Title: IMPROVED DOSAGE FORM AND PROCESS

Abstract: A chewable dosage form is disclosed for the delivery of a variety of veterinary medicines to animals. The dosage form is particularly suited to the provisions of medicines which are heat and pH sensitive. This is achieved by utilising the gelatinisation of a functional protein, such as vital wheat gluten, to incorporate the medicine. Such gelatinisation occurs under relatively mild conditions of temperature, pressure and pH. A process to prepare the dosage forms is also disclosed in which the key processing steps are conducted in the temperature range of 30 °C up to a maximum of 70 °C and at a pH in the range of about 5.0 - 7.5.
Improved dosage form and process

Cross-Reference to Related Applications

The present application claims priority from Australian Provisional Patent Application No 2007902407 filed on 7 May 2007, the contents of which are incorporated herein by reference.

Field of the Invention

This invention relates to an improved dosage form for veterinary medicines, particularly to an improved chewable, semi moist, stable animal dosage form containing oral veterinary medicines, and to a process for producing such a dosage form.

Background Art

Small omnivores and carnivores, such as cats and dogs, often need to be treated with a veterinary medicine to treat a condition or to ward off a disease. For instance, it is likely that medicines such as antibiotics, non-steroidal anti-inflammatory drugs, drugs for cardiovascular disease and/or parasiticides will need to be administered to an animal at some stage during its life. The means for administering such medicine will depend on the nature of the condition to be treated. In theory, direct oral administration of a veterinary medicine to an animal is considered a quick and easy way to administer the medicine. However, there are relatively few products on the market which are palatable to the animal and therefore oral administration is often not a desirable mode of administration due to the unreliability of administering the correct dose of medicine to the animal.

There are a few products on the market which are palatable and chewable and able to deliver a variety of actives of veterinary medicine to an animal, particularly to small omnivores and carnivores such as cats and dogs. There exists in the market, tablets and a small number of "treat-like" oral vehicles containing a quantity of medicine, which if completely consumed by the animal to be treated allow the delivery of a specific dose of a desired medicine. Tablets make poor candidates for palatable and chewable dosage forms as they disintegrate readily and often have an inferior taste.
due to the fact the taste of the actives cannot be effectively masked. Visually they seem less attractive than the "treat-like" dosage forms. The "treat-like" dosage forms generally have greater acceptance by the target animals. Current "treat-like" products are primarily batch mixed followed by a separate moulding process. These processes depend on starch gelatinisation to form a solid chewable structure which requires heating. This has the disadvantage in that ingredients that are heat sensitive cannot be used in such "treat-like" products.

An alternative process to starch gelatinisation is protein gelatinisation. Traditional technology for the manufacture of textured vegetable protein (TVP) using a single screw extruder and high moisture extrusion cooking (HMEC) process technology using a twin screw extruder require elevated process temperatures of greater than 130 -150°C and elevated pressure of greater than 35-50 bar. Such processes are clearly unsuitable for temperature sensitive ingredients.

There is a clearly a need for an improved oral veterinary product and a process for producing such a product.

Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed in Australia before the priority date of each claim of this application.

Summary of the Invention

The present inventor have found an improved chewable dosage form for delivering a range of veterinary medicines including heat and pH sensitive actives, to an animal together with a process for making such a dosage form. The improved chewable dosage form is stable and palatable and comprises a unique combination of active ingredients, humectants and plasticisers in a gelatinised functional protein matrix having a specified moisture content and water activity. The present inventor have found that the improved chewable dosage form may be manufactured using a combination of protein gelatinisation and cold extrusion techniques under low temperatures and neutral pH. The conditions required by the process of the present
invention allow temperature and pH sensitive materials to be employed and in particular allows a greater range of active ingredients to be used than previously possible in prior art processes for producing palatable, chewable and stable animal dosage forms.

5 In a first aspect, there is provided a chewable, stable dosage form for animals comprising:

a) about 20.0 - 70.0% w/w of gelatinised functional protein matrix;

b) about 0.001 - 40,000% w/w of one or more active ingredients;

c) about 0.5 - 40.0% w/w of one or more plasticisers which includes one or more oils and/or water;

d) about 0.5 - 20.0% w/w of one or more humectants;

e) optionally about 0.05 - 5.00% w/w of one or more anti-microbials;

f) optionally about 0.05 - 5.00% w/w of one or more extrusion aids;

g) optionally about 0.05 - 50.00% w/w of one or more flavouring agents;

wherein c) - g) are incorporated in the gelatinised functional protein matrix and b) is incorporated in (i) the gelatinised functional protein matrix, (ii) a coating of the dosage form or (iii) both the gelatinised functional protein matrix and the coating,

the dosage form having a total moisture content in the range of about 0.5 - 40.0 % w/w and a water activity in the range of about 0.60 - 0.80.

The dosage form of the present invention comprises a gelatinised functional protein matrix in an amount of about 20.0 - 70.0% w/w. Preferably, the gelatinised functional protein is present in an amount of about 25.0 - 65.0 % w/w, more preferably about 30.0 - 60.0 % w/w.

The gelatinised functional protein matrix is formed from the gelatinisation of about 20.0 - 70.0% w/w of one or more functional proteins, preferably about 25.0 - 65.0 % w/w and more preferably about 30.0 - 60.0 % w/w.

The one or more functional proteins include but are not limited to vital wheat gluten, defatted soy flour, soy protein concentrate, soy protein isolate, corn gluten meal, mung beans, yeast by-products and mixtures thereof. In a preferred embodiment, the functional protein is vital wheat gluten.

It will be understood that the term "functional protein" refers to a protein that has a high level, usually greater then about 65%, preferably greater then about 75%, more preferably about 80% or more of intact protein i.e. wherein the tertiary and quaternary structure of the protein has undergone minimal denaturation. Preparation of
a functional protein is achieved largely through mechanical processing in a way so as to preserve the tertiary and quaternary structure.

The present inventor have found that the presence of one or more functional proteins in the protein matrix has an important effect on the quality of the binding and solid structure formation of the dosage form of the present invention. It will be understood that gelatinisation of the functional protein involves breaking of the tertiary and quaternary structure of the functional protein, by a means that includes but is not limited to hydration, to form a denatured functional protein followed by realignment of the protein, by a means that includes but is not limited to re-hydration. The inventor has found that functional proteins, such as wheat gluten, possess a special visco-elastic property when re-hydrated which contributes to the above noted rheological features of the dosage form product of the present invention.

The improved binding properties formed at low to moderate temperatures and neutral pH allows the utilisation of non-binding materials for modifying product features including but not limited to the addition of active ingredients, humectants, flavouring agents etc.

Accordingly, it will be appreciated that starches are not required in the formation of the dosage form of the invention. As explained above, to cause starches to gelatinise requires substantially higher temperatures than that envisaged in the present invention. Therefore, it is desirable that starches be excluded although it is recognised that small amounts may be included, for example, as carriers or additives in relation to other ingredients. However, the level of inclusion will not contribute to the working of the invention and will certainly not detract from achieving the dosage form through a process of gelatinisation of a functional protein. In the dosage form of the invention, there would be less then about 0.1% w/w of gelatinised starch.

The dosage form of the present invention includes one or more active ingredients in an amount of about 0.001 - 40.000 % w/w. Preferably, the one or more active ingredients is present in an amount of about 0.005 - 35.000 % w/w, more preferably about 0.01 - 30.00 % w/w.

In one embodiment, the one or more active ingredients is included only within the functional protein matrix.
In another embodiment, the one or more active ingredients is incorporated within the functional protein matrix and a coating of the dosage form of the present invention.

In yet another embodiment, the one or more actives is incorporated only within a coating of the dosage form. Preferably, one or more process sensitive actives is incorporated only within a coating of the dosage form. An example of a process sensitive active is one that does not tolerate the moisture content and/or mechanical energy used in the formation of the dosage product form.

Accordingly, the dosage form of the present invention allows the simple oral administration of veterinary medicines to animals, preferably small omnivores and carnivores, such as cats and dogs.

The present inventor have been able to incorporate temperature and/or pH sensitive and/or process sensitive active ingredients into the dosage form of the present invention. The one or more actives include but are not limited to the group consisting of antibiotics such as penicillins including penicillin-V, penicillin-G, amoxicillin, ampicillin and cloxacillin; cephalosporin's including cefalexin, cefuroxime and cefprozil; fluoroquinolones including flumequine, enrofloxacin, orbifloxacin and marbofloxacin; tetracycline's including oxytetracycline and doxycycline; macrolides including erythromycin and azithromycin; non-steroidal anti-inflammatories including carprofen, meoxicam, aspirin, phenylbutazone and etodolac; drugs for treating cardiovascular disease including benazepril, enalapril, pimobendan, milophyline and etarninphylline; parasiticides such as benzimidazoles including albendazole, fenbendazole, oxibendazole and pro-benzimidazole febantel; macrocyclic lactones such as abamectin, ivermectin, milbemycin, moxidectin, selamectin and doramectin; and other parasiticides including praziquantel, pyrantel embonate and oxantel embonate and mixtures thereof.

The dosage form of the present invention includes one or more plasticisers which includes one or more oils and/or water in an amount of about 0.5 - 40.0% w/w. Preferably, the one or more plasticisers is present in an amount of about 5.0 - 35.0% w/w, more preferably about 10.0 - 30.0% w/w.
The one or more plasticisers include one or more oils and/or water and may additionally include one or more other plasticisers. The oils include but are not limited to vegetable oil, olive oil, castor oil, sesame oil, soybean oil, sunflower oil, paraffin oil, fractionated coconut oil, cod liver oil and mixtures thereof. Other plasticisers include but are not limited to glycerol, propylene glycol, sorbitol, ethylene glycol, and mixtures thereof. Preferably, the plasticiser is a combination of vegetable oil and water.

The inventor has found that the inclusion of one or more plasticisers is important in a) ensuring that the dosage form product of the present invention retains a rubbery, pliable texture, thereby making it chewable and b) reducing friability such that the dosage form has a low friability, even during the chewing process. This has the advantage of allowing the one or more active ingredients to remain in the dosage form product until it has been chewed and then digested by the animal.

The dosage form of the present invention includes one or more humectants in an amount of about 0.5 - 20.0% w/w. Preferably, the humectant is present in an amount of about 1.0 - 17.5% w/w, more preferably about 2.5 - 15.0% w/w.

The one or more humectants traps water, making it unavailable for microbial growth. The one or more humectants include but are not limited to salts such as sodium chloride, potassium chloride and lithium chloride; glycerol; sugars such as glucose, fructose, sucrose and lactose; propylene glycol; polyols such as sorbitol, xylitol and maltitol, polymeric polyols such as polydextrose; natural extracts such as quila; urea; lactic acid and mixtures thereof. Preferred sugars include but are not limited to glucose, sucrose, fructose, and mixtures thereof. Preferred salts include but are not limited to sodium chloride, potassium chloride, and mixtures thereof. Preferably, the humectants are sucrose and/or sodium chloride or glycerol and/or propylene glycol.

The dosage form of the present invention has a total moisture content in the range of about 0.5-40.0% w/w, and may be classed as a semi-moist product or as a product having an intermediate moisture content. The present inventor have found that the presence of one or more humectants is important in protecting the semi-moist dosage form from microbial growth.
The dosage form of the present invention has a water activity in the range of about 0.60 - 0.80, preferably in the range of about 0.60 - 0.78, more preferably in the range of about 0.60 - 0.75. A water activity below 0.80 inhibits the microbial growth and also the dependence on antimicrobials.

The pH of the dosage form of the present invention is in the range of about 5.0 - 7.5, preferably about 5.5 - 7.5.

The present inventor have found that the pH and the water activity of the dosage form product of the present invention are important in determining the shelf life and hence stability of the product.

The dosage form of the present invention optionally comprises about 0.05 - 5.00% w/w of one or more anti-microbial agents. Preferably, in an amount of about 0.1 - 3.0% w/w, more preferably about 0.25 - 2.50% w/w. The inclusion of one or more anti-microbial agents serves to inhibit possible microbial growth. The one or more anti-microbials include but are not limited to sorbate salts such as sodium or potassium sorbate; sorbic acid; citric salts such as sodium or potassium citrate; citric acid; propionate salts such as sodium or potassium propionate; propionic acid; methyl, ethyl, propyl, paraben; pH modifiers such as phosphoric acid; and mixtures thereof.

The dosage form of the present invention optionally comprises about 0.05 - 5.00% w/w of one or more extrusion aids. Preferably, the one or more extrusion aids is present in an amount of about 0.075 - 4.000% w/w, more preferably 0.1 - 2.5 % w/w.

The one or more extrusion aids include but are not limited to elemental sulphur; sulphur containing amino acids; polysaccharides such as alginate; guar gum; gelatine; carrageenan; and emulsifiers such as lecithin; and mixtures thereof.

The present inventor have found that the utilisation of one or more extrusion aids enhances the binding characteristics of the chosen functional proteins.

The dosage form of the present invention optionally comprises about 0.05 - 50.00% w/w of one or more flavouring agents. Preferably, the one or more flavouring agents is present in an amount of about 1.0 - 45.0 % w/w, more preferably about 10.0 - 40.0 % w/w.
The one or more flavouring agents enhance the palatability of the dosage form product of the present invention. The one or more flavouring agents include but are not limited to meat meals; meat by-product meals; poultry meals; poultry by-product meals; fish meals; fish by-product meals; digests; and mixtures thereof.

The dosage form of the present invention may additionally comprise one or more other ingredients such as: colouring agents including but not limited to iron oxide; non-binding fillers including but not limited to grain flour and anti-oxidants, preferably in an amount of 0.01 - 0.10 % w/w including but not limited to butylated hydroxytoluene and butylated hydroxyanisole.

The dosage form of the present invention may optionally be coated to an amount of 0.1 — 5.0% w/w. The coating may be selected from any coating for pet food known in the art and includes but is not limited to protective coatings such as povidone and methyl cellulose, etc. The coating may further include other ingredients including but not limited to microbial inhibitors, vitamins, minerals, flavour enhancers and active ingredients, particularly those that are process sensitive. Accordingly, the coating may be used to add a barrier against moisture, to add microbial inhibitors, vitamins and minerals, flavour enhancers and/or include actives into the formulation, particularly process sensitive actives.

In a preferred embodiment according to the first aspect of the invention, there is provided a chewable, stable dosage form for animals comprising:

a) about 20.0 - 70.0% w/w of gelatinised functional protein matrix;
b) about 0.001 - 40.000% w/w of one or more active ingredients;
c) about 0.5 - 40.0% w/w of one or more plasticisers which includes one or more oils and/or water;
d) about 0.5 - 20.0% w/w of one or more humectants;
e) optionally about 0.05 - 5.00% w/w of one or more anti-microbials;
f) optionally about 0.05 - 5.00% w/w of one or more extrusion aids;
g) optionally about 0.05 - 50.00% w/w of one or more flavouring agents;

wherein b) - g) are incorporated in the gelatinised functional protein matrix and the dosage form has a total moisture content in the range of about 0.5 - 40.0 % w/w and a water activity in the range of about 0.60 - 0.80.
In a more preferred embodiment according to the first aspect of the invention, there is provided a chewable, stable dosage form for animals comprising:

a) about 30.0 - 60.0% w/w of gelatinised functional protein matrix preferably formed from gelatinisation of one or more functional proteins selected from the group consisting of: vital wheat gluten, defatted soy flour, soy protein concentrate, soy protein isolate, corn gluten meal, mung beans, yeast by-products and mixtures thereof.

b) about 0.01 - 30.00% w/w of one or more active ingredients, preferably selected from the group consisting of penicillins; cephalosporins; fluoroquinolones; tetracycline's; macrolides; non-steroidal antiinflammatories; drugs for treating cardiovascular disease; parasiticides; macrocyclic lactones and mixtures thereof;

c) about 10.0 - 30.0% w/w of one or more plasticisers which includes one or more oils and/or water and optionally one or more plasticisers selected from the group consisting of glycerol; propylene glycol; ethylene glycol; sorbitol; and mixtures thereof;

d) about 2.5 - 15.0% w/w of one or more humectants, preferably selected from the group consisting of sugars, salts, glycerol, and mixtures thereof;

e) about 0.25 - 2.50% w/w of one or more anti-microbials, preferably selected from the group consisting of sorbate salts, preferably sodium or potassium sorbate; sorbic acid; citric salts, preferably sodium or potassium citrate; citric acid; propionate salts, preferably sodium or potassium propionate; propionic acid; methyl, ethyl, propyl, paraben; pH modifiers, preferably phosphoric acid; and mixtures thereof;

f) about 0.1 - 2.5% w/w of one or more extrusion aids, preferably selected from the group consisting of elemental sulphur; sulphur containing amino acids; polysaccharides, preferably alginate; guar gum; gelatine; carrageenan; and emulsifiers, preferably lecithin, and mixtures thereof;

g) about 10.0 - 40.0% w/w of one or more flavouring agents, preferably selected from the group consisting of meat meals; meat by-product meals; poultry meals; poultry by-product meals; fish meals; fish by-product meals; digests; and mixtures thereof;

wherein b) - g) are incorporated in the functional protein matrix and the dosage form has a total moisture content of about 0.5 - 40.0% w/w and a water activity of about 0.60 - 0.80.
In a second aspect, there is provided a process for preparing a chewable, stable animal dosage form comprising the steps of:

i) combining:
   a) about 20 - 70% w/w of one or more functional proteins;
   b) optionally about 0.001 - 40.000% w/w of one or more active ingredients;
   c) optionally about 0.5 - 40.0% w/w of one or more plasticisers which includes one or more oils and/or water;
   d) about 0.5 - 20.0% w/w of one or more humectants;
   e) optionally about 0.05 - 5.0% w/w of one or more anti-microbials;
   f) optionally about 0.05 - 5.00% w/w of one or more extrusion aids;
   g) optionally about 0.05 - 50.00% w/w of one or more flavouring agents;

and mixing for a time sufficient to form a premix in which a) - g) are dispersed therein;

ii) adding to the premix:
   h) 0.05 - 40.00% w/w water;
   i) optionally about 0.5 - 40.0% of one or more of the plasticisers which includes one or more oils and/or water;

and mixing for a time sufficient to allow hydration of the one or more functional proteins to form a hydrated protein premix, wherein the one or more plasticisers is added before, during or after hydration;

iii) providing sufficient mechanical work input to the hydrated protein premix so as to form a gelatinised functional protein matrix having b) - i) incorporated therein;

iv) extruding the gelatinised functional protein matrix containing b) - i) into a dosage form;

v) optionally drying the dosage form;

vi) optionally cooling the dosage form; and

vii) optionally coating the dosage form with a coating which optionally includes about 0.001 - 40.000% w/w of one or more active ingredients;

   to provide a dosage form having a total moisture content in the range of about 0.5 - 40.0 % w/w and a water activity in the range of about 0.60 - 0.80;

   wherein the one or more plasticisers is added at step i), step ii) or at both steps i) and ii) and the one or more active ingredients is added at step i), in the coating at step vii), or at both steps i) and vii); and

   wherein steps i) - v) are carried out at a temperature in the range of from about 30°C up to a maximum of 70°C and at a pH in the range of about 5.0 - 7.5.
In a third aspect, there is provided a chewable, stable animal dosage form produced according to the process defined in the second aspect of the invention.

The one or more functional proteins, one or more active ingredients; one or more plasticisers; one or more humectants; one or more anti-microbials; one or more extrusion aids; one or more flavouring agents and coating are as described above in the first aspect of the invention.

According to the first aspect of the invention, the ingredients c) - g) and optionally b) are incorporated within the functional gelatinised matrix, while in the second aspect the functionalised gelatinised matrix has ingredients b) - i) incorporated therein. Preferably, ingredients c) - g) and optionally b) in the first aspect and ingredients b) - i) in the second aspect are dispersed throughout the functional gelatinised matrix, more preferably uniformly dispersed throughout the matrix.

The process for preparing a chewable semi-moist animal dosage form according to the present invention is a new low temperature protein extrusion process for the formation of a protein based structure that includes one or more active ingredients.

Step i) of the process of the invention requires combining ingredients a) - g) of the formulation and mixing for a time sufficient to form a premix in which a) - g) are dispersed. Preferably, the ingredients are uniformly dispersed in the premix. Even more preferably, the premix is a dry blend. The present inventor have found that adequate mixing prior to processing is important, particularly with respect to the one or more active ingredients.

The b) one or more active ingredients is added at step i), in the coating at step vii), or at both steps i) and vii). It will be understood, that the total amount of the one or more active ingredients added in the process is in the amount of about 0.001 - 40.000% w/w. In cases where the one or more actives is added in step i) and the concentration of the one or more actives is low, such as below a concentration of 1%, then pre-dispersion of the active with another excipient prior to addition to the premix is preferable in order to assist in obtaining a uniform premix.

Mixing may be carried out in batch or continuous mixing modes. Mixing may be carried out in any suitable vessel. Examples of suitable mixing vessels for batch mixing include but are not limited to ribbon blenders, cone blenders, vertical mixers.
and auger mixers. Examples of suitable mixing vessels for continuous mixing include but are not limited to vertical mixers and ribbon blenders.

Hydration of the one or more functional proteins to form a hydrated protein premix occurs in step (ii) of the process. Throughout the specification, this step may be referred to as the pre-conditioning step. Accordingly, in order for hydration to occur, step ii) of the process of the invention requires that h) about 0.5 - 40.0% w/w water is added to the premix. Preferably, the hydration time is in the range of 40 - 110 seconds, more preferably 50 - 100 seconds.

It will be understood that the hydration step breaks up the 3-dimensional structure of the one or more functional proteins. The present inventor have found that the provision of sufficient hydration time to allow wetting of the functional protein in the dry blend to form a hydrated protein blend is an important factor of the process. The inventor has found that a sufficiently long process time of greater than 40 seconds and less than about 100 seconds desirably leads to uniform hydration of the protein substrates. By wetting, it is meant that sufficient hydration has occurred to allow a suitable granule of the hydrated protein premix to be formed with adequate mechanical force. Whilst it is preferably that the one or more proteins are completely hydrated, it will be appreciated that partial hydration of the one or more proteins is also possible according to the invention.

The one or more plasticisers may be added at step i), step ii) or at both steps i) and ii). It will be understood that the total amount of one or more plasticisers added in the process is in the amount of about 0.5 - 40.0% w/w. Preferably, one or more of the plasticisers is added at step ii).

In a preferred embodiment, step ii) further comprises the addition of one or more oxidants, preferably in an amount of 0.01 - 0.1 % w/w. Preferably the ingredients in step ii) of the process are homogenised.

Step ii) preferably takes place in a pre-conditioner vessel such as a ribbon blender, or any variation thereof.

Step iii) of the process of the invention requires sufficient mechanical work input to the hydrated protein premix so as to form a gelatinised functional protein
matrix containing b) - i). The mechanical work forces the hydrated protein blend from step (ii), wherein the one or more proteins is in a denatured form, to realign. It will be understood that mechanical work input refers to the specific mechanical energy (SME) needed to mix and/or knead the hydrated protein blend to form the gelatinised functional protein matrix having the desired texture and consistency required to hold the final dosage form together. Preferably, the specific mechanical energy (SME) is in the range of about 0.03 - 0.06 kW/h/kg, more preferably, about 0.035 - 0.055 kW/h/kg.

It will be appreciated that the heating and/or cooling may occur during step (iii) to aid in achieving the desired consistency and/or texture. The present inventor have found that it is very important to ensure that the maximum exposure temperature within the vessel during step iii) is no greater than 70°C and that the maximum exposure time to the elevated temperature of 70°C within the vessel is preferably very short in the range of 20 - 40 seconds, i.e. it is important that the dry blend containing the hydrated protein premix and the forming gelatinised functional protein are exposed to a temperature of no greater than 70°C. According to the process of the present invention, the temperature is in the range of from about 30°C up to a maximum of 70°C, more preferably about 35- 65°C and even more preferably about 37.5 - 62.5°C.

Preferably step iii) takes place in an extrusion vessel. Extruders include but are not limited to single, double (co- or counter-rotating) extruders or any variation thereof.

Step iv) of the process involves extruding the gelatinised functional protein matrix into a dosage form. This includes sizing and shaping the gelatinised functional protein matrix into the desired size and shape.

It may or may not be necessary to dry and/or cool the dosage form. For instance, if the water content is too high, further drying may be required.

Step v) of the process involves optionally drying the dosage form. Drying may be achieved using continuous or batch style drying, including but limited to the use of a tray dryer or fluid bed.

Step vi) involves optionally cooling the dosage form. Cooling may be achieved using a continuous or batch styled cooler, including but not limited to the use of a tray cooler. Preferably cooling takes place at temperature in the range of about 2 - 30°C.
Step vii) involves optionally coating the dosage form. This may be carried out according to standard procedures. Other ingredients as indicated above in the first aspect of the invention may be included in the coating at this stage.

The process of the present invention provides a dosage form having a total moisture content of about 0.5-40 % w/w, preferably about 5 - 30 % w/w, more preferably about 10 - 25% w/w. A moisture content in this range has been found by the inventor to form a semi-moist chewable and pliable product.

The process of the present invention provides a dosage form having a water activity of about 0.60 - 0.8. A water activity below 0.8 inhibits the microbial growth and also the dependence on antimicrobials.

The present inventor have found that it is very important that steps i) - v) are carried out at a temperature in the range of from about 30°C up to a maximum of 70°C, preferably about 35 - 65°C, and more preferably about 37.5 - 62.5 °C. Carrying out the process in this temperature range allows the use of temperature sensitive ingredients, such as temperature sensitive active ingredients.

Steps i), ii) and v) of the process of the present invention are preferably carried out at ambient pressure. Preferably steps iii) and iv ) of the process are carried out at elevated pressures, preferably for short periods of time such as 50 - 60 seconds.

A further advantage of the process of the present invention is the fact that it is carried at close to neutral pH, specifically in the pH range of about 5.0 - 7.5, preferably about 5.5 - 7.0. This again allows a range of ingredients to be used in the process, specifically pH sensitive ingredients.

The process of the present invention may further comprise the addition of one or more other ingredients such as: colouring agents including but not limited to iron oxide; non-binding fillers including but not limited to grain flour and anti-oxidants including but not limited to butylated hydroxy toluene and butylated hydroxyanisole.

The process of the invention may further include the optional step of coating the dosage form. The dosage form may optionally be coated to an amount of 0.1 - 5.0%
w/w. The coating is as described above in relation to the first and second aspects of the invention.

In a preferred embodiment, there is provided a process for preparing a chewable, stable animal dosage form comprising the steps of:

i) combining:
   a) about 20.0 - 70.0% w/w of one or more functional proteins;
   b) about 0.001 - 40.000% w/w of one or more active ingredients;
   c) about 0.5 - 20.0% w/w of one or more humectants;
   d) optionally about 0.05 - 5.00% w/w of one or more anti-microbials;
   e) optionally about 0.05 - 5.00% w/w of one or more extrusion aids;
   f) optionally about 0.05 - 50.00% w/w of one or more flavouring agents;

and mixing for a time sufficient to form a premix in which a) - f) are dispersed therein;

ii) adding to the premix:
   g) 0.05 - 40.00% w/w water;
   h) about 0.5 - 40.0% of one or more of the plasticisers which includes one or more oils and/or water;

   and mixing for a time sufficient to allow hydration of the one or more functional proteins to form a hydrated protein premix, wherein the one or more plasticisers is added before, during or after hydration;

iii) providing sufficient mechanical work input to the hydrated protein premix so as to form a gelatinised functional protein matrix having b) - h) incorporated therein;

iv) extruding the gelatinised functional protein matrix containing b) - h) into a dosage form;

v) optionally drying the dosage form;

vi) optionally cooling the dosage form; and

vii) optionally coating the dosage form with a coating;

   to provide a dosage form having a total moisture content in the range of about 0.5 - 40 % w/w and a water activity in the range of about 0.60 - 0.80;

   wherein steps i) - v) are carried out at a temperature in the range of from about 30°C up to a maximum of 70°C and at a pH in the range of about 5.0 - 7.5.

In a more preferred embodiment, there is provided a process for preparing a chewable, stable animal dosage form comprising the steps of:
i) combining in a vessel, preferably selected from the group consisting of ribbon blenders, cone blenders, vertical mixers and auger mixers:

   a) 20 - 70% w/w one or more functional proteins, preferably selected from the group consisting of vital wheat gluten, defatted soy flour, soy protein concentrate, soy protein isolate, corn gluten meal, mung beans, yeast by-products and mixtures thereof;

   b) 0.001 - 40% w/w one or more active ingredients, preferably selected from the group consisting of penicillins; cephalosporin's; fluoroquinolones; tetracycline's; macrolides; non-steroidal antiinflammatories; drugs for cardiovascular disease, preferably benazepril; parasiticides; macrocyclic lactones and mixtures thereof;

   c) 0.5 - 20 % w/w one or more humectants selected from the group consisting of sugars, salts, glycerol, and mixtures thereof;

   d) 0.5 - 5 % w/w one or more anti-microbials, preferably selected from the group consisting of sorbate salts, preferably sodium or potassium sorbate; sorbic acid; citric salts preferably sodium or potassium citrate; citric acid; propionate salts preferably sodium or potassium propionate; propionic acid; methyl, ethyl, propyl, paraben; pH modifiers preferably phosphoric acid; and mixtures thereof;

   e) 0.05 - 5 % w/w one or more extrusion aids, preferably selected from the group consisting of elemental sulphur; sulphur containing amino acids; polysaccharides preferably alginate; guar gum; gelatine; carrageenan; and emulsifiers preferably lecithin and mixtures thereof;

   f) 0.05 - 50% w/w one or more flavouring agents, preferably selected from the group consisting of meat meals; meat by-product meals; poultry meals; poultry by-product meals; fish meals; fish by-product meals; digests; and mixtures thereof;

   and batch mixing in a blender, preferably a cone blender or a ribbon blender, or continuously mixing in a mixer, preferably a vertical mixer, for a time sufficient to form a dry premix in which a) - f) are uniformly dispersed;

   ii) transferring the dry blend to a pre-conditioner vessel and adding to the dry premix:

   g) 0.5 - 40% w/w water;

   h) 0.5 - 40% w/w one or more plasticisers, selected from the group consisting of water; glycerol; propylene glycol; and sorbitol;

   i) 0.01 - 0.1% w/w one or more oxidants;

   mixing for a time sufficient to allow complete hydration of the one or more proteins to form a hydrated protein blend;

   iii) transferring the hydrated protein blend to an extrusion vessel, preferably selected from the group consisting of single or double (co- or counter-rotating) screw extruders,
and providing specific mechanical energy (SME) in the range of 0.04 - 0.06 kW/h/kg to form a gelatinised functional protein matrix containing b) - i);
iv) extruding the gelatinised functional protein matrix containing b) - i) into a dosage form;
v) optionally drying the dosage form; and
vi) optionally cooling the dosage form;

... 0.06 kW/h/kg to form a gelatinised functional protein matrix containing b) - i);
iv) extruding the gelatinised functional protein matrix containing b) - i) into a dosage form;
v) optionally drying the dosage form; and
vi) optionally cooling the dosage form;

... provide a dosage form having a total moisture content of about 10-30 % w/w and a water activity of about 0.60 - 0.8;
... steps i) - v) are carried out at a temperature in the range of from about 3 °C up to a maximum of 7 °C and at a pH in the range of about 5.0 - 7.5.

In a particularly preferred embodiment, there is provided a process for preparing a chewable, stable animal dosage form comprising the steps of:
i) combining in a vessel a ribbon blender:
a) 20 - 70 % w/w vital wheat gluten;
b) 0.001 - 40% w/w one or more active ingredients, preferably selected from the group consisting of penicillins; cephalosporin's; fluoroquinolones; tetracycline's; macrolides; non-steroidal anti-inflammatory drugs; drugs for cardiovascular disease, preferably benazepril; parasiticides; macrocyclic lactones and mixtures thereof;
c) 0.5 - 20 % w/w mixture of sugar and salt;
d) 0.5 - 5 % w/w potassium sorbate;
e) 0.05 - 50% w/w mixture of meat meal and poultry meal;
and batch mixing in the ribbon blender for a time sufficient to form a dry premix in which a) - e) are uniformly dispersed;
H) transferring the dry premix to a pre-conditioner vessel and adding to the dry premix a homogenised mixture of:
f) 0.5 - 40% w/w water;
g) 0.5 - 40% w/w vegetable oil;
h) 0.01 - 0.1% w/w butylated hydroxy toluene;
mixing for a time sufficient to allow complete hydration of the one or more proteins to form a hydrated protein premix;
iii) transferring the hydrated protein premix to an extrusion vessel and providing specific mechanical energy (SME) in the range of 0.035 - 0.06 kW/h/kg to form a gelatinised functional protein matrix containing b) - h);
iv) extruding the gelatinised functional protein matrix containing b) - h) into a dosage form; and
v) drying the dosage form;

to provide a dosage form having a total moisture content of about 10-30 % w/w and a water activity of about 0.60 - 0.8;

wherein steps i) - v) are carried out at a temperature in the range of from about 30°C up to a maximum of 70°C and at a pH in the range of about 5.0 - 7.5.

The dosage form of the present invention is able to be chewed by an animal in need of administration of a veterinary medicine. Whilst the dosage form is applicable to all animals able to effectively chew a pliable structure it is particularly suited to small omnivores and carnivores such as cats and dogs.

Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

As used herein the term "stable" means chemical and physical stability of the active ingredients of the dosage form over at least a 3 month period, preferably 6 months, when stored at about 30°C/60% relative humidity. By "chemical stability", it is intended to mean that the concentration of the active ingredients, remains within about ±10%w/w of the stated concentration of the active ingredients and the pH of the dosage form remains in the range of about 5.0 - 7.5. By "physical stability", it is intended to mean that the appearance and texture of the formulation is semi-moist and pliable, such that the moisture content remains in the range of about 10 - 30 %w/w.

The availability of ingredients is shown in the below Tables.

Table 1 - Availability of preferred active ingredients

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Available from</th>
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<tbody>
<tr>
<td>Meloxicam</td>
<td>Pacific Resources International</td>
</tr>
<tr>
<td>Praziquantel</td>
<td>Pacific Resources International</td>
</tr>
<tr>
<td>Pyrantel Embonate</td>
<td>Pacific Resources International</td>
</tr>
<tr>
<td>Febantel</td>
<td>Tiger Chemical</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>Pacific Resources International</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Pacific Resources International</td>
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</table>
Table 2 - Availability of preferred functionalised proteins

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Available from</th>
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<tbody>
<tr>
<td>Vital Wheat Gluten</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Soy Protein Isolate</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Corn Gluten Meal</td>
<td>Sinopharm</td>
</tr>
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</table>

Table 3 - Availability of preferred plasticisers

<table>
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<tr>
<td>Vegetable Oil</td>
<td>Croda</td>
</tr>
<tr>
<td>Sesame Oil</td>
<td>Bronson and Jacobs</td>
</tr>
<tr>
<td>Fractionated Coconut Oil</td>
<td>Croda</td>
</tr>
<tr>
<td>Propylene Glycol</td>
<td>Campbell Brothers</td>
</tr>
<tr>
<td>Glycerol</td>
<td>Asia Pacific Specially Chemicals</td>
</tr>
</tbody>
</table>

Table 4 - Availability of preferred anti-microbials

<table>
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<th>Ingredient</th>
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</tr>
</thead>
<tbody>
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<td>Phenonip</td>
<td>Bronson and Jacobs</td>
</tr>
<tr>
<td>Sodium Propionate</td>
<td>Asia Pacific Specially Chemicals</td>
</tr>
<tr>
<td>Potassium Sorbate</td>
<td>Asia Pacific Specially Chemicals</td>
</tr>
</tbody>
</table>

Table 5 - Availability of preferred humectants

<table>
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<th>Ingredient</th>
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<tr>
<td>Propylene glycol</td>
<td>Pacific Resource</td>
</tr>
<tr>
<td>Polyethylene glycol</td>
<td>Pacific Resource</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>Manildra</td>
</tr>
</tbody>
</table>
Table 6 - Availability of preferred flavour enhancers

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Available from</th>
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<tbody>
<tr>
<td>Meat Meal</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Poultry Meal</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Digests</td>
<td>Sinopharm</td>
</tr>
</tbody>
</table>

Modes for Carrying out the Invention

In order to better understand the nature of this invention, a number of examples will now be described.

Example 1 - Dosage Form

A chewable, stable dosage form according to the invention has the ingredients as listed in Table 7.

Table 7:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity w/w (%)</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meloxicam</td>
<td>0.5%</td>
<td>Pacific Resources International</td>
</tr>
<tr>
<td>Vital Wheat Gluten</td>
<td>31.0%</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Meat Meal</td>
<td>19.5%</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Poultry Meal</td>
<td>19.5%</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Salt</td>
<td>0.5%</td>
<td>Manildra</td>
</tr>
<tr>
<td>Sugar</td>
<td>1.25%</td>
<td>Manildra</td>
</tr>
<tr>
<td>Potassium Sorbate</td>
<td>1.0%</td>
<td>APS</td>
</tr>
<tr>
<td>Butylated hydroxytoluene</td>
<td>0.75%</td>
<td>APS</td>
</tr>
<tr>
<td>Glycerol</td>
<td>11.0%</td>
<td>APS</td>
</tr>
<tr>
<td>Vegetable Oil</td>
<td>1.5%</td>
<td>APS</td>
</tr>
<tr>
<td>Iron Oxide</td>
<td>0.5%</td>
<td>Sigma Aldrich</td>
</tr>
<tr>
<td>Water</td>
<td>13.0%</td>
<td>Potable Water</td>
</tr>
</tbody>
</table>
The dosage form has a surface pH of about 6.01, a water content of about 13% w/w and a water activity of about 0.71.

Example 2

A chewable, stable dosage form according to the invention has the ingredients as listed in Table 8, wherein the active ingredient is a combination of pyrantel, febantel and praziquantel.

Table 8

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity w/w (%)</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praziquantel</td>
<td>3.65%</td>
<td>Pacific Resources International</td>
</tr>
<tr>
<td>Pyrantel</td>
<td>10.47%</td>
<td>Pacific Resources International</td>
</tr>
<tr>
<td>Febantel</td>
<td>18.31%</td>
<td>Tiger Chemical</td>
</tr>
<tr>
<td>Vital Wheat Gluten</td>
<td>31.0%</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Meat Meal</td>
<td>3.54%</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Poultry Meal</td>
<td>3.54%</td>
<td>Sinopharm</td>
</tr>
<tr>
<td>Salt</td>
<td>0.5%</td>
<td>Manildra</td>
</tr>
<tr>
<td>Sugar</td>
<td>1.25%</td>
<td>Manildra</td>
</tr>
<tr>
<td>Potassium Sorbate</td>
<td>1.0%</td>
<td>APS</td>
</tr>
<tr>
<td>Butylatedhydroxytoluene</td>
<td>0.75%</td>
<td>APS</td>
</tr>
<tr>
<td>Glycerol</td>
<td>11.0%</td>
<td>APS</td>
</tr>
<tr>
<td>Vegetable Oil</td>
<td>1.5%</td>
<td>APS</td>
</tr>
<tr>
<td>Iron Oxide</td>
<td>0.5%</td>
<td>Sigma Aldrich</td>
</tr>
<tr>
<td>Water</td>
<td>14.0%</td>
<td>Potable Water</td>
</tr>
</tbody>
</table>

The dosage form has a surface pH of about 6.01, a water content of about 13% w/w and a water activity of about 0.71.
Example 3

A process steps of forming the dosage form according to Example 1 will now be described.

i. Meloxicam, vital wheat gluten, meat and poultry meal, salt, sugar, potassium sorbate and iron oxide were combined into a ribbon blender and mixed for approximately 10 minutes,

ii. The vegetable oil, glycerol and butylatedhydroxy toluene were homogenised for approximately 2 minutes in a 10 litre tank with stirrer.

iii. The dry mix from (i) was transferred to the preconditioner, and water followed by the homogenised mix from (ii) were added. Resonance in the preconditioner was in the order of 50 < t < 100 seconds.

iv. The preconditioned mix was transferred to the extruder, and a specific mechanical energy in the order of 0.035 — 0.055 kW/h/kg applied at a temperature in the order of 30-70°C.

v. The extrudate was sized and cut accordingly, and dried to a total moisture content of 16% using a continues oven drier/coolor at a temperature <60°C for 20 minutes to form a dosage form according to the invention.

The resulting dosage form has a pH of about 6.01 and a water activity of about 0.71.

Digestibility Studies

Digestibility studies were carried out on a dosage form according to Example 1. It was found that about 92.5% of the product was soluble in pepsin.

It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.
CLAIMS:

1. A chewable, stable dosage form for animals comprising:
   a) about 20.0-70.0% w/w of gelatinised functional protein matrix, the functional protein having an intact protein contact of greater then about 65% w/w;
   b) about 0.001 - 40.000% w/w of one or more active ingredients;
   c) about 0.5 - 40.0% w/w of one or more plasticisers which includes one or more oils and/or water;
   d) about 0.5 - 20.0% w/w of one or more humectants;
   e) optionally about 0.05 - 5.00% w/w of one or more anti-microbials;
   f) optionally about 0.05 - 5.00% w/w of one or more extrusion aids;
   g) optionally about 0.05 - 50.00% w/w of one or more flavouring agents;

   wherein c) - g) are incorporated in the gelatinised functional protein matrix and b) is incorporated in (i) the gelatinised functional protein matrix, (ii) a coating of the dosage form or (iii) both the gelatinised functional protein matrix and the coating,

   the dosage form having a total moisture content in the range of about 0.5 - 40.0 % w/w and a water activity in the range of about 0.60 - 0.80; and less than about 0.1 w/w of a gelatinised starch.

2. A dosage form according to claim 1 wherein the gelatinised functional protein matrix is in an amount of from about 20.0 to 70.0% w/w.

3. A dosage form according to claim 2 wherein the gelatinised functional protein matrix is in an amount of from about 25.0 to 65.0 % w/w.

4. A dosage form according to claim 3 wherein the gelatinised functional protein matrix is in an amount of from about 30.0 to 60.0 % w/w.

5. A dosage form according to any one of claims 1 to 4 wherein the functional protein is selected from the group consisting of vital wheat gluten, defatted soy flour, soy protein concentrate, soy protein isolate, corn gluten meal, mung beans, yeast by-products and mixtures thereof.

6. A dosage form according to claim 5 wherein the functional protein is vital wheat gluten.
7. A dosage form according to any one of claims 1 to 6 wherein the functional protein has an intact protein contact of greater than about 75% w/w.

8. A dosage form according to claim 7 wherein the functional protein has an intact protein contact of greater than about 80% w/w.

9. A dosage form according to any one of claims 1 to 8 wherein the one or more active ingredients are included only within the functional protein matrix.

10. A dosage form according to any one of claims 1 to 8 wherein the one or more active ingredients are included within the functional protein matrix and the coating.

11. A dosage form according to any one of claims 1 to 8 wherein the one or more active ingredients are included only within the coating.

12. A dosage form according to any one of claims 1 to 11 wherein the one or more active ingredients is selected from the group consisting of antibiotics such as penicillins including penicillin-V, penicillin-G, amoxicillin, ampicillin and cloxacillin; cephalosporins' including cefalexin, cefuroxime and cefprozil; fluoroquinolones including flumequine, enrofloxacin, orbifloxacin and marbofloxacin; tetracycline's including oxytetracycline and doxycycline; macrolides including erythromycin and azithromycin; non-steroidal antiinflammatories including carprofen, meloxicam, aspirin, phenylbutazone and etodolac; drugs for treating cardiovascular disease including benazepril, enalapril, pimobendan, milophyline and etaminphylline; parasiticides such as benzimidazoles including albendazole, fenbendazole, oxibendazole and pro-benzimidazole febantel; macrocyclic lactones such as abamectin, ivermectin, milbemycin, moxidectin, selamectin and doramectin; and other parasiticides including praziquantel, pyrantel embonate and oxantel embonate and mixtures of any of the foregoing.

13. A process for preparing a chewable, stable animal dosage form comprising the steps of:
   i) combining:
      a) about 20 - 70% w/w of one or more functional proteins;
      b) optionally about 0.001 - 40.000% w/w of one or more active ingredients;
c) optionally about 0.5 - 40.0% w/w of one or more plasticisers which includes one or more oils and/or water;
   d) about 0.5 - 20.0% w/w of one or more humectants;
   e) optionally about 0.05 - 5.0% w/w of one or more anti-microbials;
   f) optionally about 0.05 - 5.00% w/w of one or more extrusion aids;
   g) optionally about 0.05 - 50.00% w/w of one or more flavouring agents;
   and mixing for a time sufficient to form a premix in which a) - g) are dispersed therein;
   ii) adding to the premix:
      h) 0.05 - 40.00% w/w water;
      i) optionally about 0.5 - 40.0% of one or more of the plasticisers which includes one or more oils and/or water;
      and mixing for a time sufficient to allow hydration of the one or more functional proteins to form a hydrated protein premix, wherein the one or more plasticisers is added before, during or after hydration;
   iii) providing sufficient mechanical work input to the hydrated protein premix so as to form a gelatinised functional protein matrix having b) - i) incorporated therein;
   iv) extruding the gelatinised functional protein matrix containing b) - i) into a dosage form;
   v) optionally drying the dosage form;
   vi) optionally cooling the dosage form; and
   vii) optionally coating the dosage form with a coating which optionally includes about 0.001 - 40.000% w/w of one or more active ingredients;
   to provide a dosage form having a total moisture content in the range of about 0.5 - 40.0% w/w and a water activity in the range of about 0.60 - 0.80;
   wherein the one or more plasticisers is added at step i), step ii) or at both steps i) and ii) and the one or more active ingredients is added at step i), in the coating at step vii), or at both steps i) and vii); and
   wherein steps i) - v) are carried out at a temperature in the range of from about 3°C up to a maximum of 70°C and at a pH in the range of about 5.0 - 7.5.

14. The process according to claim 13 wherein step i) comprises a dry blend premix.

15. The process according to claim 13 or claim 14 wherein the hydration time is from 40 seconds to less then about 100 seconds.
16. The process according to any one of claims 13 to 15 wherein the sufficient mechanical work is in the range of from about 0.03 to 0.06 kW/h/kg.

17. The process according to any one of claims 13 to 16 wherein steps i) - iv) are carried out at a temperature in the range of from 35-65°C.

18. The process according to claim 17 wherein steps i) - iv) are carried out at a temperature in the range of from 37.5-62.5°C.

19. The process according to any one of claims 13 to 18 wherein steps i) - iv) are carried out at a pH of from about 5.5 to 7.0.

20. The process of any one of claims 13 to 19 wherein a coating is applied to the dosage form in an amount of from 0.1-5.0% w/w.

21. A dosage form as hereinbefore defined with reference to any one of the Examples.

22. A process for preparing a dosage form as hereinbefore defined with reference to any one of the Examples.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

A61K 47/42 (2006.01) A23J 3/16 (2006.01) A23K/1/16 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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

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

CAplus and WPIDS and keywords: chew, moist, palatability, treat, gel, jelly, plasticiser, oil, water, glycerol, protein, gluten, soy, com, mung, yeast, wheat, humectant, sucrose, sugar, sodium chloride, salt, drug, medicine, active, veterinary, dose, dosage, extrusion and A23K/IPC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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<tbody>
<tr>
<td>----</td>
<td>See the abstract, page 4 line 8 to page 31 line 11, page 32 line 19 to page 34 line 15, examples 1-3</td>
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<td>A</td>
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<td>WO 2001/025414 A1 (GENERAL MILLS, INC.) 12 April 2001</td>
<td>13-20, 22</td>
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<td>See page 8 lines 4-26, page 9 line 6 to page 10 line 27, page 15 line 4 to page 16 line 8, page 21 first paragraph, page 25 lines 19-26, page 26 line 10 to page 7 line 13, page 42 lines 20-24</td>
<td>1-12, 21</td>
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* Further documents are listed in the continuation of Box C

X See patent family annex

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<tr>
<td>Special categories of cited documents</td>
<td>earlier application or patent published on or after the international filing date</td>
<td>later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or those underlying the invention</td>
<td>document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td>
<td>document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td>
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<tr>
<td>document defining the general state of the art which is not considered to be of particular relevance</td>
<td>document cited to establish the date of priority for another citation or other special reason (as specified)</td>
<td>document in respect of which doubts are thrown by priority claims</td>
<td>document referring to an oral disclosure, use, exhibition or other means</td>
<td>document published prior to the international filing date but later than the priority date claimed</td>
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Date of the actual completion of the international search
1 July 2008

Date of mailing of the international search report
8 JUL 2003

Name and mailing address of the ISAMU

AUSTRALIAN PATENT OFFICE
PO BOX 200, WODEN ACT 2606, AUSTRALIA
E-mail address pct@ipaustral.as.gov.au
Facsimile No +61 2 6283 7999

Authorized officer

LEAH WALKER

AUSTRALIAN PATENT OFFICE
(ISO 9001 Quality Certified Service)
Telephone No (02) 6283 6170

Form PCT/ISA/2 10 (second sheet) (April 2007)
### DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tr>
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<td>WO 2001/017364 A1 (EFFEM FOODS PTY LTD) 15 March 2001 See the abstract, page 5 line 22 to page 10 line 22, page 11 line 14 to page 13 line 14</td>
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<td>WO 2007/059558 A1 (NOVARTIS AG) 17 February 2005 See the abstract, page 2 lines 13-24, page 10 line 21 to page 11 line 11, paragraph bridging pages 13 and 14 and the examples</td>
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