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Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E. _____ S. _____

SUPERINDUSTRIA Y COMERCIO

Radicación : 00003458 00000011

Folios: 2

Fecha (AMD): 2004-03-29 17:28:45

Trámite : 002 PATENTES D 1 REGISTRO/ 538 PETICION

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Ref.: Expediente No. 00.003.458

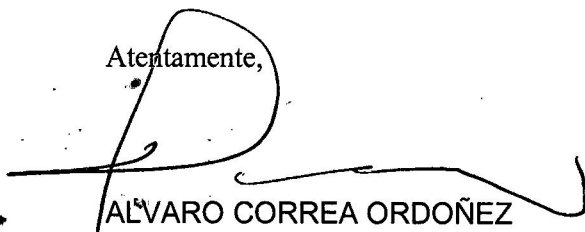
Solicitud de Patente de Invención titulada: "MÉTODOS
PARA REDUCIR LA TASA DE MORTALIDAD EN
AVES DE CORRAL."

Solicitante: DUCOA, LP.

**SOLICITUD DE EXAMEN DE FONDO SEGÚN EL ARTICULO 44 DE LA
DECISION 486, GACETA No. 532**

ALVARO CORREA ORDOÑEZ, mayor de edad y vecino de Bogotá, D.C., identificado según aparece al pie de mi firma, en mi condición de apoderado del solicitante, respetuosamente me permito solicitar, dando cumplimiento a lo establecido en el artículo 44 de la Decisión 486 de la Comisión de la Comunidad Andina de Naciones, que se examine si la invención reúne los requisitos de patentabilidad previstos en la misma. Adjunto recibo de pago por valor de \$ 353.000 pesos para cubrir la tasa correspondiente, según la Resolución 37323 del 30 de Diciembre de 2003.

Atentamente,


ALVARO CORREA ORDOÑEZC.C. No. 79.143.366 de Usaquén
T.P. 20.281

Anexos: Recibo No.04-21,115

YMD/Solic.Ex.Fondo 00.003.458 290304

[Handwritten signature]

**DILIGENCIA DE RECONOCIMIENTO
Y PRESENTACION PERSONAL**

Ante el Notario Once del Circulo de Santafé de Bogotá, compareció

Quien exhibió la C.C. No.

expedida en

y declaró que la firma y huella que aparecen en el presente memorial son suyas y que el contenido del mismo es cierto.

Memorial dirigido a INTERESADO

Santafé de Bogotá, D.C. **29 MAR 2004**

Firma del Declarante

HUELLA

Autorizó la anterior Diligencia

REPUBLICA DE COLOMBIA
NOTARIO ONCE DEL CIRCULO DE SANTAFÉ DE BOGOTÁ DEL CIRCULO DE
SANTAFÉ DE BOGOTÁ, D.C.

[Handwritten signature]
ZULMA NAVARRO DE BAUTISTA
NOTARIA ONCE

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SUPERINDUSTRIA Y COMERCIO

Folios: 2

Radicacion : 00003458 00000011

Fecha (ARD): 2004-03-29 17:28:45

Tramite : 002 PATENTES D 1 REGISTRO/ 538 PETICION

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 04 - 21,115
FECHA : MARZO 15 DE 2004

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	Vr. PAGO
JULIAN ANDRES VARGAS	CONSIGNACION	BANCO POPULAR	050-00110-6	20225347	15/03/2004	68,832,360.00

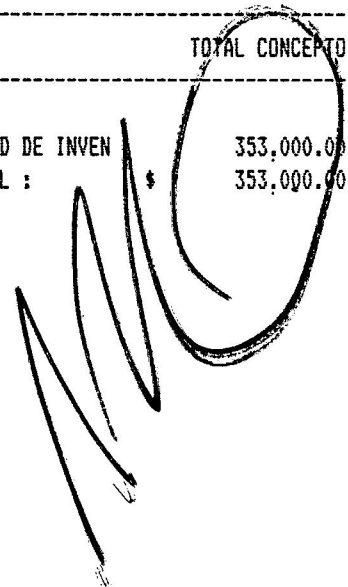
***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	85 EXAMEN DE PATENTABILIDAD DE INVEN	353,000.00
		TOTAL :	353,000.00

SON: TRESCIENTOS CINCUENTA Y TRES MIL PESOS

RESPONSABLE : 

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____



DIVISION DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. **00-3458**

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION** FUE PUBLICADO
EN LA GACETA DE PROPIEDAD INDUSTRIAL No **532**, DE FECHA **30 DE SEPTIEMBRE DE**
2003, EL TERMINO HABIL SEÑALADO POR LA LEY EXPIRA EL **30 DE DICIEMBRE DE 2003**.

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____ NO **X**

Bogotá D.C., Septiembre 08 de 2004

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2004-10-28

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES

2020

Bogotá, DC, 12 de octubre de 2004

Apoderado: Alvaro Correa Ordoñez

Oficio:

10031

ASUNTO

Radicación: 0-3458

Trámite 002

Evento 001

Actuación 430

Folios

Como resultado del examen de fondo, realizado con fundamento en el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica:

Documentos estudiados:

- capítulo descriptivo, folios 44 a 68;
- capítulo reivindicatorio, folios 69 a 71;
- 1° examen de forma, folios a 36 y 37 ;
- respuesta técnica al 1(examen de forma, folios 42 y 43;
- solicitud de la cual se reivindica prioridad, junto con la traducción mínima requerida, folios 73 a 100;
- examen de forma, folio 113;
- Solicitud del examen de patentabilidad, folios 155 y 156.

Objeto de la invención:

El título de la invención es "MÉTODOS PARA REDUCIR LA TASA DE MORTALIDAD EN AVES DE CORRAL".

El objeto de la presente solicitud se refiere a usar alimentos que contiene contienen natamicina para el tratamiento de aves de corral enfermas de ascitis.

Claridad de la solicitud:

En el artículo 30 de la Decisión 486 de la Comisión de la Comunidad Andina se establece: "Las reivindicaciones definirán la materia que se desea proteger mediante la patente. Deben ser claras y concisas y estar enteramente sustentadas por la descripción".

La reivindicación 10 no es clara, puesto que en la reivindicación original decía "por libra" y se le dijo que corrigiera las unidades de acuerdo con el sistema internacional de unidades y estableció que una libra es equivalente a "2,205 Kg", lo cual no es cierto.

Excepciones de Patentabilidad:

El artículo 20 de la Decisión 486 de la Comisión de la Comunidad Andina establece en su inciso d) que no serán patentables: "los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales".

Las reivindicaciones 1 a 11 se pretende proteger un método para tratamiento del cuerpo animal, el cual incluye la administración de una composición farmacéutica que contiene el antibiótico natamicina, por lo tanto está inmersa bajo el alcance del artículo 20 de la Decisión 486.

Determinación del estado de la técnica:

El artículo 16 de la Decisión 486 de la Comisión establece: "El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida.

Sólo para el efecto de la determinación de la novedad, también se considerará dentro del estado de la técnica, el contenido de una solicitud de patente en trámite ante la oficina nacional competente, cuya fecha de presentación o de prioridad fuese anterior a la fecha de presentación o de prioridad de la solicitud de patente que se estuviese examinando, siempre que dicho contenido esté incluido en la solicitud de fecha anterior cuando ella se publique o hubiese transcurrido el plazo previsto en el artículo 40."

Item	Documento	Fecha de publicación	Título
D1	US 4.536.494	28- agosto-1985	Animal feed method employing natamycin
D2	US 5.266.347	30-nov-1993	Antibiotic biomasa animal feed composition

Evaluación de los requisitos de patentabilidad:

El artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina establece: "Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial."

En cumplimiento con este artículo, se procedió a evaluar los requisitos de novedad, nivel inventivo y aplicación industrial con el fin de establecer la patentabilidad de la invención reivindicada en la solicitud en estudio.

Evaluación de la Novedad:

El art.16 de la Decisión 486 de la Comisión de la Comunidad Andina establece: *"Una invención se considerará nueva cuando no está comprendida en el estado de la técnica. El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida".*

La solicitud en estudio se refiere un método de tratamiento para tratar la ascitis en aves de corral, el tratamiento consiste en tratar las aves de corral que tengan los síntomas de la enfermedad con una cantidades efectiva de natamicina.

- La anterioridad D1 enseña las composiciones usadas la solicitud en estudio para el tratamiento de la ascitis. Esta anterioridad que enseña composiciones específicos y métodos de elaboración de las mismas que indican con antelación a la fecha de presentación que las composiciones usadas en los métodos terapéuticos reclamados en la solicitud en estudio, eran conocidos.

La anterioridad D2, se enseña que la natamicina que es un antibiótico polieno de ocurrencia natural, en el cultivo de *Streptomyces natalensis*, aislado en 1957. En esta anterioridad igualmente se describe las formulaciones en forma de suspensiones, premezcla para alimentos, en forma de suspensiones, en dispersiones acuosas para aerolisar, y también en mezcla de biomasa que comprende el antibiótico polieno en forma de alimento animal, en la columna 1; columna 5, renglones 30 a 35.

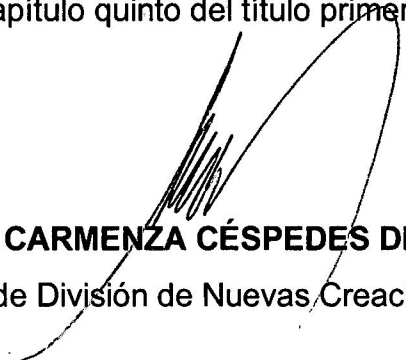
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Además se debe tener en cuenta que la Decisión 486 dice:

Artículo 21.- *Los productos o procedimientos ya patentados, comprendidos en el estado de la técnica, de conformidad con el artículo 16 de la presente Decisión, no serán objeto de nueva patente, por el simple hecho de atribuirse un uso distinto al originalmente comprendido por la patente inicial.*

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta días contados a partir de la fecha de notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la circular única No. 10 de 2001.



ALIX CARMENZA CÉSPEDES DE VERGEL

Jefe de División de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista, de fecha 28 OCT. 2004

CONCEPTO TÉCNICO No 1343	EXAMINADOR TÉCNICO Código No.202012
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United States Patent [19]

Carter

[11] Patent Number: 4,536,494

[45] Date of Patent: Aug. 20, 1985

[54] ANIMAL FEED METHOD EMPLOYING NATAMYCIN

[76] Inventor: A. Franklin Carter, 705 E. Highpoint, Springfield, Mo. 65807

[21] Appl. No.: 608,796

[22] Filed: May 10, 1984

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 552,771, Nov. 17, 1983, abandoned.

[51] Int. Cl.³ A61K 31/71; C07H 17/08

[52] U.S. Cl. 514/31; 536/6.5

[58] Field of Search 424/180; 536/6.5; 514/31

[56] References Cited

U.S. PATENT DOCUMENTS

2,903,356 9/1959 Lampen et al. 424/180
3,945,993 3/1976 Schaffner et al. 536/6.5
3,957,754 5/1976 Aszalos et al. 536/6.5

OTHER PUBLICATIONS

Coates et al., "A Mode of Action of Antibiotics in Chick Nutrition," *J. Sci. Food Agric.*, Jan. 3, 1952, pp. 43-48.

Groschke et al., "Effect of Antibiotics, Synthetic Vitamins, Vitamin B₁₂, and an APF Supplement on Chick Growth," *Research Notes*, pp. 616-618, 1950.

Cuthbertson, "Antibiotics in Nutrition," *J. Sci. Food Agric.*, Feb. 3, 1952, pp. 49-53.

Fontaine et al., "The Effects of an APF Concentrate Containing Aureomycin on the Growth and Well-Being of Young Dairy Calves", (abstract), *J. Animal Science*, vol. 9, No. 1, Feb. 1950, pp. 646-647.

Underkofler et al., *Industrial Fermentations*, vol. II, 1954, pp. 342-343.

Clark et al., "Pimaricin, A New Food Fungistat," *Microbial Inhibitors in Food*, Fourth International Symposium on Food Microbiology, 1964, at Swedish Institute for Food Preservation Research.

Morris et al., "Pimaricin—What Is It?", *Cultured Dairy Products Journal*, vol. 13, No. 3, p. 22, Aug., 1978.

Holz, "Polyene Antibiotics: Nystatin, Amphotericin B, and Filipin," *Antibiotics*, vol. V, Part 2, pp. 313-315, 1979.

Hockenhull, ed., "Production of Polyene Antifungal Agents by Streptomycetes," *Progress in Industrial Microbiology*, vol. 6, pp. 3-19.

Lampen et al., "Differences in Action of Large and Small Polyene Antifungal Antibiotics," *Bulletin of the Research Council of Israel*, vol. 11A, No. 1, 1962.

De Kruijff et al., "Polyene Antibiotic-Sterol Interactions in Membranes of *Acholeplasma Laidlawii* Cells and Lecithin Liposomes," *Biochimica et Biophysica Acta*, 339, pp. 30-43, 1974.

Zygmunt, "Intracellular Loss of Potassium in *Candida albicans* after Exposure to Polyene Antifungal Antibiotics," *Applied Microbiology*, Nov. 1966, pp. 953-956.

Primary Examiner—Johnnie R. Brown

Attorney, Agent, or Firm—Lowe, King, Price & Becker

[57] ABSTRACT

An animal feed composition which comprises a conventional animal feed and a feed efficiency-effective amount of natamycin. The feed composition may comprise natamycin in a range of about 0.000055 to 0.011 weight percent. A premix for incorporation into such animal feeds preferably comprises about 2-25 grams of natamycin admixed with about one pound of an inert carrier, such as rice hulls or calcium carbonate. One pound of premix is added to about one ton of the conventional animal feed.

9 Claims, No Drawings

ANIMAL FEED METHOD EMPLOYING NATAMYCIN

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application is a continuation-in-part of application Ser. No. 552,771, filed Nov. 17, 1983, now abandoned.

FIELD OF THE INVENTION

The present invention relates to feed efficiency agents and to animal feeds having these feed efficiency agents incorporated therein. The present invention also relates to methods for producing and using such feed efficient compositions.

BACKGROUND ART

It is known in the art to add various materials to animal feeds to achieve a number of purposes. One such purpose is set forth in applicant's above-identified parent application wherein natamycin is added to conventional animal feeds as an antifungal agent.

Numerous additives have been proposed for animal feeds as growth promoting agents. Antibiotics in particular have been proposed as growth promoting additives. For example, Coates et al., "J. Sci. Food Agric.", 3, pp. 43-48, January 1952, suggest procaine penicillin as an agent of this type. Coates et al. also discuss similar effects of streptomycin, sulphasuccidine, sulphaquinoxaline, 4-hydroxy-3-nitrophenylarsonic acid, aureomycin, terramycin, and polymyxin, disclosed in work by other authors. Groschke et al., "Research Notes", pp. 616-618 (1950), discuss chick growth effects of vitamin B₁₂, stertomycin, and aureomycin. In "J. Sci. Food Agric.", 3, pp. 49-53, February 1952 Cuthbertson discloses the value of vitamin B₁₂, and antibiotic supplements such as penicillin, as chick food additives. In an abstract by Fountaine et al., "Journal of Animal Science", Vol. 9, pp 646-647, February 1950, the use of aureomycin as a growth supplement for calves is discussed. Further, Underkofler and Hickey, in "Industrial Fermentations" pp. 342-343 (1954), discuss the use of antibiotics such as streptomycin as growth promoters. All of the antibiotics disclosed in these publications are antibacterial antibiotics and are believed to be useful because they eliminate harmful bacteria or reduce the number of microorganisms in the intestinal tract, as discussed by Underkofler and Hickey.

As disclosed in U.S. Pat. No. 2,903,356, to Lampen et al. a growth promoting supplement comprising a combination of an antibacterial antibiotic with a member of the class consisting of nystatin and amphotericin is useful. This composition was said to accelerate the growth of animals by administration of feedstuffs containing the growth promoting supplement. In this patent there is discussed the need to include a sufficient amount of a factor identified as an animal protein factor in order to promote maximum growth. Thus, as defined in this patent, the expression "growth promoting agent" is an agent which will achieve an acceleration in the growth rate of animals superior to that obtainable with a normal diet.

Nystatin is a member of the class of antibiotics known as polyene antibiotics. These antibiotics have activity against yeasts and fungi, but have no significant activity against bacteria.

The present invention is also concerned with animal feed additives. However, in the present invention, a feed efficiency agent is incorporated into the animal food, said feed efficiency agent being effective to cause an animal to grow to its normal weight while requiring less feed than normal. Thus, the additive of the present invention is to be distinguished from growth promotion agents as discussed, for example, in U.S. Pat. No. 2,903,356.

SUMMARY OF THE INVENTION

It is accordingly one object of the present invention to provide a novel feed efficiency agent and feed compositions containing the feed efficiency agent.

It is a further object of the present invention to provide a method for increasing the efficiency of animal feed compositions by the addition thereto of a feed efficiency agent comprising natamycin.

A still further object of the present invention is to provide a method for the efficient growing of animals and poultry which comprises feeding said animals on a diet comprising conventional animal food containing the feed efficiency agent natamycin.

Other objects and advantages of the present invention will become apparent as the description thereof proceeds.

In satisfaction of the foregoing objects and advantages, the present invention provides an animal feed composition comprising a conventional animal feed and a food-efficiency amount of natamycin. The present invention also provides a method for treating animal feeds to improve their feed efficiency which comprises adding thereto an effective amount of natamycin as a feed efficiency agent.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

As pointed out above, the present invention is concerned with a feed efficiency agent, methods for incorporation of the feed efficiency agent into animal feeds, and methods for growing animals by feeding said animals a conventional animal food containing natamycin as a feed efficiency agent.

It has been found according to the present invention that natamycin is an unusually effective feed efficiency agent for incorporation into animal feeds. Incorporation of the feed efficiency agent of this invention will permit an animal to attain a normal weight in the conventional period of time using less feed than normally required. The feed efficiency agent is incorporated into the animal feed at the rate of about 10-50 grams per ton of feed. The preferred method of incorporation of the feed efficiency agent is by dry blending since the feed efficiency agent is a solid.

The feed efficiency agent of this invention is natamycin. This material is also known as pimarinin or tennectin. It is a known compound and was isolated in the late 1950's from the fermentation broth of a culture of *Streptomyces natalensis*. (See Struyke et al., *Antibiotics Annual*, 1957-1958, page 876.) This organism was discovered in a soil sample taken from near Pietermaritzburg in South Africa. Natamycin is also produced by *Streptomyces chattanoogensis*.

Natamycin is a creamy white, odorless, tasteless, practically insoluble crystalline amphoteric powder. It belongs to the polyene macrolide or macrocyclic lactone group of compounds. (See generally, Clark et al. "Pimaricin, A New Food Fungistat", *Microbial Inhibi-*

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tors in Food, Food International Symposium on Food Microbiology 1964 at the Swedish Institute for Food Preservation Research.) In low concentrations, natamycin is a potent inhibitor of fungal microorganisms. It is reported to have been tested in vitro on over five hundred fungal organisms with very positive effects.

Natamycin is relatively stable when in a dry state or when mixed with dry diluents. However, the molecule is sensitive to ultraviolet light, oxygen, or extreme pH values. It is relatively insoluble in water in which its solubility is of the order 0.005-0.010 weight/weight percent. Additionally, even in solution, natamycin is rather unstable. Aqueous solutions of 6 mcg/ml of natamycin become microbiologically inactive after twenty-four hour exposure to light. Inactivation of natamycin by light, peroxides or oxygen proceeds at the fastest rate in solution or suspension. Natamycin is also sensitive to heavy metals, and may lose up to 75% of its effectiveness in four or five hours in their presence.

Natamycin has been used to treat several human clinical fungal infections, such as Candidiasis and Trichomoniasis. As reported in the British National Formulary, natamycin is sold under the trade name "Pimaricin", produced by Brocades in oral suspension, suspension for inhalation, cream and vaginal tablet formulations. Natamycin has also been used for various epidermal fungal infections such as corneal ulcers.

Natamycin has also been of interest in treatment of food products because it is highly active against yeasts and molds, as opposed to bacteria. (See Morris and Hart, "Pimaricin—What Is It?", *Culture Dairy Products Journal*, Vol. 13, page 22, 1978.) Reportedly, natamycin has been applied to food products in several ways. It has been added in dry form to liquids, slurries, pastes and semisolids when adequate mixing can be accomplished, or the pure natamycin can be mixed with one or more of the dry ingredients and then added to a given food product. Solid foods requiring surface protection can be dipped, misted, fogged or dusted with a solution or suspension of natamycin. Additionally, it has been suggested that protection from yeast and molds may be achieved in solid food by incorporating natamycin homogeneously into the food itself. (See Clark et al., cited above.)

As described in my copending application Ser. No. 552,771, filed Nov. 17, 1983, natamycin can be added to animal feeds to achieve an antifungal effect in the food.

Natamycin has also been used to retard spoilage of dressed poultry, to protect cottage cheese, and has been widely used in the dip-treatment of cheeses to coat them with the fungicide which is absorbed slightly, and dries to form a solid, surface coating. Various other reports suggest that natamycin is effective in the treatment of fresh berries, tomatoes, strawberries and raspberries. These reports indicate that natamycin has an antiyeast activity when added to wines, and various fruit juices, such as apple juice or orange juice. (See Morris and Hart, and Clark, cited above.) Natamycin is also used on meat products such as sausage.

Natamycin is a member of the class of antibiotics known as polyenes, which are toxic to yeast and fungi but not to bacteria. Nystatin, filipin, amphotericin B and candicidin are also polyene antibiotics. The polyenes have molecular weights of approximately 1,000. They possess large lactone rings which contain a non-polar transconjugated double bond system and a polar polyhydroxylic portion. However, the antibiotics differ in (1) the size of the ring, and (2) the number of conjugated

double bonds. See Holz, "Antibiotics", Vol. V, Part 2, pp. 313-315 (1979). As reported by Hockenhull, "Progress in Industrial Microbiology", Vol. 6, pp. 3-19, at page 4, natamycin has six hydroxyl groups whereas nystatin, for example, has thirteen hydroxyl groups.

While natamycin is a polyene antibiotic, it appears to differ substantially in structure and activity from other members of the class. Thus, as pointed out by Lampen et al. in "Bulletin of the Research Council of Israel", Section A, Chemistry, Proceedings of the XXXth Meeting of the Israel Chemical Society, Vol. 11A, No. 1, pp. 286-291 (April, 1962), two distinct groups of polyenes exist, and they may be divided into the two groups on the basis of the number of C atoms and glucolysis inhibition activity. As shown in Table I on page 289, nystatin is a large polyene, whereas pimaricin (natamycin) is a small polyene.

Similar differences are noted by De Kruijff et al., *Biochim. et Biophys. Acta*, 339, pp. 30-43 (1974), where it is pointed out that pimaricin or natamycin has significant permeability differences when compared with the other polymers studied. Thus, pimaricin was the only polyene which was not able to produce permeability changes in *A. laidlawii* cells and egg lecithin liposomes.

In a publication by Zygmunt, "Applied Microbiology", pp. 953-956 (November 1966), the polyene antibiotics as a class were studied for their effect on growth and fate of intracellular K⁺. As reported in this publication, these antibiotics appear to exhibit growth-inhibitory activities. From this publication, and those discussed above with respect to the mechanism of effect by the anti-bacterial antibiotics, it would not be expected that any of the polyenes would have a growth effect.

It was therefore unexpected that the natamycin would have any effect when added to animal feeds. The unexpectedly achieved effect is not that of a growth promoting agent, but is rather activity as a feed extender or feed efficiency agent. The advantage realized by the addition of natamycin to an animal feed is that less feed can be fed to raise an animal to its conventional weight in the normal period of time. This is a substantial advantage in the commercial livestock and poultry industries.

In a composition aspect, the present invention provides an animal feed composition comprising a conventional animal feed and a feed efficiency agent effective amount of natamycin. In a further composition aspect, this invention relates to an animal feed comprising about 0.000055 to 0.011 weight percent of natamycin as a feed efficiency agent in combination with a suitable inert carrier, with the balance of the composition being a conventional animal feed. In this specification, the term "animal feed" includes feed for poultry as well as for animals such as livestock.

A further composition aspect of the present invention relates to a premix for incorporation into a conventional animal feed, most preferably comprising about 8 to 15 grams of natamycin admixed with about one to three pounds of an inert carrier per ton of feed. The inert carrier may be formed of such ingredients as rice hulls or calcium carbonate.

In a method of use aspect, the present invention relates to a method for treating animal feed, comprising dry blending of about 0.000055 to 0.011 weight percent of natamycin combined with a suitable premix carrier with a conventional animal feed.

In a further method aspect, this treated animal feed is fed to animals at a rate to achieve the conventional

weight gain of the animal over the normal period of time but using less total feed.

The present invention is generally directed to a feed composition that includes natamycin as a feed efficiency agent. Animal feed is largely composed of grain and cereal products, but may also include meat byproducts as a minor ingredient. Additionally, animal feed may include citrus pulp and grape hulls, either or both being present at less than about 5% by weight. Animal feed also include added fats, minerals and vitamins such as riboflavin, and trace metals.

Animal feed for feeding poultry, which is a preferred feature of the invention, includes protein, fat, fiber, calcium and phosphorus. A preferred feed would include corn and/or wheat, fat, meat meal, soybean meal, minerals and vitamins.

Animal feed is generally formed by cracking or grinding grain, rather than by incorporating the intact grain particles. These ground or cracked particles in the feed are roughly 1/100 of the original grain size. Animal feeds are composed of many different particles, typically in a range between 1/32 of an inch, or less, to 1/2 of an inch in diameter. Additionally, the cracking process exposes higher moisture and different nutrient concentrations than are typically present at the surface of the grain particle, which usually has a hull or other coating. Thus, the increased moisture content of conventional feeds further decreases the stability of natamycin according to the literature in this art.

Feed is usually exposed to light during its manufacture. It is then typically stored in dark bins with lids to keep out moisture. However, the moisture content of feed ranges from 10-30%. Additionally, in use, uneaten leftover feed is thoroughly exposed to light, as it is retained in the pans which are typically found in automated feed systems. Thus, some feed may be retained for a week or more before it is consumed in an environment of high moisture and with exposure to ultraviolet and visible light rays.

Surprisingly, it has been found that natamycin, when added to animal feedstuffs, exhibits a significant feed efficiency factor despite the extended presence of moisture which tends to inactivate the compound. Natamycin, as indicated above, is quickly inactivated upon exposure to ultraviolet light of certain wave lengths, and in the presence of riboflavin, visible light also inactivates the natamycin. This theoretically also renders natamycin relatively less stable in feed. The presence of heavy metals in trace amounts would be expected to still reduce natamycin stability.

A surprising aspect of the present invention, as shown by the actual experiments described hereinafter, is that when natamycin is added in the indicated amounts to the animal feedstuffs, the natamycin appears to act to increase the efficiency of the feed. Thus, when the animals are fed a conventional diet, normal weight can be obtained for the age of the animal while reducing the amount of feed which is necessary to achieve the normal weight. The data set forth in the experimental portion of this application show that feed efficiency is substantially improved in normal feeding procedures. Thus, in twenty-one day performance data, using chicks as the animal, a significantly improved feed efficiency was obtained without adverse effects.

Natamycin is available under the trade name Delvocid produced by the Gist Brocades company of the Netherlands. As supplied, Delvocid contains about 50% natamycin. Natamycin may be dissolved with

stirring at room temperature for about five minutes by adding about 2-25 grams, for example, of natamycin crystals to propylene glycol or methanol, or other solvent in which natamycin will dissolve. Because of natamycin's limited solubility, it will not go completely into solution, but may form a suspension. As optimal volume for suspending 2-25 grams of natamycin is approximately 30-60 ml. Preferably, such an amount of natamycin will be added to about one pound of a conventional premix, and will not overly wet it. The one pound of premix is then added to about one ton of feed.

Preferable premix compositions include rice hulls which are readily available from grain brokers, or from the J. B. Hunt Company in Rodgers, Ark. Rice hulls are preferred because of their relatively low price; however, other premix materials may be used, such as calcium carbonate (limestone), soybean mill feed, or corn cob fractions, as examples. Other premix materials may be utilized, but they must be inert as are the other suggested premix materials. The natamycin suspension is added to the premix material, and then mixed for about ten minutes in a standard horizontal or vertical blender. Alternatively, natamycin in a dry powder form could be directly blended into feed; however, more extended mixing times would be required.

The preferred additive range of natamycin in the finished feed is about 0.000055 to 0.011 weight percent (about 0.5 to 100 grams per ton of feed), preferably about 0.000055 to 0.0055 weight percent (about 0.5 to 50 grams per ton), more preferably about 0.00022 to 0.0028 weight percent (about 2 to 25 grams per ton), and most preferably about 0.00088 to 0.0017 weight percent (about 8 to 15 grams per ton). This amount of natamycin is prepared, as discussed above, by suspending it in an appropriate carrier solvent and adding it to about one pound of a premix carrier. There is no evidence that use of the higher amounts would cause any toxicity problems in treated animals; however, the considerations of cost and undue wetting of the premix carrier may become significant. Because the premix will be added to one-ton charges of feed, the correspondence between resulting concentration in the feed is such that about one gram of natamycin added to the premix yields about a one ppm concentration of natamycin in the feed (about 0.0001 weight percent). Thus, 10 grams of natamycin added to one pound of premix, which in turn is added to a ton of feed, yields about a 10 ppm effective natamycin concentration.

Feed is conventionally prepared in a large bin or mixer in which the feed ingredients are added in descending weight order according to their prevalence in the ultimate feed mixture. Thus, cracked grain would be the primary ingredient. Minor ingredients are then added. Micro-ingredients are added last. These include vitamins, drugs, growth promoters, antibiotics, and the natamycin. Thus, natamycin is one of the micro-ingredients and is added to the feed in the final blending step. The feed is blended for conventional time periods. Individual farmers can also mix a natamycin premix with feed but this would require a small mixer such as is conventionally run by the power takeoff of a tractor. Five minutes is usually sufficient to blend natamycin in its premix form with small batches of feed materials.

The feed comprising the natamycin is fed to animals at standard feed dosage ranges and rates. No changes in feeding patterns are necessitated by the inclusion of natamycin into the animal feedstuff. Natamycin is suitable for incorporation in the feed of swine, poultry,

turkeys, dairy animals, horses, dogs, rabbits, fish and other animals which are not specifically mentioned.

The following examples illustrate the preparation of a natamycin treated premix:

EXAMPLE I

In 300 ml of propylene glycol, add 100 gm of natamycin. Stir at room temperature for about five minutes to dissolve some of the natamycin and to form a suspension with the remaining natamycin. Then, take 4 lb of dried rice hulls and place in a small, conventional horizontal mixer. Pour the 300 ml of natamycin solution/suspension over the rice hulls in the mixer and mix for ten minutes. By this technique, enough natamycin-treated premix can be prepared to treat about 4 tons of feed in order to achieve about a 25 ppm natamycin feedstuff (about 0.0028 weight percent).

EXAMPLE II

In this evaluation, the natamycin additive was evaluated on male broiler performance using commercial male broiler chicks. The broiler chicks included fifty male broiler chicks which were placed in pens to provide a bird density of 0.7 square foot per bird. Normal vaccination and other procedures were followed. Feed and water were given ad libitum. Reused litter was used, all pens were top dressed with two inches of new wood shavings. The broiler diet which meets NRC recommendations is set forth in the following Table I and shows the starter diet, the grower diet and the finisher diet. The starter diet is for the first two weeks, and the finisher diet is for the last week. The grower diet is for the period between start and finish. The table is as follows:

TABLE I

Broiler Diets Formulas and Nutrient Specifications			
Percentage	Starter	Grower	Finisher
Corn/Wheat	59.0	64.0	69.0
Fat	4.0	4.0	4.0
Meat Meal	5.0	5.0	5.0
Soybean Meal	30.0	25.0	20.0
dl-methionine	0.18	0.17	0.1
Defl. Phos.	1.25	1.2	1.15
Salt	0.25	0.25	0.25
Trace Minerals	0.05	0.05	0.05
Vitamin PMX	0.15	0.15	0.15
Protein	99.88	99.82	99.7
Fat	22.0	20.0	18.0
Fiber	6.5	6.7	6.85
Ca	>3.0	>3.3	3.5
Phos., available	1.0	0.8	0.6
Kcal (M.E.)	0.45	0.42	0.4
	1420.0	1450.0	1480.0

Treatments were assigned at random with blocks of six pens. All the treatments contained flavomycin at the rate of 1 gram per ton and Coban at the rate of 100 ppm. The feed was prepared as crumbles at 0-21 days and as pellets from 21-42 days. No withdrawal feed was given since all birds and unused feed were destroyed at final weighing date. The feeds also contained the indicated amount of natamycin, treatment 1 not containing any natamycin and thus being used as the control. Treatments 2, 3 and 4 contained 10, 20 and 50 grams per ton of natamycin. The following table sets forth the treatment data including the additive and pen numbers together with observations.

TABLE II

Treatment	Flavomycin g/ton	Coban g/ton	Natamycin g/ton	Pen Nos.
1	1	100	0	1,6,9,13,19,22
2	1	100	10	3,7,12,14,19,21
3	1	100	20	2,8,11,15,17,24
4	1	100	50	4,5,10,16,20,23

Observations and Data:

1. Weights by pen at 21 and 42 days of age.
2. Feed consumption for first 21 days and for the entire period.
3. Mortality daily and possible cause for death.
4. Gross observation was recorded for litter moisture, shank color, feathering and organic abnormalities.
5. All birds and unused feed were destroyed and not sold for human consumption.

The results of these experiments are set forth in the following table. In Table III each of the treatment groups is identified by treatment number, pen number, the number of birds started, the mortality rate and the weights of the birds, the average weight in grams and the feed efficiency. The results in Table III are 21 day performance data and are as follows:

TABLE III

Treatment	Pen No.	No. Birds		Average Weight grams	Feed Efficiency
		Star- ted	Mor- tality		
1	1	50	1	49	504
	6	50	1	49	533
	9	50	0	50	542
	13	50	1	49	549
	19	51	0	51	522
	22	49	1	48	519
Total and Average		300	4	296	528
2	3	49	1	48	513
	7	50	0	50	540
	12	49	0	49	541
	14	50	0	50	506
	18	47	0	47	557
	21	55	1	54	509
Total and Average		300	2	298	528
3	2	50	1	49	518
	8	50	2	48	535
	11	49	0	49	531
	15	50	2	48	523
	17	49	0	49	537
	24	52	0	52	500
Total and Average		300	5	295	524
4	4	50	0	50	522
	5	50	0	50	556
	10	49	0	49	522
	16	55	0	55	551
	20	54	1	53	530
	23	49	0	49	543
Total and Average		307	1	306	537

As will be seen in Table III, there is a strong indication that the natamycin-treated chicks provided better feed efficiency without adverse effects. Thus, a comparison of Treatment Group 1, whose feed did not contain natamycin, shows that the total and average feed efficiency was 1.64. This is substantially higher than the feed efficiency for Group 2, which is 1.57, Group 3, which is 1.60, and Group 4, which is 1.55. A comparison of the last two columns of Table III shows comparable or greater average weight of the chicks using less

feed. This thus demonstrates the effectiveness of natamycin as a feed efficiency agent.

The following table sets forth the 42 day performance summary of the chicks including rank by average weight. Table IV is as follows:

TABLE IV

42-day Performance Summary		
Treatment	Average Weight	Rank
2	1743	1
3	1735	2
4	1720	3
1	1716	4
Adjusted Feed Efficiency		
2	1.80	1
3	1.81	2
4	1.82	3
1	1.85	4

As will be noted from Table IV, Treatment 2 had the best overall performance with the highest average body weights and the lowest feed efficiency of 1.80.

The following table sets forth the liveability rate of the chicks during the treatment period. This rate is from 0 to 42 days and shows that the mortality rate was comparable for the treated and untreated chicks. In fact, the Treatment 2 group is substantially improved over the control and the Treatment 1 group. Table V is as follows:

TABLE V

Liveability - 0-42 Days						
Treatment	Pen No.	No. Started	No. Ended	Loss	% Mortality	Probable Cause
1	1	50	49	1	2.0	NGL
	6	50	48	2	4.0	NGL, AR
	9	50	50	0	0	
	13	50	48	2	4.0	NGL, AR
	19	51	51	0	0	
	22	49	48	1	2.0	NGL, CU
Total & Avg.		300	294	6	2.0	
2	3	49	48	1	2.0	AR
	7	50	50	0	0	
	12	49	49	0	0	
	14	50	50	0	0	
	18	47	47	0	0	
	21	55	53	2	4.0	NGL, CU
Total & Avg.		300	297	3	1.0	
3	2	50	49	1	2.0	AR
	8	50	48	2	4.0	NGL, NGL

TABLE V-continued

Liveability - 0-42 Days						
Treatment	Pen No.	No. Started	No. Ended	Loss	% Mortality	Probable Cause
	11	49	49	0	0	
	15	50	47	3	6.0	AR, AR, NGL
	17	49	49	0	0	
	24	52	51	1	1.9	NGL
Total & Avg.		300	293	7	2.3	
4	4	50	48	2	4.0	NGL, AR
	5	50	48	2	4.0	NGL, INJ
	10	49	48	1	2.0	CU
	16	55	55	0	0	
	20	54	53	1	1.9	CU
	23	49	49	0	0	
Total & Avg.		307	307	301	6	2.0

CODE:

AR - Aortic Rupture

CU - Cull

NGL - No Gross Lesions

INJ - Injury

The invention has been described herein with reference to certain preferred embodiments; however, as obvious variations thereof will become apparent to those skilled in the art, the invention is not to be considered as limited thereto.

I claim:

1. A method for improving the use of animal feed by an animal which comprises incorporating about 0.000055 to 0.011 weight percent of natamycin into the animal feed as a feed efficiency agent.

2. A method according to claim 1 wherein the natamycin is incorporated into the animal feed in admixture with an inert carrier as a premix.

3. A method according to claim 1 wherein the natamycin is dry blended into the animal feed.

4. A method according to claim 2 wherein the premix comprises about 8 to 15 grams of natamycin admixed with about 1 to 3 pounds of an inert feed as the carrier.

5. A method according to claim 4 wherein the inert carrier is selected from the group consisting of rice hulls, calcium carbonate, soy bean mill feed, and corn cob fractions.

6. A method according to claim 1 wherein the natamycin is added to the animal feed as a solvent suspension.

7. A method according to claim 1 wherein the animal feed comprises grain and cereal products.

8. A method according to claim 7 wherein the animal feed includes meat by-products, citrus pulp and grape hulls.

9. A method according to claim 1 wherein the natamycin is incorporated into the feed composition in an amount of about 0.00088 to 0.0017 weight percent.

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[54] **ANTIBIOTIC BIOMASS ANIMAL FEED COMPOSITIONS**

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[51] **Int. Cl.⁵** **A23K 1/00**

[52] **U.S. Cl.** **426/623; 426/60; 426/805; 426/807**

[58] **Field of Search** **426/623, 635, 60, 805, 426/807; 514/31; 424/119; 435/267**

[56] **References Cited**

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Primary Examiner—R. B. Penland

[57] **ABSTRACT**

An animal feed which is improved by the addition of a nonviable antibiotic biomass. The biomass may be obtained by drying a fermented biomass of an organism capable of producing an antibiotic which is effective against mycotoxin contamination. The resultant animal feed is substantially free of fungal mycotoxin contamination.

9 Claims, No Drawings

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ANTIBIOTIC BIOMASS ANIMAL FEED COMPOSITIONS

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to animal feed compositions enhanced with certain antibiotic biomass and processes for preparing the same. More specifically, the invention relates to an animal feed admixed with an antibiotic-containing biomass derived from the fermentation of amphotericin A or B, virginiamycin, leucomycins, levorin, filimarisin, partricin or trichomycin

2. Description of the Related Art

Polyene antibiotics have been produced in purified form and are known, in this form, to be effective antibiotic agents for a number of uses in post-formed formulations such as aqueous suspensions.

Natamycin, an effective antifungal agent, has been disclosed as an animal feed supplement to enhance growth (see U.S. Pat. No. 4,536,494). In this feed supplement, dry crystalline natamycin in effective amounts is physically mixed with feed grain or the like.

U.S. Pat. No. 4,132,777 discloses aqueous suspensions of natamycin formulated as an aqueous suspension for use on animals to control diseases such as ringworm.

Similarly, U.S. Pat. No. 4,950,477 discloses aqueous aerosol suspensions of pure polyenes including pimarin for control of various fungal diseases in humans and animals.

Canadian Patent 684,259 discloses feed additives of *Candida albicans* fermentation product, with or without the inclusion of an antifungal agent such as nystatin or pimarin. This reference also discloses that chlortetracycline has been used in feed and can be admixed with *Candida albicans* fermentation product.

U.K. Patent Application 2,106,498 discloses the use of *Streptomyces* SF-1(ASA), NC1B 11738 to produce a new tetraene and also pimarin. The activity of the fermentation broth is recorded, but no use of the fermentation biomass is disclosed.

U.S. Pat. No. 4,395,491 discloses the use in fodder of salinomycin in its biomass to promote growth of ruminants and pigs. Similar disclosures are contained in U.S. Pat. No. 4,291,053.

U.S. Pat. No. 3,802,998 relates to a process for producing levorin. The activity of levorin is measured in the fermentation broth, but no specific use is disclosed nor are there any disclosures of using this polyene as a dry biomass. Similarly, levorin and levoristatin activities are measures in the fermentation broth, as disclosed in U.K. Patent 1,254,212.

SUMMARY OF THE INVENTION

The present invention relates to admixing a nonviable, antibiotic-containing biomass with an animal feed. The antibiotic biomass is obtained by drying the biomass of an organism which produces the polyene antibiotic during fermentation.

It is an object of the invention to provide an enhanced animal feed by adding an antibiotic biomass to the feed. The antibiotic biomass enhances the quality and nutritional integrity of the feed by reducing, if not eliminating, contamination of the feed associated with fungal growth and possible mycotoxin release.

DETAILED DESCRIPTION OF THE INVENTION

It has now been found that for many uses, particularly in an animal feed mixture, it may be desirable not to extract and purify the antibiotic from a fermented biomass. More specifically, it has been found that the biomass from an antibiotic fermentation broth is a superior ingredient in animal feeds, particularly grain based feeds, such as poultry feed. Not only does the antibiotic biomass contain biologically effective quantities of an antibiotic to protect against fungal mycotoxin production, but it also contains significant nutrient values such as protein, trace compounds, or the like, which are desirable for maximizing animal growth.

The animal feed compositions of the present invention comprise, by way of example but not limited thereto, an animal feed such as a cracked grain feed for chickens, turkeys, and/or other poultry as well as similar feed for various animals, in combination with a biologically effective amount of an antibiotic, which is included within a nonviable antibiotic biomass.

"Antibiotic biomass" for purposes of this invention is defined as the product of fermenting an organism which releases an antibiotic. The antibiotic biomass is rendered nonviable by any suitable technique, which permits the biomass to be used as an ingredient in animal feed. The biomass comprises at least one of the cells of the antibiotic releasing organism, antibiotic, residual fermentation medium, fermentation broth (e.g., an aqueous phase which typically includes by-products), etc.

"Biologically effective amount" for purposes of this invention means that the nonviable antibiotic biomass is present in a sufficient quantity and will remain effective for a time sufficient to give adequate antifungal control for the animal feed to minimize mycotoxin production. The antifungal control is adequate to protect the animal feed against mycotoxins (e.g., due to growth of fungi, mold, yeast, etc.) contamination over the entire storage period.

"Animal feed" means a foodstuff which includes an antibiotic biomass that is provided to animals including at least one of chickens, horses, poultry, swine, turkeys, ruminants (e.g., bovine), pets, etc. The foodstuff typically comprises at least one of cereal grains (e.g., corn), soybeans, oil seeds, etc., which have been crushed or ground. The antibiotic biomass may be admixed with the foodstuff before, during and/or after being crushed or ground to obtain the animal feed.

"Stored" defines any technique whereby the animal feed is kept in a ready-to-use form for a prolonged period of time, namely about 1 to at least about 2 weeks. Storage may be in elevators, bins, bags, etc. An important aspect of the invention is that the storage is for the purpose of substantially retaining the animal feed in its initial as-stored condition, without significant change or contamination by microorganism attack.

"Dried" means that the nonviable antibiotic biomass, either sun dried or heat dried, has had its initial moisture content of at least about 30% by weight decreased to about 15% or lower, normally about 7%.

The term "non-toxic" embraces the concentration of the nonviable antibiotic biomass and substances used therewith in accordance with the invention for effective biological protection of the animal feed. Non-toxic does not include unacceptable quantities of either toxic chemicals from an antibiotic biomass or mycotoxins from fungal contamination.

Ciba patents in the area of antibiotics

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and other desirable ingredients that might normally have been lost during filtration.

Following concentration, the antibiotic biomass is dried by any suitable technique such as by spray dryer, fluid bed dryer, shelf dryer, etc. The temperature used for drying ranges from about 0° through at least about 120° C. and depends on the drying technique used and the thermal stability of the antibiotic to a given technique.

The antibiotic fermentation, antibiotic biomass recovery and treatment processes generally yield a antibiotic biomass which contains about 5 through at least about 35% antibiotic on a dry weight total antibiotic biomass basis.

For example, the solids from a fermentation broth comprising at least one of amphotericin A, amphotericin B, levorin, etc., may be separated, for example, by centrifuging. The supernate may be discarded and the biomasses may be divided into particles. The biomasses may be dried in a fluid bed dryer at 70° C. until a moisture content of about 7-8% by weight is obtained. The dried antibiotic biomasses may be mixed with a chicken feed comprising corn, wheat and soybean meal at a rate of about 100 grams of biomass per ton of chicken feed. Alternatively, a feed premix may be prepared by mixing about 100 grams of the antibiotic biomasses with about 1-5 pounds of rice hulls and/or soybean flour. The premixes may be admixed with a chicken feed comprising corn, wheat and soybean meal to obtain an enhanced feed including typically about 10 through 15 grams of antibiotic per ton of feed. The resultant feed is (1) protected from fungi contamination, (2) permits enhanced chicken growth rates and (3) controls and prevents diseases in the chicken associated with a fungi infection or mycotoxin production.

While not wishing to be bound by any theory or explanation, it is believed that the antibiotic biomass is active or effective against growth of fungi, mold and yeast, but not against bacteria. One explanation may be that fungi (but not bacteria) contain ergosterol in their membranes.

In general, the fungi will grow, if the environment is appropriate, until contacting the antibiotic within the antibiotic biomass. The mechanism of antibiotic action suggested is a binding of the antibiotic molecule and ergosterol present in the cell membrane of the fungi. The binding or complexing with ergosterol is substantiated by the neutralizing effects of ergosterol addition on the antifungal activities of the antibiotic against fungi. A complex between the antibiotic and the cell membrane of the fungi is believed to alter membrane permeability since the antibiotic typically is a relatively large molecule which creates an increased surface pressure which may tend to induce a reorientation of the ergosterol present in the membrane; thus altering permeability of the cell and resulting in osmotic shock. This osmotic shock is sufficient to interrupt, if not halt, the metabolic activities of the fungi (e.g., the antibiotic may cause irregular fungi growth, sporulation, discoloration, etc.), and therefore, reduce mycotoxin contamination.

Moreover, in one aspect of the invention, an energy source such as sugar (e.g., lactose) may already be present and/or admixed with the antibiotic biomass which is added to the animal feed. Particularly, without wishing to be bound by any theory or discussion, it is believed that the energy source may enhance the mechanism, discussed above, through which the antibiotic is believed to be effective against the fungi.

In addition to the energy source, other materials may be used in conjunction with the antibiotic biomass. Particularly, there are certain readily available materials which may tend to reduce growth of the undesired fungi. For example, fish meal, certain vitamins, etc., may be added to the feed which is consumed by the animals that may adversely affect the environment of the undesired fungi (e.g., the growth rate of the fungi is reduced). However, the presence of, for example, fish meal alone is not sufficient to protect animal feed from fungi contamination. Therefore, in certain aspects of the invention, a combination of the antibiotic biomass with other materials is effective against fungal contamination.

The antibiotic biomass is also compatible with other additives which may be admixed with the animal feed. Suitable additives include the members from the following group: protein, fat, fiber, calcium (e.g., calcium carbonate), phosphorus, trace metals, vitamins, citrus pulp, grape hulls, rice hulls, or the like.

The antibiotic biomass which has been added to the animal feed possesses an acceptable shelf life. Depending upon the storage conditions, the antibiotic can be expected to be effective against fungal contamination of the animal feed for several weeks or months. However, to ensure maximum effectiveness of the antibiotic biomass within the animal feed, the feed should be shielded from extended exposure to light (e.g., feed should be stored in the dark within a dry container).

Any antibiotic within the antibiotic biomass which is consumed by the animal is normally not absorbed or retained within the animal. As a result, the antibiotic is generally not incorporated into the eggs and/or flesh of the animal and, accordingly, if desired, does not affect human consumption of any animal which has consumed the feed of the invention. However, animals which are exposed to the fungi may incorporate the fungi, and in some cases toxins thereof, into their eggs and flesh. These fungi may be harmful to humans which consume the eggs and/or flesh of contaminated animals and, accordingly, it is desirable to prevent any significant exposure of such animals to fungi. Therefore, one aspect of the present invention permits enhanced production of animals which are not contaminated with undesirable fungi.

In certain aspects of the invention, it may be advantageous to introduce the antibiotic biomass in the animal feed in conjunction with other treatment processes and/or substances. More importantly, the antibiotic biomass of the invention does not preclude using the animal feed in conjunction with any medication, end use product or event (e.g., the antibiotic biomass may be fed to an animal undergoing a certain medical treatment).

Having thus described and exemplified the invention with a certain degree of particularity, it should be appreciated that the following claims are not to be so limited but are to be afforded a scope commensurate with the wording of each element of the claim and equivalents thereof.

What is claimed:

1. An animal feed additive composition consisting essentially of (a) a dried antibiotic biomass containing at least one polyene antibiotic selected from the group consisting of amphotericin A and B, virginiamycin, leucomycin, levorin, filimarisin, partricin, and trichomycin in admixture with (b) a non-toxic carrier material, the weight ratio of antibiotic to carrier in the ad-

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mixture being from 0.167 to 5, wherein said dried biomass prevents fungal attack of feed during storage.

2. The composition of claim 1 containing 5 to 35 parts by weight of antibiotic per 100 parts by weight residual biomass solids.

3. The composition of claim 1 mixed with animal feed to contain about 0.5 g to 100 g antibiotic per ton of animal feed.

4. The composition of claim 3 wherein the animal feed is grain-based poultry feed.

5. An animal feed composition consisting essentially of (a) a dried antibiotic biomass containing at least one polyene antibiotic selected from the group consisting of amphotericin A and B, virginiamycin, leucomycin, levorin, filimarisin, partricin, and trichomycin unseparated from the residual biomass solids from fermentation of the antibiotic-producing organism in admixture with (b) an animal foodstuff, the amount of antibiotic in the admixture being sufficient to reduce contamination of the foodstuff with fungal growth and mycotoxin during storage.

6. The composition of claim 5 containing from 5 to 35 parts by weight of antibiotic per 100 parts by weight residual fermentation solids.

7. The composition of claim 5 containing about 0.5 g to 100 g antibiotic per ton of animal feed.

8. The composition of claim 7 wherein the animal feed comprises cracked grain-based poultry feed.

9. The method of preparing an animal feed consisting essentially of: preparing at least one polyene antibiotic selected from the group consisting of amphotericin A and B, virginiamycin, leucomycins, levorin, filimarisin, patricin and trichomycin in a fermentation broth containing fermentation medium and organisms capable of producing said antibiotic; separating from the fermentation broth said antibiotic and other biomass solids including organisms; drying said antibiotic and biomass solids; and adding the dried antibiotic and biomass solids to an animal feed, the amount of antibiotic in the admixture being sufficient to reduce contamination of the foodstuff with fungal growth and mycotoxin during storage.

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