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(54) **Title:** ENTERIC DELIVERY OF FUNCTIONAL INGREDIENTS FOR ANIMALS

(57) **Abstract:** Microencapsulated materials and methods for manufacture are provided which may be suitable for animals, including ruminant animals, while providing acceptable enteric delivery properties. Functional ingredients, such as essential oils, pharmaceuticals, vitamins, minerals and the like is microencapsulated into an enteric matrix and/or enteric microcapsules. Further, a coating of an enteric material is applied. The microencapsulated materials is also coated with a coating that has a solubility less than about 20% at a pH of about 5.5 or greater. The functional ingredient may also be infused into a feed material and coated for delivery to an animal.



ENTERIC DELIVERY OF FUNCTIONAL INGREDIENTS FOR ANIMALS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit of United States Provisional Application Number 61/768,091, filed February 22, 2013, which is hereby incorporated herein by reference in its entirety.

FIELD

[0002] The present application relates to microencapsulated materials for consumption by animals. More particularly, the microencapsulated materials include functional ingredients in an enteric matrix effective for delivering the function ingredients to farm and domestic animals, including ruminant animals.

BACKGROUND

[0003] Enteric delivery of functional materials in food and feed applications has been limited. Enteric delivery systems are commonly utilized when the functional materials or medicaments are known to be sensitive to certain conditions such that they become less effective or if the functional materials cause problems during consumption, such as stomach problems with aspirin. Further, enteric delivery systems are commonly utilized when the functional materials or medicaments are known to be sensitive or unstable at low pH or in ruminant conditions or have undesirable flavor and /or taste characteristics which cannot be effectively masked by other methods.

[0004] Generally, enteric delivery, as most common in pharmaceutical practice, is accomplished by coating tablets and gel capsules. However, those particular delivery methods are not well suited for food or animal feed-type applications. In particular, neither tablets nor capsules are sized to be integrated into most existing food or animal feed-type products.

[0005] An alternative process for enteric delivery is microencapsulation. However, one issue with microencapsulation is the recovery rate, or microencapsulation efficiency of the process. Generally, a certain significant percentage of the material to be microencapsulated is not captured. The uncaptured material may be recovered for reuse, recycled, or a percentage of the uncaptured material remains adhered to the outer surface of the microencapsulated particulates.

[0006] In the situation where uncaptured material remains adhered to the micro-encapsulated particles, the product tends to have a taste profile associated with the uncaptured material, which is often undesirable. This is particularly true when the uncaptured material includes oxidizable triglycerides such as unsaturated and polyunsaturated lipids, oxidizable flavors and essential oils, or other organic compounds that may naturally have strong undesirable taste and/or flavor. For example, functional ingredients, such as essential oils, are known to possess health benefits and protect against intestinal parasites. However, one limitation of incorporating essential oils into foods, beverages, and animal feed is their strong, pungent smell and taste.

[0007] Further, delivery of functional ingredients to domestic and/or farm animals introduces additional complications. For example, animals have different transit times during digestion such that the timing of release of the functional ingredients must be carefully managed. Additionally, ruminant animals introduce further complexity due to the different chewing and digestive process in such animals. Ruminant animals generally chew feedstuff to tear and increase the surface area of the feed which helps to break down the feed during digestion. For example, ruminant animals, such as cows, often move their flat teeth side to side to tear the feed into a pulp. Therefore, enteric materials need to be sized such that they do not substantially break down during chewing. Ruminant animals also digest food/feed differently from domestic animals and humans. For example, ruminant animals have four ruminant sacks where feed, plant material and the like is digested by fermentation of cellulosic material by microorganisms such as conversion of carbohydrates into volatile fatty acids and gases. This process allows the ruminant animal to convert cellulosic fiber into energy.

[0008] To complicate matters in ruminant digestion, ruminant animals also regurgitate boluses of non-digested material (cud) for re-mastication. Boluses tend to float on top in the ruminant fluid in one of the ruminant sacks. Therefore, if the enteric material is included in the boluses, they are susceptible to re-mastication, thereby increasing the risk that the materials will break down prior to reaching the desired location in the digestive tract during repetitive chewing processes.

[0009] Ruminants also produce large amount of saliva. Saliva in ruminant animals serves two functions, buffering and suppressing foam. Saliva in ruminants typically has a pH value of approximately 8.2 and a high sodium bicarbonate level. This means that the saliva helps to counteract the effects of acid-producing feedstuffs, such as cereals, molasses,

potatoes and fodder beets, on the ruminal pH (rumen's pH is typically 5.5-7.0 depending on the feed). Further, saliva helps to suppress the foaming effect in the rumen.

[0010] During digestion, the feed particles become smaller as the bacteria work and the rumination process continues. The feed particles gradually absorb fluid and sink to the bottom of the rumen. The contents in the bottom of the reticulo-rumen or the first and second of four chambers in the animal generally has a dry matter content of 5%. Further, the rumen generally contracts about once or twice every minute or so, such as with cows. The contractions allow mixing of fluid and solid contents in the rumen to stimulate fermentation and avoid stagnation. Contractions also serve to release gases trapped in either the mat or fluid portion of the rumen. The fermentation gases are then released by belching. Disruption of this process can result in bloat. Feed particles of the correct size and density are segregated into the fluid in the reticulum by the ruminal contractions. Subsequent contractions force these particles and some of the fluid contents out of the reticulo-rumen and into the omasum or the third of four chambers in a ruminant's stomach.

[0011] The rumen and reticulum are basically one compartment, but with different functions. While much of fermentative action occurs in the rumen (first chamber), the reticulum (second chamber) serves as a staging area for passage into the omasum or regurgitation. The omasum is the third compartment of the ruminant animal's stomach. It is characterized by the presence of a large number of leaves, which provide a wide absorption surface (about 4-5 m²). This surface absorbs water (30-60% of the water intake) and nutrients such as potassium and sodium. The omasum also prevents the passage of large particles through the digestive system. The abomasum is believed to be the equivalent of human stomach, having an acidic pH (2-3), where proteins are broken down. True digestion finally occurs in the fourth stomach. The abomasum glands produce hydrochloric acid, pepsin and lipase which break down the food into all its constituent nutrients.

[0012] When the feed has passed through the acid abomasum it enters the small intestine. Here, the pH value increases because the feed is mixed with bile and pancreatic secretions, with a pH value of 8. The main functions of small intestine are to enzymatically break down nutrients so that they can be absorbed and absorb nutrients (i.e., fatty acids, sugars, and amino acids) and water via the intestinal villi.

[0013] The varying chewing and digestion processes in animals, including ruminant animals, introduce complexity in designing and preparing enteric materials. Therefore, a

number of different factors, such as multiple mastication, varying pH and digestive conditions, multiple chamber digestive systems, and particle size and durability should be taken into consideration when designing and preparing enteric materials.

SUMMARY

[0014] Microencapsulated materials and methods of manufacturing are provided that are suitable for animals, including ruminant animals, while still providing acceptable enteric delivery properties in view of the complex digestive process in animals. For example, functional ingredients, such as essential oils may be microencapsulated into an enteric matrix suitable for animal digestion and, in particular, ruminant digestion. Further, a coating of an enteric material may be applied. The microencapsulated materials may also be coated with a coating or layer that has a solubility less than about 20% at a pH of about 5.5 or greater.

[0015] In one form, a microencapsulated composition for use with animal feed is provided. The composition includes a functional ingredient composition, an enteric material coating the functional ingredient composition, and an outer coating having a solubility less than about 20% at a pH of about 5.5 or greater.

[0016] According to one form, a microencapsulated composition for use with animal feed is provided. The composition includes a granulated core and an outer coating. The granulated core includes a plurality of particles in combination with a granulating material. The particles include a functional ingredient composition microencapsulated in an enteric material. The outer coating at least substantially surrounds the granulated core and has a solubility less than about 20% at a pH of about 5.5 or greater.

[0017] In accordance with one form, an animal feed composition is provided. The composition includes a feed material, a functional ingredient composition, an enteric coating and an outer coating. The feed material includes an interior and an exterior and is selected from the group consisting of grains, cereals, legumes, wheat, soy, rice and combinations thereof. The functional ingredient composition is located on the interior of the feed material. The enteric coating covers at least one of the functional ingredient composition and the feed material. The outer coating has a solubility less than about 20% at a pH of about 5.5 or greater and is located on the exterior of the feed material.

[0018] In one form, the enteric material coating is selected from the group consisting of zein, caseinate, shellac and combinations thereof.

[0019] According to one form, the composition further includes a coating having a delayed release material selected from the group consisting of gum arabic, gelatin, ethylcellulose, hydroxypropyl methylcellulose and combinations thereof.

[0020] In accordance with one form, the functional ingredient comprises a hydrophilic material in a matrix.

[0021] In one form, the composition further includes an intermediate coating between the enteric material coating and the outer coating, the interior coating comprising ethylcellulose.

[0022] According to one form, the functional ingredient composition includes a hydrophobic material which is entrapped within a matrix of an enteric material selected from shellac, caseinate, zein, and combinations thereof.

[0023] In accordance with one form, the functional ingredient comprises essential oils.

[0024] In one form, the outer coating is selected from the group consisting of methyl methacrylate, N,N-dimethylaminoethylmethacrylate, cross-linked chitosan, poly (2-vinylpyridine-co-styrene) and combinations thereof.

[0025] According to one form, the microencapsulated composition includes particles having a size in the range of about 75 to about 500 μm .

[0026] In accordance with one form, the microencapsulated composition includes particles having a density of about 1.0 to about 2.0 g/cc.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] FIG. 1 is a diagrammatic representation of an enteric material including a core and a plurality of optional coatings;

[0028] FIG. 2 is a diagrammatic representation of an enteric material having a plurality of microcapsules within a core;

[0029] FIG. 3 is a diagrammatic representation of an enteric material infused within a feed material;

[0030] FIG. 4 is a diagrammatic representation of an enteric material comprising a plurality of microcapsules infused within a feed material;

[0031] FIG. 5 is a process flow diagram for one form for preparing a microencapsulated composition; and

[0032] FIG. 6 is an illustration of samples particles subjected to simulated ruminant digestion.

DETAILED DESCRIPTION

[0033] Disclosed is a microencapsulated composition including a functional ingredient and a method for manufacture. Generally, the composition includes one or more enteric materials as well as one or more coatings that can be used in combination to delay the release of the functional ingredient prior to a desired dissolution location, such as in the intestine. Such a combination of features may be suitable for animals and/or in animal feed, functional feed and the like, and are particularly suited for ruminant digestion.

[0034] It should be noted that “functional feed” generally encompasses any type of feed that incorporates a functional ingredient to be delivered to the human and/or animal. Functional feed can be used to decrease and/or eliminate the need to handle the animals, such as by forcing the animals to ingest or otherwise receive the functional ingredients. Such a delivery can help where the functional ingredient is large or has an undesirable taste. If the person or animal is unwilling to ingest the functional ingredient, delivery can be problematic. Therefore, by incorporating the functional ingredient in a functional feed, the functional ingredient can be made more appetizing.

[0035] The microencapsulated composition may include encapsulated materials, as well as encapsulated materials in the form of a matrix. Generally, it should be understood that the term matrix as used herein refers to a type of encapsulation that is somewhat different from traditional core and shell encapsulation which has a single functional material coated by the encapsulating material. Matrix encapsulation is generally directed to a three dimensional material, which may be spherical, semi-spherical and the like (or other shapes), with multiple active particulates, liquids and/or solids distributed and/or embedded throughout the matrix particle. For example, in one form, the matrix includes a plurality of oil droplets dispersed throughout the matrix material. Therefore, the matrix particle may include a plurality of oil droplets dispersed in the matrix material. In one form, the matrix may stabilize and/or protect the functional ingredients within. The matrix particle may then be further encapsulated with one or more coatings.

[0036] As shown in FIG. 1, one form of a microencapsulated material 10 is shown. In one form, the microencapsulated material 10 includes a core 12, a first coating 14 and a second coating 16 effective to provide enteric delivery to animals and, in particular, ruminants. While two coatings or layers are shown, the microencapsulated material 10 may include any number of coatings effective for providing a composition which is suitable for animals and/or in animal feed, and particularly ruminant digestion. Further, it should be noted that the microencapsulated material 10 may take a variety of shapes, including irregular shapes.

[0037] The core 12 generally may include a number of different components, such as a functional ingredient, a non-active carrier, one or more enteric materials and the like in a matrix. According to one form, the selection of materials for the core 12 may be such that the core 12, by itself, has enteric properties and, in addition, may also be coated with one or more optional enteric coatings as shown in FIG. 1. In another form, the core 12 does not have enteric properties by itself, but may be coated by one or more optional enteric coating(s). The core 12 may include functional ingredients such as essential oils, non-active carriers such as lipids, and enteric materials forming the matrix such as soy protein, sodium caseinate, shellac, zein, hydroxypropyl methylcellulose, and combinations thereof, to suggest a few enteric materials.

[0038] According to one form, the core includes about 1 to about 90 wt.% of enteric materials and about 40 to about 95 wt.% of functional ingredients, both on a dry weight basis of the core ingredients. In another form, the core includes about 15 to about 35 wt.% of enteric materials and about 65 to about 85 wt.% of functional ingredients, both on a dry weight basis of the core ingredients. In one form, the core includes about 10 to about 60 wt.% enteric materials and in other forms about 20 to about 60 wt.% enteric materials. According to one form, the core includes about 10 to about 70 wt.% enteric materials. In another form, the core includes about 20 to about 60 wt.% of each of the soy protein and sodium caseinate. In yet another form, the enteric matrix is zein, shellac, and mixtures thereof.

[0039] The core 12 may include hydrophobic materials, hydrophilic material, hydrophobic/hydrophilic materials and the like. Further, the core may include pharmaceuticals, medicines, vitamins, minerals, and the like which are suitable for animals. For example, the core 12 may include omega-3 oils, probiotics, polyphenols, anti-parasitic

materials, vaccines, antibiotics, essential oils, micro-nutrients such as amino acids, fatty acids, minerals, and the like.

[0040] In one form, where the core includes hydrophilic ingredients entrapped in an enteric matrix, the hydrophilic material may be entrapped in the core 12 such as via spray drying. In this approach, the hydrophilic actives can be entrapped in a slow release hydrophilic polymer via spray drying. For example, hydrophilic functional ingredients can be combined with hydroxypropyl methylcellulose (HPMC) and then spray dried to form a HPMC-type matrix entrapping the hydrophilic ingredients. Other polymers can also be used. The spray dried materials can also be granulated to achieve a desirable size for later coating. In some cases, the particles may be granulated to sizes greater than about 100 μm .

[0041] Optionally, the hydrophilic actives can be entrapped in an enteric type polymer by hydrating/dispersing the hydrophilic material in an enteric polymer solution which can then either be spray dried or spray fluid dried to contain the functional material distributed within an enteric matrix.

[0042] When hydrophobic materials are included in the core 12, the hydrophobic materials may be emulsified with one or more enteric materials to form a matrix. In this regard, the hydrophobic active can be emulsified with zein, shellac, sodium caseinate, soy and the like and then acid titrated to form the core 12 defining a matrix of zein, shellac, sodium caseinate, soy, and the like enteric materials. The matrix may be formed by methods as described in U.S. Patent Publication No. 2010/0310726, which is incorporated by reference herein in its entirety.

[0043] Alternatively, the hydrophobic material may be emulsified/dispersed in a binary solvent, such as a combination of water and alcohol, such that the solvent may be later removed via spray drying or other methods to entrap the functional material within an enteric matrix.

[0044] Other materials may be included in the core 12 as will be discussed below in more detail. For example, the core 12 may include enteric materials such as zein and shellac and may also include other materials to accommodate the hydrophobic and/or hydrophilic nature of the functional ingredients in the core 12. The core 12 may take a variety of forms, including, but not limited to core capsules, a matrix and the like. In one form, the composition may be composed of core capsules containing proteins such as sodium

caseinate and soy prepared at and/or below their isoelectric point to maintain enteric properties.

[0045] The core microcapsules 12 may then be coated with a unique combination of food grade, enteric polymers to provide one or more coatings or layers suitable for animal digestion and, in some cases, ruminant digestion. According to one form, the first coating is prepared from a binary solvent (alcohol/water) based zein and/or shellac solution, and the second coating, which in some cases may be the outermost coating, is also prepared from a material that provides delayed release in ruminant animals. It is believed that the combination of the two coatings with the core materials may be used to provide delayed enteric release in animals, including ruminant animals that have pH requirements (6-8) and digestion times (up to 20 hours) prior to stomach and intestinal digestion, much different than humans.

[0046] The first coating 14 may include a variety of different materials, including, but not limited, to enteric materials. For example, in one form, the first coating 14 includes at least one of zein, shellac, in combination with modified cellulose polymers such as ethylcellulose and hydroxypropyl methylcellulose. According to another form, the first coating 14 includes an alcohol-based zein (which generally refers to a binary solvent of alcohol and water). The first coating 14 may be provided in a variety of amounts and thicknesses as desired. For example, in one form, the first coating 14 includes about 1 to about 80 wt.% zein and/or shellac on a dry basis relative to the total composition. According to one form, the first coating 14 includes about 5 to about 80 wt.% zein and/or shellac. In another form, the first coating 14 includes about 10 to about 60 wt.% zein and/or shellac on a dry basis relative to the total microencapsulated material 10. It should be noted that other materials may be included in the first coating 14 as will be described below in more detail.

[0047] Zein may be used as the first coating, which in an inner coating that is otherwise protected by the second coating such as a coating of ethylcellulose in one approach. The zein may be used to provide a more controlled enteric release of the functional ingredient at the desired pH when ingested by the user.

[0048] The second or outer coating 16 may be a rumen protective coating and may also include a variety of different materials, including, but not limited to materials which provide for delayed release in ruminant animals. The second or outer coating may be any coating

that is stable or resistant to pH values greater than about 6, but is soluble beyond the rumen pouch and dissolves at a stomach pH of less than about 5.5, and is also stable to microorganism fermentation or resistant to microbial enzymes. For example, in one form, the second coating 14 includes polycationic polymers such as methyl methacrylate and N,N-dimethylaminoethylmethacrylate (DMAEM). These polymers have minimal solubility at or above about pH 5.5 and higher solubility at stomach pH, which is generally less than about 5.5.

[0049] The coating may also include cross-linked chitosan and combinations of chitosan with other materials. In one approach, the cross-linked chitosan may be cross-linked with glutaraldehyde. The second coating 16 may be provided in a variety of amounts and thicknesses as desired. For example, in one form, the composition includes about 1 to about 70 wt.% of the second coating on a dry weight basis of the total composition. In some approaches, the composition includes about 10 to about 70 wt.% of the second coating. In another form, the second coating 16 is provided such that the second coating 16 is included in an amount of about 10 to about 50 wt.% relative to the microencapsulated material. The second coating may also include plasticizers. In another approach, the second coating includes about 1 to about 50 wt.% zein on a dry weight basis of the total composition. In another form, the second coating includes shellac in an amount of about 1 to about 50 wt.% relative to the microencapsulated material.

[0050] In another approach, the second or outer coating may be or include a high melting fat, such that it has a melting point of at least about 40°C or other body temperature of the ingesting entity that is water impermeable in the rumen and configured to dissolve or release in the intestinal tract due to lipase. Further, in one form, for better wettability, it may be preferable to add the high melting point fat prior to adding a polycationic layer. It should be noted that other materials may be included in the second coating 16 as will be described below in more detail. In one form, the second coating has solubility of less than about 20% at a pH greater than about 5.5. In some cases, the second coating has a solubility of about 10 to about 20% at a pH greater than about 5.5. It should be noted that other coatings, such as for providing protection in the rumen, may be included such as poly (2-vinylpyridine-co-styrene).

[0051] The composition may also include a variety of additional coatings. For example, the composition may include a plurality of different enteric materials. The composition may also include optional intermediate coatings, such as water barrier type polymer materials.

One example may be to use ethylcellulose to provide further delayed release. This intermediate coating may be a water barrier.

[0052] In one form, the microencapsulated material 10 has a density of about 0.7 to about 2 g/cc. In another form, the microencapsulated material 10 has a density of about 1.0 to about 1.5 g/cc. In some forms, it may be desirable to have a density of greater than about 1.0 g/cc in view of lower density particles being regurgitated and re-masticated in ruminants. In other forms, the material 10 may have a density of about 0.8 to 2 g/cc, and in other forms, about 1.2 to about 1.4 g/cc. Additional densifying materials such as iron oxide, weighting agents, elemental iron, and mixtures thereof, may be added to increase the density. Selection of density may aid in achieving target release of the actives in certain animals, such as ruminants. For example, the densities above help aid in eliminating buoyancy of the microencapsulated material 10 such that it will sink in the ruminant fluid and not be regurgitated with boluses of non-digested material for re-mastication. Further, denser particles may also shorten the transit time to the intestines. In some approaches, densities of about 1 to about 1.5 g/cc may be effective to sink in the ruminant fluid.

[0053] According to one form, the individual microencapsulated material or particle 10 has a particle size of about 75 to about 1000 microns, and more particularly, about 100 to about 500 microns. In other approaches, about 75 to about 500 microns, and in yet other approaches, about 100 to about 300 microns. In another form, the microencapsulated material has a particle size of about 100 to about 300 microns. For example, particle sizes above may help aid in the microencapsulated material 10 from not being ground in the animal's mouth during mastication, and in the case of ruminants, re-mastication and the repetitive chewing process. In some approaches, an average particle size of an particles, which may be individual particles or agglomerated particles, may be about 1 to about 2 mm, in some cases, less than 1mm, to aid in the reduction and prevention of damage to the particle during mastication.

[0054] Another form of microencapsulated material is provided in FIG. 2. Referring to FIG. 2, a microencapsulated material or granulated microcapsule 20 is provided having a plurality of microcapsules 22 contained in a core and/or granulating material 26. The microcapsules 22 can include a plurality of microencapsulated materials 10 as described above in FIG. 1. In this regard, the microcapsules 22 can include one or more enteric coatings, can include enteric matrix forms and include other features as described above with respect to FIG. 1.

[0055] While FIG. 2 illustrates the microcapsules 22 spread out or uniformly distributed in the core 24, it should be understood that the core 24 may be packed with microcapsules 22 such that the microcapsules 22 are generally contacting one another. Further, the core 24 may include a granulating material 26 to assist in forming the core 24. For example, the granulating material 26 may help the microcapsules to agglomerate together. Suitable granulating material includes carbohydrates such as maltodextrin, corn syrup solids, sugars, mono, di and oligosaccharides, silica, hydroxypropyl methylcellulose, starch, proteins, and mixtures thereof. Zein and/or shellac may also be used as granulating material. The granulating material may be provided to agglomerate the microcapsules into robust, larger particles having multiple microcapsules. The formed granules may be strong and robust to withstand further processing handling and/or mastication. The granulating material may be provided in a variety of ranges, such as from about 1 to about 50% of the overall composition (in some approaches, about 5 to about 50% and other approaches about 1 to about 20%). The particle 20 may be formed by a granulation process.

[0056] The core 24 may also include any number of different coatings, similar to the discussion regarding FIG. 1. For example, the core 24 may include enteric coatings and other coatings for delaying release of the core materials when chewed and digested in animals, including ruminant animals. Furthermore, the core 24 may include an outer coating 28 similar to second coating 16 in FIG. 1. In this regard, the outer coating 28 may include methyl methacrylate, N,N-dimethylaminoethylmethacrylate, cross-linked chitosan and combinations thereof. Other materials such as poly (2-vinylpyridine-co-styrene) may also be used.

[0057] In one form, the microencapsulated material 20 has a density of about 0.8 to about 2.0 g/cc. In another form, the microencapsulated material 20 has a density of about 1.0 to about 1.5 g/cc and in other forms about 1.2 to about 1.5 g/cc. Additional materials such as iron oxide may be added to the granulating material 26, the microcapsules 22, and/or the various coatings to increase the density. According to one form, the microencapsulated material 20 has a particle size of about 5 microns to about 6 mm (in some approaches up to about 1 mm) and more particularly about 100 microns to about 3 mm and in other forms about 100 microns to about 300 microns. The density and particle size are selected to aid in re-mastication prevention and buoyancy reduction as described with the previous version. Further, the particles may have a density and particle size to facilitate less damage during mastication.

[0058] Referring now to FIG. 3, a further embodiment of an enteric material is shown. As seen in FIG. 3, an animal feed composition 30 is shown. The composition is advantageous because it utilizes the natural feed of the animal, such as in the form of a functional feed, as part of the enteric targeted delivery system. The animal feed composition 30 includes feed material 32, such as grain, cereal, corn, soy beans, wheat, rice, and the like, and mixtures thereof, that is combined with actives or functional ingredients and protective enteric coatings and encapsulation. The feed 32 material may be dehulled, whole, half, grit and meal. The feed material 32 also includes actives or functional ingredients (not shown) which have been incorporated with or into the interior of the feed material 32. The functional ingredients can be incorporated such as by infusing the functional ingredients into the feed material 32 as will be described in more detail below.

[0059] The animal feed 30 also includes an enteric coating 34, such as using materials described above in FIG. 1 for layer 14. For example, the enteric coating 34 may include zein, shellac, ethylcellulose and other enteric polymers. As discussed above, the thickness of the enteric coating 34 will be selected to provide the desired target release in the animal tract, and can vary for transit time of the animal. In one approach, the thickness of layer 34 may be about 1 to about 100 microns.

[0060] The animal feed 30 may also include other layers, such as a second or outer coating 36, that can be used to provide protection against release in ruminant animals and may be any of the materials and include any of the characteristics of layer 16 described above. For example, the second coating 36 can include methyl methacrylate, N, N-dimethylaminoethylmethacrylate (DMAEM) and cross-linked chitosan. The second or outer coatings may also be or include a high melting point fat coating that may be water impermeable in the rumen and then provides release characteristics in the intestinal tract due to lipase action. Due to wettability, it is preferred as a middle coat. The feed 30 may also include an optional middle or intermediate coating similar to that described with particle 10 above.

[0061] The animal feed 30 may be prepared by, first, infusing the grain with the actives or functional ingredients and, second, applying the various coatings and protectants described above. More specifically, the process may first optionally swell the grain material 32 with cold or hot water and then infuse the feed material 32 with the functional ingredient and any other materials that are desired on the interior of the feed material 32. For example, in the case of hydrophilic functional ingredients, the functional ingredient can be combined

with water and then infused into the feed material 32. In the case of hydrophobic materials, the functional ingredient can be emulsified and then infused into the feed material 32. For hydrophobic actives, pre-emulsification in water is generally used in some approaches to achieve submicron size oil droplets. Further, sugars and salts can be used to help increase the infusion rate. An organic solvent such as ethanol or ethanol/water blend can be utilized as a carrier for the hydrophobic actives such as essential oils discussed below. Optionally, the infusion solution can also include a protective polymer/film former for better infusion rate and have a low solution viscosity to help achieve good infusion.

[0062] In some forms, the grain is pre-treated to increase the micropores and therefore facilitate higher infusion rates and volumes.

[0063] After the functional ingredient is infused into the feed material 32, the feed material 32 is dried to entrap the functional ingredient therein and provide shelf stability to the feed material 32. The coatings (such as, layers 34 and 36) may then be applied such as using a fluid bed coating for small feed material and pan coating for larger feed materials. Any number of different coatings may be applied to provide desired release characteristics, as described above.

[0064] Referring now to FIG. 4, a variation on the embodiment of FIG. 3 is shown. As seen in FIG. 4, an animal feed 40 is shown having a feed material 42, similar to FIG. 3. However, FIG. 4 incorporates the functional ingredient in the feed material 42 in the form of microcapsules 44, similar to the embodiment of FIG. 2. For example, the microcapsules 44 may be in the form of functional ingredients combined with an enteric material which results in the microcapsules 44. After the microcapsules 44 are infused into the feed material 42, the feed material may then be dried and then coated, such as with coatings 48 and 50 similar to the coatings and protectants described above with FIG. 3. Coatings 48 and 50 can include further enteric coatings and coatings suitable for ruminant animals.

[0065] In one form, the functional ingredient for the embodiments described above can include any mixture of hydrophobic liquids and solids, such as solids mixed or combined therewith or dissolved or solubilized therein. As an example, functional ingredients can be selected to include materials which are desired to be released in the small intestine rather than the stomach due to pH sensitivity. As an example, the functional ingredient can include compositions described in U.S. Patent Publication No. 2008/0145462 to Enan or include esterified forms of such compositions. For instance, the functional ingredient

includes about 25 to about 35% by weight para-cymene, about 1 to about 10% by weight linalool, about 1 to about 10% by weight alpha-pinene, about 35 to about 45% by weight thymol, and about 20 to about 30% by weight soybean oil.

[0066] In particular, the functional ingredient described herein can include an essential oil blend which possesses anti-parasitic properties. In one embodiment, the essential oil blend is organic compounds blended with food grade oil, i.e., soybean oil. Further, the organic compounds can include thymol and linalool. In a further embodiment, the organic compounds include alpha-pinene and para-cymene. One exemplary blend of an essential oil includes, by weight, about 17.5 percent soybean oil, about 8 percent alpha-pinene (liquid), about 44 percent para-cymene (liquid), about 5 percent linalool (liquid) and about 25.5 percent thymol (crystal). In another embodiment, the functional ingredient may also include modified forms of the hydrophobic liquid, as described in provisional Patent Application Serial No. 61/422,439, filed December 13, 2010, which is incorporated herein in its entirety by reference. In yet another embodiment, the hydrophobic liquid includes esters, such as esters of linalool and thymol, as described in Application Serial No. 12/479,444, filed June 5, 2009, which is incorporated herein in its entirety by reference. Another exemplary form includes about 10 wt.% para-cymene, 5 wt.% alpha-pinene, 15 wt.% linalyl acetate, and about 70 wt.% thymyl octanoate.

[0067] The functional ingredient can include a portion that is modified, such as by esterification, and can comprise from about 1 to about 99 percent of the functional ingredient by weight. In some approaches, the modified functional ingredient can include from at least about 10 percent of the functional ingredient by weight and, in other approaches, about 30 percent by weight. In another embodiment, the modified functional ingredient can include from about 25 to about 65 percent of the functional ingredient by weight.

[0068] In one embodiment, the blend of non-active carrier and functional ingredient can include, by weight, about 15 to about 30 percent canola oil, about 1 to about 10 percent alpha pinene, about 5 to about 25 percent para-cymene, about 5 to about 20 percent linalyl ester and about 20 to about 60 percent thymyl ester. In other approaches, the blend of non-active carrier and functional ingredient can include, by weight, about 20 to about 25 percent canola oil, about 2 to about 7 percent alpha pinene, about 10 to about 20 percent para-cymene, about 7 to about 15 percent linalyl ester and about 35 to about 50 percent thymyl ester.

[0069] By one approach, the selected esterified form of the functional ingredient may have increased functionality due to an increased rate of hydrolysis over the parent form after ingestion and release from the enteric matrix in an intestinal tract. Esters may be obtained from natural sources or synthesized using any suitable chemical or biochemical reactions between functional ingredients, such as thymol and linalool, and organic or inorganic oxoacids that yield esters. Suitable oxoacids may include carboxylic acid, amino acids, phosphoric acid, sulfuric acid, and nitric acid. The hydroxyl group can be derived from a homogenous source (e.g., thymol) or mixed source (thymol and linalool). Exemplary monocarboxylic acids include, but are not limited to, acetic, propionic, butyric, pentanoic, hexanoic, octanoic, decanoic, stearic, lactic, cinnamic, pyruvic, benzoic, and gluconic acids. Exemplary dicarboxylic acids include, but are not limited to, oxalic, malonic, maleic, fumaric, tartaric, succinic, glutaric, glucaric, adipic, pimelic, suberic, azelaic, and sebacic acids. Exemplary tricarboxylic acids, include, but are not limited to, citric and isocitric acids. Other exemplary esters that may be formed by reactions of terpenes with oxoacids include dithymol succinate, dithymol adipate, and dithymol sebacate.

[0070] In another form, the modified functional ingredient can include an ester formed, regardless of chemical or biochemical reaction approach for its preparation, between terpene esters and other esters. In particular, the functional group can be formed using transesterification. For example, the functional group can include an ester formed by reacting thymol acetate with methyl octanoate or tripalmitin.

[0071] Alternatively, it is anticipated that the functional ingredient can include other modified compounds. In one form, the modified functional group can include any glycoside formed by chemical or biochemical reaction between the hydroxyl group(s) of a terpene and a single sugar group (monosaccharide) or several sugar groups (oligosaccharide). For example, thymol and/or linalool glycosides can be the modified functional ingredient. The sugar group can include any glycoside with the glycone portion composed of mono, di, tri, and/or polysaccharides of any kind and the aglycone portion being any hydroxy-terpene (e.g., thymol, linalool). The sugar group can also include reducing sugars and/or non-reducing sugars. Exemplary sugars include, but are not limited to, glucose, fructose, galactose, ribose, sucrose, mannose, maltose, lactose, and cellobiose.

[0072] In another form, it is anticipated that the functional group can include any ionic or nonionic salt or complex formed involving a hydroxy-terpene and another chemical species. For example, thymol and linalool salts or complexes can be the modified functional

ingredient. One example may be sodium and/or potassium salts. In another form, the modified functional ingredient may include thymol salts that do not have fixed stoichiometries. For example, thymol salts may be prepared as partial or mixed salts having different ratios of cations and thymol comprising one or more specific cations (Na^+ , K^+ , Mg^{++} , etc.) to prepare solid complexes. The solidified complexes may or may not be obtained in crystalline form. The salt or complex may be formed by any suitable method, but in some cases is formed by a chemical reaction or association between one or more hydroxy-terpene and one or more alkaline reagent. Exemplary alkaline reagents may include, but are not limited to, alkaline hydroxide, oxide, bicarbonate, or carbonate. The salt or complex can include any alkali metal, alkaline earth metal, or transition metal element, or combination thereof. Suitable salts or complex for use in foods may include those formed from sodium, potassium, lithium, calcium, magnesium, iron, manganese, zinc, and aluminum. Other exemplary salts include any mono, di, or trivalent salt of thymol, including sodium thymolate (e.g., sodium thymoxide) and any mono, di, or trivalent salt of phenol, including calcium phenoxide.

[0073] Furthermore, the functional ingredient may include various forms of modification that are combined. For example, a portion of the modified functional ingredient composition may include one or more of salts, glycosides, complexes and esterified forms of one or more essential oils.

[0074] Modifications to the functional ingredient may include a variety of forms that modify the perceived taste and/or organoleptic properties of the functional ingredient. For example, the modification may cause a change to the flavor and/or taste threshold of the functional ingredient. In one form, the modification causes a change to the volatility and/or vapor pressure of the modified functional ingredient with respect to the non-modified, parent form of the functional ingredient. In particular, the organoleptic properties of the modified form may include a higher taste threshold. As a result, in some cases a modified functional ingredient on the surface of the enteric matrix may produce a less undesirable flavor profile than the presence of unmodified functional ingredients. Further, the modifications may include salt, glycoside, complex and/or esterification of the functional ingredient.

[0075] When ingested and released in the intestinal tract, the modified form of the functional ingredient reverts back, at least in part, into the parent form and provides the same functional benefits as if the parent functional ingredient was microencapsulated and

consumed. In one form, the modified functional ingredient hydrolyzes from the modified form back into the parent, non-modified form of the functional ingredient during digestion.

[0076] In some approaches, the functional ingredient described herein can include compounds which possess functional properties, such as anti-parasitic, anti-protozoan, and anti-fungal. In one embodiment, the organic compounds further include alpha-pinene and para-cymene.

[0077] Other suitable examples of a materials which may be included in the core include unsaturated and polyunsaturated OMEGA 3, other unsaturated and polyunsaturated lipids or fatty acids and triglycerides thereof, beta-carotene, and oil soluble vitamins, stomach irritants, or any other hydrophobic materials that are either sensitive to acidic pH conditions or impart strong undesirable taste.

[0078] Due to the low water solubility and/or increased hydrophobicity, an ester may have higher microencapsulation efficiency, such as described above, than non-esterified parent compounds, such as thymol and linalool. Preferably, the efficiency increases about 50 to about 200 percent over the efficiency observed when using non-esterified functional ingredients, more preferably about 100 to about 150 percent. Further, esters have a higher olfactory perception threshold than the parent compounds, such that amount of esters necessary to be perceived is more than the amount of non-esterified thymol and linalool.

[0079] Methods are provided for microencapsulating one or more functional ingredients therein, such as described above. One method for microencapsulating a functional ingredient, such as a hydrophobic material, is generally described in FIG. 5. It should be noted that hydrophilic materials may be processed differently, such as by spray drying, as described above. As shown in FIG. 5, water, an enteric material and optionally an emulsifier are subjected to agitation until the enteric material and emulsifier are combined with the water to form a solution, such as at step 120. Generally, the emulsifier and enteric material can be added to the water together or separately, with either being added first. In some cases, the pH of the solution is generally greater than about 7, and generally greater than about 7.1 to about 9. In other cases, a base, such as sodium, ammonium or potassium hydroxide, carbonates, bicarbonates and combinations thereof, can be added to the solution to maintain the pH greater than about 7, and in yet other cases from greater than about 7 to about 9 to maintain dissolution of the enteric polymers in water substantially free of organic solvents.

[0080] The functional ingredient is then added to the enteric material solution, such as at step 130. The enteric material solution containing the functional ingredient is then mixed, such as at step 140. In one form, the materials are agitated or mixed to form an emulsion. By one approach, "agitation" or "agitated" generally refers to the use of a top mixer with impeller or a rotor/stator mixing device operating at a speed of less than about 10,000 RPM. Other mixing devices may also be employed.

[0081] After mixing, the materials are then acid titrated to precipitate out the functional ingredient microencapsulated with the enteric material, such as at step 150, in a matrix core structure that is generally tiny droplets of functional ingredients substantially homogeneously dispersed in the matrix material.

[0082] As shown at step 150, the material is titrated with acid in an amount effective to decrease the pH below the isoelectric or solubility point of the enteric materials causing phase separation and inducing precipitation of the enteric material out of solution with the functional ingredient being microencapsulated therein, thus creating a slurry of an aqueous solution and precipitate. The slurry includes a particulate precipitate having a particle size from about 1 to about 1000 micrometers, in some cases about 10 to about 500 micrometers, and in yet other cases from about 75 to about 250 micrometers. In some approaches, precipitation occurs at a pH ranging from about 3 to about 6.5, and in other approaches from about 3 to about 5, and in one approach at a pH of about 4.5. In the method illustrated in FIG. 5, and in the case of using sodium caseinate and soy protein, in order to maintain the enteric properties of the particulate precipitate, a fine, stable emulsion of sodium caseinate and soy protein may be titrated with an acid to a pH corresponding to the insolubility at the isoelectric point of sodium caseinate, such as about 4.4 to about 4.6. In some approaches, the slurry may be allowed to settle, resulting in a clear division of the liquid or supernatant and the settled particulate.

[0083] While not wishing to be limited by theory, it is believed that as the pH of the emulsion drops below the solubility point, enteric materials, such as soy protein and sodium caseinate may cross-link to like particles or to one another to form a matrix, the hydrophobic liquid being microencapsulated within the matrix. As a result of the cross-linking, the functional ingredient is homogeneously dispersed throughout the matrix. The matrix further provides a seal for the functional ingredient. As a result, the impact of the functional ingredient on the organoleptic qualities of the finished product is generally correlated to any

functional ingredient remaining adhered to the outer surface of the enteric material that is not coated.

[0084] The acid used for step 150 can be any acid, including, but not limited to, food grade acid. In one approach, the acid is a weak food grade acid. For example, the acid may be citric acid.

[0085] As noted above, the composition of the enteric material affects the dissolution rate and the protection provided by the enteric matrix. As a result, the rate and amount of acid addition varies based on the enteric matrix materials used.

[0086] To reclaim the precipitate, the slurry may be optionally filtered to produce a wet cake, then washed and dried to produce a dried cake. In some approaches, the particulate and the supernatant are both filtered to produce a cake, then washed and dried to provide a dried cake. In another approach, the slurry or supernatant and particulate are filtered to provide a wet cake. The wet cake is then washed, refiltered and rewashed prior to drying. In some approaches, the surface oil on the outer surface of the particulate precipitate is less than about 1 percent by weight of the final product. In one embodiment, a surface oil remover may be added to aid in removing residual surface oil from the precipitate, as described in co-pending Application Serial No. 12/479,433, filed June 5, 2009, which is incorporated herein in its entirety by reference. Further, the surface oil remover can also be added at any point in the preparation after acid titrating.

[0087] Next, the first coating is applied to the microencapsulated functional ingredient, as shown in step 160. After the first coating is applied, a second coating may be applied, such as shown in step 170. It should be noted that additional coatings may be included beyond the first and second coatings. Optionally, the coatings may include a small amount of a suitable plasticizer, such as one that is soluble/miscible in water.

[0088] In some approaches, each solution to prepare the first and second outer coatings can include about 5 percent to about 20 percent enteric material and about 1 percent to about 3 percent plasticizer including, but not limited to, glycerin and other suitable plasticizers. In some approaches, the final, coated microencapsulated particles can include between about 1 to about 15 percent by weight of each of the first and second coatings.

[0089] The coating materials can be applied to the enteric matrix by mixing, spraying or other suitable application. In one approach, the coating materials are first solubilized in water. A base can optionally be added to the solubilized outer coating material to increase

the pH to greater than about 7, in some cases between about 7.1 and about 12. The solubilized material can then be atomized and sprayed onto the uncoated particulate product.

[0090] In some instances, the first and second coatings each have coating thicknesses of about 1 micrometer to about 5 micrometers. If desired, the coated matrix particles can then be sieved to meet the desired particle size. The thickness of the first coating 14, 34, or 48 tends to provide the desired target release in the intestinal tract. In some cases, the thickness can be varied based on transit time in the animal. For instance, for a ruminant with a rumination transit time of 15-20 hours, the thickness of the first coating will be at the high end of the range such as about 4 to about 5 micrometers. The thickness may be modified to accommodate different transit times, animal sizes and the like. In some cases, the thickness may be up to about 10 microns or even higher depending on the circumstances.

[0091] Additional processing steps after the second coating may also be included. For example, such steps may include drying and/or otherwise removing moisture from the coated microcapsules to form a material having less than about 10%, and, in some forms, less than 5% moisture.

[0092] In one instance, the coating materials are applied by spraying a fine mist of the respective coating onto fluidized core capsules to create uniformly coated particles. Such a process can include top and/or bottom spraying. In one form, such a process can combine simultaneous layer coating with instant drying.

[0093] Other coating techniques may also be employed. For example, larger particles, such as in the case of infused grain and/or agglomerated particles, may be more suited to pan coating. Pan coating may be more suitable in view of the size and/or density which may limit the air fluidization of such particles. In one form of pan coating, the particles are tumbled in a rotating drum with baffles while the coating is atomized and sprayed on the particles. In this form, spraying and drying may be carried out simultaneously.

[0094] Other steps may also be included, such as grinding the dried material to form a powder. Further, other intermediate steps may also be included in the process. For example, such steps may include, but are not limited to, washing the microencapsulated material to remove unencapsulated functional ingredients, pH adjustments and the like.

[0095] Further, the powder can be pulverized to reduce the particle size of the powder precipitate, and then further dried to a moisture content of less than about 5 percent, such as

with a fluidized bed dryer. By one approach, the resultant particles have a particle size ranging from about 1 to about 1000 micrometers, in some approaches from about 10 to about 500 micrometers, and in other approaches from about 75 to about 250 micrometers.

[0096] When drying the powder, the temperature may be maintained between about 25°C to about 70°C, in some approaches between about 35°C to about 60°C, and in other approaches between about 35°C and about 45°C. During other processing steps, the temperature may be maintained between about 4°C to about 40°C, in some cases about 4°C to about 30°C, and in other cases from about 15°C to about 28°C.

[0097] According to one form, the core is substantially free of organic solvents. As used herein, "substantially free of organic solvent" generally refers to an amount of added organic solvent, such as isopropanol or ethanol or any other food-grade organic solvent, which is less than the amount of organic solvent required to enable solubilization of the enteric material under the processing conditions. Preferably, the amount of added organic solvent is less than about 0.1 percent by weight of the combination of water, emulsifier and enteric material. As used herein, "organic solvent" generally refers to a non-aqueous, hydrocarbon-based liquid. According to another form, the core and/or coating may include organic solvents.

[0098] The enteric material used herein is any food grade enteric polymer, or a combination or two or more food grade enteric polymers. In one form, the enteric material is a caseinate, such as sodium caseinate, soy protein or a combination thereof.

[0099] Other enteric materials that may be included in the core include shellac and zein. The shellac can be provided as an alkaline ($\text{pH} > 7$) aqueous solution, such as a water-based solution having a solid content of about 25 percent by weight or it can be prepared from refined, bleached and dewaxed shellac powder. The shellac is substantially free of organic solvent, although it may contain trace amounts of organic solvents, such as isopropyl alcohol (such as can be included in commercial products), to act as a carrier for other ingredients in the shellac solution, such as methyl and propyl parabens. Preferably, the prepared shellac solution does not contain any added organic solvents.

[00100] In one approach, the enteric material consists essentially of soy protein and sodium caseinate. It should be noted that soy protein and sodium caseinate may not be thought of as traditional enteric materials. However, when the soy protein and sodium caseinate are prepared near their isoelectric points (about 4.4 to about 4.6 for soy protein and

sodium caseinate), the materials take on enteric functionality such that they would be considered enteric materials.

[00101] The enteric matrix material and optional emulsifier may be solubilized in water, in one form alkaline water, substantially free of an organic solvent. However, it has been discovered that the combination of the soy protein and sodium caseinate provides an emulsification capability so that the addition of an emulsifier is not required in this approach. Further, the combination of soy protein and sodium caseinate improves stability of the resulting microencapsulated functional ingredient over the duration of the shelf life of the microencapsulated functional ingredient. In one approach, the soy protein and sodium caseinate are solubilized separately in separate aqueous solutions and then combined in a single solution. In some cases, a desired ratio of soy protein to sodium caseinate ranges from about 1:60 to about 60:1 in other cases the ratio ranges from about 1:10 to about 10:1 and in yet other cases the ratio ranges from about 2:1 to about 1:2.

[00102] The emulsifier described herein is any food grade emulsifier. In one form, the emulsifier is polysorbate, polyglycerol ester, sucrose stearate, sucrose esters, proteins, lecithins or combinations thereof.

[00103] The methods described herein combine water, an optional emulsifier, the enteric materials and the functional ingredient in a manner effective to microencapsulate the functional ingredient in the enteric materials. In one form, such as with hydrophobic core ingredients, the methods use water in amounts from about 50 percent to about 95 percent of the combination by weight and, in some approaches, from about 70 to about 95 percent, and, in other approaches, from about 80 to about 90 percent. The optional emulsifier is generally less than about 5 percent of the combination by weight, in some instances from about 0.01 to about 1 percent by weight, and, in other instances, about 0.01 to about 0.1 percent by weight of the combination. The enteric material ranges from about 3 percent to about 35 percent by weight, in some approaches from about 3 to about 23 percent, and, in other approaches, from about 10 percent to about 15 percent by weight of the combination. The functional ingredient generally is in amounts of about 1 to about 15 percent by weight of the combination, and in other approaches, about 3 to about 6 percent by weight, as measured in a wet state prior to titration.

[00104] The microencapsulated hydrophobic liquid produced by the above described methods may have an increased payload. Payload generally refers to the weight percentage

of the functional ingredients in relation to the final particulate product. The total payload generally refers to the total weight percentage of all the encapsulated functional ingredients, including any carrier oil, in relation to the final particulate product. Therefore, an increase in payload corresponds to an increase in functional ingredient per a given amount of enteric matrix.

[00105] Advantages and embodiments of the methods described herein are further illustrated by the following Examples. However, the particular conditions, processing schemes, materials, and amounts thereof recited in these Examples, as well as other conditions and details, should not be contrasted to unduly limit this method. All percentages are by weight unless otherwise indicated.

EXAMPLES

[00106] Example 1

[00107] A model system was developed to analyze the enteric delivery performance at various pH levels to determine if the combination of enteric and encapsulating materials would be suitable for targeted ruminant delivery of functional ingredients. A composition was prepared having the components listed below in Table 1. An annatto/medium chain triglyceride oil was used as a functional ingredient in this exemplary system as annatto oil was easy to evaluate for purposes of determining the performance in a targeted ruminant delivery system. It should be noted that other materials (such as the functional ingredients and essential oils previously discussed) would be expected to be incorporated in a similar manner and would be expected to have similar performance at the various pH levels tested.

[00108] Table 1. Composition

<u>Ingredient</u>	<u>Amount</u>
RO water	3650 g
sodium caseinate powder	210 g
25% shellac solution (ammoniac shellac, prepared with alkalized solution of shellac with ammonium hydroxide at pH 7-8)	560 g

[00109] The composition was prepared by hydrating the caseinate powder in water with overhead mixing for at least about 30 minutes. Next, shellac was added slowly while mixing to form the starting composition. About 120 g of Annatto/MCT (medium chain triglyceride)

oil blend (about 2% Annato in MCT oil) was added to prepare a coarse emulsion. The coarse emulsion was homogenized through a two stage high pressure homogenizer at about 500/5000psi. Next, the emulsion was titrated with about 12% citric acid while continuously mixing to pH 4.5 to precipitate particulates and form slurry. The slurry was permitted to mix for about 5-10 minutes. The slurry had water removed by pressing at about 40 psi for about 30 minutes to make a filter cake. The filter cake was then subjected to coarse grinding in food processor to form chunks. The coarse ground cake is then extruded through an LCI extruder at about 90 rpm through a die with an about 1.2 mm to about 2.0 mm holes. Strands of extrudates were collected and bench dried for about 48 hours. The resulting material had a final moisture content of about 3.5%. The dried material was milled and sifted to a desired particle size of about 1.2 mm to about 1.4 mm.

[00110] The dried material was then coated, which was carried out on two separate days. Three types of coating were applied: zein (inner coat), shellac (middle coat), and poly(2-Vinylpyridine-co-styrene) as an outer coat.

[00111] On the first day, zein was coated first, followed by shellac. The zein coating composition was an alcohol based solution as found in Table 2 below.

[00112] Table 2. Coating solution formulation (10% zein):

<u>Ingredients</u>	<u>Weight in grams</u>
ethyl Alcohol 200 Proof	94.5
DI water	40.5
zein	15

[00113] About 100 g of previously prepared and dried particles were loaded into a fluidized bed and coated with the zein solution of Table 2. The weight of coating solution used was about 112 g such that the coating applied is about 10 wt.% of the core capsules.

[00114] Table 3. Parameters observed during coating

air inlet temp	55-60
product temp	33-35°C
spray rate	1.0-1.5 g/min
fluid air pressure	0.5 bar
atomization pressure	2.0 bar

[00115] Next, the shellac coating was carried out without removing the material out of the coating chamber. The shellac solution used is shown below in Table 4.

[00116] Table 4. Coating solution formulation (12.5% shellac):

<u>Ingredients</u>	<u>Weight in grams</u>
25% aqueous shellac solution	75
DI water	75

[00117] The weight of the shellac coating solution used was about 104 g. The coating conditions used were the same as those for zein and found in Table 3.

[00118] On day 2, the co-polymer coating was applied. About 112 g of zein and shellac coated material was recovered from day 1 coating and reloaded for the co-polymer coating. The copolymer coating composition is shown below in Table 5.

[00119] Table 5. Copolymer coating solution formulation

<u>Ingredients</u>	<u>Weight in grams</u>
ethyl alcohol 200 Proof	275
poly(2-vinylpyridine-co-styrene) polymer	50
5M hydrochloric acid	125
DI water	50

[00120] The coating solution was prepared by dispersing the polymer in alcohol and then adding acid. Deionized water was added about 20 minutes after mixing the alcohol polymer and acid. The combined composition was mixed until a clear solution formed, which was after about 1-2 hours. The weight of solution used for coating was about 480 g.

[00121] Table 6. Parameters observed during coating

air inlet temp	55-60
product temp	35-42°C
spray rate	1.0-1.5 g/min
fluid air pressure	0.5 bar
atomization pressure	2.0 bar

[00122] The final coated product was collected and sifted to remove fines and overage.

[00123] Example 2

[00124] The material prepared according to Example 1 was subjected to digestion testing over various pH levels for simulation of ruminant digestion. Two sets of material were prepared, each with three samples. The first set of material (Samples 1, 2 and 3) was coated

and prepared according to Example 1. The second set of material (Samples 4, 5 and 6) was generally prepared in accordance with Example 1, but was not coated with the polymer coating. Generally, the first set of materials contained particles that were larger and more rounded as a result of the multiple coatings whereas the second set contained particles that were somewhat smaller.

[00125] About 1.00 g of capsules of each of samples 1-6 were added into separate 50mL Teflon centrifuge tubes. About 19 g of sodium bicarbonate buffer solution (pH=8.2) was added to all samples and were swirled to mix. The centrifuge tubes were placed on a shaker bath at about 39°C and shaken for about 16 hours at about 80 shakes/min. After shaking, Samples 1 and 4 were centrifuged at about 6000 rpm for about 10 minutes. This treatment is a simulation of a first portion of a ruminant digestion, such as in ruminant saliva and rumen contents.

[00126] Sample 1, which was coated in accordance with Example 1, contained particles that appeared substantially unchanged. Sample 4, which was a sample that was not coated with polymer, was substantially dissolved into solution.

[00127] Samples 2, 3, 5 and 6 were further tested by adding concentrated HCl to adjust the pH to about 2-3. Samples 2, 3, 5 and 6 were placed back in the shaking water bath at about 39°C for about 30 minutes. After shaking, Samples 2 and 5 were removed and centrifuged at about 6000 rpm for about 10 minutes. This treatment is a simulation of a second portion of a ruminant digestion, such as ruminant stomach contents.

[00128] Sample 2 contained particles that were smaller than the original size, but approximately the same size as the starting particles for the second set. Such a change in particle size for sample 2 is understandable as the outer polymer coating is believed to have been substantially removed such that the particles would be similar to the starting particles for the second set. Sample 5 appeared generally the same as Sample 4 as the particles had previously dissolved into solution in the first step.

[00129] Samples 3 and 6 were further tested by adding 0.5N NaOH to adjust the pH to about 7-8. These tubes were then placed back in the shaking water bath at about 39°C for about 18 hours. After shaking, the tubes were removed and centrifuge at about 6000 rpm for about 10 minutes. This treatment is a simulation of a third portion of ruminant digestion, such as ruminant small intestine contents.

[00130] The particles in Sample 3 were substantially dissolved into solution. The particles in Sample 6 were also unchanged and remained dissolved into solution.

[00131] An illustration of Samples 1, 2 and 3 during the various portions of the simulated ruminant digestion are shown in FIG. 6. As previously noted, Samples 4, 5 and 6 were completely degraded during the first portion of the ruminant digestion and therefore are not shown in the figure. As seen in FIG. 6, Sample 1, which is shown after the simulation of the first portion of ruminant digestion includes relatively large particles that are substantially unchanged. In FIG. 6, Sample 2 is shown after the simulation of the second portion of ruminant digestion where the particles are smaller than the particles in Sample 1 shown next to it (as evidenced by the reduced volume of the particles in Sample 2). Sample 3 is shown after the third portion of ruminant digestion where the particles are degraded and otherwise in solution.

[00132] It is understandable that Samples 4, 5, and 6 were degraded after simulating the first portion of ruminant digestion, ruminant saliva and rumen contents (about pH of 8.2), since their outer coating is meant to be stable in acid but to degrade in alkaline environments. Further digestions steps did not have an effect as the capsules were already completely degraded by the first step. These capsules would not be suitable for delivering an anthelmintic payload to a ruminant as ruminant saliva and rumen conditions would rapidly degrade the capsules before they reached their target location, the small intestine.

[00133] The coated materials, as exemplified by Samples 1, 2 and 3, however, behaved very differently. The particles survive the simulation of the first portion of ruminant digestion unaltered, and their appearance at the bottom of the tube is very similar to their appearance in the dry state. After the second treatment step simulating the second portion of ruminant digestion, stomach contents (pH=2-3), the particles still appear to be intact, but with their outer layer removed, and their appearance is now similar to the uncoated capsules in the dry state. After the third treatment step simulating the third portion of ruminant digestions, such as in the small intestine, the particles appear to be completely degraded. These results demonstrate that these particles are suitable for delivering an anthelmintic payload to a ruminant as the particles remain intact until they reach their target location, the small intestine.

[00134] Example 3

[00135] An animal feed composition may be prepared having one or more functional ingredients located on an interior of the feed material. The feed material can be selected from a variety of different grains, cereals, legumes, wheat, soy, rice and the like, as well as combinations thereof. An enteric coating covers at least one of the functional ingredient composition and the feed material. Further, the feed can include an outer coating having a solubility less than about 20% at a pH of about 5.5 or greater, the outer coating located on the exterior of the feed material.

[00136] The animal feed may be prepared by combining a feed material and a functional ingredient composition to infuse the functional ingredient composition into an interior of the feed material. Next, the feed material is dried to entrap the functional ingredient composition within the feed material, forming a dried feed material. The dried feed material can then be coated with at least one of an enteric coating and an outer coating having a solubility less than about 20% at a pH of about 5.5 or greater.

[00137] In one form, the enteric material is selected from the group consisting of zein, shellac and combinations thereof.

[00138] The animal feed may further include a coating having a delayed release material selected from the group consisting of gum arabic, gelatin, ethylcellulose, hydroxypropyl methylcellulose and combinations thereof.

[00139] The animal feed may further include an intermediate coating on the exterior of the feed material, the intermediate coating comprising ethylcellulose.

[00140] The animal feed may further include a water barrier coating selected from the group consisting of a lipid-type material, a high melting point fat, wax and combinations thereof.

[00141] In one form, the functional ingredient composition includes a hydrophobic material which is entrapped within a matrix of the enteric material.

[00142] The functional ingredient can include essential oils.

[00143] The outer coating can be selected from the group consisting of methyl methacrylate, N,N dimethylaminoethylmethacrylate, cross linked chitosan, and combinations thereof.

[00144] The animal feed composition can include particles having a size in the range of about 75 to about 500 μm .

[00145] The animal feed composition can include particles having a density of greater than about 1.0 g/cc.

[00146] While the compositions and methods have been particularly described with specific reference to particular process and product embodiments, it will be appreciated that various alterations, modifications, and adaptations may be based on the present disclosure, and are intended to be within the spirit of this disclosure. Furthermore, the compositions described herein are particularly suited for ruminant animals. However, the compositions can also be used with non-ruminant animals and, in some instances, will be free of the ruminant protective coating 16, 28, 36, and 50 in certain applications.

CLAIMS

What is claimed is:

1. A microencapsulated composition comprising:
a functional ingredient composition;
an enteric material coating the functional ingredient composition; and
an outer coating having a solubility less than about 20% at a pH of about 5.5 or greater.
2. The microencapsulated composition of claim 1 wherein the enteric material coating is selected from the group consisting of zein, caseinate, shellac and combinations thereof.
3. The microencapsulated composition of claims 1 or 2 further comprising a coating having a delayed release material selected from the group consisting of gum arabic, gelatin, ethylcellulose, hydroxypropyl methylcellulose and combinations thereof.
4. The microencapsulated composition of any of the preceding claims wherein the functional ingredient comprises a hydrophilic material in a matrix.
5. The microencapsulated composition of any of the preceding claims further comprising an intermediate coating between the enteric material coating and the outer coating, the interior coating comprising ethylcellulose.
6. The microencapsulated composition of any of the preceding claims wherein the functional ingredient composition includes a hydrophobic material which is entrapped within a matrix of an enteric material selected from shellac, caseinate, zein, and combinations thereof.
7. The microencapsulated composition of claim 6 wherein the functional ingredient is selected from the group consisting of omega-3 oils, probiotics, polyphenols, anti-parasitic materials, vaccines, antibiotics, essential oils, micro-nutrients, fatty acids, minerals, and combinations thereof.

8. The microencapsulated composition of any of the preceding claims wherein the outer coating is selected from the group consisting of methyl methacrylate, N,N-dimethylaminoethylmethacrylate, cross-linked chitosan, poly (2-vinylpyridine-co-styrene), and combinations thereof.

9. The microencapsulated composition of any of the preceding claims wherein the microencapsulated composition includes particles having a size in the range of about 75 to about 500 μm .

10. The microencapsulated composition of any of the preceding claims wherein the microencapsulated composition includes particles having a density of about 1.0 to about 2.0 g/cc.

11. A microencapsulated composition comprising:
a granulated core including a plurality of particles in combination with a granulating material, the particles comprising a functional ingredient composition microencapsulated in an enteric material; and
an outer coating at least substantially surrounding the granulated core, the outer coating having a solubility less than about 20% at a pH of about 5.5 or greater.

12. The microencapsulated composition of claim 11 wherein the enteric material is selected from the group consisting of zein, shellac, and combinations thereof.

13. The microencapsulated composition of claims 11 or 12 further comprising a coating having a delayed release material selected from the group consisting of gum arabic, gelatin, ethylcellulose, hydroxypropyl methylcellulose and combinations thereof.

14. The microencapsulated composition of any of claims 11 to 13 further comprising an interior coating between the granulated core and the outer coating, the interior coating comprising ethylcellulose.

15. The microencapsulated composition of any of claims 11 to 14 wherein the functional ingredient composition includes a hydrophobic material which is entrapped within a matrix of the enteric material.

16. The microencapsulated composition of claim 15 wherein the functional ingredient is selected from the group consisting of omega-3 oils, probiotics, polyphenols, anti-parasitic materials, vaccines, antibiotics, essential oils, micro-nutrients, fatty acids, minerals, and combinations thereof.

17. The microencapsulated composition of any of claims 11 to 16 wherein the outer coating is selected from the group consisting of methyl methacrylate, N,N-dimethylaminoethylmethacrylate, cross-linked chitosan, poly (2-vinylpyridine-co-styrene), and combinations thereof.

18. The microencapsulated composition of any of claims 11 to 17 further comprising a water barrier coating selected from the group consisting of a lipid-type material, a high melting point fat, wax and combinations thereof.

19. The microencapsulated composition of any of claims 11 to 18 wherein the composition includes particles having a size in the range of about 75 to about 500 μm .

20. The microencapsulated composition of any of claims 11 to 19 wherein the composition includes particles having a density of greater than about 1 g/cc.

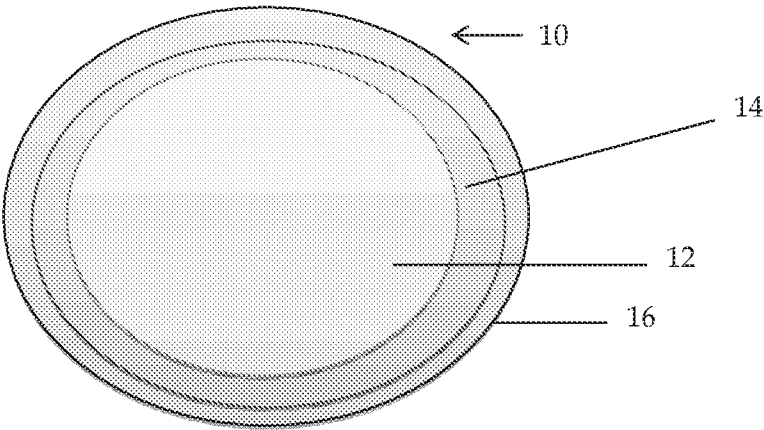


Fig. 1

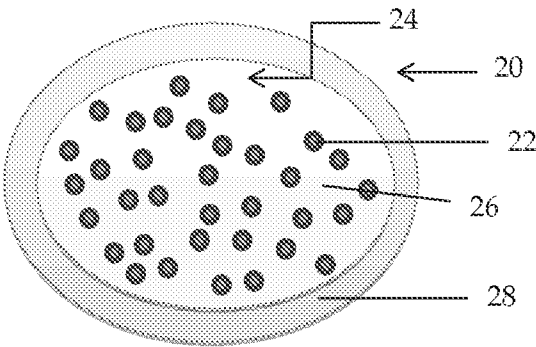


Fig. 2

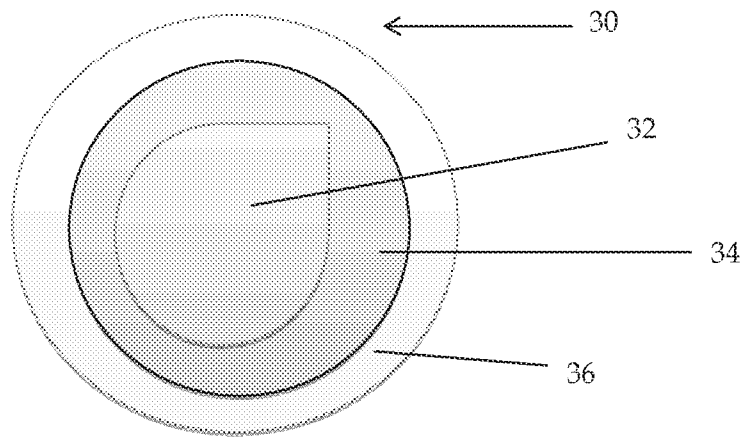


Fig. 3

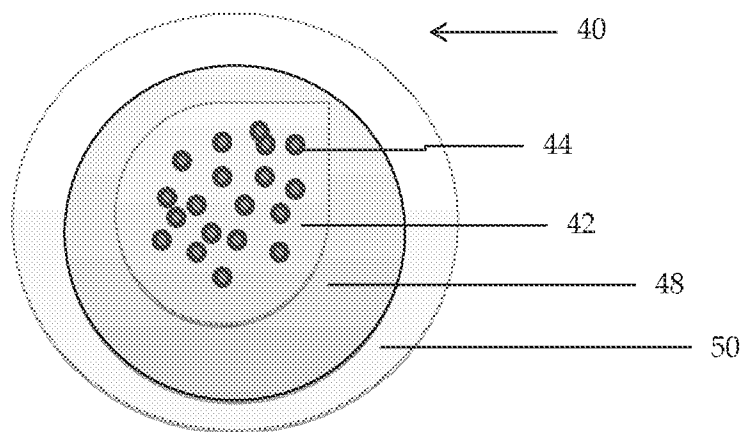


Fig. 4

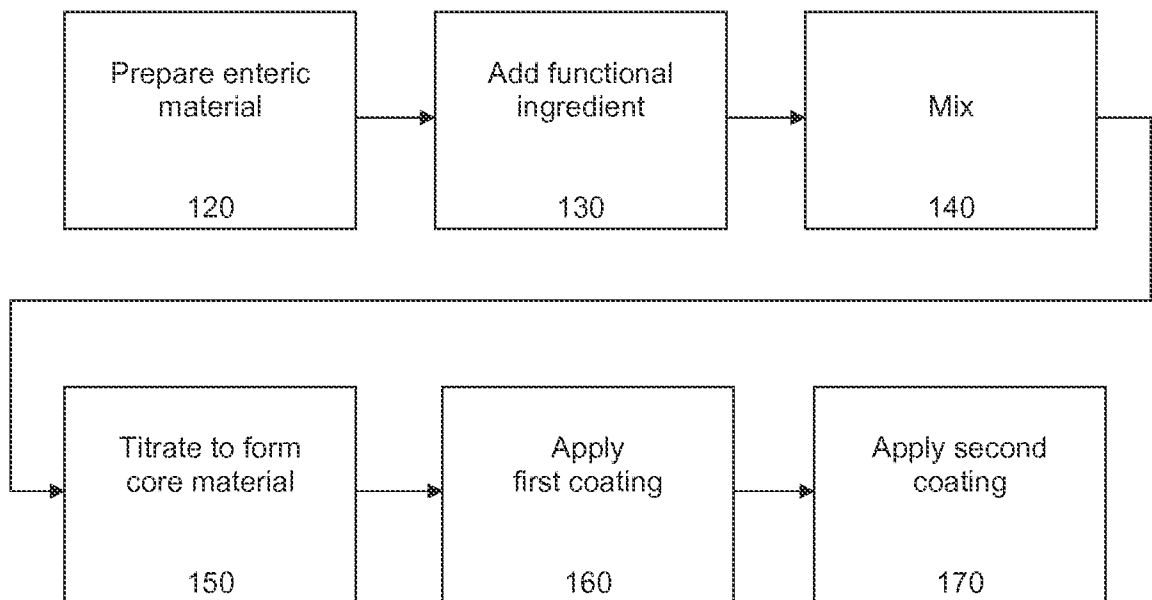
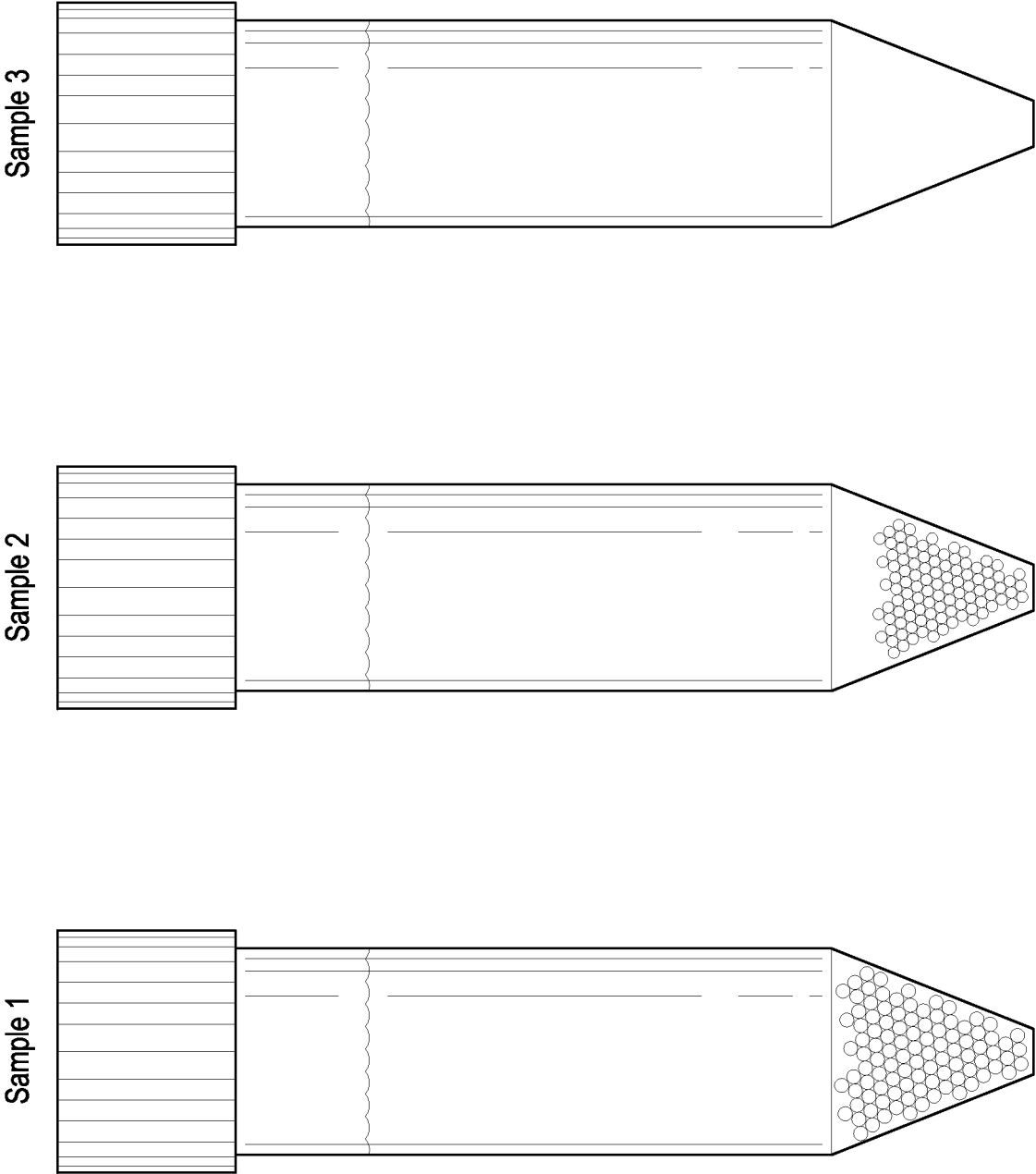
Fig. 5

Fig. 6



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/017656

A. CLASSIFICATION OF SUBJECT MATTER
INV. A23K1/00 A23K1/18
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)
A23K A61K

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 351 760 A2 (MITSUBISHI CHEM IND [JP]; AJINOMOTO KK [JP]) 24 January 1990 (1990-01-24) page 3, line 7 - line 22; claims 1,8,12,13; examples 2-4 page 3, line 25 - line 34 page 4, line 8 - line 18 page 5, line 5 - line 18 page 6, line 9 - line 51 ----- -/--	1-4, 7-13,16, 17,19,20

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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"E" earlier application or patent but published on or after the international filing date

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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

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"&" document member of the same patent family

Date of the actual completion of the international search

18 June 2014

Date of mailing of the international search report

27/06/2014

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2014/017656

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X	WO 99/13869 A1 (LUKOWSKI GEROLD [DE]) 25 March 1999 (1999-03-25)	1,2,4, 7-12,16, 17,19,20
Y	claims 1,4,6,7,9,10,13,15,16; figures 1-4 page 1, line 5 - line 6 page 2, line 29 - page 3, line 4 page 3, line 29 - page 4, line 3 page 4, line 7 - line 20 page 5, line 9 - line 16 page 6, line 15 - line 19 -----	5,6,14, 18
Y	AU 614 943 B2 (RHONE POULENC SANTE) 19 September 1991 (1991-09-19) page 8, line 16 - line 19; claims 1,2,3,5-7 page 12, line 6 - line 20 page 14, line 2 - line 15 page 17, line 2 - line 18 -----	5,6,14, 18

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