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(54) Benævnelse: **FREMGANGSMÅDE TIL FREMSTILLING AF TYGBARE DOSERINGSFORMER TIL LÆGEMIDDELADMINISTRATION OG PRODUKTER DERMED**

(56) Fremdragne publikationer:
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US-A- 5 380 535
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DESCRIPTION

FIELD OF THE INVENTION

[0001] The invention relates to a specific process for manufacturing a palatable soft chewable pharmaceutical product ("soft chew"). The field in general refers to orally administrable pharmaceutical dosage units; in particular, units in the form of an edible mass, such as a chunk.

BACKGROUND OF THE INVENTION

[0002] Formulation of a drug into an edible medication, such as a chewable tablet or confection, can increase patient acceptance of the medication, especially animals, who tend to resist swallowing hard tablets or capsules. Unfortunately, many drugs and other active ingredients (collectively, "actives") have a strongly bitter or otherwise unpalatable taste, making chewing them unpleasant.

[0003] Flavorings are commonly added to chewable medications to enhance their palatability. For example, a veterinary medication might include animal product-based flavorings such as uncooked dried meat parts such as beef, pork, chicken, turkey, fish and lamb; organ meats such as liver; meat meals, bone meals and ground bone; and animal-derived food such as casein, milk (which may include dry forms and lowered fat forms, such as dry skim milk), yogurt, gelatin, cheese and egg (collectively, "animal origin flavorings") may be utilized.

[0004] However, use of many animal origin flavorings (especially of meat, poultry or seafood origin) risks exposure to infectious agents, not only to the recipient of the drug, but also through contamination of manufacturing equipment on which the flavored dosage units are made. For this reason, manufacturing facilities that prepare pharmaceutical products with animal origin flavorings are often devoted exclusively to their preparation, at a correspondingly greater cost than would be incurred if manufacturing could be performed in a facility capable of concurrently processing multiple products.

[0005] Texture is also an issue for chewable medications. One of the most commonly used form for chewable dosage units is the compressed tablet, whose ingredients (including the actives and inactive ingredients such as binders) can make the tablet gritty or otherwise unappealing, especially to animals. Thus, a preferred alternative dosage form for use especially with animals is the "soft chew," generally a meat-like mass or chunk also widely found in consumable pet treats.

[0006] Soft chews are typically manufactured by blending and extrusion. Pre-mixed ingredients are introduced into an extruder barrel with a screw therein, then mixed, coagulated, expanded

and sheared into a blended mixture, followed by application of additional heat if a harder texture is desired. Water introduced into the mixture must generally be of pharmaceutical grade, as it will be retained within the mixture. The blended mixture is then formed into a desired shape on a die plate, then cut into individual units.

[0007] The heat generated during the extrusion process can cause deterioration in the stability (potency or integrity) of the active in the mixture, causing the effective dose provided by each unit formed to vary. Consistency of texture, shape and weights of the chews from batch to batch of extruded material can also suffer.

[0008] For example US 5 380 535 A discloses a non-aqueous process for preparing non-aqueous, chewable composition for oral delivery of unpalatable drugs, comprising a therapeutically-effective amount of one or more unpalatable drugs intimately dispersed or dissolved in a pharmaceutically-acceptable lipid which is a solid at ambient temperature, or a mixture of said lipids, the method comprising: (a) providing a therapeutically-effective amount of one or more unpalatable drugs and a pharmaceutically-acceptable molten lipid; (b) feeding said drug and molten lipid into a fluidized bed apparatus comprising means for fluidizing said drug and lipid; and (c) fluidizing said drug and lipid in said fluidized bed apparatus in the absence of a solvent for a time sufficient to solidify the molten lipid and drug into particles comprising said drug and lipid, wherein said particles have a number average particle size of from 10-150 microns, wherein said drug is present in an amount of from about 0.1-75 weight percent of said composition and said lipid is present in an amount of from about 5-50 weight percent of said composition.

[0009] Document WO 96/18387 A1 describes a method of preparing a soft, chewable dosage form, comprising the steps of: mixing under high shear force, a hydrogenated starch hydrolysate, a water soluble bulking agent, and a water insoluble bulking agent until a uniformly blended matrix is obtained.

[0010] Furthermore, US 2004/234579 A1 discloses a method of preparing a dietary supplement comprising a medicament, the method comprising:

providing a natural substance to form a carrier matrix for the medicament;

slurrifying the natural substance to form a slurry;

mixing an effective amount of the medicament with the slurry to form a mixture;

pouring the mixture into a mold;

freezing the mixture; and

removing moisture from the mixture to form a shelf-stable dietary supplement.

[0011] Moreover, WO 2004/016252 A1 describes a process for preparing a specific chewable veterinary formulation, which comprises the step of:

1. (a) blending the pharmaceutical agent, binder, disintegrant, and non-animal containing flavor or a flavor derived from a non-animal source;
2. (b) adding the water and the humectant to the mixture from step (a) and mixing the mixture; and
3. (c) without drying, extruding the mixture.

[0012] Finally, WO 2005/013714 A1 discloses a process for the production of a specific highly palatable ductile chewable-veterinary composition, comprising (i) feeding the hopper of an extruder with an effective amount of one or more ingredients that are active against animal pests, pathogens or animal diseases; meat flavoring; partially gelatinized starch; a softener; and up to 9% (w/w) of water, (ii) cooling constantly down the mixture of active ingredients and carriers so that the temperature of the extrudate that leaves the tip of the extruder does during the whole extrusion process at no time exceed 40 °C, (iii) pressing the extrudate through a die that is decisive for the shape of the chewable product, and (iv) cutting the extrudate that leaves the extruder into equal pieces.

[0013] There is a need, therefore, for a method of manufacture for soft chewable medications in which the blending of actives into the chew mixture is achieved without generation of heat. It is also desirable that the chews be susceptible to manufacture without use of costly, pharmaceutical grade water as an ingredient. There is also a need in the art for a soft chew medication whose taste appeals to animals without use of ingredients that may include infectious agents or contaminants. Further, it is highly desirable for the manufacturing means employed to produce chewable medications to do so in a manner that ensures consistent chew weights, texture and active dosages.

SUMMARY OF THE INVENTION

[0014] The invention provides a process for manufacturing a palatable soft chewable pharmaceutical product ("soft chew") comprising:

blending at least one active ingredient with inactive ingredients to form a mixture having the at least one active ingredient uniformly blended therein, wherein dry ingredients are blended first, then liquid ingredients are added and blended therein, without applying heat and by using a horizontal mixer which spins the mixture into particulate form;

wherein the inactive ingredients are selected from the group consisting of a food grade flavoring; a binder; a bulking agent; a softening agent; an anti-caking agent or lubricant; a humectant comprising glycerin or propylene glycol; and at least one excipient comprising a starch, a cellulose or a mixture thereof; and forming the mixture into individual soft chews

without need for a cooling step, wherein forming comprises knocking out the soft chews from a cavity of a mold plate. The soft chews obtained by the process of the invention, in the following referred to as "soft chews of the invention" as well, are particularly palatable to pet animals. They contain inactive ingredients of at least food grade quality, and most preferably do not contain inactive ingredients of animal origin. As such, the soft chews may be manufactured without concern about transmission of infectious agents or contaminants, and without risk of cross-contaminating other products produced in the same manufacturing facility.

[0015] The manufacturing processes of the invention allow the soft chews to be produced without application of heat to the ingredient mixture. Stability of the actives is therefore preserved, and a well-blended, soft texture is provided. Further, no water is used as an ingredient of the chews, thereby avoiding the need for use of costly pharmaceutical grade water, while reducing the opportunity for microbial growth or loss of potency by the active.

[0016] To these ends, the soft chews of the invention are manufactured using, preferably large capacity, horizontal mixers which spins the chew mixture into particulate form. The mixing action causes the ingredients in the mixture to be cast away from the mixing vessel walls, crisscrossing the vessel to provide a uniformly blended mixture formed without application of heat. Because no cooling step is required, the time to produce chews is shortened compared to cooking extrusion methods.

[0017] The highly blended mixture produced is placed into molds to form individual dosage units and allowed to set without application of heat. Soft chews can be produced in any desired shape. Preferred mixing and molding equipment utilized in the invention can provide individual soft chews with consistently blended ingredients, stably provided actives and consistent weights.

[0018] The soft chews of the invention are produced in palatable form without the use of any non-food grade inactive ingredients (or, preferably, any animal origin inactive ingredients). The manufacturing processes may therefore be performed without risk of potential cross-contamination of other equipment in the facility with infectious agents or contaminants derived from sources such as the animal-origin meat flavorings commonly used in chewable medications for animals.

DETAILED DESCRIPTION OF THE INVENTION

A. <u>Materials For Use In Soft Chews Of The Invention</u>

[0019] In general, soft chewable medications and treats include as inactive ingredients matter such as binding agents, vitamins, and colors to enhance the manufacturability, texture and

appearance of the product. Those of ordinary skill in the art will be familiar with such inactive ingredients, which need not include water for use in the invention.
The soft chews of the present invention contain at least one active ingredient and inactive ingredients. The inactive ingredients are selected from the group consisting of a food grade flavoring; a binder; a bulking agent; a softening agent; an anti-caking agent or lubricant; a humectant comprising glycerin or propylene glycol; and at least one excipient comprising a starch, a cellulose or a mixture thereof.

[0020] For use in the invention, no inactive ingredients of the soft chew should be of less than food grade quality and may be of higher quality (e.g., USP or NF grade). In this context, "food grade" refers to material that does not contain or impart chemicals or agents hazardous to health. Thus, a food grade flavoring, if of animal origin, will be one that has been prepared to substantially reduce or eliminate the presence of infectious agents or contaminants therein; e.g., by processes such as pasteurization, pressurization or irradiation.

[0021] The latter process in particular can effectively eliminate infectious agents such as *E. coli* O157:H7, *Salmonella* and *Campylobacter* from a wide variety of food and animal-derived substances, such as raw meat products, vegetables, grains and fruits. Preferably, however, soft chews of the invention will not contain any animal origin ingredients, and most preferably will not contain any animal origin flavorings. All ingredients should be pharmaceutically acceptable (e.g., food grade, USP or NF, as appropriate).

[0022] Flavorings are preferably present in soft chews of the invention that are at least food grade in quality, and most preferably exclude animal origin flavorings. Preferred non-animal origin flavorings are plant proteins, such as soy protein, to which edible artificial food-like flavorings has been added (e.g., soy-derived bacon flavoring). Depending on the target animal, other non-animal flavorings could include anise oil, carob, peanuts, fruit flavors, sweeteners such as honey, sugar, maple syrup and fructose, herbs such as parsley, celery leaves, peppermint, spearmint, garlic, or combinations thereof.

[0023] A particularly preferred flavoring for use in the invention is Provesta™ 356, made by ABF Ingredients, Inc. It is a light tan, water- soluble powder that builds on the properties of yeast extracts and reaction flavors to provide a pleasant smoky, cured bacon flavor. Provesta 356 contains no animal derived ingredients.

[0024] For administration to horses and other grazing animals, as well as small animals such as rabbits, hamsters, gerbils, and guinea pigs, grains and seeds are especially appealing additional flavoring agents. The grains may be present in any form consistent with the production of the chew including flour, bran, cereal, fiber, whole grain and meal forms, including gluten meals, and may be rolled, crimped, ground, dehydrated or milled. Minerals may also be added as flavorings, such as salt and other spices. Preferably, the grain utilized is dehydrated, milled or flaked. Vegetables such as dehydrated carrots and seeds such as safflower seeds or milo seeds are especially appealing to small animals and may be included.

[0025] Further, agents which enhance the manufacturability and texture of a soft chew may include softening agents, an anti-caking agent or lubricant, and a humectant comprising glycerin or propylene glycol. Illustrative examples of lubricants or anti-caking agents which may be used in the invention include magnesium stearate, calcium stearate, solid polyethylene glycols, sodium lauryl sulfate, or mixtures thereof. Magnesium stearate is particularly preferred for lubrication and as a component to aid in setting the soft chews after molding.

[0026] Humectants include glycerol and propylene glycol. Wetting agents including cetyl alcohol and glycerol monostearate are disclosed. Glycerin is a preferred humectant useful in maintaining the softness of the soft chew over the shelf life of the product. Glycerin is a clear, colorless, odorless, viscous, hygroscopic liquid.

[0027] Vegetable oils (such as corn, safflower, cottonseed, soybean and olive oils) may also be utilized to lubricate the chew mixture and maintain its softness. Oil also aids in flavor palatability. A particularly preferred oil is soybean oil.

[0028] Paraffin wax or polyethylene glycol 8000 (carbowax) will preferably be included in the soft chew mixture before molding at 1.0% to 3.0%. If wax is used, it is melted at 50°C before being added to the soft chew mixture after mixing. After molding, the soft chews with the added wax will set-up, usually over a period of 8 to 24 hours. The wax congeals quickly, softens the chew mixture, and prevents the soft chew units from sticking together after molding.

[0029] Additional softening agents utilized are those which limit density and hardness of the soft chew product. Such agents may include polysaccharides and fiber. A polysaccharide may be included in the form of a complex food such as a fruit, a plant starch such as potato or tapioca starch. Polysaccharide may also be provided separately, for example, in the form of chondroitin sulfate or glucosamine HCl.

[0030] Fiber may be also provided as filler or as a bulking agent and to provide or maintain porosity in the soft chew. Fibers used to this end may be derived from fruits, grains, legumes, vegetables or seeds, or provided in forms such as wood fiber, paper fiber or cellulose fiber such as powdered cellulose fiber. A particularly preferred such bulking agent for use in the invention is bran, such as oat bran,

[0031] Other bulking agents that may be utilized include any food grade material, including hydrocolloid thickeners and binders, such as gum arabic, pectins, modified starches, alginates, carrageenans, xanthan gums, carboxymethylcellulose, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, propylene glycol alginate, polyvinylpyrrolidone (PVP), carboxyvinyl polymers (such as Carbopol®), polyethylene oxide polymers (such as Polyox®), talc, dicalcium phosphate, and antacids.

[0032] Binders utilized in soft chews may be a sticky substance or a substance which becomes sticky in combination with other ingredients such as. water, but will preferably give the soft chew product a food-like texture. In general, binders may include molasses, corn syrup, peanut

butter, food gum, a starch such as potato starch, tapioca starch or corn starch, honey, maple syrup and sugars. Preferred binders for use in soft chews of the invention are starches and powdered sweeteners.

[0033] A particularly preferred binder is Starch 1500, a pregelatinized starch made by Colorcon Corporation. Pregelatinized starch is a starch that has been chemically and/or mechanically modified to rupture all or part of the starch granules and so render the starch flowable. It contains 5% of free amylase, 15% of free amylopectin and 80% unmodified starch. The source is from corn.

[0034] Powdered sugar (sucrose) serves well as a sweetener as well as a binder. Sucrose is obtained from either sugar cane or sugar beets. Salt and/or other spices may be added as appropriate, with salt being especially preferred to enhance flavor.

[0035] A preservative such as potassium sorbate, sodium benzoate or calcium propionate may be included in order to retard growth of microorganisms and fungi. Tenox 4 is a combination of BHA and BHT anti-oxidants, made by Eastman Chemicals. It is a preferred and convenient preservation system.

[0036] Vitamins may be provided according to the nutritional requirements of the target animal, and may be provided as an element of oils utilized. Vitamins are also present in various oils that may be added as softening agents, i.e. as inactive ingredient; for example, canola oil, corn oil, soybean oil and vegetable oil.

[0037] Excipients that may be utilized include starches, cellulose or mixtures thereof, in amounts ranging, for example, from about 1 to about 60 percent (w/w), preferably from about 2 to about 50 percent, more preferably from about 15 to 50 percent. For example, the excipient may consist of sodium starch glycolate, pregelatinized corn starch (Starch 1500), crospovidone (Polyplasdone XL™, International Specialty Products), and croscarmellose sodium (Ac-Di-Sol™, FMC Corp.), and derivatives thereof. Excipients may be used to create a trituration of an active. For example, to create a 10% trituration, 100 grams of the active is combined with 900 grams of an excipient, such as a preferred excipient, Starch 1500. The dry mixture is fluidized and is then preferably coated.

[0038] If a coating is to be provided (to help protect the stability of the active and mask its taste), food grade coatings are preferred, such as an aqueous film coat from Colorcon Corporation sold as OPADRY™. OPADRY is a methylcellulose based product with a plasticizer and pigment. Since the coating is aqueous based, no special handling precautions are required during manufacture of the soft chew. However, after administration, the aqueous film coat will start to erode and/or dissolve within minutes when exposed to water or other liquids in the stomach. Therefore, disintegration and dissolution of the soft chew should not be delayed after it is administered to the subject.

[0039] Any orally administrable active drug or other biologically active compound may be

provided in the soft chews of the invention. Those of ordinary skill in the human and/or veterinary pharmaceutical arts will be entirely familiar with the identity of such actives which may include, without limitation, antibiotics, analgesics, antivirals, antifungals, anthelmetics, endo- and ecto-parasticides, hormones and/or derivatives thereof, anti-inflammatories (including non-steroidal anti-inflammatories), steroids, behavior modifiers, vaccines, antacids, laxatives, anticonvulsants, sedatives, tranquilizers, antitussives, antihistamines, decongestants, expectorants, appetite stimulants and suppressants, minerals and vitamins.

[0040] The amounts of each of the components in the final product may be varied considerably, depending upon the nature of the drug, the weight and condition of the subject treated, and the unit dosage desired. Those of ordinary skill in the art will be able to adjust dosage amounts for particular actives in the soft chews in light of the teachings of this disclosure. Generally, however, the active may be provided by range in weight based on the total weight of the composition from about 0.001% to 75% (w/w), more preferably 0.095% to 40%, and most preferably not in excess of 50%. For example, for administration of an anthelmetic to dogs, such as ivermectin for treatment of heartworms (see, Example 1) triturated with starch could be added to comprise 31.2% of the foregoing mixture.

[0041] The formula described for the exemplary product may be easily modified for delivery of actives to other species. For example, equine soft chews may be based on the same basic formula, substituting molasses powder, oat bran and apple for the bacon. Flavorings particularly appealing to cats include artificial soy based compounds with a fish-like flavor. Human recipients may prefer sweeter flavorings, such as sugars or molasses.

[0042] The soft chews of the invention may be packaged individually for administration and stable storage. Examples of suitable packaging materials include HDPE bottles or foil/foil packaging.

B. <u>Processes for Manufacturing Soft Chews of the Invention</u>

[0043] Active and inactive ingredients for a soft chew of the invention are added to a mixing vessel of a horizontal mixer capable of blending the material and casting it against the side of the mixing vessels. This action permits the ingredients to be well and consistently blended without application of heat or addition of pharmaceutical grade water to the mixture.

[0044] Horizontal mixers generally comprise a mixing chamber, an elongated, horizontal mixing shaft which rotates, and a plurality of mixing tools which depend generally perpendicularly from the horizontal shaft to rotate around the inside of the chamber. (See, e.g., U.S. Patent No. 5,735,603, the disclosure of which is incorporated herein by this reference). The mixing tools are configured and dimensioned as required for the mixing process to follow the shape of the chamber walls as rotated for proper mixing of all of material present. Some such mixing chambers are cylindrically shaped, while others are trough-shaped, such as mixers which are commonly referred to in the art as double-arm mixers or ribbon mixers.

[0045] In general, a horizontal mixer will have a horizontal mixing shaft extending out of the chamber at both ends. In a motorized mixer, at one end of the shaft, referred to as the drive end, the shaft is operably coupled to a drive motor for rotating the shaft. At the drive end, the shaft is typically coupled through a bearing structure located between the drive motor and the chamber. The bearing structure provides support of the shaft drive end and also ensures smooth rotation. A separate seal structure is often provided further in along the length of the shaft to seal it against leakage of material into and out of the mixing chamber.

[0046] A particularly preferred mixer for use in the invention used is a plough type ribbon mixer with optional agitating blades, sold under the FXM SERIES™ trademark by Littleford Day Corporation. A 200 kg capacity blender can be used for commercial scale production, and is capable of producing as little as 50 kg of chew mixture for research scale work. No heat is applied during mixing, and the blended product produced has a consistent weight, ingredient distribution and texture from batch to batch.

[0047] Preferably, dry ingredients of the chew mixture are blended first, then liquid ingredients (e.g., humectants and softening agents) are added and blended therein to form a thoroughly blended mixture. After blending, the chew mixture is discharged from a port through the blender into a suitable container for processing into individual dosage units with a forming machine.

[0048] A variety of forming equipment may be utilized in the invention, but those particularly preferred for use are molding machines developed for use in producing molded food products, such as pre-formed hamburger patties and chicken nuggets. For example, the molding machines disclosed in U.S. Patent Nos. 3,486,186; 3,887,964; 3,952,478; 4,054,967; 4,097,961; 4,182,003; 4,334,339; 4,338,702; 4,343,068; 4,356,595; 4,372,008; 4,535,505; 4,597,135; 4,608,731; 4,622,717; 4,697,308; 4,768,941; 4,780,931; 4,818,446; 4,821,376; 4,872,241; 4,975,039; 4,996,743; 5,021,025; 5,022,888; 5,655,436; and 5,980,228 (the disclosures of which are incorporated herein) are representative of forming equipment that may be utilized in the invention.

[0049] Preferred forming equipment for use in the invention includes the Formax F6™ molding machine made by the Formax Corporation. The F6 machine has the capabilities of 60 stokes per minute. A square forming die of 6" by 6" can be used to form approximately 16 chunk-like soft chew units per stroke, each unit weighing 4 grams and being approximately 5/8" by 5/8" in size. Dies for production of other shapes (e.g., bone shaped chews) may also be utilized.

[0050] In such a machine, a rotary valve opens to cause the chew mixture to flow through fill slots beneath into a first set of mold cavities. A mold plate is advanced, forcing the chew mixture into a second set of cavities, then the mold plate is retracted so the cycle can begin again. The molding mechanism is hydraulic, and works by light pressure on the molding plate, without application of heat.

[0051] A knockout mechanism is provided with cups that align with the cavities to eject molded mixture from all the mold plate cavities simultaneously. For molding soft chews of the invention, such a machine could produce an output per hour of approximately 57,600 units, assuming use of a blender mixture yielding 50,000 units per sub batch. Each batch of chews may be packaged in bulk or, preferably, each chew is then individually packaged for storage.

[0052] The invention having been fully described, its practice is illustrated by the examples provided below. Standard abbreviations and measurements apply throughout the examples unless a contrary definition is given. The examples do not limit the scope of the invention, which is defined entirely by the appended claims.

Example 1

IVERMECTIN SOFT CHEW FOR TREATMENT OF HEARTWORMS

[0053] An example of a soft chew suitable for delivery of an active is set forth in Formula 1 below.

Formula 1:	**Concetration % w/w**	**Ingredient**
41.90		Starch 1500, USP
1.0		Powdered Sugar, USP
2.0		Oat Bran, Food Grade
15.0		Bacon Flavor (Provesta™ 356), Food Grade
2.0		Polyethylene glycol 6000
20.0		Glycerin, USP
7.0		Vegetable Oil (soybean), USP
0.1		Tenox 4, Food Grade
1.0		Magnesium Stearate, USP
1.0		Yeast Flavoring
3.0		Croscarmellose, sodium N.F.
0.001		FD&C Carmine Dye

Example 2

METHOD FOR COATING ACTIVE INGREDIENTS OF SOFT CHEWS OF THE INVENTION

[0054] The active (ivermectin) was milled and screened through a 20 mesh screen. A 10% trituration was made by dry blending 100 grams of ivermectin and 900 grams of Starch 1500 for 3 to 5 minutes. The resultant trituration was fluidized in a fluidized bed column and a food grade coating (OPADRY™) was applied using a Wurster coater, a top spray fluidized coater, or other suitable device.

Example 3

EXEMPLARY METHOD OF MANUFACTURE FOR SOFT CHEWS OF THE INVENTION

[0055] All dry ingredients listed in Examples 1 and 2 except the oat bran were sifted through a 20 mesh screen, then placed with the bran into the mixing vessel of a horizontal mixing blender and mixed for 5 minutes. The glycerin was added slowly followed by the slow addition of the vegetable oil and Tenox 4 which had been added to the oil. The product was mixed for 3 minutes. The PEG 8000 was melted then added relatively quickly to the chew mixture, which was then mixed for an additional minute. The mixture resembled a "cookie dough-like" appearance.

[0056] The mixture was formed into individual chunks using a-Formax F6™ molding machine with dies for production of chunk-like shapes, and packaged for storage.

[0057] The invention having been fully described, its scope is defined by the claims appended hereto.

REFERENCES CITED IN THE DESCRIPTION

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Patentkrav

1. Fremgangsmåde til fremstilling af et velsmagende blødt, tygbart farmaceutisk produkt ("blødt tyggestykke" ("soft chew")), hvilken fremgangsmåde omfatter:
blanding af mindst én aktiv bestanddel med inaktive bestanddele til dannelse af en blanding med den mindst ene aktive bestanddel ensartet blandet deri, hvor tørre bestanddele blandes først, hvorefter flydende bestanddele tilsættes og iblandes uden påføring af varme og ved anvendelse af en horisontalmixer, der hvirvler blandingen til en partikelformig form;
hvor de inaktive bestanddele er valgt fra gruppen bestående af et smagsstof af fødevarekvalitet; et bindemiddel; et fyldemiddel; et blødgøringsmiddel; et antiklumpningsmiddel eller glittemiddel; et befugtningsmiddel, der omfatter glycerin eller propylenglycol; og mindst ét hjælpestof, der omfatter en stivelse, en cellulose eller en blanding deraf; og
formning af blandingen til individuelle bløde tyggestykker uden behov for et afkølingstrin, hvor formningen omfatter udstansning af de bløde tyggestykker fra et hulrum i en formplade.

2. Fremgangsmåde ifølge krav 1, hvor den mindst ene aktive bestanddel er valgt fra gruppen bestående af antibiotika, analgetika, antivirale midler, antifungale midler, anthelmintika, endoparasiticider, ektoparasiticider, hormoner, anti-inflammatoriske midler (herunder ikke-steroide anti-inflammatoriske midler), steroider, adfærdsmodificerende midler, vacciner, antacida, afføringsmidler, antikonvulsiva, sedativa, beroligende midler, antitussiva, antihistaminer, dekongestionsmidler, slimløsnende midler, appetitstimulerende og -undertrykkende midler, mineraler og vitaminer.

3. Fremgangsmåde ifølge krav 1, hvor smagsstoffet omfatter et smagsstof af ikke-animalsk oprindelse.

4. Fremgangsmåde ifølge krav 1, hvor fyldemidlet omfatter klid, gummi arabicum, pektiner, modificerede stivelser, alginater, carrageeniner, xanthangummier, carboxymethylcellulose, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, propylenglycolalginat,

polyvinylpyrrolidon, carboxyvinylpolymerer, polyethylenoxidpolymerer, talkum, dicalciumphosphat eller antacida.

5. Fremgangsmåde ifølge krav 1, der endvidere omfatter trinnet med at præparere en triturering af den aktive bestanddel med hjælpestoffet, inden den aktive bestanddel tilsættes til de inaktive bestanddele.

6. Fremgangsmåde ifølge krav 1, hvor den aktive bestanddel er overtrukket.

7. Fremgangsmåde ifølge krav 2, hvor den mindst ene aktive bestanddel er et anthelmintikum.

8. Fremgangsmåde ifølge krav 1, hvor blandingen blandes i en horisontalmixer, der omfatter et blandekammer, en langstrakt, horisontal blandeaksel, der roterer, og en flerhed af blandeværktøjer, som strækker sig vinkelret fra den horisontale aksel med henblik på at rotere omkring kammerets inderside.

9. Fremgangsmåde ifølge krav 1, hvor antiklumpningsmidlet eller glittemidlet omfatter magnesiumstearat, calciumstearat, fast polyethylenglycol, natriumlaurylsulfat eller blandinger deraf.

10. Fremgangsmåde ifølge krav 1, hvor blødgøringsmidlet omfatter vegetabilsk olie.