar a 30-35°C y a una velocidad del aire de 8-10 m/s durante unos 60 m; y decapar, cortar y montar las cápsulas secas en la unidad de proceso (7).



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REIVINDICACIONES

1. Cápsula botánica de revestimiento duro, que comprende:

- 5 76,15-81,04 % de agua purificada;
- 18-22 % de celulosa botánica (HPMC) con una viscosidad de 4-8 cps a una temperatura de 20°C con una concentración del 2 % como materia prima;
- 10 0,8-1,2 % de goma Gellan, que es un estabilizador de la viscosidad;
- 0,05-01, % de citrato de sodio;
- 0,01-0,05 % de glicerina, que es un plastificante; y
- 15 0,1-0,5 % de éster de ácido graso de sacarosa, que es un emulsionante.

2. Procedimiento para la fabricación de una cápsula botánica de revestimiento duro, que comprende las etapas de:

20 mantener la temperatura de una disolución para fabricar cápsulas botánicas a 55-60°C mientras una cubeta de inmersión (1) de una máquina de moldeo de cápsulas circula a una velocidad de 25-30 rpm;

25 introducir unos pivotes de moldeo (2) en una disolución en dicha cubeta de inmersión (1) durante 10-15 segundos, transfiriendo rápidamente los pivotes de moldeo (2) a un equipo de enfriamiento (3) que se encuentra unido a la zona inferior de dicha cubeta de inmersión (1), y enfriar dichos pivotes de moldeo (2) durante 5-10 segundos;

30 elevar verticalmente dichos pivotes de moldeo (2) hacia el equipo de enfriamiento (5) de la zona superior, enfriando dichos pivotes de moldeo (2) durante 100-120 segundos, y controlar el flujo de películas que se forman en dichos pivotes de moldeo (2) mediante aire frío; y

mover dichos pivotes de moldeo (2) que han pasado a través de dicho equipo de enfriamiento (5) de dicha zona superior hacia el túnel de secado (6), y secar a una temperatura de 30-35°C y a una velocidad del aire de 8-10 m/s durante 60 minutos aproximadamente.

35 3. Procedimiento de fabricación de una cápsula botánica de revestimiento duro según la reivindicación 2, en el que la temperatura de dicho equipo de enfriamiento (3,5) de las citadas zona superior o inferior es de 15-20°C, y la velocidad del aire es de 4-6 m/s.

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FIG.1

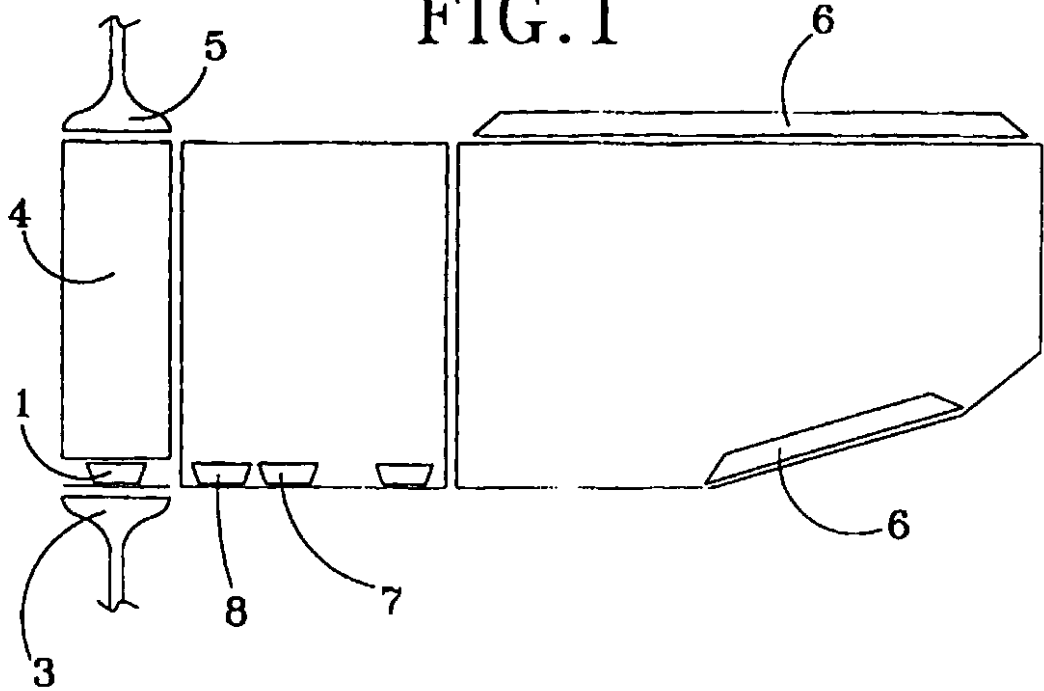
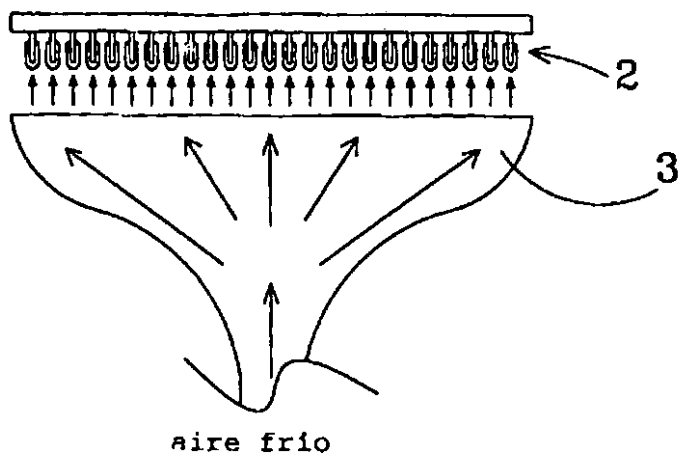


FIG.2



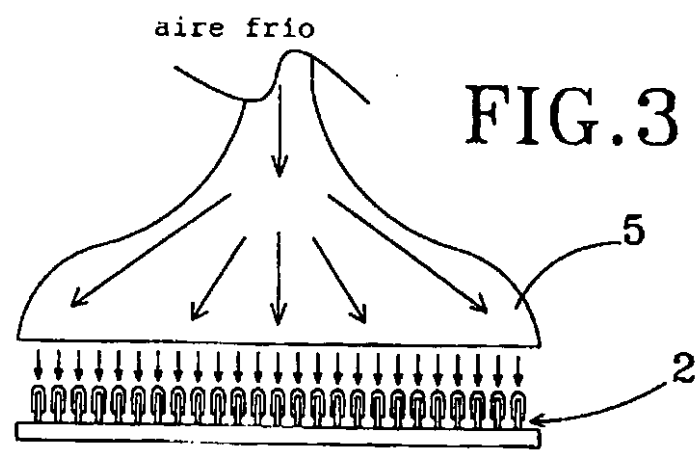
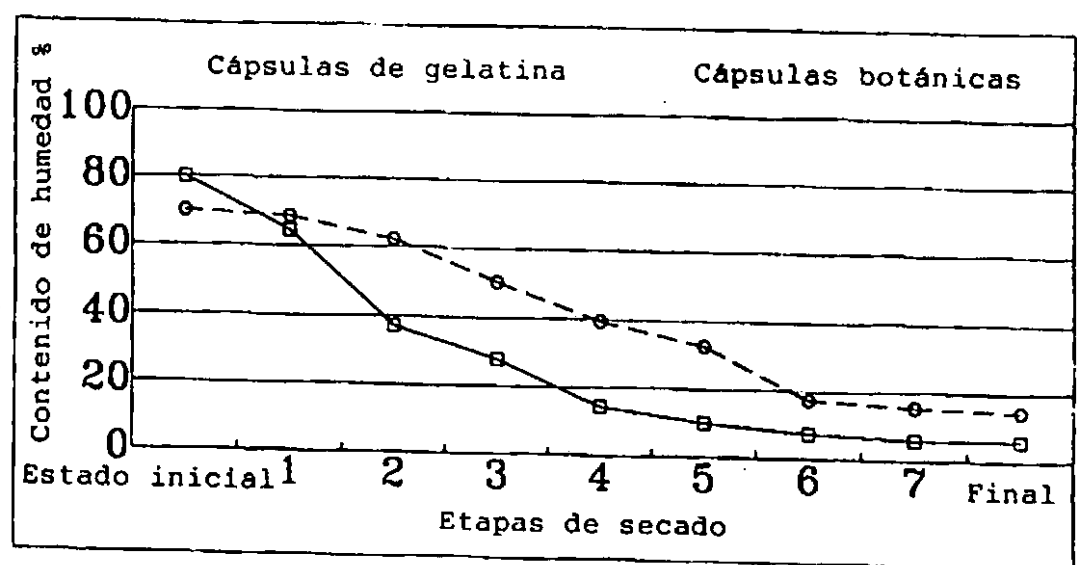


FIG.4



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Publication number: **0 622 408 A1**

EUROPEAN PATENT APPLICATION

Application number: **94201069.5**

Date of filing: **19.04.94**

Int. Cl. 5: **C08L 5/00, C08L 5/14, C08J 5/18, A61K 9/62, //(C08L5/00,5:14),(C08L5/14, 5:00)**

Priority: **27.04.93 US 53578**

Date of publication of application: **02.11.94 Bulletin 94/44**

Designated Contracting States: **CH DE DK ES FR GB IT LI NL**

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Composition and process for gelatin-free soft capsules.

The present invention relates to a polymer composition comprised of gellan, carrageenan and mannan gums and a process for producing flexible films for encapsulation comprising the gellan, carrageenan and mannan gum composition. The mannan gums include the galactomannans and the glucomannans. Advantageously, soft capsules of the above composition are produced using the novel process. The composition comprises a blend of a gellan gum: (carrageenan/mannan gum) wherein the gellan gum concentration ranges from about 0.1 to 50 weight percent and the ratio of carrageenan/locust bean gum ranges from 3:1 to 1:3. Additional reagents are added to this gum blend to form a film-forming polymer composition useful in the production of gelatin-free capsules or microcapsules.

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BACKGROUND OF THE INVENTION

The present invention relates to a polymer composition comprised of gellan, carrageenan and mannan gums and a process for producing flexible films for encapsulation comprising the gellan, carrageenan and mannan gum composition. Advantageously, soft capsules of the above composition are produced using the novel process.

The art reveals that processes and compositions for encapsulation or producing soft capsules generally are composed of gelatin or animal based gels. Soft capsules have primarily been made from low bloom gelatin which melts at low temperatures so that in the manufacturing process two sheets of gelatin are sealed simultaneously with the filling of the capsule. There is a need, however, for producing soft capsules containing liquid or solid contents selected from food or nutritional supplements including vitamins or minerals and the like wherein the capsules are edible and derived from non animal based sources and the capsules can be produced on the existing machinery which is utilized to produce the gelatin based capsules and films. Various polysaccharides and various processes for making them and using them are known. See: U.S. 4,326,052; 4,326,053; 4,377,636; 4,385,123; 4,647,470; 4,746,528 and 5,112,445. U.S. Pat. No. 4,746,528 describes combinations of gellan, xanthan gum and a galactomannan and/or glucomannan gum used to produce elastic gels. U.S. Pat. No. 4,647,470 describes blends of low-acetyl gellan gum with xanthan gum and locust bean gum, konjak, tara or cassia gums which are useful for modifying the brittleness of gellan food products. Gelled food product compositions comprising blends of gellan gum/K-carrageenan gum and mannan gums in weight ratios of about 80:20 to 10:90 of K-carrageenan to mannan and about 95:5 to 20:80 of gellan gum to (K-carrageenan/mannan) are known. See GB 2219803 A.

The art also reveals that heretofore many of the film-forming water soluble materials have high melting temperatures and/or decompose at melting temperatures thus rendering them unsuitable for producing non-animal based capsules. There is an additional need to provide soft capsules which may be utilized to encapsulate bath oils and the like wherein the capsular material is composed of non-gelatin based sources and is water soluble. There is an additional need for novel processes related to the production of non-animal based soft capsules or flexible films such as those claimed and disclosed in the present invention. The present invention therefore satisfies the need for producing capsules wherein the particular non-animal derived compositions comprise suitable material which has the essential low melting and stability characteristics of the animal derived gelatins and thus can be produced on existing capsule machinery.

SUMMARY OF THE INVENTION

The present invention relates to a polymer composition comprised of gellan, carrageenan and mannan gums and a process for producing flexible films for encapsulation, specifically soft capsules. There is a need for non-animal sourced, i.e. gelatin-free, encapsulating polymer systems that will remelt under controlled conditions to form soft capsules to seal the encapsulated contents that may be selected from liquid or solid active or inactive ingredients within two polymer sheets. The present invention therefore involves a polymer composition and a process for producing a complete capsule wherein the capsule contains the selected contents including active and inactive ingredients in solid or liquid form which may then readily be administered to or taken by a target organism.

The total polymer concentration of the film-forming composition ranges from 1 to 10 weight percent of the total weight of the capsule. The gellan gum concentration ranges from about 0.1 to 50 weight percent and the carrageenan to mannan gum weight ratio ranges from 3:1 to 1:3. In order to achieve remelting of the film composition at a soft capsule processing temperature of less than 100 °C, sufficient water must be available to inhibit polymer association and subsequent increase in the melting temperature above 100 °C.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a polymer composition comprised of gellan, carrageenan and mannan gums wherein the mannan gums are selected from a galactomannan or a glucomannan and a process for producing flexible films for encapsulation, specifically soft capsules. There is a need for non-animal sourced, i.e. gelatin-free, encapsulating polymer systems that will remelt under controlled conditions to form soft capsules to seal the encapsulated contents that may be selected from liquid or solid active or ingredients within two polymer sheets. The present invention therefore involves a polymer composition and a process for producing a complete capsule wherein the capsule contains the selected contents including active and inactive ingredients in solid or liquid form which may then readily be administered to or taken by a target organism. Advantageously, a gum-blend composition comprising a gellan gum: (carrageenan gum/

mannan gum) wherein the gellan gum concentration ranges from about 0.1 to 50 weight percent and the ratio of carrageenan/mannan gum ranges from 3:1 to 1:3 is used in the present invention to form the various film-forming polymer compositions. The present invention also relates to a gum-blend composition comprising a gellan gum: (carrageenan gum/mannan gum) wherein the gellan gum concentration ranges from about 5 0.1 to about 19% weight percent and the ratio of carrageenan/mannan gum ranges from 3:1 to 1:3.

The total polymer concentration of the film-forming composition ranges from 1 to 10 weight percent of the total weight of the capsule. The gellan gum concentration ranges from about 0.1 to 50 weight percent and the carrageenan to mannan gum weight ratio ranges from 3:1 to 1:3. In order to achieve remelting of the film composition at a soft capsule processing temperature of less than 100 °C, sufficient water must be 10 available to inhibit polymer association and subsequent increase in the melting temperature above 100 °C.

The melting property of the flexible film disclosed in the present application is critical to the proper sealing of the capsules produced during production of said soft capsules. The present invention makes use of a unique combination of hydrocolloids which interact to give synergistic film properties. Furthermore, by controlling the solids content of the film during the encapsulation process, a melting temperature of less 15 than 100 °C for the polymer composition within the scope of the present invention is achieved. The compositions and processes of the present invention have numerous advantages including biodegradability, strength, thermal reversibility, water solubility and reduced processing time.

Gellan gum refers to the extracellular polysaccharide obtained by the aerobic fermentation of the microorganism, Pseudomonas elodea, in a suitable nutrient medium. Various forms of gellan gum have 20 been described and may be utilized in the present invention. These gums include native, deacetylated, deacetylated clarified, partially deacetylated, and partially deacetylated clarified. As used hereafter, "gellan gum" shall refer to low acetyl (LA) gellan gum which has an acetyl level of 0.3 to 0 % weight and to high acetyl (HA) gellan gum which has an acetyl level greater than 0.3 % weight and to blends or combinations of LA and HA gellan gum.

Mannan gums include the galactomannan gums and the glucomannan gums or mixtures thereof. Locust bean gum (lbg) is an extract of the locust bean or carob, Ceratonia siligua and is a member of the galactomannan class. It is commercially available and used as a stabilizer in various food products. Glucomannans are also included within the scope of the present invention and may be selected from, for 25 example, konjac gum, tara and/or cassia gums. Konjac or konjac gum is a glucomannan extracted from the plant Amorphophallus konjac. Tara gum is a vegetable gum derived from the seed of the legume Cesalpinia spinosa. Cassia gum is a pod extract derived from Cassia occidentalis or fistula.

k-carrageenan is a hydrocolloid obtained by extraction with water or other polar solvents from some members of the algae class Rhodophyceae (red algae) and consists of a mixture of the ammonium, calcium, magnesium, potassium, and sodium esters of galactose and 3-6-anhydrogalactose copolymers. 30 Carrageenans include the κ , λ , and ι forms. These additives are used predominantly as suspending or gelling agents in the pharmaceutical or food industries.

The present invention is directed to a tri-combination of the above components in particular ratios which under the appropriate conditions as described herein may be utilized to produce polymeric films useful in producing non-gelatin capsules which are soft and water soluble. The mannan gum component is 40 preferably selected from either locust bean gum or konjac gum. Of course, mixtures of the mannan gums may also be utilized in the present invention. The tri-combination may be formulated and is preferably formulated in the following ratios for the film-forming polymeric compositions:

gellan gum	k-carrageenan	locust bean gum
0.100	0.225	0.675
0.100	0.675	0.225
0.100	2.475	0.7425
0.800	1.900	0.950
5.000	1.250	3.750
5.000	3.750	1.250

This tri-gum combination or a combination wherein a mannan gum such as konjac gum is substituted 55 for the locust bean gum or any tri-combination within the scope of the present invention may be further combined with a salt such as potassium citrate and additional ingredients such as sorbitol, glycerine, corn syrup and deionized water to form a film-forming polymeric composition. Sodium citrate and potassium chloride may also be added to form an aqueous composition useful in the preparation of film-forming compositions. Sequestrants selected from a sodium or potassium phosphate or citrate salt or combinations



thereof may be utilized in the present invention. For example, sodium phosphate and/or sodium citrate may be added to the composition and are useful in chelating the divalent ions such as magnesium and calcium and allow complete hydration of the gellan gum. The added potassium salt level in the gum/film forming composition is useful as it relates to the melting and setting temperature of the film.

5 The following gelling salts may be utilized in the present invention: sodium chloride, sodium sulfate, and other sodium salts of appropriate organic or inorganic acids. Potassium sulfate and other potassium salts of appropriate organic or inorganic acids may also be utilized as gelling salts in the present invention. One skilled in the art will appreciate that under certain circumstances and conditions, certain ions are necessary to gel certain gums such as the kappa form of a carrageenan gum. Therefore, when κ -carrageenan is used, 10 potassium ions must be present to obtain the maximum performance of the gum. Furthermore, the use of mono- or di-valent ions to gel gellan gum is determined by the requirement of gel texture and modulus.

A process for preparing compositions within the scope of the present invention and for manufacturing soft capsules from the compositions comprises the steps of:

15 (1) A tri-gum blend comprising gellan gum, locust bean gum and k-carrageenan gum in the relative ratios as described above such as, for example, (a) low-acyl gellan gum with a relative weight percentage of about 20%; (b) k-carrageenan gum with a relative weight percentage of about 50%; (c) locust bean gum with a relative weight percentage of about 25%; and a salt such as potassium citrate in a relative weight percentage of about 9% wherein the potassium citrate is used as a sequestrant/gelling salt is mixed into cold (20-30 °C) deionized water and then the ingredients sorbitol, glycerine and corn syrup are added 20 with agitation. The plasticizers or other reagents useful in the present invention may be selected from sorbitol, glycerine, propylene glycol, polyethylene glycol, corn syrup, sucrose, fructose or combinations thereof. The mixture is then heated to a temperature of about 75-100 °C. Advantageously, the mixture is heated to 90 °C with agitation and held at this temperature for about 10 minutes;

25 (2) The hot solution produced in step 1 is then, for example, transferred to an encapsulation machine wherein a 30-40 mil film is formed on rotating steel drums. Two films thus formed on the steel drums proceed through rotating dies that are designed to simultaneously form, cut and fill various sized and shaped capsules. The fill material may be either solid or liquid material. The edges of the capsule formed in this process are heat and pressured sealed and the filled capsules are then washed, dried to a pre-determined moisture content such as 3-4% and packaged. The moisture content of the film during 30 the encapsulation process controls the melting temperature and the proper sealing of the capsules.

In the above process, the locust bean gum can readily be substituted with a mannan gum such as konjak gum or mixtures of locust bean gums and konjak gums in a ratio of 1:100 to 100:1. Gelatin free soft capsules utilizing these compositions may readily be prepared.

35 **EXAMPLES**

The following gum-blends and/or gum blend aqueous compositions may readily be prepared. The relative ratios of the gums and additional reagents are generally expressed in relative weight percentages. The variations in relative composition may also be reflected in simple weight ratio comparisons. The 40 following examples are reflected in weight percentages and reflect the number of grams used to prepare the compositions.

When water is added to form the film-forming polymeric composition, the units in the following examples are expressed in either weight percentages or in milliliters (mls). It is understood, however, that any quantities within the claimed ratios may be prepared depending upon the needs of the preparer and 45 upon the quantity needed to manufacture.

EXAMPLE 1

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	wt%
Low-acyl gellan gum	19.05%
k-carrageenan	47.62%
locust bean gum	23.81%
Potassium citrate	9.52%

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EXAMPLE 2

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High-acyl gellan gum	19.05%
k-carrageenan	47.62%
locust bean gum	23.81%
Potassium citrate	9.52%

10 The gum blends such as those described in Examples 1 or 2 or other gum blends within the scope of the present invention may be further combined with additional ingredients to form a film-forming polymer composition. The following examples are representative of those film-forming polymeric compositions useful for the production of capsules and the like and are not to be construed as limiting the scope of the present invention.

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EXAMPLE 3

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Gum blend (EX 1)	4.00 %
Sorbitol	5.67 %
Glycerine	5.67 %
Corn syrup	5.67 %
Deionized water	78.99 %

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EXAMPLE 4

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Gum blend (EX 2)	4.00 %
Sorbitol	5.67 %
Glycerine	5.67 %
Corn syrup	5.67 %
Deionized water	78.99 %

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In addition to the examples described above, the following film-forming polymeric compositions may also be prepared.

40 EXAMPLE 5

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Gellan gum (LA)	0.66 %
k-carrageenan	0.66 %
locust bean gum	0.66 %
Glycerine	0.60 %
sodium citrate	0.10 %
Potassium chloride	0.10 %
Deionized water	97.22 %

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EXAMPLE 6

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Gellan gum (HA)	0.40 %
k-carrageenan	1.00 %
Locust bean gum	1.00 %
Polydextrose	13.40 %
Sorbitol	4.00 %
Sodium citrate	0.10 %
Potassium chloride	0.10 %
Deionized water	80.0 %

15 EXAMPLE 7

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25

Gellan gum (HA)	0.29 %
k-carrageenan	1.62 %
locust bean gum	0.81 %
Sorbitol	6.00 %
Glycerine	6.00 %
corn syrup	6.00 %
Potassium citrate	0.29 %
Deionized water	78.99 %

EXAMPLE 8

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Gellan gum (LA)	0.66%
k-carrageenan	1.33%
konjac	2.33%
Glycerine	9.97%
Sodium citrate	0.30%
Deionized water	85.41%

40 The physical properties of examples 3-7 are listed below and demonstrate the effectiveness of the films prepared within the scope of the present invention. In addition to the described physical properties, the capsules or other products formed from the film-forming compositions are particularly useful because they provide a gelatin-free polymeric composition.

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Example Number	Tensile Strength (psi)	Elongation at break (%)
3	525	143
4	531	177
5	2423	78
6	1087	107
7	396	122

55 Films of the example solutions while hot were cast with a knife blade set at 100 mil clearance and allowed to air dry 24 hours at 60 % relative humidity and 22 °C prior to being tested on an INSTRON Model 1011 tensile-testing instrument.

EXAMPLE 9

The composition within the scope of the present invention was prepared according to the following process:

- 5 (1) A tri-gum blend comprising gellan gum, locust bean gum and k-carrageenan gum in the relative ratios as described above such as, for example, (a) high-acyl gellan gum (.29 grams); (b) k-carrageenan gum (1.62 grams); (c) locust bean gum (.81 grams); and a salt such as potassium citrate (.29 grams) wherein the potassium citrate is used as a sequestrant/gelling salt was mixed into cold (20-30 °C) deionized water (about 80 mls) and then the ingredients sorbitol (6 grams), glycerine (6 grams) and corn syrup (6 grams) were added with agitation. The mixture was then heated to a temperature of about 90 °C with agitation and held at this temperature for about 10 minutes;
- 10 (2) The hot solution produced in step 1 was then, for example, transferred to an encapsulation machine well known to those skilled in the art which was first developed in 1932 by R.P. Scherer, wherein a 30-40 mil (.030-.040 inches) (a mil is defined as .001 inch and is a common measurement of film thickness) film was formed on rotating steel drums. The rotating steel drums can vary in size from 12 inches in diameter to 30 inches or more depending on the size of the encapsulation machine. The width of the rotating steel cylinder can also vary from 6-12 inches. The drums are hollow and can be heated or cooled by injecting liquids within the drum. The two films thus formed on the steel drums proceed through counter-rotating dies that were designed to simultaneously form, cut and fill various sized and shaped capsules. The counter-rotating dies are normally made of solid brass and are cylinders approximately six inches in diameter and 12 inches long depending on the width of the encapsulating film. Various shapes of capsules may be cut into the brass circumference of the die. The fill material may be either solid or liquid material.

The fill material used in the above examples was mineral oil and fragrances since this material may be utilized in the production of bath beads which generally contain mineral oil and fragrances. Of course, the fill-material may be selected from any desired known solid or liquid material which the manufacturer deems necessary. The edges of the capsule formed in this process were heat and pressured sealed at a temperature range of 75-85 °C and a pressure range of 0.1-2 psi and the filled capsules were then washed with a petroleum based solvent to remove the traces of mineral oil, dried to a pre-determined moisture content of 3-4% and packaged. The moisture content of the film during the encapsulation process controls the melting temperature and the proper sealing of the capsules.

Capsules produced in the above process can further be utilized in a method of treating a nutritional deficiency in a mammalian organism in need of treatment thereof comprising administering to said mammalian organism an edible soft capsule of the composition according to claim 1, wherein the capsule contains contents selected from an essential vitamin or nutrient and a method of administering a bath capsule to a bath comprising adding to said bath a soft capsule of a water soluble composition according to claim 1, wherein the capsule contains contents selected from a bath oil or detergent or perfume. Of course, additional ingredients may be added to the capsule contents during the manufacturing process to produce a suitable target capsule.

Gelatin-free carbonless paper utilizing microcapsules containing dyes may readily be prepared using the claimed composition and process. Furthermore, the present invention also encompasses microencapsulation of any water-immiscible liquids to, for example, mask unpleasant tastes or to protect substances from oxidation and also to allow controlled release of encapsulated material and physical separation of reactive materials.

Claims

1. A gum-blend composition comprising a gellan gum: (carrageenan gum/ mannan gum) wherein the gellan gum concentration ranges from about 0.1 to about 19 weight percent and the ratio of carrageenan/mannan gum ranges from 3:1 to 1:3.
2. The gum-blend composition according to Claim 1, wherein the ratios by weight of gellan to carrageenan to mannan gum comprise:

gellan gum	k-carrageenan	mannan gum
0.100	0.225	0.675;
0.100	0.675	0.225;
0.100	2.475	0.7425.

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3. A film-forming polymeric composition comprising from 1 to 10 weight percent of a gum-blend composition which comprises a gellan gum:(carrageenan gum/mannan gum) wherein the gellan gum concentration ranges from about 0.1 to 50 weight percent and the ratio of carrageenan/mannan gum ranges from 3:1 to 1:3 and a gelling salt and a sequestrant.
4. The film-forming polymeric composition according to Claim 3 comprising a composition wherein the gellan gum concentration ranges from 0.1 to 50 weight percent of the gum-blend composition and the carrageenan to mannan gum weight ratio ranges from 3:1 to 1:3 wherein the mannan gum is selected from locust bean gum, konjac gum, tara gum or cassia gum or combinations thereof and the gelling salt is selected from a sodium or potassium inorganic or organic salt or combinations thereof and the sequestrant is selected from a sodium or potassium citrate or phosphate or combinations thereof.
5. The film-forming polymeric composition according to Claim 4, further comprising a plasticizer selected from sorbitol, glycerine, propylene glycol, polyethylene glycol, corn syrup, sucrose, fructose or combinations thereof.
6. A film comprising the film-forming polymer composition according to Claim 3 wherein the film is characterized in that it is biodegradable.
7. A film comprising the film-forming polymer composition according to Claim 3 wherein the film is characterized in that tensile strength ranges from 300-3000 psi and elongation-at-break at a minimum of 50 %.
8. A film comprising the film-forming polymer composition according to Claim 3 wherein the film is characterized in that it is re-melttable after film formation.
9. A film comprising the film-forming polymer composition according to Claim 3 wherein the film is characterized in that it is water soluble.
10. A gelatin-free soft capsule, comprising the composition according to claim 3 and capsule contents wherein the capsule contents are selected from a solid or liquid.
11. A process for producing a gelatin-free soft capsule, comprising the steps of:
 - (a) transferring a hot aqueous mixture containing the film-forming composition according to Claim 3 to a plurality of rotating drums;
 - (b) casting a 30-40 mil film on the plurality of rotating drums;
 - (c) passing at least two of the 30-40 mil films over rotating dies;
 - (d) simultaneously forming, filling with contents selected from a liquid or a solid, heat-sealing and cutting a plurality of capsules selected from a plurality of shapes and sizes; and
 - (e) washing and drying said plurality of capsules.
12. A process according to Claim 11, wherein the capsule contains contents selected from a bath oil or detergent or perfume.
13. A method of treating a nutritional deficiency in a mammalian organism in need of treatment thereof comprising administering to said mammalian organism an edible soft capsule of the composition according to claim 1, wherein the capsule contains contents selected from an essential vitamin or nutrient.
14. Use of a composition according to claim 1, together with an essential vitamin or nutrient, in the manufacture of an edible capsule for the treatment of a nutritional deficiency.