United States Patent

Grant et al.

[15] **3,697,640**

[45] **Oct. 10, 1972**

[54] **RUMEN STABLE MEDICAMENT AND/OR NUTRIENT COMPOSITIONS**

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[22] Filed: **Oct. 27, 1970**

[21] Appl. No.: **84,295**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 758,874, Sept. 10, 1968.

[52] **U.S. Cl.** **424/35**, 99/2, 424/319

[51] **Int. Cl.** **A61k 9/00**

[58] **Field of Search** 424/35; 99/2

[56] **References Cited**

UNITED STATES PATENTS

3,562,806	2/1971	Grant et al.	424/35
2,940,901	6/1960	Hiatt et al.	424/35
2,196,768	4/1940	Hiatt	424/35

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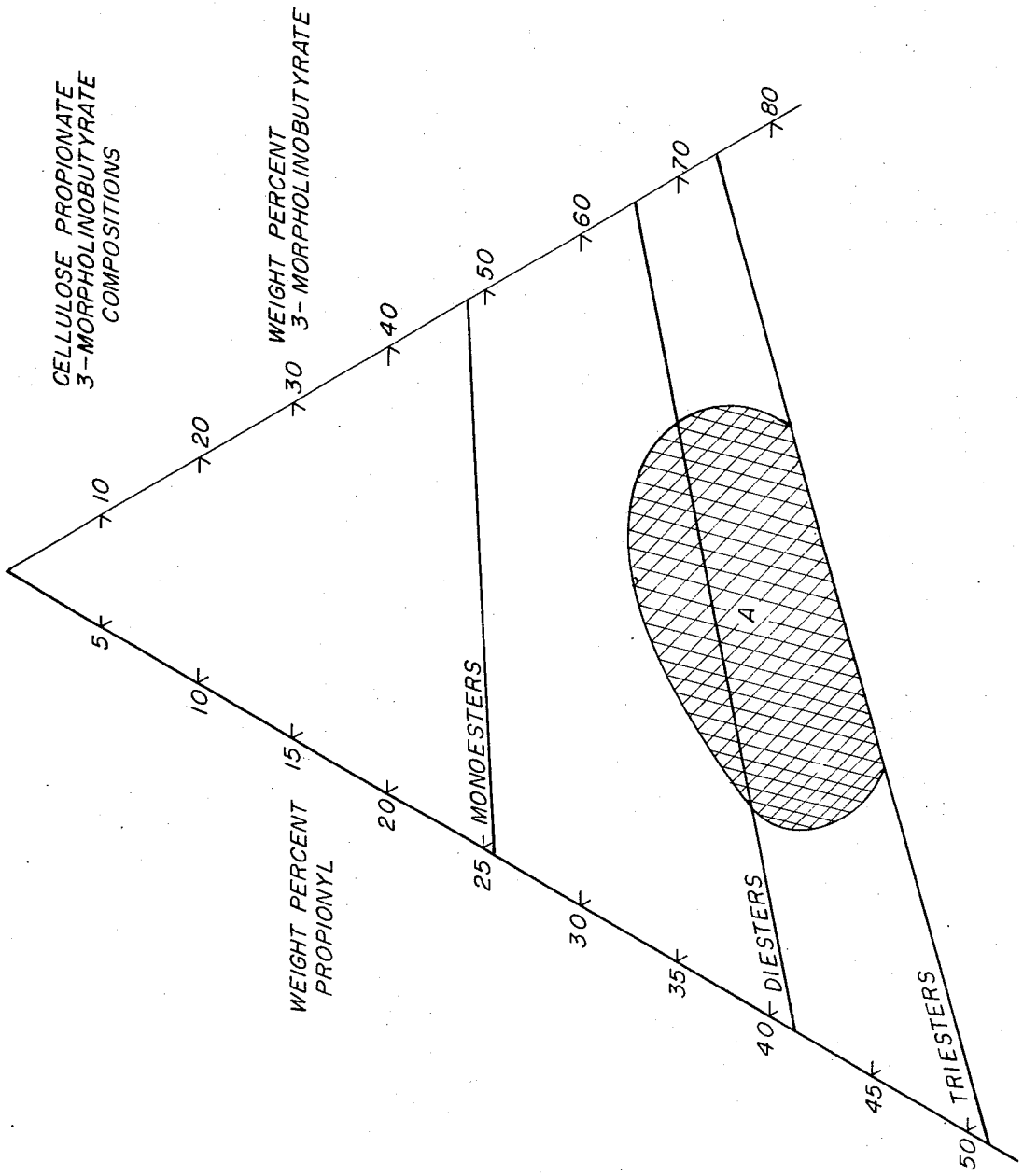
[57] **ABSTRACT**

Materials such as medicaments and nutrients that decompose when they are fed orally to ruminants because of their instability in the in vivo rumen environment can be protected from the ruminant environment by effectively coating such materials with special nitrogen-containing cellulosic materials having the ability to resist being degraded in the rumen, but also having the additional ability to dissolve in the in vivo abomasal fluid.

24 Claims, 1 Drawing Figure



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RUMEN STABLE MEDICAMENT AND/OR NUTRIENT COMPOSITIONS

This application is a continuation-in-part of copending U.S. patent application Ser. No. 758,874 filed Sept. 10, 1968 now U.S. Pat. No. 3,562,806, granted Feb. 9, 1971.

The present invention relates to special compositions that are specially useful for preserving sensitive materials from undesired reaction when they are subjected to degradative environments. More specifically this invention relates to compositions containing a significant amount of a cellulosic material such as cellulose propionate 3-morpholinobutyrate effective in inhibiting such undesired reaction.

Methods for protecting reactive materials such as medicaments temporarily while the medicaments are exposed to environments which ordinarily tend to degrade or decompose the medicament have been known for many years. For example, certain drugs that would ordinarily react in an undesirable manner in the acidic environment of the stomach have been coated heretofore with various materials that are resistant to the action of acids. In this manner, drugs for human consumption are sometimes protected during their passage through the stomach. The protective coatings are selected so that, after the passage of the coated material through the stomach, the coating decomposes in the more basic environment of the intestine, thereby releasing the drugs (chemically unchanged) at the place in the body where the drug will be most effectively absorbed. Such coatings have been termed "enteric coatings."

In the case of ruminants such as sheep and cattle, medicaments having "enteric" coating are, unfortunately, not protected from the drastic treatments afforded in the rumens of such animals. Medicaments given orally to ruminants pass directly first into the rumen (which has a large population of microorganisms and is either neutral or slightly acidic). From the rumen the materials then pass into the more acidic abomasum, and subsequently into the animal's intestine. In the case of such ruminants, many medicaments, including many desirable nutrients such as vitamins, amino acids, and the like, are decomposed or metabolized to at least some extent in an undesirable manner in the environment of the rumen. Such decomposition makes oral treatment of ruminants with such susceptible materials either expensive or impossible. Thus, there is a definite need, particularly in the fields of veterinary medicine and ruminant nutrition, for a method whereby materials that are ordinarily degraded in the rumen environment can be administered orally to ruminants without such a high degree of degradation taking place.

It has now been discovered that materials intended to be administered orally to ruminants can be effectively protected from the rumen environment if the materials are first coated with a cellulosic material having the proper characteristics. Materials having the "proper characteristics" are those that resist not only the extremely "corrosive" microorganism environment of the rumen, but also the solubilizing action of the in vivo rumen fluid (which has a pH of from about 5.5 to about 6.5 or more). The cellulosic materials that have been found particularly useful in this respect to provide protected medicament and/or nutrient compositions are

those in which the medicament or nutrient is coated with cellulose propionate 3-morpholinobutyrate having certain ratios of its various substituents on the cellulose "backbone." The cellulose propionate 3-morpholinobutyrate having the properties essential for the success of the present invention are those containing ratios of propionyl, hydroxyl and morpholino-butyryl groups such that they fall within the shaded area designated "A" in the drawing. Particularly preferred cellulose propionate 3-morpholinobutyrates in this group are those containing from about 13 to about 30 percent of propionyl from about 0 to about 4 weight percent of hydroxyl, and from about 22 to about 50 weight percent of morpholinobutyryl.

Processes for manufacturing and stabilizing such products are disclosed and described in detail in U.S. Pat. application Ser. Nos. 653,645 (U.S. Pat. No. 3,514,442) and 653,646 (now abandoned), the disclosures of which are incorporated by reference into the present disclosure.

The protected medicament and nutrient compositions of this invention can be used successfully when the composition consists mainly of the material to be protected, covered with a very thin continuous coating of the effective nitrogen-containing cellulosic material (wherein the weight of the coating can represent as little as about 0.5 weight percent or less, but is preferably at least about 1 weight percent, of the total weight of the composition). It is generally preferred, in the successful practice of this invention, that the medicament and/or nutrient compositions of this invention be blends of (a) one or more medicaments and/or nutrients with (b) one or more of the effective cellulosic materials. Generally, in such blends, the effective cellulosic material (s) will represent at least about 10 weight percent of the total medicament compositions. Preferably, but not necessarily, the medicament or nutrient portion of the rumen-stable compositions of this invention should be solid at temperatures below about 40° C. Typical, non-limiting, examples of medicaments that can be utilized in the practice of this invention include antibiotics (such as chlortetracycline, chloramphenicol, bacitracin zinc, erythromycin, oxytetracycline and the like) antibacterials, antivirals, growth stimulants, sulfonamides, anthelmintics, coccidiostats, hormones, vaccines, estrogens, androgens, steriods, tranquilizers and analgesics as well as materials that are often considered as "nutrients" such as carbohydrates, proteins, amino acids, vitamins and minerals. For purposes of the present invention discussion such "nutrients" can be considered the equivalent of "medicaments." Actually, any material to which it is desired to impart protection from the rumen environment of ruminants can be effectively protected by utilizing one or more of the effective nitrogen-containing cellulose derivative as described herein.

In order to obtain coated medicaments in the practice of the present invention, one needs simply to dissolve the special cellulosic coating material in an organic solvent such as acetone, methylene chloride, ethylacetate, alcohol, alcohol mixtures, and the like, and subsequently spray the resulting solution over particles of the medicament that is to be protected. The particles generally result from simply compressing the material to be protected into a so-called unit dosage

form such as a tablet or a smaller particle, several of which can be used simultaneously as a unit dose, if desired. As the solid medicament particles are tumbled in a conventional pill-coating machine while the solution of the cellulosic protectant is sprayed onto the particles, and the solid particles are subsequently subjected to a moving air stream, the solvent can readily be evaporated from the surface of the particles, thereby leaving behind the desired continuous protective coating. Such particles generally have a desirable, hard shiny appearance. Other conventional methods for coating particulated medicaments and nutrients such as, for example, pore coating, or fluidized bed procedures can also be used. The resulting coated medicament and/or nutrient material is suprisingly rumen-stable. One of the reasons why it is surprising that the compositions of this invention are rumen-stable is that the rumen environment is designed specially to degrade cellulosic materials, while the protecting materials of this invention are cellulosic in nature. Thus, one would ordinarily expect the useful cellulosic materials of this invention to be unstable in the rumen environment.

A surprisingly high degree of protection can also be afforded medicament materials in the rumen environment if the medicaments are physically blended, initially, with one or more of the nitrogen-containing cellulosic materials of this invention. In the preparation of such blends, the medicament can simply be admixed in a conventional stainless steel dough-mixer, for example, preferably with a small amount of solvent for the cellulosic material. Sometimes it is desirable to apply a relatively small amount of heat to the mixture of materials in the blender while the ingredients are being blended. After the medicament and the cellulosic material have been blended for at least a few minutes, the resulting blend can simply be removed from the mixer, cooled if necessary to thoroughly solidify the blend, and ground or crushed to yield particles of the desired size.

In the treatment of ruminants, the rumen-stable medicament and/or nutrient compositions of the present invention are generally admixed with the ordinary feed that the ruminants are to consume. Therefore, improved feed compositions comprising a blend of common animal food material with a solid, particulated rumen-stable nitrogen-containing cellulosic material that can be solubilized in the presence of a strong acid (which materials have been described in detail hereinbefore), wherein the rumen-stable cellulosic material is of one of the cellulose propionate 3-morpholinobutyrates having substituents such that it falls within the shaded area in the drawing (stabilized with an antioxidant), constitutes the preferred embodiment of the present invention.

For some reason, the nitrogen-containing cellulosic materials that are useful in the practice of the present invention degrade spontaneously when they are exposed to air and warmed to slightly elevated temperatures (above about 100° F) or when they are stored under ambient conditions for an extended period of time. Such degradation results in the ultimate insolubilization of the material in the desired medium. It has been found, however, that although the protected compositions of the present invention have utility as rumen-stable compositions over very long periods of time when the nitrogen-containing cellulosic material, per se, is used, the "shelf life" of the compositions of this invention can be significantly prolonged if there is also present in such compositions an effective amount of an organic antioxidant material. (The stabilization of nitrogen-containing cellulosic materials with organic antioxidants is disclosed and described in detail in copending U.S. patent application Ser. No. 653,646, which is now abandoned). Typical examples of organic antioxidants that can be used successfully to accomplish the desired stabilization of cellulose propionate 3-morpholinobutyrate include, for example, butylated hydroxytoluene, p-methoxyphenol, p-tertiary-butylphenol, t-butyl hydroquinone, hydroquinone, thymol, 2,5-bis(1,1-dimethylpropyl) hydroquinone and mixtures thereof. Of these, particularly preferred materials are butylated hydroxytoluene and p-methoxy phenol. Although the actual amount of organic antioxidant that is found necessary to effectively stabilize a particular nitrogen-containing cellulosic derivative will vary somewhat, depending upon such factors as the degree of stabilization desired, the particular antioxidant (or antioxidant mixture) that is utilized, and even the particular nitrogen-containing cellulosic derivative to be stabilized thereby, generally from about 0.05 to about 5 weight percent or more (and preferably from about 0.2 and about 2 weight percent), based on the weight of the nitrogen-containing cellulosic material being stabilized can be used.

It should be understood that the cellulosic compositions of this invention need not necessarily be used in the pure state for successful results. For example, other materials (in addition to the medicament and/or nutrient) can also be present in significant amounts in the compositions of this invention, so long as the basic protective abilities of the present cellulosic materials is not destroyed. Materials such as dyes, pigments, plasticizers (such as diethyl phthalate, triacetin, triphenyl phosphate, polyethylene glycol and the like) can be present in the protected medicaments and/or nutrients of this invention, is some instances, in amounts up to as much as 5 weight percent or more, if desired. In one aspect of this invention; namely, that involving the use of the rumen-stable cellulosic materials as protective coatings over the material being protected, it is generally preferred that one or more plasticizers be present in the coating layers in order to give the coating improved flexibility.

In the following examples, the effectiveness of cellulose propionate 3-morpholinobutyrates in the medicament and/or nutrient compositions of this invention is demonstrated. In these examples, all "parts" are by weight unless otherwise specified.

EXAMPLE 1

Into a conventional stainless steel sigma blade mill are introduced 75,000 parts of (82 percent active) chlortetracycline (CTC), 25,000 parts of a blend of (1) cellulose propionate 3-morpholinobutyrate containing 2% hydroxyl, 19% propionyl, 43% 3-morpholinobutyryl, and having an average molecular weight of about 45,000, with (2) 125 parts of butylated hydroxyphenol (an antioxidant), and 125,000 parts of methylene chloride. The resulting mixture is blended for 20

minutes. The resulting thick, viscous mass is air dried to remove the methylene chloride, whereupon it becomes solid. It is then ground to pass through a U.S. standard 16 mesh screen.

The resulting product is then blended with a complete lamb feed at the level of 20 grams of CTC per ton of feed. After 10 weeks, the average weight gain of 10 lambs fed with this feed composition has increased more that 5.5 pounds per lamb (15.8 percent) as compared with the weight gained by a "control" group of 10 lambs that had been fed the same type of treated feed, except that the CTC in the feed given to the "control" group was not blended with any of the nitrogen-containing cellulosic materials in accordance with the present invention.

It is particularly noteworthy that not every cellulosic material that is resistant to the action of the in vivo rumen environment is useful in the practice of this invention. (Nor is every nitrogen-containing cellulosic material useful in the practice of this invention). Thus, whereas some materials are extremely resistant to the rumen environment, those materials are very likely to also be insoluble in the abomasum, as well as being insoluble in the remainder of the animal's digestive tract. For usefulness in the practice of the present invention, however, the coating of protecting material must be resistant to the in vivo rumen environment, but must also readily dissolve in the more acidic abomasal fluid. Data set out in Table 1, below, illustrates these points. In order to obtain the data in Table 1, a piece of thin film of the material being tested is fastened inside a nylon fabric bag, which in turn is suspended for 24 hours (through a rumen cannula) inside the rumen of a living sheep. The weight of the film before and after such treatment indicates the resistance of the film to the in vivo rumen environment. An acceptable material (insofar as the successful practice of this invention is concerned) must be practically completely resistant to degradation under this test. Since an acceptable material must also dissolve in a strong aqueous acid environment, the solubility of the tested materials after 10 minutes' exposure in in vitro abomasal fluid (pH=2.5) is shown in TABLE 1.

TABLE I

Ex. No.	Polymers	In Vivo Rumen Stability[a]	Solubility in Abomasal Fluid
2	Cellulose Propionate 3-Morpholino-butyrate	97	Yes
3	Cellulose acetate	100	No
4	Cellulose acetate butyrate	97	No
5	ethyl cellulose	100	No
6	Copolymer (25% dimethylamino ethyl methacrylate, 67% methyl metha crylate, 8% ethyl acrylate)	2	Partly
7	Copolymer (15% dimethylamino ethyl methacrylate, 67% methyl metha crylate, 18% ethyl acrylate)	97	No
8	poly(1-methyl-amido-4-dimethylamino benzene)	90	No
9	deacetylated chitin	100	No

[a]Figures show percent of original weight recovered after exposure.

Deacetylated chitin (of Example 9) consists of chains of glucosamine residues connected through 1,4'-β-glucosidic linkages. It is, therefore, analogous to cellulose which is chains of glucose residues connected through 1,4'-β-glucosidic linkages.

Two-hundred sixty-seven milligrams of granules of a blend of cellulose propionate 3-morpholinobutyrate and CTC prepared as in Example 1, above (that pass through a U.S. Standard 16-mesh screen, but are retained on a U.S. Standard 60-mesh screen) containing 75% CTC and 25% cellulose propionate 3-morpholinobutyrate are administered abomasally to a live sheep via abomasal cannula. As a control, 200 mg. of CTC are administered in the same manner (but without the cellulose propionate 3-morpholinobutyrate) to a second live sheep. Urine is continually collected through a urethral catheter. It is then analyzed for CTC. Practically the same amount of CTC is recovered from both sheep, indicating that CTC is readily and effectively released in the in vivo abomasal fluid from compositions of the present invention. It should be noted that, whereas the medicament compositions described above are stable when thy are subjected to the rumen environment and also will dissolve in an aqueous acidic solution having a pH below about 5, the utility of the coated compositions and blends described hereinbefore is not at all limited to application to ruminants. Thus, it has been discovered that the medicament compositions of this invention demonstrate an effectively prolonged storage life when the compositions are exposed to relatively higher temperatures and humid atmospheres. Hence, the coating procedures and blending procedures described above are useful in conjunction with any material that will ultimately be exposed to an aqueous acidic environment (such as is present in the stomach of any animal, including man) and for which is a desire to improve the stability of the material to be protected either when the material is exposed to human conditions or when it is exposed initially to alkaline, neutral, or slightly acidic environments.

EXAMPLE 3

Fifteen hundred parts of cellulose propionate 3-morpholinobutyrate (having 1.75 propionyl groups and 1.25 morpholinobutyryl groups per anhydroglucose unit and stabilized with 0.7 weight percent of butylated hydroxytoluene) and 375 parts of diethyl phthalate (plasticizer) are dissolved in 10,000 parts of a solvent blend of acetone: methylene chloride: ethanol in weight ratios, respectively of 35:60:5. This solution is divided into ten equal portions, each of which is poured gradually over 50,000 parts of deep concave 11/32-inch core tablets of compressed dicalcium orthaphosphate, while the tablets are slowly stirred. After each portion of solution is poured onto the tablets, the solvent is evaporated therefrom by stirring the tablets continuously in a dry, cool air stream. After

10 "coats," the resulting coated tablets have an excellent, smooth appearance. The tablets do not dissolve or disintegrate in water at room temperature, even after 2 hours such exposure. However, they dissolve readily (in less than 2 minutes) in fresh abomasal fluid from a sheep and in U.S.P. simulated gastric fluid.

EXAMPLE 4

Two hundred parts of cellulose propionate 3-morpholinobutyrate (having 1.55 propionyl units, 1.05 morpholinobutyryl units and 0.4 hydroxyl units per anhydroglucose unit and stabilized with 0.5 weight percent of p-tertiary butylphenol) and 30 parts of diethyl phthalate (plasticizer) are dissolved in 350 parts of methylene chloride. The resulting solution is sprayed gradually onto 6,700 parts of dicalcium phosphate deep concave tablets in a conventional tablet coating pan. When finish dried, the resulting tablets are found to have the type of smooth, hard, glossy finish that is considered to be very desirable as a tablet coating finish by the pharmaceutical trade. These tablets do not disintegrate or dissolve in water at room temperature, even though they are stored in contact with water for 1 week. They can be dissolved in U.S.P. simulated gastric fluid in only 1 minute, however.

EXAMPLE 5

Six parts of the cellulose propionate 3-morpholinobutyrate used in Example 4 is dissolved in 50 parts of methylene chloride. Into this solution is mixed 1 part of powdered chlortetracycline hydrochloride. The resulting slurry is then permitted to dry at room temperature. It is then a hard plaque. It is ground into 12/30 mesh size granules. These granules release only 2 percent of their medicament into water in 24 hours, but dissolve completely in U.S.P. simulated gastric fluid in only 2 minutes, completely releasing the medicament into the gastric fluid.

EXAMPLE 6

Spherical pellets of methionine passing a No. 12 screen and retained on a No. 16 screen were coated with cellulose propionate 3-morpholinobutyrate using the fluidized bed spray coating method. The cellulose propionate 3-morpholinobutyrate had an apparent acetyl content of 25.6 percent, a nitrogen content of 2.93 percent, 1.72 propionyl groups, 1.23 morpholinobutyryl groups, and 0.4 hydroxyl groups per anhydroglucose unit and demonstrated an intrinsic viscosity of 1.2 in acetone. The coating solution was prepared by dissolving 2 grams of this material in 100 ml of a solvent mixture which consisted of 19 parts dichloromethane and 1 part methanol (v/v). The coating solution was then sprayed onto the fluidized methionine pellets at the rate of 60–70 ml per minute to a coating level of 21.5 percent by weight of cellulose propionate 3-morpholinobutyrate.

The effectiveness of this coating was evaluated by examining the effects of three buffers on the solubility of the methionine pellets. These tests were carried out in a Burrell wrist action shaker at room temperature using 2 grams of the coated pellets and 100 ml of the buffer. After 24 hours exposure to pH 6.8 buffer, 99.0 percent of the methionine was still in the protective pellet. After 24 hours exposure to pH 5.4 buffer, 96.0 percent of the methionine was still in the protective pellet. After 0.5 hours exposure to pH 2.9 buffer, 0.0 percent of the methionine pellets were intact.

EXAMPLE 7

Two grams of methionine as a coated preparation, prepared as described in Example 6, were introduced into the abomasum of each of two sheep twice daily via an abomasal cannula. Blood samples were taken from the jugular vein and the plasma was analyzed for free methionine.

The concentrations of methionine in the plasma of sheep No. 1 and 2 are shown in Table II both before and a series of samples after the abomasal administration of coated methionine. The concentration of methionine in the blood rose sharply after administration of coated methionine and in one case rose to a level over 15 times that found before administration. The same pattern of response was found for both animals.

The sharp rise in blood methionine after abomasal administration confirms the release of methionine from the coated methionine preparation.

TABLE II

Effect of Abomasal Administration of Coated Methionine on the Blood Plasma Concentration of Methionine

Hour	Plasma Methionine (μg/ml of plasma) Sheep No. 1	Sheep No. 2
Before Administration	6.5	5.8
	Coated	Administered
0830	Methionine	Abomasally
1000	52.5	88.5
1400	21.3	68.8
	Coated	Administered
1530	Methionine	Abomasally
1800	38.3	70.7
Next day		
0800	7.4	9.6
	Coated	Administered
0830	Methionine	Abomasally
1000	59.2	70.6
1400	24.0	37.8
1600	16.8	20.7

EXAMPLE 8

Ten grams of methionine in a coated preparation prepared in accordance with the method described in Example 6 were administered to each of two sheep directly into the rumen through a tube inserted in the esophagus. Blood samples were taken before administration and at various periods after administration from the jugular vein and the plasma was analyzed for free methionine.

Table III contains the plasma concentrations of free methionine at various sampling periods. Both animals showed a similar pattern of response to the coated methionine in blood plasma. Plasma concentrations of free methionine were relatively low for 8 to 12 hours, after which they then rose sharply and the concentration remained relatively high for 16 to 20 hours.

The relatively low levels during the early sampling periods illustrate an expected rumen retention of the

Enlate-coated particles. The sharp rise in plasma methionine after 8 to 12 hours indicated passage out of the rumen of the undamaged methionine. The extended high concentration of methionine in the blood indicated that the coated methionine preparation was capable of staying in the rumen environment for an extended period of time (over 30 hours) undamaged and then after its stay in the rumen, was capable of releasing the methionine in a position in the digestive tract, presumably the abomasum, where it was absorbed into the blood in either the abomasum or the small intestine. This data therefore confirms the rumen stability of the coated methionine preparation and, after it passes out of the rumen, the release and absorption of the methionine.

TABLE III

Free Plasma METHIONINE Levels Following Rumen Administration of Enlate-Coated Methionine

	Hour	Sheep No. 4	Sheep No. 5
Previous day	1600	1.7	3.6
	0800	4.9	3.3
	0815	rumen admini	stration of coated methionine
	1215	10.3	**12.0**
	1615	22.6	13.7
	2000	20.4	44.0
	2400	28.7	66.8
Next day	400	37.6	65.5
	800	34.9	42.3
	1200	20.3	7.3
	1600	20.9	7.4

This invention has been described in detail with particular reference to a preferred embodiment thereof, but it will be understood that variations and modifications can be effected within the spirit and scope of the invention as described hereinabove and as defined in the appended claims.

We claim:

1. A rumen-stable composition which is protected from degradation when said composition is passed through the rumen of a ruminant and which is soluble in abomasal fluid, said composition comprising:
   a. a pellet of material selected from the group consisting of methionine and mixtures thereof with oral ruminant medicament and nutrients; and coated with
   b. a cellulose propionate 3-morpholinobutyrate.

2. A rumen-stable composition as in claim 1, wherein said composition also contains an amount of antioxidant; said amount being effective to inhibit the spontaneous degradation of said cellulose propionate 3-morpholinobutyrate.

3. A rumen-stable composition as in claim 2, wherein said composition contains at least about 10 weight percent of said cellulose propionate 3-morpholinobutyrate, based on the combined weight of (a) and (b), and (a) and (b) are uniformly admixed in said composition.

4. A rumen-stable composition as in claim 3, wherein said cellulose propionate 3-morpholinobutyrate has a composition that falls within the area designated A in the drawing.

5. A rumen-stable composition as in claim 2, wherein said cellulose propionate 3-morpholinobutyrate contains from about 13 to about 30 weight percent propionyl, from about 22 to about 50 weight percent morpholinobutyryl, and from about 0 to about 4 weight percent hydroxyl.

6. A rumen-stable medicament composition as in claim 5, wherein said other medicament is an antibiotic.

7. A rumen-stable medicament composition as in claim 6, wherein said antibiotic is chloramphenicol.

8. A rumen-stable medicament composition as in claim 6, wherein said antibiotic is chlortetracycline.

9. A rumen-stable medicament composition as in claim 6, wherein said antibiotic is oxytetracycline.

10. A rumen-stable medicament composition as in claim 6, wherein said antibiotic is erythromycin.

11. A rumen-stable medicament composition as in claim 6, wherein said antibiotic is bacitracin zinc.

12. A rumen-stable nutrient composition as in claim 3, wherein said other nutrient is selected from the group consisting of carbohydrates, proteins, amino acids, vitamins, minerals, and mixtures thereof.

13. A rumen-stable nutrient composition as in claim 12, wherein said other nutrient is vitamin A.

14. A rumen-stable composition as in claim 2, wherein said cellulose propionate 3-morpholinobutyrate is present as an external coating over said material and in an amount equal to at least about 0.5 weight percent.

15. An improved feed composition comprising a blend of (a) common animal food material coated with (b) a solid particulated, rumen-stable composition that is soluble in an aqueous solution having a pH below about 5; said rumen-stable composition comprising:
   i. a material selected from the group consisting of methionine and mixtures thereof with other medicaments and nutrients, and coated with
   ii. a cellulose propionate 3-morpholinobutyrate.

16. An improved feed composition as in claim 15, wherein said material to be protected from direct contact with rumen fluids includes methionine and a medicament.

17. An improved feed composition as in claim 15 wherein said material to be protected from direct contact with rumen fluids includes methionine and a nutrient.

18. A coated composition comprising:
   a. a core material selected from the group consisting of methionine and mixtures thereof with oral ruminant medicaments and nutrients, and coated with
   b. a coating material; said coating material comprising a cellulose propionate 3-morpholinobutyrate.

19. A coated composition as in claim 18, wherein said cellulose propionate 3-morpholinobutyrate is stabilized to inhibit spontaneous degradation by the presence in said coating material of an effective amount of an antioxidant, and said nitrogen-containing cellulosic derivative is present in said coated composition in an amount equal to at least about 1 weight percent.

20. A coated composition as in claim 19, wherein said cellulose propionate 3-morpholinobutyrate has a composition that falls within the area designated A in the drawing.

21. A coated composition as in claim 20, wherein said coating material also contains at least one plasticizer.

22. A coated composition as in claim 19, wherein said organic base is a secondary amine.

23. An improved feed composition as in claim 15, wherein said organic base is a secondary amine.

24. A rumen-stable composition as in claim 2, wherein said organic base is a secondary amine.

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