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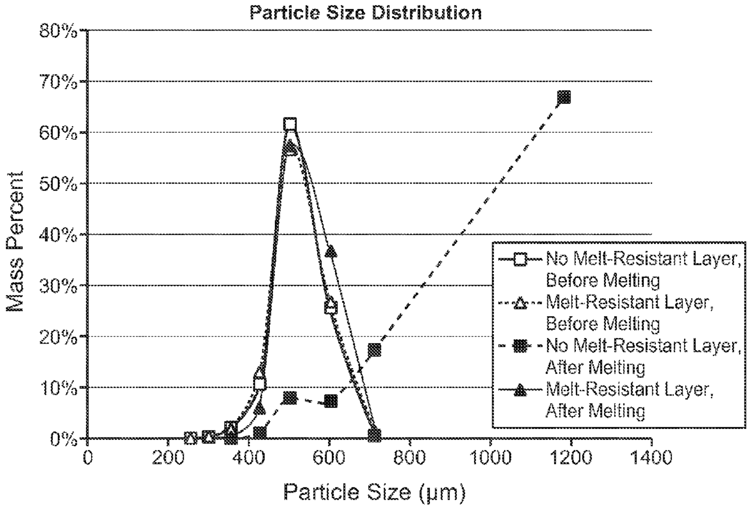

FIG. 4

(57) **Abstract**: The present teachings provide an improved layered granule comprising a melt-delayed layer located internal to a melt-resistant layer. The melt-delayed granules can be used in a variety of contexts, including animal feed. Methods of making and using the melt-delayed granules are also provided.

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MELT-DELAYED GRANULE

PRIORITY

This application claims benefit of priority from US Provisional Application Serial No. 61/673,183, filed 18 July 2012 and is incorporated by reference herein in its entirety.

FIELD

This disclosure is directed towards improved compositions for granules containing active agents and methods of making and using.

BACKGROUND

Industrially-produced enzymes have come to play a prominent role in many commercial areas. For example, the use of enzymes in foods and animal feed has become a common practice. Enzymes are known to improve digestibility of food and animal feed, reduce anti-nutritional factors in food and animal feed, and improve animal productivity. Additionally, enzymes are widely employed in various household cleaning products, including laundry and dish detergents. Enzymes are also prominently used in such areas as starch processing, biofuels, and dairy industries.

Inactivation of enzymes can occur during industrial food and feed processes (such as pelleting) by, for example, heat treatment, high pressure, shear stress, and chemical treatment (such as pH, surfactant, and solvents). The inactivation is at least partially reversible if the enzyme reactivates after processing, for example, upon cooling after steam treatment and pelleting; the inactivation is irreversible if the catalytic activity does not resume after processing, for example, upon cooling after steam treatment and pelleting. The irreversible inactivation and reduced activity of an enzyme is generally not desirable in processes such as pelleting. There is a need in the food and feed industries for stable, durable enzyme granules to serve as components in formulations that are subjected to steam treatment pelleting processes without appreciable loss of enzyme activity.

Approaches to avoid the problem of irreversibly inactivating enzymes or reducing the activity of the enzyme in industrial processes include identifying new sources of an enzyme (e.g. the identification of a known enzyme in an extreme thermophile microorganism) or identifying means to stabilize known enzymes. Klibanov, 1983, (*Stabilization of Enzymes against Thermal Inactivation*, Advances in Applied Microbiology, volume 29, page 1-28) discloses that there are three basic means for stabilizing enzymes: (1) immobilization, (2) chemical modification and (3) inclusion of additives. However, Klibanov (1983) further discloses that any one of these methods could lead to stabilization or destabilization, or have no effect at all. The present teachings seek to overcome some of these problems by use of an improved granule formulation.

In some situations, it can be desirable to melt a coating of material that has already been applied to a granule, for example from an aqueous suspension or dispersion of such a material. This would be hoped to cause the individual particles in the coating to melt and fuse together, creating a continuous coating with improved barrier properties. However, in situations where the particles are in intimate contact with one another, such as in fluid bed or pan coating, this will cause the particles to agglomerate and fuse together due to the tackiness of the now-molten coating destroying the intactness of individual granules and creating chips or other defects in the outer coating of the granules.

While others have attempted to make granules using melted layers (see US Patent 4657784), these approaches have not been successful. For example, such approaches use coatings that are applied in melted form. As a result of applying the layers in melted form, significant manufacturing challenges occur, such as difficulty in maintaining the spray nozzles from clogging, and difficulties associated with temperature control.

The present teachings address these and other problems through a novel granule design and method of making.

In addition to the animal feed industry, the granules provided by the present teachings can provide use in any of a variety of contexts, including the starch processing industry, the dairy industry, the biofuels industry, and the detergent industry, including household cleaning applications such as dish and laundry detergents.

For ease of reference we have described elements of the present teachings under one or more headings. It is to be noted that the teachings under each of the headings also apply to the teachings under the other headings. For example, each of the stated embodiments and aspects concerning the use of the present teachings is equally an embodiment or aspect concerning the method of the present teachings or the composition of the present teachings. Likewise, each of the stated embodiments and aspects concerning the method or use of the present teachings is equally an embodiment or aspect concerning the composition of the present teachings.

All patents, patent applications, publications, documents, and articles cited herein are all incorporated herein by reference in their entireties.

BRIEF SUMMARY

The present teachings provide a granule comprising; a core, wherein the core comprises an active agent; a melt-delayed layer containing an aggregation inhibitor; and, a melt-resistant layer. In some embodiments, the present teachings provide a method of making a granule comprising; providing a core; coating a melt-delayed layer onto the core; and, coating a melt-resistant layer onto the melt-delayed layer to make a granule. In some embodiments, the present teachings provide a process for producing an animal feed composition according to any of the preceding claims, comprising: preparing granules having a core comprising an active agent, a melt-delayed layer, and a melt-resistant layer; mixing the granules together with an unpelleted mixture; and, pelleting the unpelleted mixture at a temperature of 70℃-95℃.

Additional methods, uses, and compositions are also provided.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts an illustrative melt-delayed granule according to the present teachings.

Figure 2 depicts illustrative granules according to some embodiments of the present teachings.

Figure 3 depicts illustrative granules according to some embodiments of the present teachings.

Figure 4 depicts illustrative data according to some embodiments of the present teachings.

Figure 5 depicts illustrative data according to some embodiments of the present teachings.

DETAILED DESCRIPTION

The practice of the present teachings will employ, unless otherwise indicated, conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, biochemistry, and animal feed pelleting, which are within the skill of the art. Such techniques are explained fully in the literature, for example, Molecular Cloning: A Laboratory Manual, second edition (Sambrook et al., 1989); Oligonucleotide Synthesis (M. J. Gait, ed., 1984; Current Protocols in Molecular Biology (F. M. Ausubel et al., eds., 1994); PCR: The Polymerase Chain Reaction (Mullis et al., eds., 1994); Gene Transfer and Expression: A Laboratory Manual (Kriegler, 1990), and Fairfield, D. 1994. Chapter 10, Pelleting Cost Center. In Feed Manufacturing Technology IV. (McEllhiney, editor), American Feed Industry Association, Arlington, Va., pp. 110-139.

Unless defined otherwise herein, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the present teachings belong. Singleton, et al., Dictionary of Microbiology and Molecular Biology, second ed., John Wiley and Sons, New York (1994), and Hale & Markham, The Harper Collins Dictionary of Biology, Harper Perennial, NY (1991) provide one of skill with a general dictionary of many of the terms used in this invention. Any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present teachings.

Numeric ranges provided herein are inclusive of the numbers defining the range.

Definitions

As used herein, the term “granule” refers to a particle which contains a core, an active agent, and optionally at least one coating layer.

As used herein, the term “core” refers to the inner nucleus of a granule. The cores of the present teachings may be produced by a variety of fabrication techniques including: rotary atomization, wet granulation, dry granulation, spray drying, disc granulation, extrusion, pan coating, spheronization, drum granulation, fluid-bed agglomeration, high-shear granulation, fluid-bed spray coating, crystallization, precipitation, emulsion gelation, spinning disc atomization and other casting approaches, and prill processes. Such processes are known in the art and are described in US Pat. No. 4689297 and US Pat. No. 5324649 (fluid bed processing); EP656058B1 and US Pat. No. 454332 (extrusion process); US Pat. No. 6248706 (granulation, high-shear); and EP804532B1 and US Pat. No. 6534466 (combination processes utilizing a fluid bed core and mixer coating). The melt-delayed granule of the present teachings comprises a core upon which at least two coating layers are built.

The core includes the active agent, which may or may not be coated around a seed. Suitable cores for use in the present teachings are preferably a hydratable or porous material (i.e., a material which is dispersible or soluble in water) that is a feed grade material. The core material can either disperse in water (disintegrate when hydrated) or solubilize in water by going into a true aqueous solution. Clays (for example, the phyllosilicates bentonite, kaolin, montmorillonite, hectorite, saponite, beidellite, attapulgite, and stevensite), silicates, such as sand (sodium silicate), nonpareils and agglomerated potato starch or flour, or other starch granule sources such as wheat and corn cobs are considered dispersible. (Nonpareils are spherical particles made of a seed crystal that has been built onto and rounded into a spherical shape by binding layers of powder and solute to the seed crystal in a rotating spherical container. Nonpareils are typically made from a combination of a sugar such as sucrose, and a powder such as cornstarch.) In one embodiment of the present teachings the core is a sodium chloride or sodium sulfate crystal, also referred to as a seed, or other inorganic salt crystal. In another embodiment of the present teachings, the core is a sucrose crystal. Particles composed of inorganic salts and/or sugars and/or small organic molecules may be used as the cores of the present teachings. Suitable water soluble ingredients for incorporation into cores include: inorganic salts such as sodium chloride, ammonium sulfate, sodium sulfate, magnesium sulfate, zinc sulfate; or urea, citric acid, sugars such as sucrose, lactose and the like. Cores of the present teachings may further comprise one or more of the following: active agents, feed or food grade polymers, fillers, plasticizers, fibrous materials, extenders and other compounds known to be used in cores. Suitable polymers include polyvinyl alcohol (PVA), including partially and fully hydrolyzed PVA, polyethylene glycol, polyethylene oxide, polyvinyl pyrrolidine, and carbohydrate polymers (such as starch, amylose, amylopectin, alpha and beta-glucans, pectin, glycogen), including mixtures and derivatives thereof. Suitable fillers useful in the cores include inert materials used to add bulk and reduce cost, or used for the purpose of adjusting the intended enzyme activity in the finished granule. Examples of such fillers include, but are not limited to, water soluble agents such as salts, sugars and water dispersible agents such as clays, talc, silicates, cellulose and starches, and cellulose and starch derivatives. Suitable plasticizers useful in the cores of the present teachings are low molecular weight organic compounds and are highly specific to the polymer being plasticized. Examples include, but are not limited to, sugars (such as, glucose, fructose and sucrose), sugar alcohols (such as, glycerol, lower molecular weight polyethylene glycols, sorbitol, xylitol and maltitol and other glycols), polar low molecular weight organic compounds, such as urea, or other known plasticizers such as water or feed grade plasticizers. Suitable fibrous materials useful in the cores of the present teachings include, but are not limited to: cellulose, and cellulose derivatives such as HPMC (hydroxy-propyl-methyl cellulose), CMC (carboxy-methyl cellulose), HEC (hydroxy-ethyl cellulose). In one embodiment, particularly for feed applications, of the present teachings, the core is a water-soluble or dispersible corn cob material or sugar or salt crystal. In another embodiment particularly suitable for household cleaning applications, the core is a water-soluble or dispersible sugar or salt crystal or a nonpareil. Those skilled in the art will recognize that, for feed and food applications, the cores (and any polymers, fillers, plasticizers, fibrous materials, and extenders), are acceptable for food and/or feed applications. For household cleaning applications, such a restriction need not apply.

The term “coating layer” and “layer” are used herein interchangeably. The first coating layer generally encapsulates the core in order to form a substantially continuous layer so that the core surface has few or no uncoated areas. Subsequent coating layers can encapsulate the growing granule to form one or more additional substantially continuous layer(s). The materials (e.g. the active agents and components detailed herein) used in the granule and/or multi-layered granule can be suitable for the use in foods and/or animal feeds, and accordingly can be food grade or feed grade.

The term “outer coating layer” as used herein refers to the coating layer of a multi-layered granule which is the furthest from the core (i.e. the last coating layer which is applied). In some embodiments, the outer coating layer can be the melt-resistant layer.

The term “melt-delayed layer” refers to the layer of a multi-layered granule that melts at a lower temperature than the melt-resistant coating layer, is located internal to the melt-resistant layer, and is applied to a growing granule in un-melted form, but later melted after the application of the melt-resistant layer. The melt-delayed layer comprises at least one “melt-delayed material”, and at least one aggregation inhibitor. Illustrative melt-delayed materials include waxes including carnauba wax, paraffin wax, bees wax, polyethylene glycol (PEG) and stearic acid. In some embodiments, the melt-delayed material is carnauba wax.

The term “melt-resistant layer” refers to the layer of a multi-layered granule that melts at a higher temperature than the melt-delayed layer, and which is located external to the melt-delayed layer.

The term “aggregation inhibitor” refers to the presence of at least one material that inhibits aggregation which may lead to the precipitation of the melt-delayed materials. Since the melt-delayed materials of the present teachings are applied as an aqueous dispersion or an aqueous emulsion, it can be desirable to include an aggregation inhibitor in the form of a surfactant, dispersant or wetting agent to keep the particles or droplets of melt-delayed materials from aggregating and precipitating in solution. Suitable surfactants, dispersants or wetting agents include polysorbates such as polysorbate 80, sodium dodecyl sulfate, alcohol ethoxylates and polyvinyl alcohol.

The term “melt-resistant layer material” refers to any of a collection of materials that comprise the melt-resistant layer, and which together have the property of a melting temperature that is higher than the melting temperature of the melt-delayed layer. Illustrative melt-resistant layer materials include HPMC, polyethylene oxide, gum arabic, sucrose, starch, sodium sulfate, magnesium sulfate and other salts. In some embodiments, the melt-resistant layer material is composed of PVA and talc.

As used herein, the term “active agent” may be any material that is to be added to a granule to provide the intended functionality for a given use. The active agent may be a biologically viable material, a food or feed ingredient, an antimicrobial agent, an antibiotic replacement agent, a prebiotic, a probiotic, an agrochemical ingredient, such as a pesticide, fertilizer or herbicide; a pharmaceutical ingredient or a household care active ingredient, or combinations thereof. In a preferred embodiment, the active ingredient is a protein, enzyme, peptide, polypeptide, amino acid, carbohydrate, lipid or oil, vitamin, co-vitamin, hormone, or combinations thereof. In another embodiment, the active ingredient is an enzyme, bleach, bleach activator, perfume, or other biologically active ingredient. Inherently thermostable active agents are encompassed by the present teachings and can exhibit enhanced thermostability in the granules. Most preferred active ingredients for food and feed applications are enzymes, peptides and polypeptides, amino acids, antimicrobials, gut health promoting agents, vitamins, and combinations thereof. Any enzyme may be used, and a nonlimiting list of enzymes include phytases, xylanases, β-glucanases, phosphatases, proteases, amylases (alpha or beta or glucoamylases) cellulases, lipases, cutinases, oxidases, transferases, reductases, hemicellulases, mannanases, esterases, isomerases, pectinases, lactases, peroxidases, laccases, other redox enzymes and mixtures thereof. Particularly preferred enzymes include a xylanase from *Trichoderma reesei* and a variant xylanase from *Trichoderma reesei*, both available from DuPont Industrial Biosciences or the inherently thermostable xylanase described in EP1222256B1, as well as other xylanases from *Aspergillus niger, Aspergillus kawachii, Aspergillus tubigensis, Bacillus circulans, Bacillus pumilus, Bacillus subtilis, Neocallimastix patriciarum,Penicillium species, Streptomyces lividans, Streptomyces thermoviolaceus, Thermomonospora fusca, Trichoderma harzianum, Trichoderma reesei, Trichoderma viride*. Additional particularly preferred enzymes include phytases, such as for example Finase L®, a phytase from Aspergillus sp., available from AB Enzymes, Darmstadt, Germany; Phyzyme™ XP, a phytase from E. Coli, available from DuPont Nutrition and Health, and other phytases from, for example, the following organisms: Trichoderma, Penicillium, Fusarium, Buttiauxella, Citrobacter, Enterobacter, Penicillium, Humicola, Bacillus, and Peniophora, as well as those phytases described in US patent applications 61/595,923 and 61/595,941, both filed February 12, 2012. An example of a cellullase is Multifect® BGL, a cellulase (beta glucanase), available from DuPont Industrial Biosciences and other cellulases from species such as Aspergillus, Trichoderma, Penicillium, Humicola, Bacillus, Cellulomonas, Penicillium, Thermomonospore, Clostridium, and Hypocrea. The cellulases and endoglucanases described in US20060193897A1 also may be used. Amylases may be, for example, from species such as Aspergillus, Trichoderma, Penicillium, Bacillus, for instance, *B. subtilis*, *B. stearothermophilus*, *B. lentus*, *B. licheniformis*, *B. coagulans*, and *B. amyloliquefaciens.* Suitable fungal amylases are derived from *Aspergillus*, such as *A. oryzae* and *A. niger.* Proteases may be from *Bacillus amyloliquefaciens*, *Bacillus lentus*, *Bacillus subtilis, Bacillus licheniformis, and Aspergillus and Trichoderma species*. Phytases, xylanases, phosphatases, proteases, amylases, esterases, redox enzymes, lipases, transferases, cellulases, and β-glucanases are enzymes frequently used for inclusion in animal feed. Enzymes suitable for inclusion into tablets for household care applications are similar, particularly proteases, amylases, lipases, hemicellulases, redox enzymes, peroxidases, transferases, and cellulases. In particularly preferred aspects of the present teachings, the enzymes are selected from phytases, xylanases, beta glucanases, amylases, proteases, lipases, esterases, and mixtures thereof. In one embodiment of the present teachings, two enzymes are provided in the granule, a xylanase and a beta-glucanase. The enzymes may be mixed together or applied to the granule separately. In another embodiment, three enzymes are provided in the granule, namely beta-glucanase, xylanase and phytase. The above enzyme lists are examples only and are not meant to be exclusive. Any enzyme may be used in the granules of the present teachings, including wild type, recombinant and variant enzymes of bacterial, fungal, yeast, plant, insect and animal sources, and acid, neutral or alkaline enzymes. It will be recognized by those skilled in the art that the amount of enzyme used will depend, at least in part, upon the type and property of the selected enzyme and the intended use.

As used herein, the terms “pellets” and “pelleting” refer to solid, rounded, spherical and cylindrical tablets or pellets and the processes for forming such solid shapes, particularly feed pellets and solid, extruded animal feed. Known food and animal feed pelleting manufacturing processes generally include admixing together food or feed ingredients for about 1 to about 5 minutes at room temperature, transferring the resulting admixture to a surge bin, conveying the admixture to a steam conditioner, optionally transferring the steam conditioned admixture to an expander, transferring the admixture to the pellet mill or extruder, and finally transferring the pellets into a pellet cooler. Fairfield, D. 1994. Chapter 10, Pelleting Cost Center. In Feed Manufacturing Technology IV. (McEllhiney, editor), American Feed Industry Association, Arlington, Va., pp. 110-139.

As used herein, the term “unpelleted mixtures” refers to premixes or precursors, base mixes, mash, and diluents. Premixes typically contain vitamins and trace minerals. Base mixes typically contain food and feed ingredients such as dicalcium phosphate, limestone, salt and a vitamin and mineral premix, but not grains and protein ingredients. Diluents include, but are not limited to grains (for example wheat middlings and rice bran) and clays, such as phyllosilicates (the magnesium silicate sepiolite, bentonite, kaolin, montmorillonite, hectorite, saponite, beidellite, attapulgite, and stevensite). Clays also function as carriers and fluidizing agent, or diluents, for feed premixes. Mash typically comprises a complete animal diet.

As used herein, the term “recovered activity” refers to the ratio of (i) the activity of an active agent after a treatment involving one or more of the following stressors: heating with or without moisture, increased pressure, increased pH, decreased pH, storage, drying, exposure to surfactant(s), exposure to solvent(s), and mechanical stress) to (ii) the activity of the active agent before the treatment. The recovered activity may be expressed as a percentage.

The percent recovered activity is calculated as follows:

$$\%\ \text{recovered activity} = \left(\frac{\text{activity after treatment}}{\text{activity before treatment}} \right) \times 100\ \%$$

In the context of pelleting experiments, the “activity before treatment” can be approximated by measuring the active agent activity present in the mash that does not undergo treatment in a manner that is otherwise matched to the active agent that does undergo treatment. For example, the active agent in the untreated mash is handled and stored for a similar time and under similar conditions as the active agent in the treated mash, to control for possible interactions or other effects outside of the specified treatment per se.

Exemplary Embodiments

In an embodiment illustrative of the present teachings according to Figure 1, a granule comprises a seed (such as a salt crystal, for example a sodium sulfate crystal), around which an active agent such as an enzyme is placed. The resulting core can then be subjected to a fluid-bed spray coating process for addition of the various layers to make a melt-delayed granule. As depicted here, an immature melt-delayed layer surrounds the active agent, followed by a melt-resistant layer. Following a melting step such as with heat, the immature melt-delayed layer melts to become a mature melt-delayed layer. The melt-resistant layer remains intact throughout.

Thus, by putting a thin, higher melting point coating (the melt-delayed layer) on top of the lower melting point coating (the melt-resistant layer) it was possible to melt the lower melting point coating while not melting the higher melting point layer. This has the effect of preventing agglomeration, since the external layers avoid having a tackiness that causes unwanted agglomeration. Subsequent cooling allows for the lower melting point layer (the immature melt-delayed layer) to harden into a mature melt-delayed layer, which can improve the barrier properties of this layer, and hence improve the durability and performance of the resulting melt-delayed granule.

In some embodiments, the seed and enzyme are made using fluid-bed spray coating, such that the enzyme is deposited as a coating onto a seed, to make a core. In some embodiments, the seed and enzyme are made through other means, such that the enzyme does not comprise a layer over the seed but can rather be interspersed with any of a variety of material(s).

In some embodiments, the melt-delayed layer is directly adjacent to the core, such that there are no intervening layers. In some embodiments, the melt-delayed layer is directly adjacent to the melt-resistant layer, such that there are no intervening layers. In some embodiments, the melt-resistant layer is the outer layer. In some embodiments, an additional layer or two or more can reside external to the melt-resistant layer.

In one embodiment, the entire granule is made using fluid-bed spray coating, wherein a seed is first coated with an enzyme layer, the enzyme layer is next coated with a melt-delayed layer, and finally a melt-resistant layer is added. In such a granule, no intervening layers between the core, the melt-delayed layer, and the melt-resistant layer, is implemented. However, in some embodiments, one or more additional intervening layers can be added, either between the core and the melt-delayed layer, and/or between the melt-delayed layer and the melt-resistant layer, or external to the melt-resistant layer.

In some embodiments, the melt-delayed layer can range in composition from 2% to 40% by weight of the granule. In some embodiments, the melt-delayed layer can range in composition from 3%-15%, 10%-20%, or 4%-10% by weight of the granule.

In some embodiments, the melt-resistant layer can comprise < 10% by weight of the granule. In some embodiments, the melt-resistant layer comprises < 5% by weight of the granule. In some embodiments, the melt-resistant layer comprises 1-5% by weight of the granule.

In some embodiments, the melt-delayed layer comprises between 4%-10% of the granule by weight, and the melt-resistant layer comprises < 5% of the granule by weight, and there are no intervening layers between the core (which comprises an enzyme as the active agent), melt-delayed layer, and the melt-resistant layer, and the difference in melting points between the melt-resistant layer and the melt-delayed layer is 5°C or greater.

The melting temperature of the melt-delayed layer can be any temperature lower than the melt-resistant layer, though is likely to be greater than room temperature, but less than 120°C, allowing for easy accessibility with typical process equipment such as a fluidized bed coater. In some embodiments, the difference in melting points of the melt-resistant layer and the melt-delayed layer is 5°C or greater.

In some embodiments, the melt-resistant layer is not the outer layer. In such embodiments, the outer layer would typically be a coating with any of a variety of properties desired for the outer coating, such as for example a masking color, or resistance to dust formation. A typical masking color is white and this coating is typically a mixture of Titanium Dioxide and Polyvinyl Alcohol. A typical dust resistant coating is a highly plasticized polyvinyl alcohol coating with the plasticizer typically being glycerol or low molecular weight polyethylene glycol.

EXAMPLE

The present teachings can be further understood by reference to the following Example, which is provided by way of illustration and is not meant to be limiting. In this Example, granules were made with fluid-bed spray coating that contained a melt-delayed layer, and either did or did not further comprise a melt-resistant layer. The resulting granules were heated to melt the melt-delayed layer. Pictures of the resulting two kinds of granules showed severe agglomeration occurring in those granules lacking the melt-resistant layer. However, those granules containing a melt-resistant layer were shown to be free of agglomeration. This is shown in Figures 2 and 3.

Data quantifying the agglomeration showed that in those granules lacking the melt-resistant layer, the percent of the total mass of granules in the agglomerated state (defined as those greater than 1000 microns in diameter) is 50%. However, those granules containing the melt-resistant layer had 0% of the mass of granules in this highly agglomerated state. Complete particle size distributions showing the significant increase in particle size for the granules lacking the melt-resistant layer are shown in Figure 4.

Next, the effect of melting the melt-delayed layer was examined. For the granules of this experiment, the melt-delayed layer was comprised of carnauba wax as the melt-delayed material. Carnauba wax is a commercially available material itself comprising an aggregation inhibitor. The melt-resistant layer of the granules of this experiment, when present, comprised 9% PVA/talc. In this study, enzyme activity was measured to assess the functional consequences of melting the melt-delayed layer.

For this experiment, the core was 32.21% w/w sucrose for the granule with the melt-resistant coating, and 42.21% w/w sucrose for the granule without the melt-resistant coating. On top of the core was the enzyme layer comprising 4.44% enzyme solids, 3% sucrose, 6% corn starch, 0.10% sodium phytate and 0.75% rapeseed oil. On top of the enzyme layer was the starch-sucrose layer comprising19.75% corn starch, 19.75% sucrose and 0.75% rapeseed oil. On top of the starch-sucrose layer was the melt-delayed layer comprising 4% carnauba wax. A 9% layer of partially hydrolyzed PVA (3% of granule) and talc (6% of granule) was used as the melt-resistant layer and this was on top of the melt-delayed layer.

Looking at the data in Figure 5, granules lacking melt-resistant layers were first examined (first two bars). As expected, a melting treatment of 90°C for 1 hour, as compared to the absence of such a melting treatment, resulted in a significant reduction in enzyme activity. This effect is hypothesized to be due to damage of the melt-delayed layer arising from agglomeration. Next, granules containing both a melt-delayed layer and a melt-resistant layer either were, or were not, subjected to the melting treatment to melt the melt-delayed layer. This comparison shows that granules containing the melt-delayed layer and the melt-resistant layer that were subjected to the melting treatment show a nearly 20% improvement in retained enzyme activity (fourth bar) relative to un-melted control granules (third bar).

CLAIMS

1. A granule comprising;

a core, wherein the core comprises an active agent;

a melt-delayed layer; and,

a melt-resistant layer.

2. The granule of claim 1 wherein the melt-delayed layer has melted.

3. The granule of claim 1 wherein the melt-delayed layer has not melted.

4. The granule of any of the preceding claims wherein the melt-delayed layer comprises a melt-delayed material selected from the group consisting of carnauba wax, paraffin wax, bees wax, polyethylene glycol (PEG), and stearic acid.

5. The granule of claim 4 wherein the melt-delayed material is carnauba wax.

6. The granule of any of the preceding claims wherein the melt-resistant layer comprises a melt-resistant material selected from the group consisting of HPMC, polyethylene oxide, gum Arabic, sucrose, starch, sodium sulfate, magnesium sulfate, PVA, and talc.

7. The granule of claim 6 wherein the melt-resistant material is PVA and talc.

8. The granule of any of the preceding claims wherein the melt-delayed layer comprises 4%-10% w/w of the granule.

9. The granule of any of the preceding claims wherein the melt-resistant layer comprises <5% by weight of the granule.

10. The granule of any of the preceding claims wherein the melt-delayed layer has a melting point that is at least 5 degrees C lower than a melting point of the melt-resistant layer.

11. The granule according to any of the preceding claims wherein no intervening layers exist between the core, the melt-delayed layer and the melt-resistant layer.

12. An animal feed pellet comprising the granule of any of the preceding claims.

13. An animal feed unpelleted mixture comprising the granule of any of claims 1-11.

14. A household cleaning composition comprising the granule of any of claims 1-11.

15. A method of making a granule comprising;

providing a core;

coating a melt-delayed layer onto the core; and,

coating a melt-resistant layer onto the melt-delayed layer to make a granule.

16. The method of claim 15 further comprising melting the melt-delayed layer to make a granule.

17. The method of claim 16 further comprising cooling the granule to allow the melt-delayed layer to solidify.

18. A process for producing an animal feed composition according to any of the preceding claims, comprising:

preparing granules having a core comprising an active agent, a melt-delayed layer, and a melt-resistant layer;

mixing the granules together with an unpelleted mixture; and,

pelleting the unpelleted mixture at a temperature of 70°C-95°C.

19. The use of a granule according to any of claims 1-12 in a steam-treating or pelleting process

20. The use of a granule according to any of claims 1-11 and 14 in a household cleaning process.

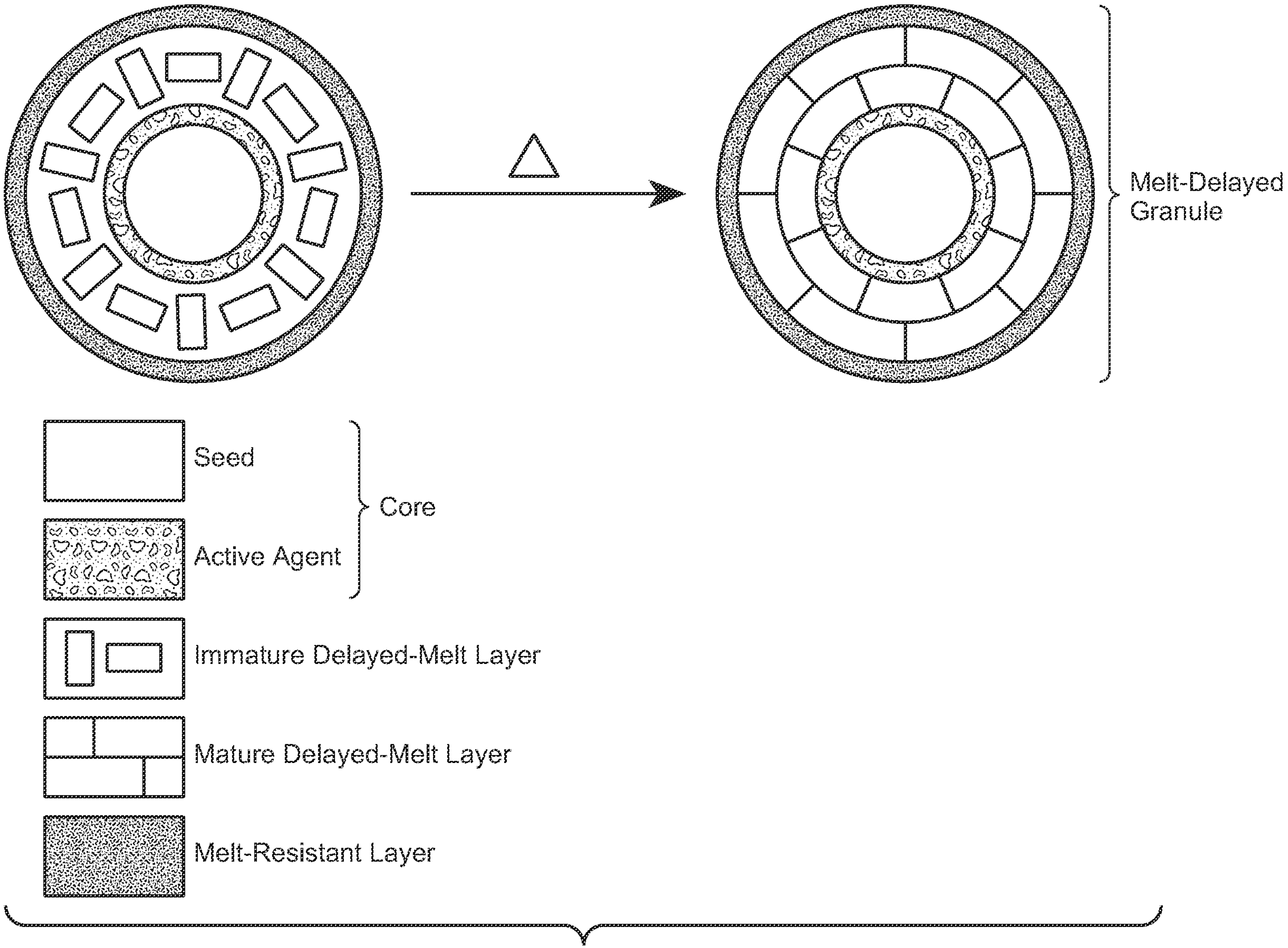
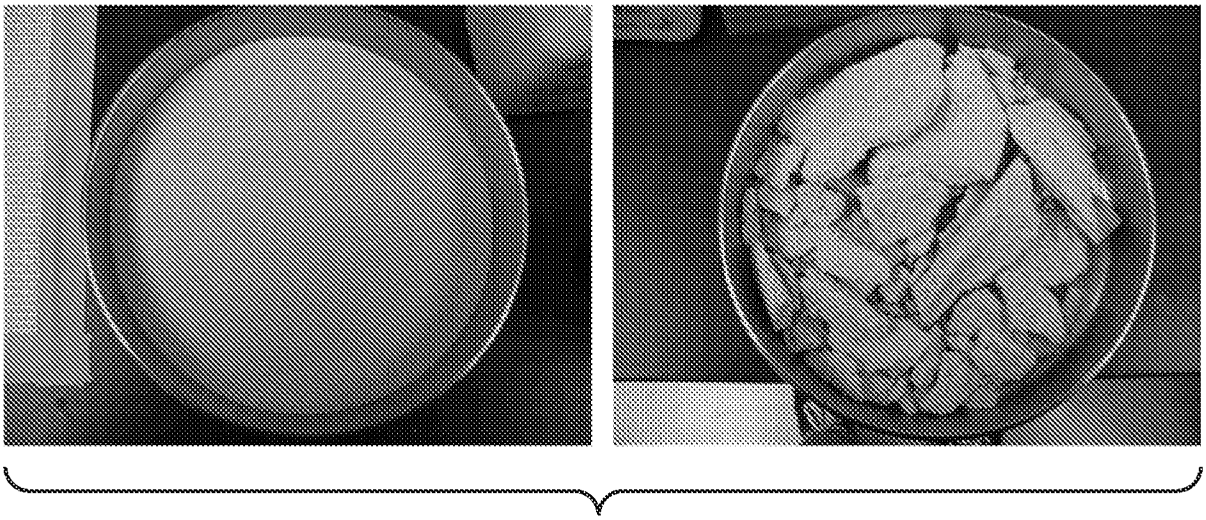

Δ
Melt-Delayed Granule
Seed
Active Agent
Core
Immature Delayed-Melt Layer
Mature Delayed-Melt Layer
Melt-Resistant Layer

FIG. 1

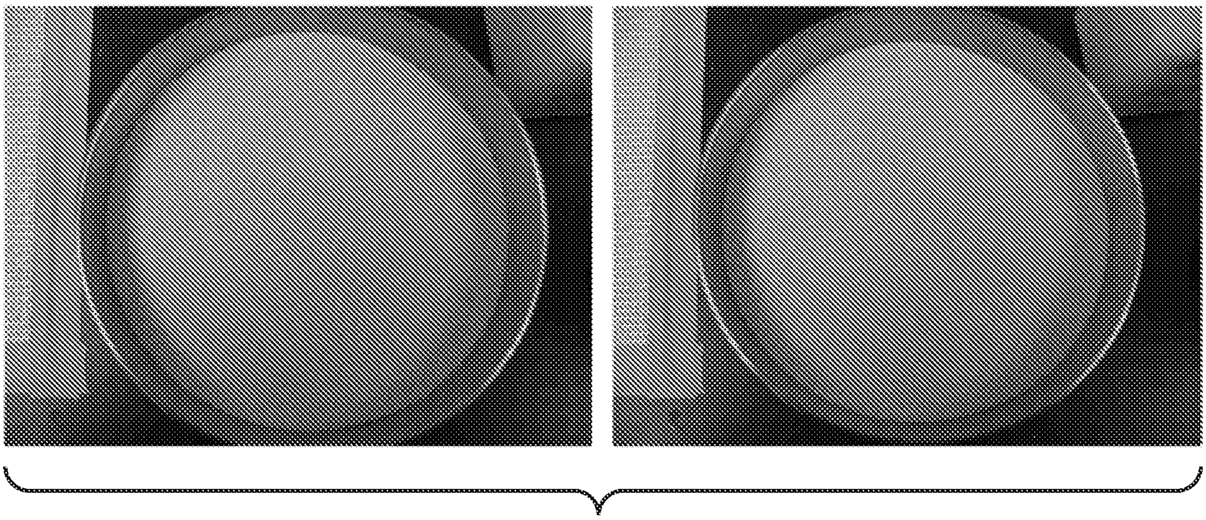


Effect of Melting Granules Lacking a Melt-Resistant Layer

Before Melting

After Melting

FIG. 2



Effect of Melting Granules Containing a Melt-Resistant Layer

Before Melting

After Melting

FIG. 3

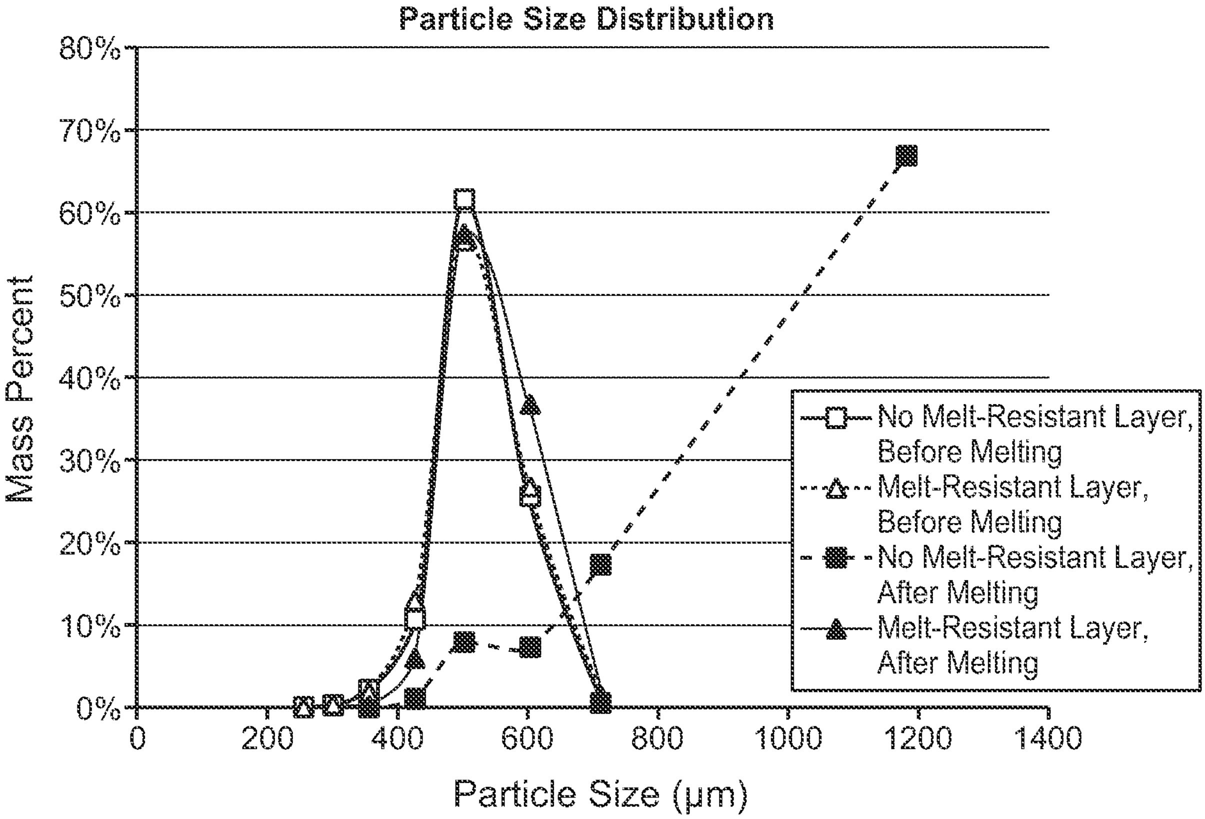

Particle Size Distribution
80%
70%
60%
50%
40%
30%
20%
10%
0%
Mass Percent
0
200
400
600
800
1000
1200
1400
Particle Size (μm)
No Melt-Resistant Layer, Before Melting
Melt-Resistant Layer, Before Melting
No Melt-Resistant Layer, After Melting
Melt-Resistant Layer, After Melting

FIG. 4

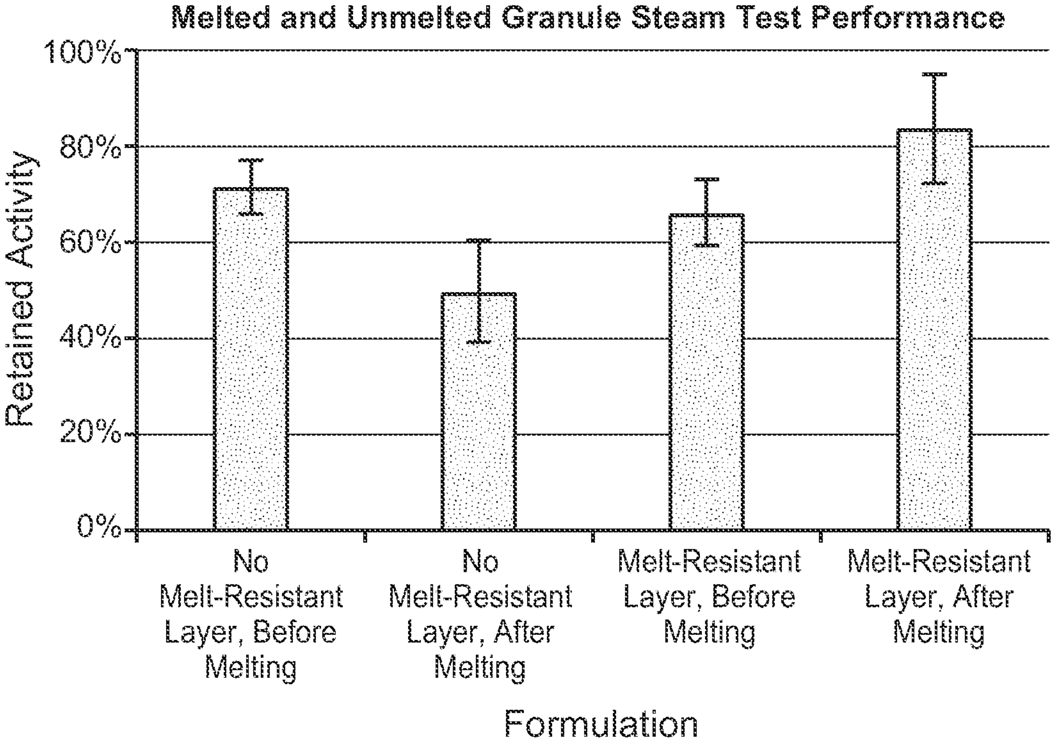

Melted and Unmelted Granule Steam Test Performance
100%
80%
60%
40%
20%
0%
Retained Activity
No Melt-Resistant Layer, Before Melting
No Melt-Resistant Layer, After Melting
Melt-Resistant Layer, Before Melting
Melt-Resistant Layer, After Melting
Formulation

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/048951

A. CLASSIFICATION OF SUBJECT MATTER
INV. A23L1/00 A23K1/00 A23K1/16 A23K1/165 A23L1/03
C11D3/386 C11D17/00
ADD.

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)
A23L A23K C11D

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

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

EPO-Internal, WPI Data, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 510 761 A1 (UNILEVER NV [NL]; UNILEVER PLC [GB]) 28 October 1992 (1992-10-28) claims 1-20; examples II,III,IV -----	1-20
X	US 4 657 784 A (OLSON KEITH E [US]) 14 April 1987 (1987-04-14) cited in the application the whole document -----	1-20
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☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" 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 theory underlying the invention

"X" 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

"Y" 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

"&" document member of the same patent family

Date of the actual completion of the international search 5 November 2013	Date of mailing of the international search report 14/11/2013
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Korb, Margit

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/048951

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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A	WO 03/059087 A1 (DSM NV [NL]; ANDELA CARL SIDONIUS MARIA [NL]; BEEKMAN WILLEM JOHAN [NL) 24 July 2003 (2003-07-24) claims 1-19; examples 1-6 -----	1-20

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