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(54) Title: CLEAR OIL-CONTAINING PHARMACEUTICAL COMPOSITIONS

(57) Abstract: The present invention relates to pharmaceutical compositions and methods for improved solubilization of triglycerides and improved delivery of therapeutic agents. Compositions of the present invention include a triglyceride and a carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. Upon dilution with an aqueous solvent, the composition forms a clear, aqueous dispersion of the triglyceride and surfactants. An optional therapeutic agent can be incorporated into the composition, or can be co-administered with the composition. The invention also provides methods of enhancing triglyceride solubility and methods of treatment with therapeutic agents using these compositions.

CLEAR OIL-CONTAINING PHARMACEUTICAL COMPOSITIONS

FIELD OF THE INVENTION

The present invention relates to drug and nutrient delivery systems, and in particular to pharmaceutical compositions and methods for the improved solubilization of triglycerides and improved delivery of therapeutic agents.

BACKGROUND

A wide variety of therapeutic agents, such as drugs, nutritional agents, and cosmeceuticals, are conventionally formulated in oil/water emulsion systems. These conventional emulsions take advantage of the increased solubility of many therapeutic agents in oils (triglycerides). Thus, one conventional approach is to solubilize a therapeutic agent in a bioacceptable triglyceride solvent, such as a digestible vegetable oil, and disperse this oil phase in an aqueous solution. The dispersion may be stabilized by emulsifying agents and provided in emulsion form. Alternatively, the therapeutic agent can be provided in a water-free formulation, with an aqueous dispersion being formed *in vivo* in the gastrointestinal environment. The properties of these oil-based formulations are determined by such factors as the size of the triglyceride/therapeutic agent colloidal particles and the presence or absence of surfactant additives.

In simplest form, a triglyceride-containing formulation suitable for delivering therapeutic agents through an aqueous environment is an oil-in-water emulsion. Such emulsions contain the hydrophobic therapeutic agent solubilized in an oil phase which is dispersed in an aqueous environment with the aid of a surfactant. The surfactant may be present in the oil-based formulation itself, or may be a compound provided in the gastrointestinal system, such as bile salts, which are known to be *in vivo* emulsifying agents. The colloidal oil particles sizes are relatively large, ranging from several hundred nanometers to several microns in diameter, in a broad particle size distribution. Since the particle sizes are on the order of or greater than the wavelength range of visible light, such emulsions, when prepared in an emulsion dosage form, are visibly "cloudy" or "milky" to the naked eye.

Although conventional triglyceride-based pharmaceutical compositions are useful in solubilizing and delivering some therapeutic agents, such compositions are subject to a

number of significant limitations and disadvantages. Emulsions are thermodynamically unstable, and colloidal emulsion particles will spontaneously agglomerate, eventually leading to complete phase separation. The tendency to agglomerate and phase separate presents problems of storage and handling, and increases the likelihood that pharmaceutical emulsions initially properly prepared will be in a less optimal, less effective, and poorly-characterized state upon ultimate administration to a patient. Uncharacterized degradation is particularly disadvantageous, since increased particle size slows the rate of transport of the colloidal particle and digestion of the oil component, and hence the rate and extent of absorption of the therapeutic agent. These problems lead to poorly-characterized and potentially harmful changes in the effective dosage received by the patient. Moreover, changes in colloidal emulsion particle size are also believed to render absorption more sensitive to and dependent upon conditions in the gastrointestinal tract, such as pH, enzyme activity, bile components, and stomach contents. Such uncertainty in the rate and extent of ultimate absorption of the therapeutic agent severely compromises the medical professional's ability to safely administer therapeutically effective dosages. In addition, when such compositions are administered parenterally, the presence of large particles can block blood capillaries, further compromising patient safety.

A further disadvantage of conventional triglyceride-containing compositions is the dependence of therapeutic agent absorption on the rate and extent of lipolysis. Although colloidal emulsion particles can transport therapeutic agents through the aqueous environment of the gastrointestinal tract, ultimately the triglyceride must be digested and the therapeutic agent must be released in order to be absorbed through the intestinal mucosa. The triglyceride carrier is emulsified by bile salts and hydrolyzed, primarily by pancreatic lipase. The rate and extent of lipolysis, however, are dependent upon several factors that are difficult to adequately control. For example, the amount and rate of bile salt secretion affect the lipolysis of the triglycerides, and the bile salt secretion can vary with stomach contents, with metabolic abnormalities, and with functional changes of the liver, bile ducts, gall bladder and intestine. Lipase availability in patients with decreased pancreatic secretory function, such as cystic fibrosis or chronic pancreatitis, may be undesirably low, resulting in a slow and incomplete triglyceride lipolysis. The activity of lipase is pH dependent, with deactivation occurring at about pH 3, so that the lipolysis rate

will vary with stomach contents, and may be insufficient in patients with gastric acid hyper-secretion. Moreover, certain surfactants commonly used in the preparation of pharmaceutical emulsions, such as polyethoxylated castor oils, may themselves act as inhibitors of lipolysis. Although recent work suggests that certain surfactant. combinations, when used in combination with digestible oils in emulsion preparations, can substantially decrease the lipolysis-inhibiting effect of some common pharmaceutical surfactants (see, U.S. Patent No. 5,645,856), such formulations are still subject to the other disadvantages of pharmaceutical emulsions and triglyceride-based formulations.

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

Yet another approach is based on formation of "microemulsions". Like an emulsion, a microemulsion is a liquid dispersion of oil in water, stabilized by surfactants. Conventional microemulsions, however, present several safety and efficiency problems. The amount of triglyceride that can be solubilized in a conventional microemulsion is generally quite small, resulting in a poor loading capacity. In order to solubilize significant amounts of triglycerides, large amounts of hydrophilic surfactant and/or solvents must be used. These high concentrations of hydrophilic surfactant and solvents raise questions of safety, since the levels of hydrophilic surfactant and solvent needed can approach or exceed bioacceptable levels.

Thus, there is a need for pharmaceutical compositions that overcome the limitations and safety concerns of conventional triglyceride-containing formulations, but without suffering from the disadvantages described above.

SUMMARY OF THE INVENTION

According to one aspect, the preset invention provides a pharmaceutical composition consisting of:

(a) a triglyceride;

(b) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic; and

(c) a therapeutic agent which is capable of being solubilized in the triglyceride, the carrier, or both the triglyceride and the carrier,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm.

In another aspect, the present invention provides a pharmaceutical composition consisting of:

(a) a triglyceride;

(b) a carrier comprising at least one hydrophilic surfactant and at least one hydrophobic surfactant; and

(c) a therapeutic agent which is capable of being solubilized in the triglyceride, the carrier, or both the triglyceride and the carrier,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ration of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm.

In yet another aspect, the present invention provides a pharmaceutical composition consisting of:

(a) a triglyceride;

(b) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic, wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm;

(c) a first amount of a therapeutic agent, said first amount being solubilized in the triglyceride, the carrier, or both the triglyceride and the carrier; and

(d) a second amount of a therapeutic agent, said second amount not solubilized in the triglyceride or the carrier.

In another further aspect, the present invention provides a pharmaceutical composition comprising:

(a) a triglyceride; and

(b) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm, and wherein the triglyceride is present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous dispersion of the triglyceride and a carrier having only one surfactant, the surfactant being hydrophilic, and having the same total surfactant concentration.

In a further aspect, the present invention provides a method of treating an animal with a therapeutic agent, the method comprising:

(a) providing a dosage form of a pharmaceutical composition consisting of:

(i) a triglyceride; and

(ii) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm;

(b) providing a therapeutic agent; and

(c) administering said dosage form to said animal.

In another aspect, the present invention provides a method of increasing the amount of a triglyceride that can be solubilized in a clear aqueous dispersion, the method comprising:

(a) providing a composition comprising a triglyceride and a carrier, the carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic; and

(b) dispersing the composition in an aqueous solution,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm, and wherein the triglyceride is present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous

dispersion of the triglyceride and a carrier having only one surfactant and having the same total surfactant concentration.

In another aspect, the present invention provides a method of treating an animal with a therapeutic agent, the method comprising:

(a) providing a dosage form of a pharmaceutical composition consisting of:

(i) an effective amount of a triglyceride; and

(ii) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm; and

(iii) said therapeutic agent; and

(b) administering said dosage form to said animal.

The present invention provides pharmaceutical compositions for improved solubilization of triglycerides, and improved delivery of therapeutic agents. It has been surprisingly found that pharmaceutical compositions containing significant amounts of triglycerides can be formed without the disadvantages of conventional triglyceridecontaining compositions by using a combination of surfactants and triglycerides in amounts such that when the pharmaceutical composition is mixed with an aqueous solution, a clear aqueous dispersion is formed. Such compositions can be co-administered with a therapeutic agent to increase the rate and/or extend of bioabsorption of the therapeutic agent, or can be provided with a therapeutic agent in the preconcentrate composition or in the diluent solution:

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

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In one embodiment, the present invention relates to pharmaceutical compositions having a triglyceride and a carrier, the carrier including at least two surfactants, at least one of which is hydrophilic. The triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion. In a particular aspect of this embodiment, the composition is capable of containing more triglyceride than can be solubilized in a clear aqueous dispersion having only one surfactant, the surfactant being hydrophilic.

In another embodiment, the present invention relates to pharmaceutical compositions having a triglyceride and a carrier, the carrier including at least one hydrophilic surfactant and at least one hydrophobic surfactant. The triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion. In a particular aspect of this embodiment, the composition is capable of containing more triglyceride than can be solubilized in a clear aqueous dispersion having a hydrophilic surfactant but not having a hydrophobic surfactant..

In another embodiment, the triglyceride itself can have therapeutic value as, for example, a nutritional oil, or absorption-promoting value as, for example, a long-chain triglyceride ("LCT", having fatty acid chains longer than C_{10} and preferably C_{12} - C_{22}) or a medium-chain triglyceride ("MCT", having C_6-C_{10} fatty acid chains). Thus, in this embodiment, the present invention provides pharmaceutical compositions including a triglyceride having nutritional and/or absorption-promoting value, and a carrier. The carrier includes at least two surfactants, at least one of which is hydrophilic. Optionally, the carrier can include at least one hydrophilic surfactant and at least one hydrophobic surfactant. The triglyceride and surfactants are present in amounts such that upon dilution with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion.

In another embodiment, the present invention relates to methods of increasing the amount of triglyceride that can be solubilized in an aqueous system, by providing a composition including a triglyceride and a carrier, the carrier including at least two surfactants, at least one of which is hydrophilic, and dispersing the composition in an aqueous solution so that a clear aqueous dispersion is formed. Within the clear aqueous dispersion, the triglyceride is capable of being solubilized in an amount greater than the

amount of the triglyceride that remains solubilized in an aqueous dispersion of the triglyceride and a carrier having only one surfactant and having the same total surfactant concentration. Optionally, the carrier can include at least one hydrophilic surfactant and at least one hydrophobic surfactant.

In another aspect, the present invention relates to triglyceride-containing pharmaceutical compositions as described in the preceding embodiments, which further include a therapeutic agent. In particular embodiments, the therapeutic agent is a hydrophobic drug or a hydrophilic drug. In other embodiments, the therapeutic agent is a nutritional agent. In still further embodiments, the therapeutic agent is a cosmeceutical agent.

In another embodiment, the present invention relates to methods of increasing the solubilization of a therapeutic agent in a composition, by providing the therapeutic agent in a composition of the present invention.

In another embodiment, the present invention relates to a pharmaceutical composition which includes a therapeutic agent, a triglyceride and a carrier. The carrier includes at least two surfactants, at least one of which is hydrophilic. Optionally, the carrier includes at least one hydrophilic surfactant and at least one hydrophobic surfactant. The triglyceride, and surfactants are present in amounts such that upon dilution with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion. The therapeutic agent is present in two amounts, a first amount of the therapeutic agent solubilized in the clear aqueous dispersion, and a second amount of the therapeutic agent that remains non-solubilized but dispersed.

In another embodiment, the present invention relates to methods of increasing the rate and/or extent of absorption of therapeutic agents by administering to a patient a pharmaceutical composition of the present invention. In this embodiment, the therapeutic agent can be present in the pharmaceutical composition pre-concentrate, in the diluent, or in a second pharmaceutical composition, such as a conventional commercial formulation, which is co-administered with a pharmaceutical composition of the present invention.

These and other features of the present invention will become more fully apparent from the following description and appended claims, or may be learned by the practice of the invention as set forth hereinafter.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention overcomes the problems described above characteristic of conventional triglyceride-containing formulations by providing unique pharmaceutical compositions which form clear aqueous dispersions upon mixing with an aqueous solution. Surprisingly, the present inventors have found that compositions including triglycerides and a combination of surfactants can solubilize therapeutically effective amounts of therapeutic agents in homogeneous, single-phase systems which are thermodynamically stable and optically clear. The optical clarity is indicative of a very small particle size within the aqueous dispersions, and this small particle size substantially reduces lipolysis dependence of the rate of bioabsorption, and other disadvantages of conventional triglyceride-containing formulations. Use of these formulations is thus believed to result in an enhanced rate and/or extent of absorption of the therapeutic agent. Advantageously, the compositions of the present invention are surprisingly able to solubilize greater amounts of triglycerides than conventional formulations, even when the total surfactant concentration is the same as in a conventional formulation.

A. Pharmaceutical Compositions

In one embodiment, the present invention provides a pharmaceutical composition including a triglyceride and a carrier. The carrier includes at least two surfactants, at least one of which is a hydrophilic surfactant. Optionally, the carrier includes at least one hydrophilic surfactant and at least one hydrophobic surfactant. The triglyceride and surfactants are present in amounts such that upon dilution with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion. It is a particular and surprising feature of the present invention that the composition is homogeneous and optically clear, despite the presence of substantial amounts of triglycerides, thereby providing surprising and important advantages over conventional triglyceride-containing formulations.

1. Triglycerides

The compositions of the present invention include one or more pharmaceutically acceptable triglycerides. Examples of triglycerides suitable for use in the present invention are shown in Table 1. In general, these triglycerides are readily available from commercial sources. For several triglycerides, representative commercial products and/or commercial suppliers are listed.

Table 1: Triglycerides

Triglyceride	Commercial Source
Aceituno oil	
Almond oil	Super Refined Almond Oil (Croda)
Arachis oil	
Babassu oil	
Blackcurrant seed oil	
Borage oil	
Buffalo ground oil	
Candlenut oil	
Canola oil	Lipex 108 (Abitec)
Castor oil	
Chinese vegetable tallow oil	
Cocoa butter	
Coconut oil	Pureco 76 (Abitec)
Coffee seed oil	
Corn oil	Super Refined Corn Oil (Croda)
Cottonseed oil	Super Refined Cottonseed Oil (Croda)
Crambe oil	
Cuphea species oil	
Evening primrose oil	
Grapeseed oil	
Groundnut oil	
Hemp seed oil	
Illipe butter	

Kapok seed oil	
Linseed oil	
Menhaden oil	Super Refined Menhaden Oil (Croda)
Mowrah butter	
Mustard seed oil	
Oiticica oil	
Olive oil	Super Refined Olive Oil (Croda)
Palm oil	
Palm kernel oil	
Peanut oil	Super Refined Peanut Oil (Croda)
Poppy seed oil	
Rapeseed oil	
Rice bran oil	
Safflower oil	Super Refined Safflower Oil (Croda)
Sal fat	
Sesame oil	Super Refined Sesame Oil (Croda)
Shark liver oil	Super Refined Shark Liver Oil (Croda)
Shea nut oil	
Soybean oil	Super Refined Soybean Oil (Croda)
Stillingia oil	
Sunflower oil	
Tall oil	
Tea seed oil	
Tobacco seed oil	
Tung oil (China wood oil)	

Ucuhuba	
Vernonia oil	
Wheat germ oil	Super Refined Wheat Germ Oil (Croda)
Hydrogenated castor oil	Castorwax
Hydrogenated coconut oil	Pureco 100 (Abitec)
Hydrogenated cottonseed oil	Dritex C (Abitec)
Hydrogenated palm oil	Dritex PST (Abitec); Softisan 154 (Hüls)
Hydrogenated soybean oil	Sterotex HM NF (Abitec); Dritex S (Abitec)
Hydrogenated vegetable oil	Sterotex NF (Abitec); Hydrokote M (Abitec)
Hydrogenated cottonseed and castor oil	Sterotex K (Abitec)
Partially hydrogenated soybean oil	Hydrokote AP5 (Abitec)
Partially soy and cottonseed oil	Apex B (Abitec)
Glyceryl tributyrate	(Sigma)
Glyceryl tricaproate	(Sigma)
Glyceryl tricaprylate	(Sigma)
Glyceryl tricaprate	Captex 1000 (Abitec)
Glyceryl triundecanoate	Captex 8227 (Abitec)
Glyceryl trilaurate	(Sigma)
Glyceryl trimyristate	Dynasan 114 (Hüls)
Glyceryl tripalmitate	Dynasan 116 (Hüls)
Glyceryl tristearate	Dynasan 118 (Hüls)
Glyceryl triarchidate	(Sigma)
Glyceryl trimyristoleate	(Sigma)
Glyceryl tripalmitoleate	(Sigma)
Glyceryl trioleate	(Sigma)

Glyceryl trilinoleate	(Sigma)
Glyceryl trilinolenate	(Sigma)
Glyceryl tricaprylate/caprate	Captex 300 (Abitec); Captex 355 (Abitec); Miglyol 810 (Hüls); Miglyol 812 (Hüls)
Glyceryl tricaprylate/caprate/laurate	Captex 350 (Abitec)
Glyceryl tricaprylate/caprate/linoleate	Captex 810 (Abitec); Miglyol 818 (Hüls)
Glyceryl tricaprylate/caprate/stearate	Softisan 378 (Hüls); (Larodan)
Glyceryl tricaprylate/laurate/stearate	(Larodan)
Glyceryl 1,2-caprylate-3-linoleate	(Larodan)
Glyceryl 1,2-caprate-3-stearate	(Larodan)
Glyceryl 1,2-laurate-3-myristate	(Larodan)
Glyceryl 1,2-myristate-3-laurate	(Larodan)
Glyceryl 1,3-palmitate-2-butyrate	(Larodan)
Glyceryl 1,3-stearate-2-caprate	(Larodan)
Glyceryl 1,2-linoleate-3-caprylate	(Larodan)

Fractionated triglycerides, modified triglycerides, synthetic triglycerides, and mixtures of triglycerides are also within the scope of the invention.

Preferred triglycerides include vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, medium and long-chain triglycerides, and structured triglycerides. It should be appreciated that several commercial surfactant compositions contain small to moderate amounts of triglycerides, typically as a result of incomplete reaction of a triglyceride starting material in, for example, a transesterification reaction. Such commercial surfactant compositions, while nominally referred to as "surfactants", may be suitable to provide all or part of the triglyceride component for the compositions of the present invention. Examples of commercial surfactant compositions containing triglycerides include some members of the surfactant families Gelucires

(Gattefosse), Maisines (Gattefosse), and Imwitors (Hüls). Specific examples of these compositions are:

Gelucire 44/14 (saturated polyglycolized glycerides)

Gelucire 50/13 (saturated polyglycolized glycerides)

Gelucire 53/10 (saturated polyglycolized glycerides)

Gelucire 33/01 (semi-synthetic triglycerides of C_8-C_{18} saturated fatty acids)

Gelucire 39/01 (semi-synthetic glycerides)

other Gelucires, such as 37/06, 43/01, 35/10, 37/02, 46/07, 48/09, 50/02, 62/05, etc.

Maisine 35-I (linoleic glycerides)

Imwitor 742 (caprylic/capric glycerides)

Still other commercial surfactant compositions having significant triglyceride content are known to those skilled in the art. It should be appreciated that such compositions, which contain triglycerides as well as surfactants, may be suitable to provide all or part of the triglyceride component of the compositions of the present invention, as well as all or part of the surfactant component, as described below. Of course, none of the commonly known triglyceride-containing commercial surfactants alone provides the unique pharmaceutical compositions and characteristics as recited in the appended claims.

Among the above-listed triglycerides, preferred triglycerides include: almond oil; babassu oil; borage oil; blackcurrant seed oil; canola oil; castor oil; coconut oil; corn oil; cottonseed oil; evening primrose oil; grapeseed oil; groundnut oil; mustard seed oil; olive oil; palm oil; palm kernel oil; peanut oil; rapeseed oil; safflower oil; sesame oil; shark liver oil; soybean oil; sunflower oil; hydrogenated castor oil; hydrogenated coconut oil; hydrogenated palm oil; hydrogenated soybean oil; hydrogenated vegetable oil; hydrogenated cottonseed and castor oil; partially hydrogenated soybean oil; partially soy and cottonseed oil; glyceryl tricaproate; glyceryl tricaprylate; glyceryl tricaprate; glyceryl triundecanoate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl trilinolenate; glyceryl tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; and glyceryl tricaprylate/caprate/stearate. Other preferred triglycerides are saturated polyglycolized glycerides (Gelucire 44/14, Gelucire 50/13 and

Gelucire 53/10), linoleic glycerides (Maisine 35-I), and caprylic/capric glycerides (Imwitor 742).

Among the preferred triglycerides, more preferred triglycerides include: coconut oil; corn oil; olive oil; palm oil; peanut oil; safflower oil; sesame oil; soybean oil; hydrogenated castor oil; hydrogenated coconut oil; partially hydrogenated soybean oil; glyceryl tricaprate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; glyceryl tricaprylate/caprate/stearate; saturated polyglycolized glycerides (Gelucire 44/14, Gelucire 50/13 and Gelucire 53/10); linoleic glycerides (Maisine 35-I); and caprylic/capric glycerides (Imwitor 742).

2. **Surfactants**

The carrier includes a combination of surfactants, at least one of which is a hydrophilic surfactant, with the remaining surfactant or surfactants being hydrophilic or hydrophobic. As is well known in the art, the terms "hydrophilic" and "hydrophobic" are relative terms. To function as a surfactant, a compound must necessarily include polar or charged hydrophilic moieties as well as non-polar hydrophobic (lipophilic) moieties; *i.e.*, a surfactant compound must be amphiphilic. An empirical parameter commonly used to characterize the relative hydrophilicity and hydrophobicity of non-ionic amphiphilic compounds is the hydrophilic-lipophilic balance (the "HLB" value). Surfactants with lower HLB values are more hydrophobic, and have greater solubility in oils, whereas surfactants with higher HLB values are more hydrophilic, and have greater solubility in aqueous solutions.

Using HLB values as a rough guide, hydrophilic surfactants are generally considered to be those compounds having an HLB value greater than about 10, as well as anionic, cationic, or zwitterionic compounds for which the HLB scale is not generally applicable. Similarly, hydrophobic surfactants are compounds having an HLB value less than about 10.

It should be appreciated that the HLB value of a surfactant is merely a rough guide generally used to enable formulation of industrial, pharmaceutical and cosmetic emulsions. For many important surfactants, including several polyethoxylated surfactants, it has been reported that HLB values can differ by as much as about 8 HLB units, depending upon the empirical method chosen to determine the HLB value (Schott, *J.*

Pharm. Sciences, 79(1), 87-88 (1990)). Likewise, for certain polypropylene oxide containing block copolymers (poloxamers, available commercially as PLURONIC® surfactants, BASF Corp.), the HLB values may not accurately reflect the true physical chemical nature of the compounds. Finally, commercial surfactant products are generally not pure compounds, but are often complex mixtures of compounds, and the HLB value reported for a particular compound may more accurately be characteristic of the commercial product of which the compound is a major component. Different commercial products having the same primary surfactant component can, and typically do, have different HLB values. In addition, a certain amount of lot-to-lot variability is expected even for a single commercial surfactant product. Keeping these inherent difficulties in mind, and using HLB values as a guide, one skilled in the art can readily identify surfactants having suitable hydrophilicity or hydrophobicity for use in the present invention, as described herein.

The carrier of the present invention includes at least one hydrophilic surfactant. The hydrophilic surfactant can be any surfactant suitable for use in pharmaceutical compositions. Suitable hydrophilic surfactants can be anionic, cationic, zwitterionic or non-ionic, although non-ionic hydrophilic surfactants are presently preferred. Preferably, the carrier includes a mixture of two or more hydrophilic surfactants, more preferably two or more non-ionic hydrophilic surfactants. Also preferred are mixtures of at least one hydrophilic surfactant, preferably non-ionic, and at least one hydrophobic surfactant.

The choice of specific surfactants should be made keeping in mind the particular triglycerides and optional therapeutic agents to be used in the composition, and the range of polarity appropriate for the chosen therapeutic agent. With these general principles in mind, a very broad range of surfactants is suitable for use in the present invention. Such surfactants can be grouped into the following general chemical classes detailed in the Tables herein. The HLB values given in the Tables below generally represent the HLB value as reported by the manufacturer of the corresponding commercial product. In cases where more than one commercial product is listed, the HLB value in the Tables is the value as reported for one of the commercial products, a rough average of the reported values, or a value that, in the judgment of the present inventors, is more reliable.

It should be emphasized that the invention is not limited to the surfactants in the Tables, which show representative, but not exclusive, lists of available surfactants.

2.1. Polyethoxylated Fatty Acids

Although polyethylene glycol (PEG) itself does not function as a surfactant, a variety of PEG-fatty acid esters have useful surfactant properties. Among the PEG-fatty acid monoesters, esters of lauric acid, oleic acid, and stearic acid are especially useful. Among the surfactants of Table 2, preferred hydrophilic surfactants include PEG-8 laurate, PEG-8 oleate, PEG-8 stearate, PEG-9 oleate, PEG-10 laurate, PEG-10 oleate, PEG-12 laurate, PEG-12 oleate, PEG-15 oleate, PEG-20 laurate and PEG-20 oleate. Examples of polyethoxylated fatty acid monoester surfactants commercially available are shown in Table 2.

Table 2: PEG-Fatty Acid Monoester Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG 4-100 monolaurate	Crodet L series (Croda)	>9
PEG 4-100 monooleate	Crodet O series (Croda)	>8
PEG 4-100 monostearate	Crodet S series (Croda), Myrj Series (Atlas/ICI)	>6
PEG 400 distearate	Cithrol 4DS series (Croda)	>10
PEG 100,200,300 monolaurate	Cithrol ML series (Croda)	>10
PEG 100,200,300 monooleate	Cithrol MO series (Croda)	>10
PEG 400 dioleate	Cithrol 4DO series (Croda)	>10
PEG 400-1000 monostearate	Cithrol MS series (Croda)	>10
PEG-1 stearate	Nikkol MYS-1EX (Nikko), Coster K1 (Condea)	2
PEG-2 stearate	Nikkol MYS-2 (Nikko)	4
PEG-2 oleate	Nikkol MYO-2 (Nikko)	4.5
PEG-4 laurate	Mapeg® 200 ML (PPG), Kessco® PEG 200ML (Stepan), LIPOPEG 2L (LIPO Chem.)	9.3
PEG-4 oleate	Mapeg® 200 MO (PPG), Kessco® PEG200 MO (Stepan),	8.3
PEG-4 stearate	Kessco® PEG 200 MS (Stepan), Hodag 20 S (Calgene), Nikkol MYS-4 (Nikko)	6.5

PEG-5 stearate	Nikkol TMGS-5 (Nikko)	9.5
PEG-5 oleate	Nikkol TMGO-5 (Nikko)	9.5
PEG-6 oleate	Algon OL 60 (Auschem SpA), Kessco® PEG 300 MO (Stepan), Nikkol MYO-6 (Nikko), Emulgante A6 (Condea)	8.5
PEG-7 oleate	Algon OL 70 (Auschem SpA)	10.4
PEG-6 laurate	Kessco® PEG300 ML (Stepan)	11.4
PEG-7 laurate	Lauridac 7 (Condea)	13
PEG-6 stearate	Kessco® PEG300 MS (Stepan)	9.7
PEG-8 laurate	Mapeg® 400 ML (PPG), LIPOPEG 4DL(Lipo Chem.)	13
PEG-8 oleate	Mapeg® 400 MO (PPG), Emulgante A8 (Condea); Kessco PEG 400 MO (Stepan)	12
PEG-8 stearate	Mapeg® 400 MS (PPG), Myrj 45	12
PEG-9 oleate	Emulgante A9 (Condea)	>10
PEG-9 stearate	Cremophor S9 (BASF)	>10
PEG-10 laurate	Nikkol MYL-10 (Nikko), Lauridac 10 (Croda)	13
PEG-10 oleate	Nikkol MYO-10 (Nikko)	11
PEG-10 stearate	Nikkol MYS-10 (Nikko), Coster K100 (Condea)	11
PEG-12 laurate	Kessco® PEG 600ML (Stepan)	15
PEG-12 oleate	Kessco® PEG 600MO (Stepan)	14
PEG-12 ricinoleate	(CAS # 9004-97-1)	>10
PEG-12 stearate	Mapeg® 600 MS (PPG), Kessco® PEG 600MS (Stepan)	14
PEG-15 stearate	Nikkol TMGS-15 (Nikko), Koster K15 (Condea)	14
PEG-15 oleate	Nikkol TMGO-15 (Nikko)	15
PEG-20 laurate	Kessco® PEG 1000 ML (Stepan)	17
PEG-20 oleate	Kessco® PEG 1000 MO (Stepan)	15

PEG-20 stearate	Mapeg® 1000 MS (PPG), Kessco® PEG 1000 MS (Stepan), Myrj 49	16
PEG-25 stearate	Nikkol MYS-25 (Nikko)	15
PEG-32 laurate	Kessco® PEG 1540 ML (Stepan)	16
PEG-32 oleate	Kessco® PEG 1540 MO (Stepan)	17
PEG-32 stearate	Kessco® PEG 1540 MS (Stepan)	17
PEG-30 stearate	Myrj 51	>10
PEG-40 laurate	Crodet L40 (Croda)	17.9
PEG-40 oleate	Crodet O40 (Croda)	17.4
PEG-40 stearate	Myrj 52, Emerest® 2715 (Henkel), Nikkol MYS-40 (Nikko)	>10
PEG-45 stearate	Nikkol MYS-45 (Nikko)	18
PEG-50 stearate	Myrj 53	>10
PEG-55 stearate	Nikkol MYS-55 (Nikko)	18
PEG-100 oleate	Crodet O-100 (Croda)	18.8
PEG-100 stearate	Myrj 59, Arlacel 165 (ICI)	19
PEG-200 oleate	Albunol 200 MO (Taiwan Surf.)	>10
PEG-400 oleate	LACTOMUL (Henkel), Albunol 400 MO (Taiwan Surf.)	>10
PEG-600 oleate	Albunol 600 MO (Taiwan Surf.)	>10

2.2 PEG-Fatty Acid Diesters

Polyethylene glycol (PEG) fatty acid diesters are also suitable for use as surfactants in the compositions of the present invention. Among the surfactants in Table 3, preferred hydrophilic surfactants include PEG-20 dilaurate, PEG-20 dioleate, PEG-20 distearate, PEG-32 dilaurate and PEG-32 dioleate. Representative PEG-fatty acid diesters are shown in Table 3.

Table 3: PEG-Fatty Acid Diester Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG-4 dilaurate	Mapeg® 200 DL (PPG), Kessco® PEG 200 DL (Stepan), LIPOPEG 2-DL (Lipo Chem.)	7
PEG-4 dioleate	Mapeg® 200 DO (PPG),	6
PEG-4 distearate	Kessco® 200 DS (Stepan)	5
PEG-6 dilaurate	Kessco® PEG 300 DL (Stepan)	9.8
PEG-6 dioleate	Kessco® PEG 300 DO (Stepan)	7.2
PEG-6 distearate	Kessco® PEG 300 DS (Stepan)	6.5
PEG-8 dilaurate	Mapeg® 400 DL (PPG), Kessco® PEG 400 DL (Stepan), LIPOPEG 4 DL (Lipo Chem.)	11
PEG-8 dioleate	Mapeg® 400 DO (PPG), Kessco® PEG 400 DO (Stepan), LIPOPEG 4 DO(Lipo Chem.)	8.8
PEG-8 distearate	Mapeg® 400 DS (PPG), CDS 400 (Nikkol)	11
PEG-10 dipalmitate	Polyaldo 2PKFG	>10
PEG-12 dilaurate	Kessco® PEG 600 DL (Stepan)	11.7
PEG-12 distearate	Kessco® PEG 600 DS (Stepan)	10.7
PEG-12 dioleate	Mapeg® 600 DO (PPG), Kessco® 600 DO(Stepan)	10
PEG-20 dilaurate	Kessco® PEG 1000 DL (Stepan)	15
PEG-20 dioleate	Kessco® PEG 1000 DO (Stepan)	13
PEG-20 distearate	Kessco® PEG 1000 DS (Stepan)	12
PEG-32 dilaurate	Kessco® PEG 1540 DL (Stepan)	16
PEG-32 dioleate	Kessco® PEG 1540 DO (Stepan)	15
PEG-32 distearate	Kessco® PEG 1540 DS (Stepan)	15
PEG-400 dioleate	Cithrol 4DO series (Croda)	>10

PEG-400 distearate	Cithrol 4DS series (Croda)	>10

2.3 PEG-Fatty Acid Mono- and Di-ester Mixtures

In general, mixtures of surfactants are also useful in the present invention, including mixtures of two or more commercial surfactant products. Several PEG-fatty acid esters are marketed commercially as mixtures or mono- and diesters. Representative surfactant mixtures are shown in Table 4.

Table 4: PEG-Fatty Acid Mono- and Diester Mixtures

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG 4-150 mono, dilaurate	Kessco® PEG 200-6000 mono, dilaurate (Stepan)	
PEG 4-150 mono, dioleate	Kessco® PEG 200-6000 mono, dioleate (Stepan)	
PEG 4-150 mono, distearate	Kessco® 200-6000 mono, distearate (Stepan)	

2.4 Polyethylene Glycol Glycerol Fatty Acid Esters

Suitable PEG glycerol fatty acid esters are shown in Table 5. Among the surfactants in the Table, preferred hydrophilic surfactants are PEG-20 glyceryl laurate, PEG-30 glyceryl laurate, PEG-40 glyceryl laurate, PEG-20 glyceryl oleate, and PEG-30 glyceryl oleate.

Table 5: PEG Glycerol Fatty Acid Esters

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG-20 glyceryl laurate	Tagat® L (Goldschmidt)	16
PEG-30 glyceryl laurate	Tagat® L2 (Goldschmidt)	16
PEG-15 glyceryl laurate	Glycerox L series (Croda)	15
PEG-40 glyceryl laurate	Glycerox L series (Croda)	15
PEG-20 glyceryl stearate	Capmul® EMG (ABITEC), Aldo® MS-20 KFG (Lonza)	13
PEG-20 glyceryl oleate	Tagat® O (Goldschmidt)	>10

PEG-30 glyceryl oleate	Tagat® O2 (Goldschmidt)	>10

2.5. Alcohol - Oil Transesterification Products

A large number of surfactants of different degrees of hydrophobicity or hydrophilicity can be prepared by reaction of alcohols or polyalcohols with a variety of natural and/or hydrogenated oils. Most commonly, the oils used are castor oil or hydrogenated castor oil, or an edible vegetable oil such as corn oil, olive oil, peanut oil, palm kernel oil, apricot kernel oil, or almond oil. Preferred alcohols include glycerol, propylene glycol, ethylene glycol, polyethylene glycol, sorbitol, and pentaerythritol. Among these alcohol-oil transesterified surfactants, preferred hydrophilic surfactants are PEG-35 castor oil (Incrocas-35), PEG-40 hydrogenated castor oil (Cremophor RH 40), PEG-25 trioleate (TAGAT® TO), PEG-60 corn glycerides (Crovol M70), PEG-60 almond oil (Crovol A70), PEG-40 palm kernel oil (Crovol PK70), PEG-50 castor oil (Emalex C-50), PEG-50 hydrogenated castor oil (Emalex HC-50), PEG-8 caprylic/capric glycerides (Labrasol), and PEG-6 caprylic/capric glycerides (Softigen 767). Preferred hydrophobic surfactants in this class include PEG-5 hydrogenated castor oil, PEG-7 hydrogenated castor oil, PEG-9 hydrogenated castor oil, PEG-6 corn oil (Labrafil® M 2125 CS), PEG-6 almond oil (Labrafil® M 1966 CS), PEG-6 apricot kernel oil (Labrafil® M 1944 CS), PEG-6 olive oil (Labrafil® M 1980 CS), PEG-6 peanut oil (Labrafil® M 1969 CS), PEG-6 hydrogenated palm kernel oil (Labrafil® M 2130 BS), PEG-6 palm kernel oil (Labrafil® M 2130 CS), PEG-6 triolein (Labrafil® M 2735 CS), PEG-8 corn oil (Labrafil® WL 2609 BS), PEG-20 corn glycerides (Crovol M40), and PEG-20 almond glycerides (Crovol A40). The latter two surfactants are reported to have HLB values of 10, which is generally considered to be the approximate border line between hydrophilic and hydrophobic surfactants. For purposes of the present invention, these two surfactants are considered to be hydrophobic. Representative surfactants of this class suitable for use in the present invention are shown in Table 6.

Table 6: Transesterification Products of Oils and Alcohols

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG-3 castor oil	Nikkol CO-3 (Nikko)	3

PEG-5, 9, and 16 castor oil	ACCONON CA series (ABITEC)	6-7
PEG-20 castor oil	Emalex C-20 (Nihon Emulsion), Nikkol CO-20 TX (Nikko)	11
PEG-23 castor oil	Emulgante EL23	>10
PEG-30 castor oil	Emalex C-30 (Nihon Emulsion), Alkamuls® EL 620 (Rhone-Poulenc), Incrocas 30 (Croda)	11
PEG-35 castor oil	Cremophor EL and EL-P (BASF), Emulphor EL, Incrocas-35 (Croda), Emulgin RO 35 (Henkel)	
PEG-38 castor oil	Emulgante EL 65 (Condea)	
PEG-40 castor oil	Emalex C-40 (Nihon Emulsion), Alkamuls® EL 719 (Rhone-Poulenc)	13
PEG-50 castor oil	Emalex C-50 (Nihon Emulsion)	14
PEG-56 castor oil	Eumulgin® PRT 56 (Pulcra SA)	>10
PEG-60 castor oil	Nikkol CO-60TX (Nikko)	14
PEG-100 castor oil	Thornley	>10
PEG-200 castor oil	Eumulgin® PRT 200 (Pulcra SA)	>10
PEG-5 hydrogenated castor oil	Nikkol HCO-5 (Nikko)	6
PEG-7 hydrogenated castor oil	Simusol® 989 (Seppic), Cremophor WO7 (BASF)	6
PEG-10 hydrogenated castor oil	Nikkol HCO-10 (Nikko)	6.5
PEG-20 hydrogenated castor oil	Nikkol HCO-20 (Nikko)	11
PEG-25 hydrogenated castor oil	Simulsol® 1292 (Seppic), Cerex ELS 250 (Auschem SpA)	11
PEG-30 hydrogenated castor oil	Nikkol HCO-30 (Nikko)	11
PEG-40 hydrogenated castor oil	Cremophor RH 40 (BASF), Croduret (Croda), Emulgin HRE 40 (Henkel)	13
PEG-45 hydrogenated castor oil	Cerex ELS 450 (Auschem Spa)	14
PEG-50 hydrogenated castor oil	Emalex HC-50 (Nihon Emulsion)	14
PEG-60 hydrogenated castor oil	Nikkol HCO-60 (Nikko); Cremophor RH 60 (BASF)	15

PEG-80 hydrogenated castor oil	Nikkol HCO-80 (Nikko)	15
PEG-100 hydrogenated castor oil	Nikkol HCO -100 (Nikko)	17
PEG-6 corn oil	Labrafil® M 2125 CS (Gattefosse)	4
PEG-6 almond oil	Labrafil® M 1966 CS (Gattefosse)	4
PEG-6 apricot kernel oil	Labrafil® M 1944 CS (Gattefosse)	4
PEG-6 olive oil	Labrafil® M 1980 CS (Gattefosse)	4
PEG-6 peanut oil	Labrafil® M 1969 CS (Gattefosse)	4
PEG-6 hydrogenated palm kernel oil	Labrafil® M 2130 BS (Gattefosse)	4
PEG-6 palm kernel oil	Labrafil® M 2130 CS (Gattefosse)	4
PEG-6 triolein	Labrafil® M 2735 CS (Gattefosse)	4
PEG-8 corn oil	Labrafil® WL 2609 BS (Gattefosse)	6-7
PEG-20 corn glycerides	Crovol M40 (Croda)	10
PEG-20 almond glycerides	Crovol A40 (Croda)	10
PEG-25 trioleate	TAGAT® TO (Goldschmidt)	11
PEG-40 palm kernel oil	Crovol PK-70	>10
PEG-60 corn glycerides	Crovol M70(Croda)	15
PEG-60 almond glycerides	Crovol A70 (Croda)	15
PEG-4 caprylic/capric triglyceride	Labrafac® Hydro (Gattefosse),	4-5
PEG-8 caprylic/capric glycerides	Labrasol (Gattefosse),Labrafac CM 10 (Gattefosse)	>10
PEG-6 caprylic/capric glycerides	SOFTIGEN® 767 (Hüls), Glycerox 767 (Croda)	19
Lauroyl macrogol-32 glyceride	GELUCIRE 44/14 (Gattefosse)	14
Stearoyl macrogol glyceride	GELUCIRE 50/13 (Gattefosse)	13

Mono, di, tri, tetra esters of vegetable oils and sorbitol	SorbitoGlyceride (Gattefosse)	<10
Pentaerythrityl tetraisostearate	Crodamol PTIS (Croda)	<10
Pentaerythrityl distearate	Albunol DS (Taiwan Surf.)	<10
Pentaerythrityl tetraoleate	Liponate PO-4 (Lipo Chem.)	<10
Pentaerythrityl tetrastearate	Liponate PS-4 (Lipo Chem.)	<10
Pentaerythrityl tetracaprylate/tetracaprate	Liponate PE-810 (Lipo Chem.), Crodamol PTC (Croda)	<10
Pentaerythrityl tetraoctanoate	Nikkol Pentarate 408 (Nikko)	

Also included as oils in this category of surfactants are oil-soluble vitamins, such as vitamins A, D, E, K, etc. Thus, derivatives of these vitamins, such as tocopheryl PEG-1000 succinate (TPGS, available from Eastman), are also suitable surfactants.

2.6. Polyglycerized Fatty Acids

Polyglycerol esters of fatty acids are also suitable surfactants for the present invention. Among the polyglyceryl fatty acid esters, preferred hydrophobic surfactants include polyglyceryl oleate (Plurol Oleique), polyglyceryl-2 dioleate (Nikkol DGDO), and polyglyceryl-10 trioleate. Preferred hydrophilic surfactants include polyglyceryl-10 laurate (Nikkol Decaglyn 1-L), polyglyceryl-10 oleate (Nikkol Decaglyn 1-O), and polyglyceryl-10 mono, dioleate (Caprol® PEG 860). Polyglyceryl polyricinoleates (Polymuls) are also preferred hydrophilic and hydrophobic surfactants. Examples of suitable polyglyceryl esters are shown in Table 7.

Table 7: Polyglycerized Fatty Acids

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Polyglyceryl-2 stearate	Nikkol DGMS (Nikko)	5-7
Polyglyceryl-2 oleate	Nikkol DGMO (Nikko)	5-7
Polyglyceryl-2 isostearate	Nikkol DGMIS (Nikko)	5-7

Polyglyceryl-3 oleate	Caprol® 3GO (ABITEC), Drewpol 3-1-O (Stepan)	6.5
Polyglyceryl-4 oleate	Nikkol Tetraglyn 1-O (Nikko)	5-7
Polyglyceryl-4 stearate	Nikkol Tetraglyn 1-S (Nikko)	5-6
Polyglyceryl-6 oleate	Drewpol 6-1-O (Stepan), Nikkol Hexaglyn 1-O (Nikko)	9
Polyglyceryl-10 laurate	Nikkol Decaglyn 1-L (Nikko)	15
Polyglyceryl-10 oleate	Nikkol Decaglyn 1-O (Nikko)	14
Polyglyceryl-10 stearate	Nikkol Decaglyn 1-S (Nikko)	12
Polyglyceryl-6 ricinoleate	Nikkol Hexaglyn PR-15 (Nikko)	>8
Polyglyceryl-10 linoleate	Nikkol Decaglyn 1-LN (Nikko)	12
Polyglyceryl-6 pentaoleate	Nikkol Hexaglyn 5-O (Nikko)	<10
Polyglyceryl-3 dioleate	Cremophor GO32 (BASF)	<10
Polyglyceryl-3 distearate	Cremophor GS32 (BASF)	<10
Polyglyceryl-4 pentaoleate	Nikkol Tetraglyn 5-O (Nikko)	<10
Polyglyceryl-6 dioleate	Caprol® 6G20 (ABITEC); Hodag PGO-62 (Calgene), PLUROL OLEIQUE CC 497 (Gattefosse)	8.5
Polyglyceryl-2 dioleate	Nikkol DGDO (Nikko)	7
Polyglyceryl-10 trioleate	Nikkol Decaglyn 3-O (Nikko)	7
Polyglyceryl-10 pentaoleate	Nikkol Decaglyn 5-O (Nikko)	3.5
Polyglyceryl-10 septaoleate	Nikkol Decaglyn 7-O (Nikko)	3
Polyglyceryl-10 tetraoleate	Caprol® 10G4O (ABITEC); Hodag PGO-62 (CALGENE), Drewpol 10-4-O (Stepan)	6.2
Polyglyceryl-10 decaisostearate	Nikkol Decaglyn 10-IS (Nikko)	<10
Polyglyceryl-10l decaoleate	Drewpol 10-10-O (Stepan), Caprol 10G10O (ABITEC), Nikkol Decaglyn 10-O	3.5
Polyglyceryl-10 mono, dioleate	Caprol® PGE 860 (ABITEC)	11

Polyglyceryl polyricinoleate	Polymuls (Henkel)	3-20

2.7. Propylene Glycol Fatty Acid Esters

Esters of propylene glycol and fatty acids are suitable surfactants for use in the present invention. In this surfactant class, preferred hydrophobic surfactants include propylene glycol monolaurate (Lauroglycol FCC), propylene glycol ricinoleate (Propymuls), propylene glycol monooleate (Myverol P-O6), propylene glycol dicaprylate/dicaprate (Captex® 200), and propylene glycol dioctanoate (Captex® 800). Examples of surfactants of this class are given in Table 8.

Table 8: Propylene Glycol Fatty Acid Esters

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Propylene glycol monocaprylate	Capryol 90 (Gattefosse), Nikkol Sefsol 218 (Nikko)	<10
Propylene glycol monolaurate	Lauroglycol 90 (Gattefosse), Lauroglycol FCC (Gattefosse)	<10
Propylene glycol oleate	Lutrol OP2000 (BASF)	<10
Propylene glycol myristate	Mirpyl	<10
Propylene glycol monostearate	ADM PGME-03 (ADM), LIPO PGMS (Lipo Chem.), Aldo® PGHMS (Lonza)	3-4
Propylene glycol hydroxy stearate		<10
Propylene glycol ricinoleate	PROPYMULS (Henkel)	<10
Propylene glycol isostearate		<10
Propylene glycol monooleate	Myverol P-O6 (Eastman)	<10
Propylene glycol dicaprylate/dicaprate	Captex® 200 (ABITEC), Miglyol® 840 (Hüls), Neobee® M-20 (Stepan)	>6
Propylene glycol dioctanoate	Captex® 800 (ABITEC)	>6
Propylene glycol caprylate/caprate	LABRAFAC PG (Gattefosse)	>6

Propylene glycol dilaurate		>6
Propylene glycol distearate	Kessco® PGDS (Stepan)	>6
Propylene glycol dicaprylate	Nikkol Sefsol 228 (Nikko)	>6
Propylene glycol dicaprate	Nikkol PDD (Nikko)	>6

2.8. Mixtures of Propylene Glycol Esters - Glycerol Esters

In general, mixtures of surfactants are also suitable for use in the present invention. In particular, mixtures of propylene glycol fatty acid esters and glycerol fatty acid esters are suitable and are commercially available. One preferred mixture is composed of the oleic acid esters of propylene glycol and glycerol (Arlacel 186). Examples of these surfactants are shown in Table 9.

Table 9: Glycerol/Propylene Glycol Fatty Acid Esters

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Oleic	ATMOS 300, ARLACEL 186 (ICI)	3-4
Stearic	ATMOS 150	3-4

2.9. Mono- and Diglycerides

A particularly important class of surfactants is the class of mono- and diglycerides. These surfactants are generally hydrophobic. Preferred hydrophobic surfactants in this class of compounds include glyceryl monooleate (Peceol), glyceryl ricinoleate, glyceryl laurate, glyceryl dilaurate (Capmul® GDL), glyceryl dioleate (Capmul® GDO), glyceryl mono/dioleate (Capmul® GMO-K), glyceryl caprylate/caprate (Capmul® MCM), caprylic acid mono/diglycerides (Imwitor® 988), and mono- and diacetylated monoglycerides (Myvacet® 9-45). Examples of these surfactants are given in Table 10.

Table 10: Mono- and Diglyceride Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Monopalmitolein (C16:1)	(Larodan)	<10
Monoelaidin (C18:1)	(Larodan)	<10
Monocaproin (C6)	(Larodan)	<10
Monocaprylin	(Larodan)	<10
Monocaprin	(Larodan)	<10
Monolaurin	(Larodan)	<10
Glyceryl monomyristate (C14)	Nikkol MGM (Nikko)	3-4
Glyceryl monooleate (C18:1)	PECEOL (Gattefosse), Hodag GMO-D, Nikkol MGO (Nikko)	3-4
Glyceryl monooleate	RYLO series (Danisco), DIMODAN series (Danisco), EMULDAN (Danisco), ALDO® MO FG (Lonza), Kessco GMO (Stepan), MONOMULS® series (Henkel), TEGIN O, DREWMULSE GMO (Stepan), Atlas G-695 (ICI), GMOrphic 80 (Eastman), ADM DMG-40, 70, and 100 (ADM), Myverol (Eastman)	3-4
Glycerol monooleate/linoleate	OLICINE (Gattefosse)	3-4
Glycerol monolinoleate	Maisine (Gattefosse), MYVEROL 18-92, Myverol 18-06 (Eastman)	3-4
Glyceryl ricinoleate	Softigen® 701 (Hüls), HODAG GMR-D (Calgene), ALDO® MR (Lonza)	6
Glyceryl monolaurate	ALDO® MLD (Lonza), Hodag GML (Calgene)	6.8
Glycerol monopalmitate	Emalex GMS-P (Nihon)	4
Glycerol monostearate	Capmul® GMS (ABITEC), Myvaplex (Eastman), IMWITOR® 191 (Hüls), CUTINA GMS, Aldo® MS (Lonza), Nikkol MGS series (Nikko)	5-9
Glyceryl mono-,dioleate	Capmul® GMO-K (ABITEC)	<10
Glyceryl palmitic/stearic	CUTINA MD-A, ESTAGEL-G18	<10
Glyceryl acetate	Lamegin® EE (Grünau GmbH)	<10

Glyceryl laurate	Imwitor® 312 (Hüls), Monomuls® 90-45 (Grünau GmbH), Aldo® MLD (Lonza)	4
Glyceryl citrate/lactate/oleate/ linoleate	Imwitor® 375 (Hüls)	<10
Glyceryl caprylate	Imwitor® 308 (Hüls), Capmul® MCMC8 (ABITEC)	5-6
Glyceryl caprylate/caprate	Capmul® MCM (ABITEC)	5-6
Caprylic acid mono,diglycerides	Imwitor® 988 (Hüls)	5-6
Caprylic/capric glycerides	Imwitor® 742 (Hüls)	<10
Mono-and diacetylated monoglycerides	Myvacet® 9-45, Myvacet® 9-40, Myvacet® 9-08 (Eastman), Lamegin® (Grünau)	3.8-4
Glyceryl monostearate	Aldo® MS, Arlacel 129 (ICI), LIPO GMS (Lipo Chem.), Imwitor® 191 (Hüls), Myvaplex (Eastman)	4.4
Lactic acid esters of mono,diglycerides	LAMEGIN GLP (Henkel)	<10
Dicaproin (C6)	(Larodan)	<10
Dicaprin (C10)	(Larodan)	<10
Dioctanoin (C8)	(Larodan)	<10
Dimyristin (C14)	(Larodan)	<10
Dipalmitin (C16)	(Larodan)	<10
Distearin	(Larodan)	<10
Glyceryl dilaurate (C12)	Capmul® GDL (ABITEC)	3-4
Glyceryl dioleate	Capmul® GDO (ABITEC)	3-4
Glycerol esters of fatty acids	GELUCIRE 39/01 (Gattefosse), GELUCIRE 43/01 (Gattefosse)	1
	GELUCIRE 37/06 (Gattefosse)	6
Dipalmitolein (C16:1)	(Larodan)	<10
1,2 and 1,3-diolein (C18:1)	(Larodan)	<10

Diclaidin (C18:1)	(Larodan)	<10
Dilinolein (C18:2)	(Larodan)	<10

2.10. Sterol and Sterol Derivatives

Sterols and derivatives of sterols are suitable surfactants for use in the present invention. These surfactants can be hydrophilic or hydrophobic. Preferred derivatives include the polyethylene glycol derivatives. A preferred hydrophobic surfactant in this class is cholesterol. A preferred hydrophilic surfactant in this class is PEG-24 cholesterol ether (Solulan C-24). Examples of surfactants of this class are shown in Table 11.

Table 11: Sterol and Sterol Derivative Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Cholesterol, sitosterol, lanosterol		<10
PEG-24 cholesterol ether	Solulan C-24 (Amerchol)	>10
PEG-30 cholestanol	Nikkol DHC (Nikko)	>10
Phytosterol	GENEROL series (Henkel)	<10
PEG-25 phyto sterol	Nikkol BPSH-25 (Nikko)	>10
PEG-5 soya sterol	Nikkol BPS-5 (Nikko)	<10
PEG-10 soya sterol	Nikkol BPS-10 (Nikko)	<10
PEG-20 soya sterol	Nikkol BPS-20 (Nikko)	<10
PEG-30 soya sterol	Nikkol BPS-30 (Nikko)	>10

2.11. Polyethylene Glycol Sorbitan Fatty Acid Esters

A variety of PEG-sorbitan fatty acid esters are available and are suitable for use as surfactants in the present invention. In general, these surfactants are hydrophilic, although several hydrophobic surfactants of this class can be used. Among the PEG-sorbitan fatty acid esters, preferred hydrophilic surfactants include PEG-20 sorbitan monolaurate (Tween-20), PEG-20 sorbitan monopalmitate (Tween-40), PEG-20 sorbitan monostearate

(Tween-60), and PEG-20 sorbitan monooleate (Tween-80). Examples of these surfactants are shown in Table 12.

Table 12: PEG-Sorbitan Fatty Acid Esters

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG-10 sorbitan laurate	Liposorb L-10 (Lipo Chem.)	>10
PEG-20 sorbitan monolaurate	Tween-20 (Atlas/ICI), Crillet 1 (Croda), DACOL MLS 20 (Condea)	17
PEG-4 sorbitan monolaurate	Tween-21 (Atlas/ICI), Crillet 11 (Croda)	13
PEG-80 sorbitan monolaurate	Hodag PSML-80 (Calgene); T-Maz 28	>10
PEG-6 sorbitan monolaurate	Nikkol GL-1 (Nikko)	16
PEG-20 sorbitan monopalmitate	Tween-40 (Atlas/ICI), Crillet 2 (Croda)	16
PEG-20 sorbitan monostearate	Tween-60 (Atlas/ICI), Crillet 3 (Croda)	15
PEG-4 sorbitan monostearate	Tween-61 (Atlas/ICI), Crillet 31 (Croda)	9.6
PEG-8 sorbitan monostearate	DACOL MSS (Condea)	>10
PEG-6 sorbitan monostearate	Nikkol TS106 (Nikko)	11
PEG-20 sorbitan tristearate	Tween-65 (Atlas/ICI), Crillet 35 (Croda)	11
PEG-6 sorbitan tetrastearate	Nikkol GS-6 (Nikko)	3
PEG-60 sorbitan tetrastearate	Nikkol GS-460 (Nikko)	13
PEG-5 sorbitan monooleate	Tween-81 (Atlas/ICI), Crillet 41 (Croda)	10
PEG-6 sorbitan monooleate	Nikkol TO-106 (Nikko)	10
PEG-20 sorbitan monooleate	Tween-80 (Atlas/ICI), Crillet 4 (Croda)	15
PEG-40 sorbitan oleate	Emalex ET 8040 (Nihon Emulsion)	18
PEG-20 sorbitan trioleate	Tween-85 (Atlas/ICI), Crillet 45 (Croda)	11
PEG-6 sorbitan tetraoleate	Nikkol GO-4 (Nikko)	8.5
PEG-30 sorbitan tetraoleate	Nikkol GO-430 (Nikko)	12

PEG-40 sorbitan tetraoleate	Nikkol GO-440 (Nikko)	13
PEG-20 sorbitan monoisostearate	Tween-120 (Atlas/ICI), Crillet 6 (Croda)	>10
PEG sorbitol hexaoleate	Atlas G-1086 (ICI)	10
PEG-6 sorbitol hexastearate	Nikkol GS-6 (Nikko)	3

2.12. Polyethylene Glycol Alkyl Ethers

Ethers of polyethylene glycol and alkyl alcohols are suitable surfactants for use in the present invention. Preferred hydrophobic ethers include PEG-3 oleyl ether (Volpo 3) and PEG-4 lauryl ether (Brij 30). Examples of these surfactants are shown in Table 13.

Table 13: Polyethylene Glycol Alkyl Ethers

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG-2 oleyl ether,oleth-2	Brij 92/93 (Atlas/ICI)	4.9
PEG-3 oleyl ether,oleth-3	Volpo 3 (Croda)	<10
PEG-5 oleyl ether,oleth-5	Volpo 5 (Croda)	<10
PEG-10 oleyl ether,oleth-10	Volpo 10 (Croda), Brij 96/97 (Atlas/ICI)	12
PEG-20 oleyl ether,oleth-20	Volpo 20 (Croda), Brij 98/99 (Atlas/ICI)	15
PEG-4 lauryl ether, laureth-4	Brij 30 (Atlas/ICI)	9.7
PEG-9 lauryl ether		>10
PEG-23 lauryl ether, laureth-23	Brij 35 (Atlas/ICI)	17
PEG-2 cetyl ether	Brij 52 (ICI)	5.3
PEG-10 cetyl ether	Brij 56 (ICI)	13
PEG-20 cetyl ether	Brij 58 (ICI)	16
PEG-2 stearyl ether	Brij 72 (ICI)	4.9
PEG-10 stearyl ether	Brij 76 (ICI)	12

PEG-20 stearyl ether	Brij 78 (ICI)	15
PEG-100 stearyl ether	Brij 700 (ICI)	>10

2.13. Sugar Esters

Esters of sugars are suitable surfactants for use in the present invention. Preferred hydrophilic surfactants in this class include sucrose monopalmitate and sucrose monolaurate. Examples of such surfactants are shown in Table 14.

Table 14: Sugar Ester Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Sucrose distearate	SUCRO ESTER 7 (Gattefosse), Crodesta F-10 (Croda)	3
Sucrose distearate/monostearate	SUCRO ESTER 11 (Gattefosse), Crodesta F-110 (Croda)	12
Sucrose dipalmitate		7.4
Sucrose monostearate	Crodesta F-160 (Croda)	15
Sucrose monopalmitate	SUCRO ESTER 15 (Gattefosse)	>10
Sucrose monolaurate	Saccharose monolaurate 1695 (Mitsubishi-Kasei)	15

2.14. Polyethylene Glycol Alkyl Phenols

Several hydrophilic PEG-alkyl phenol surfactants are available, and are suitable for use in the present invention. Examples of these surfactants are shown in Table 15.

Table 15: Polyethylene Glycol Alkyl Phenol Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
PEG-10-100 nonyl phenol	Triton X series (Rohm & Haas), Igepal CA series (GAF, USA), Antarox CA series (GAF, UK)	>10
PEG-15-100 octyl phenol ether	Triton N-series (Rohm & Haas), Igepal CO series (GAF, USA), Antarox CO series (GAF, UK)	>10

2.15. Polyoxyethylene-Polyoxypropylene Block Copolymers

The POE-POP block copolymers are a unique class of polymeric surfactants. The unique structure of the surfactants, with hydrophilic POE and hydrophobic POP moieties in well-defined ratios and positions, provides a wide variety of surfactants suitable for use in the present invention. These surfactants are available under various trade names, including Synperonic PE series (ICI); Pluronic® series (BASF), Emkalyx, Lutrol (BASF), Supronic, Monolan, Pluracare, and Plurodac. The generic term for these polymers is "poloxamer" (CAS 9003-11-6). These polymers have the formula:

$$HO(C_2H_4O)_a(C_3H_6O)_b(C_2H_4O)_aH$$

where "a" and "b" denote the number of polyoxyethylene and polyoxypropylene units, respectively.

Preferred hydrophilic surfactants of this class include Poloxamers 108, 188, 217, 238, 288, 338, and 407. Preferred hydrophobic surfactants in this class include Poloxamers 124, 182, 183, 212, 331, and 335.

Examples of suitable surfactants of this class are shown in Table 16. Since the compounds are widely available, commercial sources are not listed in the Table. The compounds are listed by generic name, with the corresponding "a" and "b" values.

Table 16: POE-POP Block Copolymers

COMPOUND	a, b values in $HO(C_2H_4O)_a(C_3H_6O)_b(C_2H_4O)_aH$	HLB
Poloxamer 105	a = 11 b = 16	8
Poloxamer 108	a = 46 b = 16	>10
Poloxamer 122	a = 5 b = 21	3
Poloxamer 123	a = 7 b = 21	7
Poloxamer 124	a = 11 b = 21	>7
Poloxamer 181	a = 3 b = 30	
Poloxamer 182	a = 8 b = 30	2
Poloxamer 183	a = 10 b = 30	
Poloxamer 184	a = 13 b = 30	

Poloxamer 185	a = 19	b = 30	
Poloxamer 188	a = 75	b = 30	29
Poloxamer 212	a = 8	b = 35	
Poloxamer 215	a = 24	b = 35	
Poloxamer 217	a = 52	b = 35	
Poloxamer 231	a = 16	b = 39	
Poloxamer 234	a = 22	b = 39	
Poloxamer 235	a = 27	b = 39	
Poloxamer 237	a = 62	b = 39	24
Poloxamer 238	a = 97	b = 39	
Poloxamer 282	a = 10	b = 47	
Poloxamer 284	a = 21	b = 47	
Poloxamer 288	a = 122	b = 47	>10
Poloxamer 331	a = 7	b = 54	0.5
Poloxamer 333	a = 20	b = 54	
Poloxamer 334	a = 31	b = 54	
Poloxamer 335	a = 38	b = 54	
Poloxamer 338	a = 128	b = 54	
Poloxamer 401	a = 6	b = 67	
Poloxamer 402	a = 13	b = 67	
Poloxamer 403	a = 21	b = 67	
Poloxamer 407	a = 98	b = 67	

2.16. Sorbitan Fatty Acid Esters

Sorbitan esters of fatty acids are suitable surfactants for use in the present invention. Among these esters, preferred hydrophobic surfactants include sorbitan monolaurate (Arlacel 20), sorbitan monopalmitate (Span-40), sorbitan monooleate (Span-

80), sorbitan monostearate, and sorbitan tristearate. Examples of these surfactants are shown in Table 17.

Table 17: Sorbitan Fatty Acid Ester Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Sorbitan monolaurate	Span-20 (Atlas/ICI), Crill 1 (Croda), Arlacel 20 (ICI)	8.6
Sorbitan monopalmitate	Span-40 (Atlas/ICI), Crill 2 (Croda), Nikkol SP-10 (Nikko)	6.7
Sorbitan monooleate	Span-80 (Atlas/ICI), Crill 4 (Croda), Crill 50 (Croda)	4.3
Sorbitan monostearate	Span-60 (Atlas/ICI), Crill 3 (Croda), Nikkol SS-10 (Nikko)	4.7
Sorbitan trioleate	Span-85 (Atlas/ICI), Crill 45 (Croda), Nikkol SO-30 (Nikko)	4.3
Sorbitan sesquioleate	Arlacel-C (ICI), Crill 43 (Croda), Nikkol SO-15 (Nikko)	3.7
Sorbitan tristearate	Span-65 (Atlas/ICI) Crill 35 (Croda), Nikkol SS-30 (Nikko)	2.1
Sorbitan monoisostearate	Crill 6 (Croda), Nikkol SI-10 (Nikko)	4.7
Sorbitan sesquistearate	Nikkol SS-15 (Nikko)	4.2

2.17. Lower Alcohol Fatty Acid Esters

Esters of lower alcohols (C_2 to C_4) and fatty acids (C_8 to C_{18}) are suitable surfactants for use in the present invention. Among these esters, preferred hydrophobic surfactants include ethyl oleate (Crodamol EO), isopropyl myristate (Crodamol IPM), and isopropyl palmitate (Crodamol IPP). Examples of these surfactants are shown in Table 18.

Table 18: Lower Alcohol Fatty Acid Ester Surfactants

COMPOUND	COMMERCIAL PRODUCT (Supplier)	HLB
Ethyl oleate	Crodamol EO (Croda), Nikkol EOO (Nikko)	<10
Isopropyl myristate	Crodamol IPM (Croda)	<10
Isopropyl palmitate	Crodamol IPP (Croda)	<10
Ethyl linoleate	Nikkol VF-E (Nikko)	<10

1	Isopropyl linoleate	Nikkol VF-IP (Nikko)	<10

2.18. Ionic Surfactants

Ionic surfactants, including cationic, anionic and zwitterionic surfactants, are suitable hydrophilic surfactants for use in the present invention. Preferred anionic surfactants include fatty acid salts and bile salts. Preferred cationic surfactants include carnitines. Specifically, preferred ionic surfactants include sodium oleate, sodium lauryl sulfate, sodium lauryl sarcosinate, sodium dioctyl sulfosuccinate, sodium cholate, sodium taurocholate; lauroyl carnitine; palmitoyl carnitine; and myristoyl carnitine. Examples of such surfactants are shown in Table 19. For simplicity, typical counterions are shown in the entries in the Table. It will be appreciated by one skilled in the art, however, that any bioacceptable counterion may be used. For example, although the fatty acids are shown as sodium salts, other cation counterions can also be used, such as alkali metal cations or ammonium. Unlike typical non-ionic surfactants, these ionic surfactants are generally available as pure compounds, rather than commercial (proprietary) mixtures. Because these compounds are readily available from a variety of commercial suppliers, such as Aldrich, Sigma, and the like, commercial sources are not generally listed in the Table.

Table 19: Ionic Surfactants

COMPOUND	HLB
FATTY ACID SALTS	>10
Sodium caproate	
Sodium caprylate	
Sodium caprate	
Sodium laurate	
Sodium myristate	
Sodium myristolate	
Sodium palmitate	
Sodium palmitoleate	
Sodium oleate	18
Sodium ricinoleate	

Sodium linoleate	
Sodium linolenate	
Sodium stearate	
Sodium lauryl sulfate (dodecyl)	40
Sodium tetradecyl sulfate	
Sodium lauryl sarcosinate	
Sodium dioctyl sulfosuccinate [sodium docusate (Cytec)]	
BILE SALTS	>10
Sodium cholate	
Sodium taurocholate	
Sodium glycocholate	
Sodium deoxycholate	
Sodium taurodeoxycholate	
Sodium glycodeoxycholate	
Sodium ursodeoxycholate	
Sodium chenodeoxycholate	
Sodium taurochenodeoxycholate	
Sodium glyco cheno deoxycholate	
Sodium cholylsarcosinate	
Sodium N-methyl taurocholate	
Sodium lithocholate	
PHOSPHOLIPIDS	
Egg/Soy lecithin [Epikuron™ (Lucas Meyer), Ovothin™ (Lucas Meyer)]	
Lyso egg/soy lecithin	
Hydroxylated lecithin	
Lysophosphatidylcholine	
Cardiolipin	
Sphingomyclin	
Phosphatidylcholine	
Phosphatidyl ethanolamine	
Phosphatidic acid	

Phosphatidyl glycerol

Phosphatidyl serine

PHOSPHORIC ACID ESTERS

Diethanolammonium polyoxyethylene-10 oleyl ether phosphate

Esterification products of fatty alcohols or fatty alcohol ethoxylates with phosphoric acid or anhydride

CARBOXYLATES

Ether carboxylates (by oxidation of terminal OH group of fatty alcohol ethoxylates)

Succinylated monoglycerides [LAMEGIN ZE (Henkel)]

Sodium stearyl fumarate

Stearoyl propylene glycol hydrogen succinate

Mono/diacetylated tartaric acid esters of mono- and diglycerides

Citric acid esters of mono-, diglycerides

Glyceryl-lacto esters of fatty acids (CFR ref. 172.852)

Acyl lactylates:

lactylic esters of fatty acids

calcium/sodium stearoyl-2-lactylate

calcium/sodium stearoyl lactylate

Alginate salts

Propylene glycol alginate

SULFATES AND SULFONATES

Ethoxylated alkyl sulfates

Alkyl benzene sulfones

α-olefin sulfonates

Acyl isethionates

Acyl taurates

Alkyl glyceryl ether sulfonates

Octyl sulfosuccinate disodium

Disodium undecylenamideo-MEA-sulfosuccinate

CATIONIC Surfactants >10

Lauroyl carnitine

Palmitoyl carnitine

Myristoyl carnitine

Hexadecyl triammonium bromide

Decyl trimethyl ammonium bromide

Cetyl trimethyl ammonium bromide

Dodecyl ammonium chloride

Alkyl benzyldimethylammonium salts

Diisobutyl phenoxyethoxydimethyl benzylammonium salts

Alkylpyridinium salts

Betaines (trialkylglycine):

Lauryl betaine (N-lauryl,N,N-dimethylglycine)

Ethoxylated amines:

Polyoxyethylene-15 coconut amine

2.19 Unionized Ionizable Surfactants

Ionizable surfactants, when present in their unionized (neutral, non-salt) form, are hydrophobic surfactants suitable for use in the compositions and methods of the present invention. Particular examples of such surfactants include free fatty acids, particularly C_6-C_{22} fatty acids, and bile acids. More specifically, suitable unionized ionizable surfactants include the free fatty acid and bile acid forms of any of the fatty acid salts and bile salts shown in Table 19.

2.20 Preferred Surfactants and Surfactant Combinations

Among the above-listed surfactants, several combinations are preferred. In all of the preferred combinations, the carrier includes at least one hydrophilic surfactant. Preferred non-ionic hydrophilic surfactants include alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl macrogolglycerides; polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols, derivatives, and analogues thereof; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols

with fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; sugar esters, sugar ethers; sucroglycerides; and mixtures thereof.

More preferably, the non-ionic hydrophilic surfactant is selected from the group consisting of polyoxyethylene alkylethers; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglyceryl fatty acid esters; polyoxyethylene glycerides; polyoxyethylene vegetable oils; and polyoxyethylene hydrogenated vegetable oils. The glyceride can be a monoglyceride, diglyceride, triglyceride, or a mixture.

Also preferred are non-ionic hydrophilic surfactants that are reaction mixtures of polyols and fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils or sterols. These reaction mixtures are largely composed of the transesterification products of the reaction, along with often complex mixtures of other reaction products. The polyol is preferably glycerol, ethylene glycol, polyethylene glycol, sorbitol, propylene glycol, pentaerythritol, or a saccharide.

Several particularly preferred carrier compositions are those which include as a non-ionic hydrophilic surfactant PEG-10 laurate, PEG-12 laurate, PEG-20 laurate, PEG-32 laurate, PEG-32 dilaurate, PEG-12 oleate, PEG-15 oleate, PEG-20 oleate, PEG-20 dioleate, PEG-32 oleate, PEG-200 oleate, PEG-400 oleate, PEG-15 stearate, PEG-32 distearate, PEG-40 stearate, PEG-100 stearate, PEG-20 dilaurate, PEG-25 glyceryl trioleate, PEG-32 dioleate, PEG-20 glyceryl laurate, PEG-30 glyceryl laurate, PEG-20 glyceryl stearate, PEG-20 glyceryl oleate, PEG-30 glyceryl oleate, PEG-30 glyceryl laurate, PEG-40 glyceryl laurate, PEG-40 palm kernel oil, PEG-50 hydrogenated castor oil, PEG-40 castor oil, PEG-35 castor oil, PEG-60 castor oil, PEG-40 hydrogenated castor oil, PEG-60 hydrogenated castor oil, PEG-60 corn oil, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, polyglyceryl-10 laurate, PEG-30 cholesterol, PEG-25 phyto sterol, PEG-30 soya sterol, PEG-20 trioleate, PEG-40 sorbitan oleate, PEG-80 sorbitan laurate, polysorbate 20, polysorbate 80, POE-9 lauryl ether, POE-23 lauryl ether, POE-10 oleyl ether, POE-20 oleyl ether, POE-20 stearyl ether, tocopheryl PEG-100 succinate, PEG-24 cholesterol, polyglyceryl-10 oleate, Tween 40, Tween 60, sucrose monostearate, sucrose monolaurate, sucrose monopalmitate, PEG 10-100 nonyl phenol series, PEG 15-100 octyl phenol series, or a poloxamer.

Among these preferred surfactants, more preferred are PEG-20 laurate, PEG-20 oleate, PEG-35 castor oil, PEG-40 palm kernel oil, PEG-40 hydrogenated castor oil, PEG-60 corn oil, PEG-25 glyceryl trioleate, polyglyceryl-10 laurate, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, PEG-30 cholesterol, polysorbate 20, polysorbate 80, POE-9 lauryl ether, POE-23 lauryl ether, POE-10 oleyl ether, PEG-24 cholesterol, sucrose monostearate, sucrose monolaurate and poloxamers. Most preferred are PEG-35 castor oil, PEG-40 hydrogenated castor oil, PEG-60 corn oil, PEG-25 glyceryl trioleate, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, polysorbate 20, polysorbate 80, tocopheryl PEG-1000 succinate, PEG-24 cholesterol, and hydrophilic poloxamers.

The hydrophilic surfactant can also be, or include as a component, an ionic surfactant. Preferred ionic surfactants include alkyl ammonium salts; bile acids and salts, analogues, and derivatives thereof; fusidic acid and derivatives thereof; fatty acid derivatives of amino acids, oligopeptides, and polypeptides; glyceride derivatives of amino acids, oligopeptides, and polypeptides; acyl lactylates; mono-,diacetylated tartaric acid esters of mono-,diglycerides; succinylated monoglycerides; citric acid esters of mono-,diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids and derivatives thereof; phospholipids and derivatives thereof; salts of alkylsulfates; salts of fatty acids; sodium docusate; carnitines; and mixtures thereof.

More preferable ionic surfactants include bile acids and salts, analogues, and derivatives thereof; lecithins, lysolecithin, phospholipids, lysophospholipids and derivatives thereof; salts of alkylsulfates; salts of fatty acids; sodium docusate; acyl lactylates; mono-,diacetylated tartaric acid esters of mono-,diglycerides; succinylated monoglycerides; citric acid esters of mono-,diglycerides; carnitines; and mixtures thereof.

More specifically, preferred ionic surfactants are lecithin, lysolecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, phosphatidic acid, phosphatidylserine, lysophosphatidylcholine, lysophosphatidylethanolamine, lysophosphatidylglycerol, lysophosphatidic acid, lysophosphatidylserine, PEG-phosphatidylethanolamine, PVP-phosphatidylethanolamine, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, cholate,

taurocholate, glycocholate, deoxycholate, taurodeoxycholate, chenodeoxycholate, glycodeoxycholate, glycochenodeoxycholate, taurochenodeoxycholate, ursodeoxycholate, tauroursodeoxycholate, glycoursodeoxycholate, cholylsarcosine, N-methyl taurocholate, caproate, caprylate, caprate, laurate, myristate, palmitate, oleate, ricinoleate, linoleate, linolenate, stearate, lauryl sulfate, teracecyl sulfate, docusate, lauroyl carnitines, palmitoyl carnitines, myristoyl carnitines, and salts and mixtures thereof.

Particularly preferred ionic surfactants are lecithin, lysolecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, lysophosphatidylcholine, PEG-phosphatidylethanolamine, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, cholate, taurocholate, glycocholate, deoxycholate, taurodeoxycholate, glycodeoxycholate, cholylsarcosine, caproate, caprylate, caprate, laurate, oleate, lauryl sulfate, docusate, and salts and mixtures thereof, with the most preferred ionic surfactants being lecithin, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, taurocholate, caprylate, caprate, oleate, lauryl sulfate, docusate, and salts and mixtures thereof.

The carrier of the present compositions includes at least two surfactants, at least one of which is hydrophilic. In one embodiment, the present invention includes at two surfactants that are hydrophilic, and preferred hydrophilic surfactants are listed above. In another embodiment, the carrier includes at least one hydrophilic surfactant and at least one hydrophobic surfactant. In this embodiment, preferred hydrophobic surfactants are alcohols; polyoxyethylene alkylethers; fatty acids; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lower alcohol fatty acids esters; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid derivatives of mono/diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; transesterified vegetable oils; sterols; sterol derivatives; sugar esters; sugar ethers; sucroglycerides; polyoxyethylene vegetable oils; and polyoxyethylene hydrogenated vegetable oils.

As with the hydrophilic surfactants, hydrophobic surfactants can be reaction mixtures of polyols and fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

Preferably, the hydrophobic surfactant is selected from the group consisting of fatty acids; lower alcohol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lactic acid derivatives of mono/diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; and reaction mixtures of polyols and fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

More preferred are lower alcohol fatty acids esters; polypropylene glycol fatty acid esters; propylene glycol fatty acid esters; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lactic acid derivatives of mono/diglycerides; sorbitan fatty acid esters; polyoxyethylene vegetable oils; and mixtures thereof, with glycerol fatty acid esters and acetylated glycerol fatty acid esters being most preferred. Among the glycerol fatty acid esters, the esters are preferably mono- or diglycerides, or mixtures of mono- and diglycerides, where the fatty acid moiety is a C_6 to C_{22} fatty acid.

Also preferred are hydrophobic surfactants which are the reaction mixture of polyols and fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols. Preferred polyols are polyethylene glycol, sorbitol, propylene glycol, and pentaerythritol.

Specifically preferred hydrophobic surfactants include myristic acid; oleic acid; lauric acid; stearic acid; palmitic acid; PEG 1-4 stearate; PEG 2-4 oleate; PEG-4 dilaurate; PEG-4 dioleate; PEG-4 distearate; PEG-6 dioleate; PEG-6 distearate; PEG-8 dioleate; PEG 3-16 castor oil; PEG 5-10 hydrogenated castor oil; PEG 6-20 corn oil; PEG 6-20 almond oil; PEG-6 olive oil; PEG-6 peanut oil; PEG-6 palm kernel oil; PEG-6 hydrogenated palm kernel oil; PEG-4 capric/caprylic triglyceride, mono, di, tri, tetra esters of vegetable oil and sorbitol; pentaerythrityl di, tetra stearate, isostearate, oleate, caprylate, or caprate; polyglyceryl 2-4 oleate, stearate, or isostearate; polyglyceryl 4-10 pentaoleate; polyglyceryl-3 dioleate; polyglyceryl-6 dioleate; polyglyceryl-10 trioleate; polyglyceryl-3 distearate; propylene glycol mono- or diesters of a C_6 to C_{20} fatty acid; monoglycerides of

C_6 to C_{20} fatty acids; acetylated monoglycerides of C_6 to C_{20} fatty acids; diglycerides of C_6 to C_{20} fatty acids; lactic acid derivatives of monoglycerides; lactic acid derivatives of diglycerides; cholesterol; phytosterol; PEG 5-20 soya sterol; PEG-6 sorbitan tetra, hexastearate; PEG-6 sorbitan tetraolcate; sorbitan monolaurate; sorbitan monopalmitate; sorbitan mono, trioleate; sorbitan mono, tristearate; sorbitan monoisostearate; sorbitan sesquioleate; sorbitan sesquistearate; PEG 2-5 oleyl ether; POE 2-4 lauryl ether; PEG-2 cetyl ether; PEG-2 stearyl ether; sucrose distearate; sucrose dipalmitate; ethyl oleate; isopropyl myristate; isopropyl palmitate; ethyl linoleate; isopropyl linoleate; and poloxamers.

Among the specifically preferred hydrophobic surfactants, most preferred are oleic acid; lauric acid; glyceryl monocaprate; glyceryl monocaprylate; glyceryl monolaurate; glyceryl monooleate; glyceryl dicaprate; glyceryl dicaprylate; glyceryl dilaurate; glyceryl dioleate; acetylated monoglycerides; propylene glycol oleate; propylene glycol laurate; polyglyceryl-3 oleate; polyglyceryl-6 dioleate; PEG-6 corn oil; PEG-20 corn oil; PEG-20 almond oil; sorbitan monooleate; sorbitan monolaurate; POE-4 lauryl ether; POE-3 oleyl ether; ethyl oleate; and poloxamers.

3. **Therapeutic Agents**

In the embodiments of the present invention which include therapeutic agents, the therapeutic agents suitable for use in the pharmaceutical compositions and methods of the present invention are not particularly limited, as the compositions are surprisingly capable of solubilizing and delivering a wide variety of therapeutic agents. The therapeutic agents can be hydrophilic, lipophilic, amphiphilic or hydrophobic, and can be solubilized in the triglyceride; solubilized in the carrier; solubilized in both the triglyceride and the carrier; or present in the diluent. Optionally, the therapeutic agent can be present in a first, solubilzed amount, and a second, non-solubilized (suspended) amount. Such therapeutic agents can be any agents having therapeutic or other value when administered to an animal, particularly to a mammal, such as drugs, nutrients, and cosmetics (cosmeceuticals). It should be understood that while the invention is described with particular reference to its value in the form of aqueous dispersions, the invention is not so limited. Thus, drugs, nutrients or cosmetics which derive their therapeutic or other value from, for example, topical or transdermal administration, are still considered to be suitable for use in the present invention.

Specific non-limiting examples of therapeutic agents that can be used in the pharmaceutical compositions of the present invention include analgesics and anti-inflammatory agents, anthelmintics, anti-arrhythmic agents, anti-asthma agents, anti-bacterial agents, anti-viral agents, anti-coagulants, anti-depressants, anti-diabetics, anti-epileptics, anti-fungal agents, anti-gout agents, anti-hypertensive agents, anti-malarials, anti-migraine agents, anti-muscarinic agents, anti-neoplastic agents and immunosuppressants, anti-protozoal agents, anti-thyroid agents, anti-tussives, anxiolytic, sedatives, hypnotics and neuroleptics, β-Blockers, cardiac inotropic agents, corticosteroids, diuretics, anti-parkinsonian agents, gastro-intestinal agents, histamine H_1-receptor antagonists, keratolytics, lipid regulating agents, muscle relaxants, anti-anginal agents, nutritional agents, analgesics, sex hormones, stimulants, peptides, peptidomimetics, DNA, RNA, oligodeoxynucleotides, genetic material, proteins, oligonucleotides, and vaccines.

In one embodiment, the therapeutic agent is a nutritional agent.

In another embodiment, the therapeutic agent is a cosmeceutical agent.

In another embodiment, the therapeutic agent is a protein, peptide or oligonucleotide. In a particular aspect of this embodiment, the therapeutic agent is a protein, peptidomimetic, DNA, RNA, oligodeoxynucleotide, genetic material, peptide or oligonucleotide having a molecular weight of less than about 1000 g/mol.

In another embodiment, the therapeutic agent is hydrophobic. Hydrophobic therapeutic agents are compounds with little or no water solubility. Intrinsic water solubilities (*i.e.*, water solubility of the unionized form) for hydrophobic therapeutic agents are less than about 1% by weight, and typically less than about 0.1% or 0.01% by weight. In a particular aspect of this embodiment, the therapeutic agent is a hydrophobic drug. In another particular aspect, the therapeutic agent is a hydrophobic drug having a molecular weight of less than about 1000 g/mol.

In another embodiment, the therapeutic agent is hydrophilic. Amphiphilic therapeutic agents are included within the class of hydrophilic therapeutic agents. Apparent water solubilities for hydrophilic therapeutic agents are greater than about 1% by weight, and typically greater than about 0.1% by weight. In a particular aspect of this embodiment, the therapeutic agent is a hydrophilic drug. In another particular aspect, the

therapeutic agent is a hydrophilic drug having a molecular weight of less than about 1000 g/mol.

Although the invention is not limited thereby, examples of therapeutic agents suitable for use in the compositions and methods of the present invention include the following representative compounds, as well as their pharmaceutically acceptable salts, isomers, esters, ethers and other derivatives:

abacavir, acarbose, acebutolol, acetazolamide, acetohexamide, acrivastine, acetretin, acyclovir, alatrofloxacin, albendazole, albuterol, alclofenac, alendronate, allopurinol, aloxiprin, alprazolam, alprenolol, alprostadil, amantadine, amiloride, aminoglutethimide, amiodarone, amiodarone HCl, amitriptyline, amlodipine, amodiaquine, amoxapine, amoxapine, amphetamine, amphotericin B, amprenavir, amrinone, amsacrine, amyl nitrate, amylobarbital, amylobarbitone, aspirin, astemizole, atenolol, atorvastatin, atovaquone, atropine, auranofin, azapropazone, azathioprine, azelastine, azithromycin, baclofen, barbital, barbitone, becaplermin, beclamide, beclomethasone, bendroflumethiazide, benzathine, benzathine penicillin, benazepril, benidipine, benorylate, bentazepam, benzhexol, benzhexol HCl, benznidazole, benzonatate, benztropine, bephenium hydroxynaphthoate, betamethasone, bezafibrate, bicalutamide, biperiden, bisacodyl, bisantrene, bovine growth hormone, bromazepam, bromfenac, bromocriptine, bromocriptine mesylate, bromperidol, brompheniramine, brotizolam, budesonide, bumetanide, bupropion, busulfan, butenafine, butenafine HCl, butobarbital, butobarbitone, butoconazole, butoconazole nitrate, calcifediol, calcipotriene, calcitonin, calcitriol, cambendazole, camptothecan, candesartan, capecitabine, capsaicin, captopril, carbamazepine, carbiniazole, carbinoxamine, carbromal, carotenes, cefazolin, cefoxitin sodium, celecoxib, cephadrine, cephalexin, cerivastatin, cetirizine, chlorpheniramine, chlophenisamine, chloproguanil, chlorambucil, chlordiazepoxide, chlormethiazole, chloroquine, chlorothiazide, chlorproguanil HCl, chlorpromazine, chlorpropamide, chlorprothixene, chlorthalidone, cholecalciferol, cilostazol, cimetidine, cinnarizine, cinoxacin, ciprofloxacin, ciprofloxacin HCl, cisapride, citalopram, cetirizine, clarithromycin, clemastine, clemastine fumarate, clemizole, clenbuterol, ciprofibrate, clioquinol, clobazam, clofazimine, clofibrate, clomiphene, clomiphene citrate, clomipramine, clonazepam, clopidogrel, clotiazepam, clotrimazole, cloxacillin, clozapine, codeine, conjugated estrogene, cortisone acetate, cortisone acetate, cromalyn sodium, cromoglicate, cromolyn, cyclizine, cyclosporin, cyproheptadine, cyproheptadine HCl,

dacarbazine, danazol, dantrolene, dantrolene sodium, darodipine, decoquinate, delavirdine, demeclocycline, desoxymethasone, dexamphetamine, dexchlorpheniramine, dexfenfluramine, dextropropyoxyphene, diamorphine, diazepam, diazoxide, dichlorophen, diclofenac, dicloxacillin, dicumarol, didanosine, diethylpropion, diflunisal, digitoxin, digoxin, dehydroepiandrosterone, dihydrocodeme, dihydroergotamine, dihydroergotamine mesylate, dihydrotachysterol, diiodohydroxyquinoline, dilitazem, dilitazem HCl, diloxanide furoate, dimenhydrinate, dinitolmide, diphenhydramine, diphenoxylate, diphenoxylate HCl, diphenylimidazole, diphenylpyrallin, dipyndamole, dinthromycin, disopyramide, divalproen, docusate, dolasetron, domperidone, doxazosin, doxazosin HCl, doxycycline, dronabinol, droperidol, econazole, econazole nitrate, editronate, efavirenz, ennapril, elhpticine, enalapril, enkephalin, enoxacin, enoximone, enrofloxacin, epalrestate, eperisone, ephedrine, eposartan, eposartan Iosartan, ergocalciferol, ergotamine, ergotamine tartrate, erythromycin, erythropoietin, essential fatty acids, estramustine, ethacrynic acid, ethambutol, ethinamate, ethynyl estradiol. ethionamide, ethopropazine, ethopropazine HCl, ethotoin, etodolac, etoperidone, etoposide, etretinate, famcyclovir, famotidine, felbamate, felodipine, fenbendazole, fenbufen, fenfluramine, fenofibrate, fenoldopam, fenoprofen, fenoprofen calcium, fentanyl, fexofenadine, finasteride, flecainide, flecainide acetate, fluconazole, fluocortolone, flucytosine, fludrocortisone, fludrocortisone acetate, fluexetine HCl, flunanisone, flunarizine, flunarizine HCl, flunisolide, flunitrazzepam, fluopromazine, fluoxetine, fluoxymesterone, fluphenthixol decatnoate, flupentixol, flupentixol decanoate, fluphenazine, fluphenazine decanoate, flurazepam, flurbiprofen, flurithromycin, fluticasone propionate, fluvastatin, foscarnet sodium, fosenopril, fosphenytoin, fosphenytoin sodium, frovatriptan, frusemide, fumagillin, finzolidone, furosemide, furzolidone, gabapentin, gancyclovir, gemfibrozil, gentamycin, glibenclamide, gliclazide, glipizide, glucagon, glybenclamide, glyburide, glyceryl Arinitrate glymepiride, glymepride, granisetron, granulocyte stimulating factor, grepafloxacin, griseofulvin, guanabenz, guanabenz, acetate, halofantrine, halofantrine HCl, haloperidol, hydrocortisone, hyoscyamine, ibufenac, ibuprofen, imipenem, indinavir, indivir, inesartan, irinotecan, isosorbide dinitrate, isosorbide mononitrate, isotretinoin, isoxazole, isradipine, itraconazole, ivermectin, ketoconazole, ketoprofen, ketorolac, ketotifen, labetalol, lamivudine, lamotrigine, lanatoside C, lansoprazole, leflunomide, levofloxacin, levothyroxine, lisinopril, lomefloxacin, Iomustine, loperamide, loratadine, lorazepam, lorefloxacin, lormetazepam, losartati, lovastatin, L-thyroxine, lysuride, lysuride maleate,

maprotiline, maprotiline HCl, mazindol, mebendazole, meclofenamic acid, meclizine, meclizine HCl, medazepam, medigoxin, medroxyprogesterone acetate, mefenamic acid, mefloquine, mefloquine HCl, megestrol acetate, melonicam, melphalan, mepacrine, mepenzolate bromide, meprobamate, meptazinol, mercaptopurine, mesalazine, mesoridazine, meshanol, mesylate, metformin, methadone, methaqualone, methoin, methotrexate, methomalen, methsuximide, methylphenidate, methylphenobarbital, methylphenobarbitone, methylprednisolone, methyltestosterone, methysergide, methysergide maleate, metoclopramide, metolazone, metoprolol, metronidazole, mianserm, mianserin HCl, miconazole, midazolam, miglitol, minoxidil, mitomycins, mitotane, mitoxantrone, mycophenolate, molindone, montelukast, morphine, mortriptyline, moxifloxacin, moxifloxacin HCl, mycophenolate, nabumetone, nadolol, nalbuphine, nalidixic acid, naproxen, naratriptan, naratriptan HCl, natamycin, nedocromil sodium, nefazodone, nelfinavir, neutontin, nevirapine, nicardipine, nicardipine HCl, nicotine, nicoumalone, nifedipine, nilutamide, nimesulide, nimodipine, nimorazole, nisoldipine, nitrazepam, nitrofurantoin, nitrofurazone, nizatidine, non-essential fatty acids, norethisterone, norfloxacin, norgestrel, nortriptyline HCl, nystatin, oestradiol, ofloxacin, olanzapine, omeprazole, ondansetron, ondansetron HCl, oprelvekin, ornidazole, oxacillin, oxpmniquine, oxantel, oxantel embonate, oxaprozin, oxatomide, oxazepam, oxcarbazepine, oxfendazole, oxiconazole, oxprenolol, oxybutynin, oxyphenbutazone, oxyphencyclimine, oxyphencyclimine HCl, paclitaxel, pamidronate, paramethadione, paracalcitol, paroxetine, paroxetine HCl, penicillins, pentaerythritol tehanitrate, pentazocine, pentobarbital, pentobarbitone, pentoxifylline, perchloperazine, perfloxacin, pericyclovir, perphenazine, perphenazine pimozide, phenacemide, phenbenzamine, phenindione, pheniramine, phenobarbital, phenobarbitone, phenoxybenzamine, phenoxybenzamme HCl, phensuximide, phentemune, phenylalanme, phenylbutazone, phenytoin, physostigmine, phytonadiol, pimozide, pindolol, pioglitazone, piroxicam, pizotifen, pizotifen maleate, pramipexol, pramipexole, pranlukast, pravastatin, praziquantel, prazosin, prazosin HCl, prednisolone, prednisone, pregabalin, primidone, probenecid, probucol, procarbazine, procarbazine HCl, prochlorperazine, progesterone. Pmguanil, proguanil HCl, propofol, propranolol, propylthiouracil, pseudoephedrine, pyrantel, pyrantel embonate, pyridostigmine, pyrimethamine quetiapine, quinapril, quinidine, quinidine sulfate, quinine, quinine sulfate, rabeprazole, rabeprazole sodium, raloxifene, raloxifene HCl, ranifdine, ranitidine HCl, recombinant human growth hormone,

refocoxib, remifentanil, repaglinide, reserpine, residronate, retinoids, ricobendazole, rifabutin, rifabutine, rifampicin, rifampin, rifapentine, rimantadine, rimexolone, risperidone, ritonavir, rizatriptan, rizatriptan benzoate, rofecoxib ropinirole HCl, robinirole, rosiglitazone, roxatidine, roxithromycin, salbutamol, salmon calcitonin (scT); saquinavir, selegiline, sertindole, sertraline, sertraline HCl, sibutramine, sibutramine HCl, sildenafil, sildenafil citrate, simvastatin, sirolimus, sodium cefazoline, somatostatin, sparfloxacin, spiramycins, spironolactone, stanozolol, stavudine, stilbestrol, sulconazole, sulconazole nitrate, sulfabenzamide, sulfacetamide, sulfadiazine, sulfadoxine, sulfafurazole, sulfamerazine, sulfamethoxazole, sulfapyridine, sulfasalazine, sulindac, sulphide, sulphacetamide, sulphadiazine, sulphadoxine, sulphafurazole, sulphamerazine, sulphamethoxazole, sulphapyndme, sulphasalazine, sulphur-pyrazone, sulpiride, sulthiame, sumatriptan, sumatriptan succinate, tacrine, tacrolimus, tamoxifen, tamoxifen citrate, tamsulosin, tamsulosin HCl, targretin, tazarotene, telmisar tan, temazepam, teniposide, terazosin, terazosin HCl, terbinafine HCl, terbutalne, terbutaline sulfate, terconazole, terfenadine, testolactone, testosterone, tetracycline, tetrahydrocannabinol, tetramisole, thiabendazole, thioguanine, thioridazine, tiagabine, tiagabine HCl, tibolone, ticlopidine, tiludronate, timolol, tinidazole, tioconazole, tirofiban, tizanidine, tizanidine HCl, tolazamide, tolbutamide, tolcapone, tolmetin, tolterodine, topiramate, topotecan, topotecan HCl, toremifene, toremifene citrate, tramadol, trazodone, trazodone HCl, tretinoin, triamcinolone, triamterene, triazolam, trifluoperazine, _ trim ethoprim, trimipramine; trimipramine maleate, troglitazone, tromethamine, tropicamide, trovafloxacin, . tumor necrosisi factor, undeoenoic acid, ursodeoxycholic acid, valacylcovir, valproic acid, valsartan, vancomycin, vasopressin, venlafaxine HCl, verteporfin, vigabatrin, vinblastme, vincristme, vinorelbine, vitamin A, Vitamin B2, vitamin D, vitamin E and vitamin K, vitamin K5, vitamin' K6, vitamin K7, vitamin K-S (II), zafirlukast, zileuton, zohnitriptan, zolpidem, and zopiclone.

Of course, salts, metabolic precursors, derivatives and mixtures of therapeutic agents may also be used where desired.

4. **Concentrations**

The components of the pharmaceutical compositions of the present invention in amounts such that upon dilution with an aqueous solution, the composition forms a clear, aqueous dispersion. The determining concentrations of components to form clear aqueous dispersions are the concentrations of triglyceride and surfactants, with the amount of the therapeutic agent, if present, being chosen as described below. The relative amounts of triglycerides and surfactants are readily determined by observing the properties of the resultant dispersion; *i.e.*, when the relative amounts of these components are within a suitable range, the resultant aqueous dispersion is optically clear. When the relative amounts are outside the suitable range, the resulting dispersion is visibly "cloudy", resembling a conventional emulsion or multiple-phase system. Although a visibly cloudy solution may be potentially useful for some applications, such a system would suffer from many of the same disadvantages as conventional prior art formulations, as described above.

A convenient method of determining the appropriate relative concentrations for any particular triglyceride is as follows. A convenient working amount of a hydrophilic surfactant is provided, and a known amount of the triglyceride is added. The mixture is stirred, with the aid of gentle heating if desired, then is diluted with purified water to prepare an aqueous dispersion. Any dilution amount can be chosen, but convenient dilutions are those within the range expected *in vivo*, about a 10 to 250-fold dilution. In the Examples herein, a convenient dilution of 100-fold was chosen. The aqueous dispersion is then assessed qualitatively for optical clarity. The procedure can be repeated with incremental variations in the relative amount of triglyceride added, to determine the maximum relative amount of triglyceride that can be present to form a clear aqueous dispersion with a given hydrophilic surfactant. *I.e.*, when the relative amount of triglyceride is too great, a hazy or cloudy dispersion is formed.

The amount of triglyceride that can be solubilized in a clear aqueous dispersion is increased by repeating the above procedure, but substituting a second hydrophilic surfactant, or a hydrophobic surfactant, for part of the originally-used hydrophilic surfactant, thus keeping the total surfactant concentration constant. Of course, this

procedure is merely exemplary, and the amounts of the components can be chosen using other methods, as desired.

It has been surprisingly found that mixtures of surfactants including two hydrophilic surfactants can solubilize a greater relative amount of triglyceride than a single surfactant. Similarly, mixtures of surfactants including a hydrophilic surfactant and a hydrophobic surfactant can solubilize a greater relative amount of triglyceride than either surfactant by itself. It is particularly surprising that when the surfactant mixture includes a hydrophilic surfactant and a hydrophobic surfactant, the solubility of the triglyceride is greater than, for example, in the hydrophilic surfactant itself. Thus, contrary to conventional knowledge in the art, the total amount of water-insoluble component (triglyceride plus hydrophobic surfactant) exceeds the amount of hydrophobic surfactant that can be solubilized by the same amount of hydrophilic surfactant. This unexpected finding shows a surprising and non-intuitive relationship between the hydrophilic and hydrophobic components.

It should be emphasized that the optical clarity is determined in the diluted composition (the aqueous dispersion), and not in the pre-concentrate. Thus, for example, U.S. Patent No. 4,719,239 shows optically clear compositions containing water, oil, and a 3:7 mixture of PEG-glycerol monooleate and caprylic-capric acid glycerol esters, but the compositions contain no more that about 75% by weight water, or a dilution of the pre-concentrate of no more than 3 to 1. Upon dilution with water in a ratio of more than about 3 to 1, the compositions of the cited reference phase-separate into multi-phase systems, as is shown, for example, in the phase diagram of Figure 2 in the '239 patent. In contrast, the compositions of the present invention, when diluted to values typical of dilutions encountered *in vivo*, or when diluted *in vivo* upon administration to a patient, remain as clear aqueous dispersions. Thus, the clear aqueous dispersions of the present invention are formed upon dilution of about 10 to about 250-fold or more.

As an alternative to qualitative visual assessment of optical clarity, the optical clarity of the aqueous dispersion can be measured using standard quantitative techniques for turbidity assessment. One convenient procedure to measure turbidity is to measure the amount of light of a given wavelength transmitted by the solution, using, for example, a UV-visible spectrophotometer. Using this measure, optical clarity corresponds to high transmittance, since cloudier solutions will scatter more of the incident radiation, resulting

in lower transmittance measurements. If this procedure is used, care should be taken to insure that the composition itself does not absorb light of the chosen wavelength, as any true absorbance necessarily reduces the amount of transmitted light and falsely increases the quantitative turbidity value. In the absence of chromophores at the chosen wavelength, suitable dispersions at a dilution of 100X should have an apparent absorbance of less than about 0.3, preferably less than about 0.2, and more preferably less than about 0.1.

Other methods of characterizing optical clarity, such as direct particle size measurement and other methods known in the art may also be used.

It should be emphasized that any or all of the available methods may be used to ensure that the resulting aqueous dispersions possess the requisite optical clarity. For convenience, however, the present inventors prefer to use the simple qualitative procedure; *i.e.*, simple visible observation. However, in order to more fully illustrate the practice of the present invention, both qualitative observation and spectroscopic measures are used to assess the dispersion clarity in the Examples herein.

If present, the therapeutic agent is solubilized in the triglyceride, the carrier, or in both the triglyceride and the carrier. Alternatively, the therapeutic agent can be solubilized in the aqueous medium used to dilute the preconcentrate to form an aqueous dispersion. The maximum amount of therapeutic agent that can be solubilized is readily determined by simple mixing, as the presence of any non-solubilized therapeutic agent is apparent upon visual examination.

In one embodiment, the therapeutic agent is present in an amount up to the maximum amount that can be solubilized in the composition. In another embodiment, the therapeutic agent is present in a first amount which is solubilized, and a second amount that remains unsolubilized but dispersed. This may be desirable when, for example, a larger dose of the therapeutic agent is desired. Although not all of the therapeutic agent is solubilized, such a composition presents advantages over conventional compositions, since at least a portion of the therapeutic agent is present in the clear aqueous dispersion phase. Of course, in this embodiment, the optical clarity of the resultant aqueous dispersion is determined before the second non-solubilized amount of the therapeutic agent is added.

Other considerations well known to those skilled in the art will further inform the choice of specific proportions of surfactants and triglycerides. These considerations include the degree of bioacceptability of the compounds, and the desired dosage of

therapeutic agent to be provided. In some cases, the amount of triglyceride or therapeutic agent actually used in a pharmaceutical composition according to the present invention will be less than the maximum that can be solubilized, and it should be apparent that such compositions are also within the scope of the present invention.

5. Solubilizers

If desired, the pharmaceutical compositions of the present invention can optionally include additional compounds to enhance the solubility of the therapeutic agent or the triglyceride in the composition. Examples of such compounds, referred to as "solubilizers", include:

alcohols and polyols, such as ethanol, isopropanol, butanol, benzyl alcohol, ethylene glycol, propylene glycol, butanediols and isomers thereof, glycerol, pentaerythritol, sorbitol, mannitol, transcutol, dimethyl isosorbide, polyethylene glycol, polypropylene glycol, polyvinylalcohol, hydroxypropyl methylcellulose and other cellulose derivatives, cyclodextrins and cyclodextrin derivatives;

ethers of polyethylene glycols having an average molecular weight of about 200 to about 6000, such as tetrahydrofurfuryl alcohol PEG ether (glycofurol, available commercially from BASF under the trade name Tetraglycol) or methoxy PEG (Union Carbide);

amides, such as 2-pyrrolidone, 2-piperidone, ε-caprolactam, N-alkylpyrrolidone, N-hydroxyalkylpyrrolidone, N-alkylpiperidone, N-alkylcaprolactam, dimethylacetamide, and polyvinylpyrrolidone;

esters, such as ethyl propionate, tributylcitrate, acetyl triethylcitrate, acetyl tributyl citrate, triethylcitrate, ethyl oleate, ethyl caprylate, ethyl butyrate, triacetin, propylene glycol monoacetate, propylene glycol diacetate, ε-caprolactone and isomers thereof, δ-valerolactone and isomers thereof, β-butyrolactone and isomers thereof;

and other solubilizers known in the art, such as dimethyl acetamide, dimethyl isosorbide (Arlasolve DMI (ICI)), N-methyl pyrrolidones (Pharmasolve (ISP)), monooctanoin, diethylene glycol monoethyl ether (available from Gattefosse under the trade name Transcutol), and water.

Mixtures of solubilizers are also within the scope of the invention. Except as indicated, these compounds are readily available from standard commercial sources.

Preferred solubilizers include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropyl cyclodextrins, ethanol, polyethylene glycol 200-600, glycofurol, transcutol, propylene glycol, and dimethyl isosorbide. Particularly preferred solubilizers include sorbitol, glycerol, triacetin, ethyl alcohol, PEG-400, glycofurol and propylene glycol.

The amount of solubilizer that can be included in compositions of the present invention is not particularly limited. Of course, when such compositions are ultimately administered to a patient, the amount of a given solubilizer is limited to a bioacceptable amount, which is readily determined by one of skill in the art. In some circumstances, it may be advantageous to include amounts of solubilizers far in excess of bioacceptable amounts, for example, to maximize the concentration of therapeutic agent, with excess solubilizer removed prior to providing the composition to a patient using conventional techniques, such as distillation or evaporation. Thus, if present, the solubilizer can be in a concentration of 50%, 100%, 200%, or up to about 400% by weight, based on the amount of surfactant. If desired, very small amounts of solubilizers may also be used, such as 25%, 10%, 5%, 1% or even less. Typically, the solubilizer will be present in an amount of about 1% to about 100%, more typically about 5% to about 25% by weight or about 10% to about 25% by weight.

6. **Enzyme Inhibitors**

When the therapeutic agent is subject to enzymatic degradation, the compositions can include an enzyme inhibiting agent. Enzyme inhibiting agents are shown for example, in Bernskop-Schnurch, A., "The use of inhibitory agents to overcome enzymatic barrier to perorally administered therapeutic peptides and proteins", *J. Controlled Release* 52, 1-16 (1998), the disclosure of which is incorporated herein by reference.

Generally, inhibitory agents can be divided into the following classes:

Inhibitors that are not based on amino acids, such as P-aminobenzamidine, FK-448, camostat mesylate, sodium glycocholate;

Amino acids and modified amino acids, such as aminoboronic acid derivatives and n-acetylcysteine;

Peptides and modified peptides, such as bacitracin, phosphinic acid dipeptide derivatives, pepstatin, antipain, leupeptin, chymostatin, elastatin, bestatin,

hosphoramindon, puromycin, cytochalasin potatocarboxy peptidase inhibitor, and amastatin;

Polypeptide protese inhibitors , such as aprotinin (bovine pancreatic trypsin inhibitor), Bowman-Birk inhibitor and soybean trypsin inhibitor, chicken egg white trypsin inhibitor, chicken ovoinhibitor, and human pancreatic trypsin inhibitor. Complexing agents, such as EDTA, EGTA, 1,10- phenanthroline and hydroxychinoline; and

Mucoadhesive polymers and polymer-inhibitor conjugates, such as polyacrylate derivatives, chitosan, cellulosics, chitosan-EDTA, chitosan-EDTA-antipain, polyacrylic acid-bacitracin, carboxymethyl cellulose-pepstatin, polyacrylic acid-Bwoman-Birk inhibitor.

The choice and levels of the enzyme inhibitor are based on toxicity, specificity of the proteases and the potency of the inhibition. The inhibitor can be suspended or solubilized in the composition preconcentrate, or added to the aqueous diluent or as a beverage.

Without wishing to be bound by theory, it is believed that an inhibitor can function solely or in combination as:

a competitive inhibitor, by binding at the substrate binding site of the enzyme, thereby preventing the access to the substrate; examples of inhibitors believed to operate by this mechanism are antipain, elastatinal and the Bowman Birk inhibitor;

a non-competitive inhibitor which can be simultaneously bound to the enzyme site along with the substrate, as their binding sites are not identical; and/or

a complexing agent due to loss in enzymatic activity caused by deprivation of essential metal ions out of the enzyme structure.

7. **Other Additives**

Other additives conventionally used in pharmaceutical compositions can be included, and these additives are well known in the art. Such additives include detackifiers, anti-foaming agents, buffering agents, antioxidants, preservatives, chelating agents, viscomodulators, tonicifiers, flavorants, colorants odorants, opacifiers, suspending agents, binders, fillers, plasticizers, lubricants, and mixtures thereof. The amounts of such additives can be readily determined by one skilled in the art, according to the particular properties desired.

8. Dosage Forms

The pharmaceutical compositions of the present invention can be formulated as a preconcentrate in a liquid, semi-solid, or solid form, or as an aqueous or organic diluted preconcentrate. In the diluted form, the diluent can be water, an aqueous solution, a buffer, an organic solvent, a beverage, a juice, or mixtures thereof. If desired, the diluent can include components soluble therein, such as a therapeutic agent, an enzyme inhibitor, solubilizers, additives, and the like.

The compositions can be processed according to conventional processes known to those skilled in the art, such as lyophilization, encapsulation, compression, melting, extrusion, drying, chilling, molding, spraying, coating, comminution, mixing, homogenization, sonication and granulation, to produce the desired dosage form.

The dosage form is not particularly limited. Thus, compositions of the present invention can be formulated as pills, capsules, caplets, tablets, granules, beads or powders. Granules, beads and powders can, of course, be further processed to form pills, capsules, caplets or tablets. When formulated as a capsule, the capsule can be a hard or soft gelatin capsule, a starch capsule, or a cellulosic capsule. Such dosage forms can further be coated with, for example, a seal coating or an enteric coating. The term "enteric coated capsule" as used herein means a capsule coated with a coating resistant to acid; *i.e.*, an acid resistant enteric coating. Enteric coated compositions of this invention protect therapeutic peptides or proteins in a restricted area of drug liberation and absorption, and reduce or even exclude extensive dilution effects. Although solubilizers are typically used to enhance the solubility of a hydrophobic therapeutic agent, they may also render the compositions more suitable for encapsulation in hard or soft gelatin capsules. Thus, the use of a solubilizer such as those described above is particularly preferred in capsule dosage forms of the pharmaceutical compositions. If present, these solubilizers should be added in amounts sufficient to impart to the compositions the desired solubility enhancement or encapsulation properties.

Although formulations specifically suited to oral administration are presently preferred, the compositions of the present invention can also be formulated for topical, transdermal, buccal, ocular, pulmonary, vaginal, rectal, transmucosal or parenteral administration, as well as for oral administration. Thus, the dosage form can be a solution, suspension, emulsion, cream, ointment, lotion, suppository, spray, aerosol, paste, gel,

drops, douche, ovule, wafer, troche, cachet, syrup, elixer, or other dosage form, as desired. If formulated as a suspension, the composition can further be processed in capsule form.

When formulated as a sprayable solution or dispersion, a dosage form of a multiparticulate carrier coated onto a substrate with the pharmaceutical compositions described herein can be used. The substrate can be a granule, a particle, or a bead, for example, and formed of a therapeutic agent or a pharmaceutically acceptable material. The multiparticulate carrier can be enteric coated with a pharmaceutically acceptable material as is well known to those skilled in the art.

Other additives may be included, such as are well-known in the art, to impart the desired consistency and other properties to the formulation.

9. Specific Embodiments

In all of the embodiments described herein, the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution, either *in vitro* or *in vivo*, a clear, aqueous dispersion is formed. This optical clarity in an aqueous dispersion defines the appropriate relative concentrations of the triglyceride and surfactant components, but does not restrict the dosage form of the compositions to an aqueous dispersion, nor does it limit the compositions of the invention to optically clear dosage forms. Thus, the appropriate concentrations of the triglyceride and surfactants are determined by the optical clarity of a dispersion formed by the composition preconcentrate and an aqueous solution in a dilution of about 10 to about 250-fold, as a preliminary matter. Once the appropriate concentrations are determined, the pharmaceutical compositions can be formulated as described in the preceding section, without regard to the optical clarity of the ultimate formulation. Of course, optically clear aqueous dispersions, and their preconcentrates, are preferred formulations.

In one embodiment, the present invention relates to pharmaceutical compositions having a triglyceride and a carrier, the carrier including at least two surfactants, at least one of which is hydrophilic. The triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion. In a particular aspect of this embodiment, the composition can contain more triglyceride than can be solubilized in a clear aqueous dispersion having only one surfactant, the surfactant being hydrophilic. Thus, this embodiment provides a higher concentration of triglyceride than is achievable with a

single hydrophilic surfactant, resulting in a reduced triglyceride to hydrophilic surfactant ratio and enhanced biocompatibility.

In another embodiment, the present invention relates to pharmaceutical compositions having a triglyceride and a carrier, the carrier including at least one hydrophilic surfactant and at least one hydrophobic surfactant. The triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion. In a particular aspect of this embodiment, the composition contains more triglyceride than can be solubilized in a clear aqueous dispersion having a hydrophilic surfactant but not having a hydrophobic surfactant..

In another embodiment, the triglyceride itself can have therapeutic value as, for example, a nutritional oil, or absorption-promoting value as, for example, a long-chain triglyceride (LCT) or a medium-chain triglyceride (MCT). Thus, in this embodiment, the present invention provides pharmaceutical compositions including a triglyceride having nutritional and/or absorption-promoting value, and a carrier. The carrier includes at least two surfactants, at least one of which is hydrophilic. Optionally, the carrier can include at least one hydrophilic surfactant and at least one hydrophobic surfactant. The triglyceride and surfactants are present in amounts such that upon dilution with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion.

In another embodiment, the present invention relates to a pharmaceutical composition which includes a therapeutic agent, a triglyceride and a carrier. The carrier includes at least two surfactants, at least one of which is hydrophilic. Optionally, the carrier includes at least one hydrophilic surfactant and at least one hydrophobic surfactant. The triglyceride, and surfactants are present in amounts such that upon dilution with an aqueous solution, either *in vitro* or *in vivo*, the composition forms a clear aqueous dispersion. The therapeutic agent is present in two amounts, a first amount of the therapeutic agent solubilized in the clear aqueous dispersion, and a second amount of the therapeutic agent that remains non-solubilized but dispersed.

In another aspect, the present invention relates to triglyceride-containing pharmaceutical compositions as described in the preceding embodiments, which further include a therapeutic agent. In particular embodiments, the therapeutic agent is a hydrophobic drug or a hydrophilic drug. In other embodiments, the therapeutic agent is a

nutritional agent. In still further embodiments, the therapeutic agent is a cosmeceutical agent.

10. Preparation of Pharmaceutical Compositions

The pharmaceutical compositions of the present invention can be prepared by conventional methods well known to those skilled in the art. Of course, the specific method of preparation will depend upon the ultimate dosage form. For dosage forms substantially free of water, *i.e.*, when the composition is provided in a pre-concentrate form for later dispersion *in vitro* or *in vivo* in an aqueous system, the composition is prepared by simple mixing of the components to form a pre-concentrate. The mixing process can be aided by gentle heating, if desired. For compositions in the form of an aqueous dispersion, the pre-concentrate form is prepared, then the appropriate amount of an aqueous solution is added. Upon gentle mixing, a clear aqueous dispersion is formed. If any water-soluble enzyme inhibitors or additives are included, these may be added first as part of the pre-concentrate, or added later to the clear aqueous dispersion, as desired. The compositions can be prepared with or without a therapeutic agent, and a therapeutic agent may also be provided in the diluent, if desired.

As previously noted, in another embodiment, the present invention includes a multi-phase dispersion containing a therapeutic agent. In this embodiment, a pharmaceutical composition includes a triglyceride and a carrier, which forms a clear aqueous dispersion upon mixing with an aqueous solution, and an additional amount of non-solubilized therapeutic agent. Thus, the term "multi-phase" as used herein to describe these compositions of the present invention means a composition which when mixed with an aqueous solution forms a clear aqueous phase and a particulate dispersion phase. The carrier and triglycerides are as described above, and can include any of the surfactants, therapeutic agents, solubilizers and additives previously described. An additional amount of therapeutic agent is included in the composition. This additional amount is not solubilized by the carrier, and upon mixing with an aqueous system is present as a separate dispersion phase. The additional amount is optionally a milled, micronized, or precipitated form. Thus, upon dilution, the composition contains two phases: a clear aqueous dispersion of the triglyceride and surfactants containing a first, solubilized amount of the therapeutic agent, and a second, non-solubilized amount of the therapeutic agent dispersed therein. It should be emphasized that the resultant multi-phase dispersion

will not have the optical clarity of a dispersion in which the therapeutic agent is fully solubilized, but will appear to be cloudy, due to the presence of the non-solubilized phase. Such a formulation may be useful, for example, when the desired dosage of a therapeutic agent exceeds that which can be solubilized in the carrier and/or triglyceride. The formulation may also contain additives, as described above.

One skilled in the art will appreciate that a therapeutic agent may have a greater solubility in the pre-concentrate composition than in the aqueous dispersion, so that meta-stable, supersaturated solutions having apparent optical clarity but containing a therapeutic agent in an amount in excess of its solubility in the aqueous dispersion can be formed. Such super-saturated solutions, whether characterized as clear aqueous dispersions (as initially formed) or as multi-phase solutions (as would be expected if the meta-stable state breaks down), are also within the scope of the present invention.

The multi-phase formulation can be prepared by the methods described above. A pre-concentrate is prepared by simple mixing of the components, with the aid of gentle heating, if desired. It is convenient to consider the therapeutic agent as divided into two portions, a first solubilizable portion which will be solubilized and contained within the clear aqueous dispersion upon dilution, and a second non-solubilizable portion which will remain non-solubilized. When the ultimate dosage form is non-aqueous, the first and second portions of the therapeutic agent are both included in the pre-concentrate mixture. When the ultimate dosage form is aqueous, the composition can be prepared in the same manner, and upon dilution in an aqueous system, the composition will form the two phases as described above, with the second non-solubilizable portion of the therapeutic agent dispersed or suspended in the aqueous system, and the first solubilizable portion of the therapeutic agent solubilized in the composition. Alternatively, when the ultimate dosage form is aqueous, the pre-concentrate can be prepared including only the first, solubilizable portion of the therapeutic agent. This pre-concentrate can then be diluted in an aqueous system to form a clear aqueous dispersion, to which is then added the second, non-solubilizable portion of the therapeutic agent to form a multi-phase aqueous composition.

B. Methods

In another embodiment, the present invention relates to methods of increasing the solubilization of a therapeutic agent in a composition, by providing the therapeutic agent in a composition of the present invention. The composition can be any of the

compositions described herein, with or without a therapeutic agent. It is surprisingly found that by using the combinations of triglycerides and surfactants described herein, greater amounts of triglycerides can be solubilized, without resort to unacceptably high concentrations of hydrophilic surfactants.

In another embodiment, the present invention relates to methods of increasing the rate and/or extent of absorption of therapeutic agents by administering to a patient a pharmaceutical composition of the present invention. In this embodiment, the therapeutic agent can be present in the pharmaceutical composition pre-concentrate, in the diluent, or in a second pharmaceutical composition, such as a conventional commercial formulation, which is co-administered with a pharmaceutical composition of the present invention. For example, the delivery of therapeutic agents in conventional pharmaceutical compositions can be improved by co-administering a pharmaceutical composition of the present invention with a conventional composition.

C. Characteristics of the Pharmaceutical Compositions

The dispersions formed upon dilution of the pharmaceutical compositions of the present invention have the following characteristics:

Rapid formation: upon dilution with an aqueous solution, the composition forms a clear dispersion very rapidly; *i.e.*, the clear dispersion appears to form instantaneously.

Optical clarity: the dispersions are essentially optically clear to the naked eye, and show no readily observable signs of heterogeneity, such as turbidity or cloudiness. More quantitatively, dispersions of the pharmaceutical compositions of the present invention have absorbances (400 nm) of less than about 0.3, and often less than about 0.1, at 100X dilution, as described more fully in the Examples herein. In the multi-phase embodiment of the compositions described herein, it should be appreciated that the optical clarity of the aqueous phase will be obscured by the dispersed particulate non-solubilized therapeutic agent.

Robustness to dilution: the dispersions are surprisingly stable to dilution in aqueous solution. The hydrophobic therapeutic agent remains solubilized for at least the period of time relevant for absorption.

As discussed above, conventional triglyceride-containing formulations suffer the disadvantage that bioabsorption of the therapeutic agents contained therein is dependent upon enzymatic degradation (lipolysis) of the triglyceride components. The solubilization

of the triglyceride in an aqueous medium is usually limited if only a hydrophilic surfactant is used to disperse the triglyceride, as is conventional. Without a sufficiently high concentration of the hydrophilic surfactant, an emulsion or milky suspension of the triglyceride is formed, and the triglyceride is present in the form of relatively large oil droplets. In this case, the large size of the triglyceride particles impedes the transport and absorption of the triglyceride or therapeutic agent solubilized in the triglyceride or in the carrier. In addition, the large, thermodynamically unstable triglyceride particles could further impose a risk when the compositions are administered intravenously, by plugging the blood capillaries.

To achieve a high level of fully-solubilized triglyceride would require an amount of the hydrophilic surfactant exceeding that which would be bioacceptable. The pharmaceutical compositions of the present invention, however, solve these and other problems of the prior art by adding a third component, a hydrophobic surfactant or a second hydrophilic surfactant. The solubilization of the triglyceride in the aqueous system is thereby unexpectedly enhanced. It is also unexpectedly found that the total amount of solubilized water-insoluble components, the triglyceride and hydrophobic surfactant, can greatly exceed the amount of the hydrophobic surfactant alone that can be solubilized using the same amount of the hydrophilic surfactant.

The unique pharmaceutical compositions and methods of the present invention present a number of significant and unexpected advantages, including:

Increased safety: The present compositions and methods allow for increased levels of triglyceride relative to hydrophilic surfactants, thereby reducing the need for excessively large amounts of hydrophilic surfactant. Further, the triglyceride-containing compositions of the present invention present small particle sizes, thus avoiding the problems of large particle size in conventional triglyceride-containing formulations and the concomitant safety concerns in parenteral administration.

Efficient transport: The particle sizes in the aqueous dispersions of the present invention are much smaller than the larger particles characteristic of vesicular, emulsion or microemulsion phases. This reduced particle size enables more efficient drug transport through the intestinal aqueous boundary layer, and through the absorptive brush border membrane. More efficient transport to absorptive sites leads to improved and more consistent absorption of therapeutic agents.

Less-dependence on lipolysis: The lack of large particle-size triglyceride components provides pharmaceutical compositions less dependent upon lipolysis, and upon the many poorly characterized factors which affect the rate and extent of lipolysis, for effective presentation of a therapeutic agent to an absorptive site. Such factors include the presence of composition components which may inhibit lipolysis; patient conditions which limit production of lipase, such as pancreatic lipase secretory diseases; and dependence of lipolysis on stomach pH, endogenous calcium concentration, and presence of co-lipase or other digestion enzymes. The reduced lipolysis dependence further provides transport which is less prone to suffer from any lag time between administration and absorption caused by the lipolysis process, enabling a more rapid onset of therapeutic action and better bioperformance characteristics. In addition, pharmaceutical compositions of the present invention can make use of hydrophilic surfactants which might otherwise be avoided or limited due to their potential lipolysis inhibiting effects.

Non-dependence on bile and meal fat contents: Due to the higher solubilization potential over bile salt micelles, the present compositions are less dependent on endogenous bile and bile related patient disease states, and meal fat contents. These advantages overcome meal-dependent absorption problems caused by poor patient compliance with meal-dosage restrictions.

Superior solubilization: The triglyceride and surfactant combinations used in compositions of the present invention enable superior loading capacity over conventional formulations. In addition, the particular combination of surfactants used can be optimized for a specific therapeutic agent to more closely match the polarity distribution of the therapeutic agent, resulting in still further enhanced solubilization.

Faster dissolution and release: Due to the robustness of compositions of the present invention to dilution, the therapeutic agents remain solubilized and thus do not suffer problems of precipitation of the therapeutic agent in the time frame relevant for absorption. In addition, the therapeutic agent is presented in small particle carriers, and is not limited in dilution rate by entrapment in emulsion carriers. These factors avoid liabilities associated with the poor partitioning of lipid solubilized drug in to the aqueous phase, such as large emulsion droplet surface area, and high interfacial transfer resistance, and enable rapid completion of the critical partitioning step.

Consistent performance: Aqueous dispersions of the present invention are thermodynamically stable for the time period relevant for absorption, and can be more predictably reproduced, thereby limiting variability in bioavailability-- a particularly important advantage for therapeutic agents with a narrow therapeutic index.

Efficient release: The compositions of the present invention are designed with components that help to keep the therapeutic agent or absorption promoter, such as a permeation enhancer, an enzyme inhibitor, etc., solubilized for transport to the absorption site, but readily available for absorption, thus providing a more efficient transport and release.

Less prone to gastric emptying delays: Unlike conventional triglyceride-containing formulations, the present compositions are less prone to gastric emptying delays, resulting in faster absorption. Further, the particles in dispersions of the present invention are less prone to unwanted retention in the gastro-intestinal tract.

Small size: Because of the small particle size in aqueous dispersion, the pharmaceutical compositions of the present invention allow for faster transport of the therapeutic agent through the aqueous boundary layer.

These and other advantages of the present invention, as well as aspects of preferred embodiments, are illustrated more fully in the Examples which follow.

EXAMPLES

Example 1: Preparation of Compositions

A simple pre-concentrate is prepared as follows. Predetermined weighed amounts of the surfactants and triglyceride are stirred together to form a homogeneous mixture. For combinations that are poorly miscible, the mixture can be gently heated to aid in formation of the homogeneous mixture. If the composition is to include a therapeutic agent, the chosen therapeutic agent in a predetermined amount is added and stirred until solubilized. Optionally, solubilizers or additives are included by simple mixing.

To form an aqueous dispersion of the pre-concentrate, a predetermined amount of purified water, buffer solution, or aqueous simulated physiological solution, is added to the pre-concentrate, and the resultant mixture is stirred to form a clear, aqueous dispersion.

Example 2: Triglyceride Solubilization in Conventional Formulations

Conventional formulations of a triglyceride and a hydrophilic surfactant were prepared for comparison to compositions of the present invention. For each surfactant-triglyceride pair, multiple dispersions were prepared with differing amounts of the two components, to determine the maximum amount of the triglyceride that can be present while the composition still forms a clear dispersion upon a 100-fold dilution with distilled water. No therapeutic agent was included in these compositions, since it is believed that the presence of the therapeutic agent does not substantially affect the clear, aqueous nature of composition. For the same reason, these compositions were free of additional solubilizers and other additives. The optical clarity was determined by visual inspection and/or by UV absorption (at 400 nm). When UV absorption was used, compositions were considered to be clear when the absorption was less than about 0.2.

Table 20 shows the maximum amount of triglyceride present in such binary mixtures forming clear aqueous dispersions. The numerical entries in the Table are in units of grams of triglyceride per 100 grams of hydrophilic surfactant.

Table 20: Binary Triglyceride-Surfactant Solubility

Hydrophilic Surfactant / Triglyceride	PEG-35 Castor Oil (Incrocas 35)	PEG-40H Castor Oil (Cremophor RH-40)	PEG-6 Caprate/ Caprylate (Softigen 767)	PEG-60 Corn Oil (Crovol M-70)	PEG-45 Palm Kernel Oil (Crovol PK-70)	Polysorbate -20 (Tween 20)	Polysorbate 80 (Tween 80)
Corn Oil (Croda, Super Refined)	10	25	3	5	8	2	10
Soybean Oil (Croda, Super Refined)	10	25	3	8	8	2	10
Glyceryl Tricaprylate/ Caprate (Captex 300)	60	40	8	30	25	20	45
Glyceryl Tricaprylate/ Caprate (Captex 355)	70	40	5	55	30	20	55
Glyceryl Tricaprylate/ Caprate/Laurate (Captex 350)	70	60	5	55	25	10	50

Glyceryl Tricaprylate/ Caprate/Linoleate (Captex 810D)	30	40	3	25	15	2	25

Example 3: Effect of Surfactant Combinations

The procedure of Example 2 was repeated for compositions containing PEG-40 hydrogenated castor oil (Cremophor RH 40) or polysorbate 80 (Tween 80) as the hydrophilic surfactant, but substituting a second hydrophilic surfactant (compositions number 6-7 and 14-16) or a hydrophobic surfactant (compositions number 4-5, 8-9, and 17-18) for part of the hydrophilic surfactant. The total amount of hydrophilic surfactant was kept constant. The results are summarized in Table 21.

Table 21A: Effects of Surfactant Combinations on the Solubilization of Triglycerides

	Composition in w/w ratio								
	1	2	3	4	5	6	7	8	9
Corn Oil	25	30	40	40	40	40	40	40	40
Cremophor RH-40	100	100	100	77	71	67	57	62	57
Peceol	---	---	---	23	29	---	---	---	---
Kessco PEG 400 MO	---	---	---	---	---	33	43	---	---
Crovol M-40	---	---	---	---	---	---	---	38	43
Appearance of the Concentrate	Clear	Hazy	Hazy	Clear	Clear	Clear	Clear	Hazy	Hazy
Abs @ 400 nm of the 100X (w/v) Dilution in Deionized Water	0.148	2.195	2.518	0.121	0.132	0.124	0.102	0.233	0.167

Table 21B

	Composition in w/w ratio								
	10	11	12	13	14	15	16	17	18
Corn Oil	10	15	20	30	15	20	30	20	25

Tween 80	100	100	100	100	67	67	67	67	67
Kessco PEG 400 MO	---	---	—	—	33	33	33	—	---
Crovol M-40	---	—	—	—	—	---	---	33	33
Appearance of the Concentrate	Clear	Clear	Hazy	Hazy	Clear	Clear	Clear	Clear	Clear
Abs @ 400 nm of the 100X (w/v) Dilution in Deionized Water	0.002	1.314	1.613	1.654	0.041	0.019	0.194	0.057	0.158

The clear or hazy appearance noted in the Table is that of the pre-concentrate, not of the aqueous dispersion. The clarity of the aqueous dispersion is shown quantitatively by UV absorption of the 100X dilution at 400 nm.

Comparing compositions 1-3, a binary corn oil-Cremophor RH-40 mixture having 25 grams of corn oil per 100 grams of the surfactant is optically clear, having an absorption of 0.148. However, upon a slight increase of the amount of corn oil to 30 grams, the dispersion becomes cloudy, with an absorbance of 2.195, indicating the formation of a conventional emulsion. Compositions 4-5 show the surprising result that when part of the hydrophilic Cremophor RH-40 is replaced by a hydrophobic surfactant (Peceol), keeping the total surfactant concentration constant, compositions having a much higher amount of triglyceride (40 grams) still form clear aqueous dispersions, with absorbances less than 0.2 and dramatically less than the comparable binary composition number 3. A similar result is shown in compositions 8-9 for a different hydrophobic surfactant, Crovol M-40. Likewise, when part of the hydrophilic surfactant is replaced by a second hydrophilic surfactant in compositions 6-7, it is surprisingly found that the amount of triglyceride solubilized is similarly increased.

The second part of the Table, Table 21B, shows a similar surprising result for a different hydrophilic surfactant, Tween 80. Simple binary corn oil-Tween 80 mixtures form clear aqueous dispersions with 10 grams of corn oil, but are cloudy and multi-phasic with 15 grams or more of the triglyceride. As the Table shows, substitution of part of the hydrophilic surfactant with a second hydrophilic surfactant or a hydrophobic surfactant dramatically increases the amount of triglyceride that can be solubilized.

Example 4: Effect of Surfactant Combinations

Example 3 was repeated, using different triglyceride-surfactant combinations. In particular, medium-chain triglycerides (MCTs) were used instead of corn oil, a long-chain triglyceride (LCT). The results are shown in the three-part Table 22.

Table 22A: Solubilization of MCTs

	Composition in w/w ratio				
	19	**20**	**21**	**22**	**23**
Pureco 76	33	50	80	50	80
Cremophor RH-40	100	100	100	40	100
Imwitor 988	---	---	---	60	100
Ethanol	---	---	---	---	33
Appearance of the Concentrate	Clear	Clear	Hazy	Clear	Clear
Abs @ 400 nm of the 100X (w/v) Dilution in Deionized Water	0.201	0.346	2.522	0.204	0.098

Table 22B

	Composition in w/w ratio			
	24	**25**	**26**	**27**
Captex 300	40	75	75	75
Cremophor RH-40	100	100	50	100
Imwitor 988	---	---	50	75
Appearance of the Concentrate	Clear	Hazy	Clear	Clear
Abs @ 400 nm of the 100X (w/v) Dilution in Deionized Water	0.180	0.557	0.208	0.078

Table 22C

	Composition in w/w ratio					
	28	29	30	31	32	33
Captex 300	20	25	33	30	40	40
Tween 20	100	100	100	70	70	66
Brij 30	---	---	---	30	30	34
Appearance of the Concentrate	Clear	Hazy	Hazy	Clear	Clear	Clear
Abs @ 400 nm of the 100X (w/v) Dilution in Deionized Water	0.078	1.192	2.536	0.017	0.234	0.103

Table 22 shows that the increased solubilization of the triglyceride is observed for MCTs as well as for LCTs, with a variety of surfactants. Table 22 additionally shows that the same effect is observed in the presence of increased amounts of surfactants (compositions 23 and 27) and solubilizers (composition 23).

Example 5: Characterization of Compositions

Various compositions were prepared and characterized by visual observation as well as by UV absorbance at 400 nm. Each composition was diluted 100-fold with distilled water. The results are shown in Table 23.

Table 23: Visual and Spectroscopic Characterization

No.	Composition		Visual Observation	Absorbance at 400 nm
24	Soybean Oil	80 mg		
	Tween 20	200 mg	Very clear solution	0.014
	Tween 80	800 mg		
25	Captex 810D	250 mg		
	Incrocas 35	500 mg	Very clear solution	0.030
	Tween 80	500 mg		
26	Captex 810D	200 mg		
	Incrocas 35	667 mg	Clear solution	0.157

	Myvacet 9-45	333 mg		
27	Corn Oil	250 mg		
	Cremophor RH-40	750 mg	Clear solution	0.085
	Peceol	150 mg		
	Propylene Glycol	100 mg		
28	Captex 355	200 mg		
	Labrafil M2125CS	300 mg	Clear solution	0.212
	Cremophor RH-40	500 mg		
	Ethanol	100 mg		
29	Captex 355	150 mg		
	Cremophor RH-40	600 mg	Clear solution	0.141
	Labrafil M2125CS	250 mg		
	Ethanol	100 mg		
30	Captex 355	300 mg		
	Incrocas 35	500 mg	Clear solution,	0.241
	Labrafil M2125CS	200 mg	Slightly hazy	
	Ethanol	100 mg		
31	Captex 355	250 mg		
	Incrocas 35	600 mg	Clear solution	0.076
	Labrafil M2125CS	150 mg		
	Ethanol	100 mg		
32	Pureco 76	160 mg		
	Cremophor RH-40	480 mg	Clear solution	0.168
	Labrafil M2125CS	160 mg		
	Ethanol	150 mg		

Example 6: Comparative Example

Prior art formulations were prepared for comparison with the compositions of the present invention. As in Example 5, the compositions were diluted 100-fold with distilled water, and characterized by visual observation and by UV absorbance. The results are shown in Table 24.

Table 24: Compositions Not Forming Clear Aqueous Dispersions

	Compositon		Visual Observation	Absorbance at 400 nm
33	Corn Oil	400 mg	Milky suspension	1.989
	Cremophor RH-40	710 mg		
	Crovol M-40	290 mg		
34	Captex 300	300 mg	Milky suspension	1.594
	Tween 20	650 mg		
	Imwitor 988	350 mg		
35	Corn Oil	400 mg	Milky suspension	2.716
	Cremophor RH-40	620 mg		
	Labrafil M2125CS	380 mg		
36	Soybean Oil	185 mg	Milky suspension	2.595
	Captex GTO	275 mg		
	Tween 80	275 mg		
	Triacetin	185 mg		
37	Pureco 76	315 mg	Milky suspension	2.912
	Cremophor RH-40	225 mg		
	Span 20	360 mg		
38	Soybean Oil	340 mg	Milky suspension	2.566
	Captex GTO	280 mg		
	Tween 80	280 mg		
39	Pureco 76	330 mg		

	Labrasol	120 mg	Milky suspension	2.233
40	Corn Oil	400 mg		
	Cremophor RH-40	570 mg	Milky suspension	2.249
	Lauroglycol FCC	430 mg		
41	Soybean Oil	160 mg		
	Tween 80	200 mg	Milky suspension	2.867
	Imwitor 988	450 mg		
	Ethanol	150 mg		
42	Corn Oil	200 mg		
	Tween 80	570 mg	Milky suspension	1.547
	Kessco PEG 400 MO	430 mg		

As the Table shows, conventional formulations such as those disclosed in U.S. Patent No. 5,645,856, form milky suspensions rather than the clear aqueous dispersions of the present invention.

Example 7: Formulations with Therapeutic Agents

Table 25 shows several formulations of compositions that can be prepared according to the present invention, using a variety of therapeutic agents.

Table 25: Formulations

No.	Composition (g)	
43	Cremophor RH-40	0.75
	Peceol	0.25
	Corn Oil NF	0.40
	Fenofibrate	0.10
44	Cremophor RH-40	0.57
	Crovol M-40	0.43
	Corn Oil NF	0.40
	Rofecoxib	0.15

45	Cremophor RH-40	0.57
	Kessco PEG 400 MO	0.43
	Soybean Oil NF	0.40
	Nabumetone	0.30
46	Tween 80	0.70
	Tween 85	0.35
	Miglyol 812	0.30
	Paclitaxel	0.10
	PEG 400	0.25
47	Cremophor RH-40	0.50
	Imwitor 988	0.50
	Captex 300	0.75
	Cyclosporin A	0.20
	Propylene Glycol	0.15
48	Tween 20	0.66
	Brij 30	0.34
	Captex 355	0.40
	Retinoic Acid	0.02
49	Tween 80	0.67
	Kessco PEG 400 MO	0.33
	Corn Oil	0.30
	Terbinafine	0.25

50	Crovol M-70	0.67
	Crovol M-40	0.33
	Captex 350	0.75
	Progesterone	0.10
	Ethanol	0.15
51	Labrasol	0.30
	Gelucire 44/14	0.70
	Dronabinol	0.02
	Ethanol	0.10
52	Incrocas 35	0.80
	Arlacel 186	0.20
	Miglyol 818	0.45
	Alendronate sodium	0.04
	Water	0.10
53	Cremophor RH-40	0.62
	Capmul MCM	0.38
	Miglyol 810	0.25
	Heparin sodium	0.03
	Water	0.10
	PEG 400	0.05

The present invention may be embodied in other specific forms without departing from its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the invention is, therefore, indicated by the appended claims rather than by the foregoing description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

What is claimed is:

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A pharmaceutical composition consisting of:

(a) a triglyceride;

(b) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic; and

(c) a therapeutic agent which is capable of being solubilized in the triglyceride, the carrier, or both the triglyceride and the carrier,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm.

2. The pharmaceutical composition of claim 1, wherein the triglyceride is selected from the group consisting of vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, synthetic triglycerides, modified triglycerides, fractionated triglycerides, and mixtures thereof.

3. The pharmaceutical composition of claim 1, wherein the triglyceride is selected from the group consisting of almond oil; babassu oil; borage oil; blackcurrant seed oil; canola oil; castor oil; coconut oil; corn oil; cottonseed oil; evening primrose oil; grapeseed oil; groundnut oil; mustard seed oil; olive oil; palm oil; palm kernel oil; peanut oil; rapeseed oil; safflower oil; sesame oil; shark liver oil; soybean oil; sunflower oil; hydrogenated castor oil; hydrogenated coconut oil; hydrogenated palm oil; hydrogenated soybean oil; hydrogenated vegetable oil; hydrogenated cottonseed and castor oil; partially hydrogenated soybean oil; partially hydrogenated soy and cottonseed oil; glyceryl tricaproate; glyceryl tricaprylate; glyceryl tricaprate; glyceryl triundecanoate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl trilinolenate; glyceryl

tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; glyceryl tricaprylate/caprate/stearate; saturated polyglycolized glycerides; linoleic glycerides; caprylic/capric glycerides; modified triglycerides; fractionated triglycerides; and mixtures thereof.

4. The pharmaceutical composition of claim 1, wherein the triglyceride is selected from the group consisting of coconut oil; corn oil; olive oil; palm oil; peanut oil; safflower oil; sesame oil; soybean oil; hydrogenated castor oil; hydrogenated coconut oil; partially hydrogenated soybean oil; glyceryl tricaprate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; glyceryl tricaprylate/caprate/stearate; saturated polyglycolized glycerides; linoleic glycerides; caprylic/capric glycerides; modified triglycerides; fractionated triglycerides; and mixtures thereof.

5. The pharmaceutical composition of claim 1, wherein the triglyceride is selected from the group consisting of a medium chain triglyceride, a long chain triglyceride, a modified triglyceride, a fractionated triglyceride, and mixtures thereof.

6. The pharmaceutical composition of claim 1, wherein the hydrophilic surfactant comprises at least one non-ionic hydrophilic surfactant having an HLB value greater than or equal to about 10.

7. The pharmaceutical composition of claim 1, wherein the hydrophilic surfactant comprises at least one ionic surfactant.

8. The pharmaceutical composition of claim 6, which further comprises at least one ionic surfactant.

9. The pharmaceutical composition of claim 6, wherein the non-ionic surfactant is selected from the group consisting of alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl macrogolglycerides; polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; sugar esters, sugar ethers; sucroglycerides; and mixtures thereof.

10. The pharmaceutical composition of claim 6, wherein the non-ionic hydrophilic surfactant is selected from the group consisting of polyoxyethylene alkylethers; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

11. The pharmaceutical composition of claim 10, wherein the glyceride is selected from the group consisting of a monoglyceride, a diglyceride, a triglyceride, and mixtures thereof.

12. The pharmaceutical composition of claim 10, wherein the reaction mixture comprises the transesterification products of a polyol and at least one member of the group

consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

13. The pharmaceutical composition of claim 10, wherein the polyol is selected from the group consisting of glycerol, ethylene glycol, polyethylene glycol, sorbitol, propylene glycol, pentaerythritol, a saccharide, and mixtures thereof.

14. The pharmaceutical composition of claim 6, wherein the hydrophilic surfactant is selected from the group consisting of PEG-10 laurate, PEG-12 laurate, PEG-20 laurate, PEG-32 laurate, PEG-32 dilaurate, PEG-12 oleate, PEG-15 oleate, PEG-20 oleate, PEG-20 dioleate, PEG-32 oleate, PEG-200 oleate, PEG-400 oleate, PEG-15 stearate, PEG-32 distearate, PEG-40 stearate, PEG-100 stearate, PEG-20 dilaurate, PEG-25 glyceryl trioleate, PEG-32 dioleate, PEG-20 glyceryl laurate, PEG-30 glyceryl laurate, PEG-20 glyceryl stearate, PEG-20 glyceryl oleate, PEG-30 glyceryl oleate, PEG-30 glyceryl laurate, PEG-40 glyceryl laurate, PEG-40 palm kernel oil, PEG-50 hydrogenated castor oil, PEG-40 castor oil, PEG-35 castor oil, PEG-60 castor oil, PEG-40 hydrogenated castor oil, PEG-60 hydrogenated castor oil, PEG-60 corn oil, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, polyglyceryl-10 laurate, PEG-30 cholesterol, PEG-25 phyto sterol, PEG-30 soya sterol, PEG-20 trioleate, PEG-40 sorbitan oleate, PEG-80 sorbitan laurate, polysorbate 20, polysorbate 80, POE-9 lauryl ether, POE-23 lauryl ether, POE-10 oleyl ether, POE-20 oleyl ether, POE-20 stearyl ether, tocopheryl PEG-100 succinate, PEG-24 cholesterol, polyglyceryl-10 oleate, Tween 40, Tween 60, sucrose monostearate, sucrose monolaurate, sucrose monopalmitate, PEG 10-100 nonyl phenol series, PEG 15-100 octyl phenol series, a poloxamer, and mixtures thereof.

15. The pharmaceutical composition of claim 6, wherein the hydrophilic surfactant is selected from the group consisting of PEG-20 laurate, PEG-20 oleate, PEG-35

castor oil, PEG-40 palm kernel oil, PEG-40 hydrogenated castor oil, PEG-60 corn oil, PEG-25 glyceryl trioleate, polyglyceryl-10 laurate, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, PEG-30 cholesterol, polysorbate 20, polysorbate 80, POE-9 lauryl ether, POE-23 lauryl ether, POE-10 oleyl ether, PEG-24 cholesterol, sucrose monostearate, sucrose monolaurate, a poloxamer, and mixtures thereof.

16. The pharmaceutical composition of claim 6, wherein the hydrophilic surfactant is selected from the group consisting of PEG-35 castor oil, PEG-40 hydrogenated castor oil, PEG-60 corn oil, PEG-25 glyceryl trioleate, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, polysorbate 20, polysorbate 80, tocopheryl PEG-1000 succinate, PEG-24 cholesterol, a poloxamer, and mixtures thereof.

17. The pharmaceutical composition of claim 7, wherein the ionic surfactant is selected from the group consisting of alkyl ammonium salts; bile salts; fusidic acid; fatty acid conjugates of amino acids, oligopeptides, and polypeptides; glyceride esters of amino acids, oligopeptides, and polypeptides; acyl lactylates; mono- and diacetylated tartaric acid; esters of mono- and diglycerides; succinylated monoglycerides; citric acid esters of mono- and diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids; carnitine fatty acid ester salts; phospholipids; salts of alkylsulfates; salts of fatty acids; sodium docusate; and mixtures thereof.

18. The pharmaceutical composition of claim 7, wherein the ionic surfactant is selected from the group consisting of bile acids and salts; lecithins, lysolecithin, phospholipids, and lysophospholipids; carnitine fatty acid ester salts; salts of alkylsulfates; salts of fatty acids; sodium docusate; acyl lactylates; mono- and diacetylated tartaric acid

esters of mono- and diglycerides; succinylated monoglycerides; citric acid esters of mono- and diglycerides; and mixtures thereof.

19. The pharmaceutical composition of claim 7, wherein the ionic surfactant is selected from the group consisting of lecithin, lysolecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, phosphatidic acid, phosphatidylserine, lysophosphatidylcholine, lysophosphatidylethanolamine, lysophosphatidylglycerol, lysophosphatidic acid, lysophosphatidylserine, PEG-phosphatidylethanolamine, PVP-phosphatidylethanolamine, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, cholate, taurocholate, glycocholate, deoxycholate, taurodeoxycholate, chenodeoxycholate, glycodeoxycholate, glycochenodeoxycholate, taurochenodeoxycholate, ursodeoxycholate, lithocholate, tauroursodeoxycholate, glycoursodeoxycholate, cholylsarcosine, N-methyl taurocholate, caproate, caprylate, caprate, laurate, myristate, palmitate, oleate, ricinoleate, linoleate, linolenate, stearate, lauryl sulfate, tetraacetyl sulfate, docusate, lauroyl carnitine, palmitoyl carnitine, myristoyl, carnitine, and salts and mixtures thereof.

20. The pharmaceutical composition of claim 7, wherein the ionic surfactant is selected from the group consisting of lecithin, lysolecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, lysophosphatidylcholine, PEG-phosphatidylethanolamine, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, cholate, taurocholate, glycocholate, deoxycholate, chenodeoxycholate, lithocholate, ursodeoxycholate, taurodeoxycholate, glycodeoxycholate, cholylsarcosine, caproate, caprylate, caprate, laurate, oleate, lauryl sulfate, docusate, lauroyl carnitine, palmitoyl carnitine, myristoyl carnitine, and salts and mixtures thereof.

21. The pharmaceutical composition of claim 7, wherein the ionic surfactant is selected from the group consisting of lecithin, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, chenodeoxycholate, lithocholate, ursodeoxycholate, taurocholate, caprylate, caprate, oleate, lauryl sulfate, docusate, lauroyl carnitine, palmitoyl carnitine, myristoyl carnitine, and salts and mixtures thereof.

22. The pharmaceutical composition of claim 1, wherein the carrier comprises at least two hydrophilic surfactants.

23. The pharmaceutical composition of claim 1, wherein the carrier comprises at least one hydrophilic surfactant and at least one hydrophobic surfactant.

24. The pharmaceutical composition of claim 1 wherein the hydrophobic surfactant is a compound or mixture of compounds having an HLB value less than about 10.

25. The pharmaceutical composition of claim 24, wherein the hydrophobic surfactant is selected from the group consisting of alcohols; polyoxyethylene alkylethers; fatty acids; bile acids; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lower alcohol fatty acid esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid esters of mono/diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block

copolymers; transesterified vegetable oils; sterols; sugar esters; sugar ethers; sucroglycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

26. The pharmaceutical composition of claim 24, wherein the hydrophobic surfactant is selected from the group consisting of fatty acids; bile acids; lower alcohol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lactic acid esters of mono/diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

27. The pharmaceutical composition of claim 24, wherein the hydrophobic surfactant is selected from the group consisting of bile acids; lower alcohol fatty acid esters; polypropylene glycol fatty acid esters; propylene glycol fatty acid esters; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lactic acid esters of mono/diglycerides; sorbitan fatty acid esters; polyoxyethylene vegetable oils; and mixtures thereof.

28. The pharmaceutical composition of claim 24, wherein the hydrophobic surfactant is selected from the group consisting of a glycerol fatty acid ester, an acetylated glycerol fatty acid ester, and mixtures thereof.

29. The pharmaceutical composition of claim 28, wherein the glycerol fatty acid ester is selected from the group consisting of a monoglyceride, diglyceride, and mixtures thereof.

30. The pharmaceutical composition of claim 29, wherein the fatty acid of the glycerol fatty acid ester is a C_6 to C_{22} fatty acid or a mixture thereof.

31. The pharmaceutical composition of claim 24, wherein the hydrophobic surfactant is a reaction mixture of a polyol and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

32. The pharmaceutical composition of claim 31, wherein the reaction mixture is a transesterification product of a polyol and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

33. The pharmaceutical composition of claim 31, wherein the polyol is selected from the group consisting of polyethylene glycol, sorbitol, propylene glycol, pentaerythritol, a saccharide, and mixtures thereof.

34. The pharmaceutical composition of claim 24, wherein the hydrophobic surfactant is selected from the group consisting of myristic acid; oleic acid; lauric acid; stearic acid; palmitic acid; PEG 1-4 stearate; PEG 2-4 oleate; PEG-4 dilaurate; PEG-4 dioleate; PEG-4 distearate; PEG-6 dioleate; PEG-6 distearate; PEG-8 dioleate; PEG 3-16 castor oil; PEG 5-10 hydrogenated castor oil; PEG 6-20 corn oil; PEG 6-20 almond oil; PEG-6 olive oil; PEG-6 peanut oil; PEG-6 palm kernel oil; PEG-6 hydrogenated palm kernel oil; PEG-4 capric/caprylic triglyceride, mono, di, tri, tetra esters of vegetable oil and

sorbitol; pentaerythrityl di, tetra stearate, isostearate, oleate, caprylate, or caprate; polyglyceryl 2-4 oleate, stearate, or isostearate; polyglyceryl 4-10 pentaoleate; polyglyceryl-3 dioleate; polyglyceryl-6 dioleate; polyglyceryl-10 trioleate; polyglyceryl-3 distearate; propylene glycol mono- or diesters of a C_6 to C_{22} fatty acid; monoglycerides of a C_6 to C_{22} fatty acid; acetylated monoglycerides of a C_6 to C_{22} fatty acid; diglycerides of C_6 to C_{22} fatty acids; lactic acid esters of monoglycerides; lactic acid esters of diglycerides; cholesterol; phytosterol; PEG 5-20 soya sterol; PEG-6 sorbitan tetra, hexastearate; PEG-6 sorbitan tetraoleate; sorbitan monolaurate; sorbitan monopalmitate; sorbitan mono, trioleate; sorbitan mono, tristearate; sorbitan monoisostearate; sorbitan sesquioleate; sorbitan sesquistearate; PEG 2-5 oleyl ether; POE 2-4 lauryl ether; PEG-2 cetyl ether; PEG-2 stearyl ether; sucrose distearate; sucrose dipalmitate; ethyl oleate; isopropyl myristate; isopropyl palmitate; ethyl linoleate; isopropyl linoleate; poloxamers; cholic acid; ursodeoxycholic acid; glycocholic acid; taurocholic acid; lithocholic acid; deoxycholic acid; chenodeoxycholic acid; and mixtures thereof.

35. The pharmaceutical composition of claim 24, wherein the hydrophobic surfactant is selected from the group consisting of oleic acid; lauric acid; glyceryl monocaprate; glyceryl monocaprylate; glyceryl monolaurate; glyceryl monooleate; glyceryl dicaprate; glyceryl dicaprylate; glyceryl dilaurate; glyceryl dioleate; acetylated monoglycerides; propylene glycol oleate; propylene glycol laurate; polyglyceryl-3 oleate; polyglyceryl-6 dioleate; PEG-6 corn oil; PEG-20 corn oil; PEG-20 almond oil; sorbitan monooleate; sorbitan monolaurate; POE-4 lauryl ether; POE-3 oleyl ether; ethyl oleate; poloxamers; cholic acid; ursodeoxycholic acid; glycocholic acid; taurocholic acid; lithocholic acid; deoxycholic acid; chenodeoxycholic acid; and mixtures thereof.

36. The pharmaceutical composition of claim 1, wherein the therapeutic agent is selected from the group consisting of a drug, a vitamin, a nutritional supplement, a cosmeceutical, and mixtures thereof.

37. The pharmaceutical composition of claim 1, wherein the therapeutic agent is a hydrophobic drug.

38. The pharmaceutical composition of claim 37, wherein the hydrophobic drug has a molecular weight of less than about 1000 g/mol.

39. The pharmaceutical composition of claim 1, wherein the therapeutic agent is a hydrophilic drug.

40. The pharmaceutical composition of claim 39, wherein the hydrophilic drug is selected from the group consisting of a peptidomimetic, a peptide, a protein, an oligonucleotide, an oligodeoxynucleotide, RNA, DNA, genetic material, and mixtures thereof.

41. The pharmaceutical composition of claim 39, wherein the hydrophilic drug has a molecular weight of less than about 1000 g/mol.

42. The pharmaceutical composition of claim 1, wherein the surfactants are present in amounts such that the triglyceride can be present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous dispersion of the triglyceride and a carrier having only one surfactant, the surfactant being hydrophilic, and having the same total surfactant concentration.

43. The pharmaceutical composition of claim 22, wherein the surfactants are present in amounts such that the triglyceride can be present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous dispersion of the triglyceride and a carrier having only one surfactant, the surfactant being hydrophilic, and having the same total surfactant concentration.

44. The pharmaceutical composition of claim 23, wherein the surfactants are present in amounts such that the triglyceride can be present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous dispersion of the triglyceride and a carrier having a hydrophilic surfactant but not having a hydrophobic surfactant, and having the same total surfactant concentration.

45. The pharmaceutical composition of claim 1, wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution to composition ratio of about 10:1 by weight, the composition forms a clear aqueous dispersion.

46. The pharmaceutical composition of claim 1, wherein the absorbance is less than about 0.2.

47. The pharmaceutical composition of claim 46, wherein the absorbance is less than about 0.1.

48 The pharmaceutical composition of claim 1, in the form of a preconcentrate in a liquid, semi-solid, or solid form, or as an aqueous or organic diluted preconcentrate.

49. A dosage form comprising the pharmaceutical composition of claim 1 processed by a technique selected from the group consisting of lyophilization, encapsulation, extruding, compression, melting, molding, spraying, coating, comminution, mixing, homogenization, sonication, granulation, and combinations thereof.

50. A dosage form comprising the pharmaceutical composition of claim 1, wherein the dosage form is selected from the group consisting of a pill, capsule, caplet, tablet, granule, bead and powder.

51. The dosage form of claim 60, which further comprises an enteric coating, a seal coating, or both.

52. A dosage form comprising the pharmaceutical composition of claim 1, wherein the dosage form is selected from the group consisting of a solution, suspension, emulsion, cream, ointment, lotion, suppository, spray, aerosol, paste, gel, drops, douche, ovule, wafer, troche, cachet, syrup and elixir.

53. A dosage form comprising a multiparticulate carrier coated onto a substrate with the pharmaceutical composition of claim 1.

54. The dosage form of claim 53, wherein the substrate is selected from the group consisting of a particle, a granule and a bead, and is formed of a material selected from the group consisting of the therapeutic agent, a pharmaceutically acceptable material, and a mixture thereof.

55. The dosage form of claim 53, wherein the multiparticulate carrier is selected from the group consisting of an enteric coating, a seal coating, and a mixture thereof.

56. The pharmaceutical composition of claim 1, wherein the therapeutic agent has a portion that is solubilized in the composition, and a portion that is not solubilized in the composition.

57. The dosage form of claim 53, wherein the dosage form is further processed by a technique selected from the group consisting of encapsulation, compression, extrusion or molding.

58. The dosage form of claim 53, wherein the dosage form is encapsulated in a capsule selected from the group consisting of a starch capsule, a cellulosic capsule, a hard gelatin capsule, and a soft gelatin capsule.

59. The dosage form of claim 54, wherein the dosage form is encapsulated in a capsule selected from the group consisting of a starch capsule, a cellulosic capsule, and a soft gelatin capsule.

60. A pharmaceutical composition consisting of:

(a) a triglyceride;

(b) a carrier comprising at least one hydrophilic surfactant and at least one hydrophobic surfactant; and

(c) a therapeutic agent which is capable of being solubilized in the triglyceride, the carrier, or both the triglyceride and the carrier,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ration of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm.

61. The pharmaceutical composition of claim 60, wherein the triglyceride is selected from the group consisting of vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, synthetic triglycerides, modified triglycerides, fractionated triglycerides, and mixtures thereof.

62. The pharmaceutical composition of claim 60, wherein the triglyceride is selected from the group consisting of almond oil; babassu oil; borage oil; blackcurrant seed oil; canola oil; castor oil; coconut oil; corn oil; cottonseed oil; evening primrose oil; grapeseed oil; groundnut oil; mustard seed oil; olive oil; palm oil; palm kernel oil; peanut oil; rapeseed oil; safflower oil; sesame oil; shark liver oil; soybean oil; sunflower oil; hydrogenated castor oil; hydrogenated coconut oil; hydrogenated palm oil; hydrogenated soybean oil; hydrogenated vegetable oil; hydrogenated cottonseed and castor oil; partially hydrogenated soybean oil; partially hydrogenated soy and cottonseed oil; glyceryl tricaproate; glyceryl tricaprylate; glyceryl tricaprate; glyceryl triundecanoate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl trilinolenate; glyceryl tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; glyceryl tricaprylate/caprate/stearate; saturated polyglycolized glycerides; linoleic glycerides; caprylic/capric glycerides; modified triglycerides; fractionated triglycerides; and mixtures thereof.

63. The pharmaceutical composition of claim 60, wherein the triglyceride is selected from the group consisting of coconut oil; corn oil; olive oil; palm oil; peanut oil;

safflower oil; sesame oil; soybean oil; hydrogenated castor oil; hydrogenated coconut oil; partially hydrogenated soybean oil; glyceryl tricaprate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; glyceryl tricaprylate/caprate/stearate; saturated polyglycolized glycerides; linoleic glycerides; caprylic/capric glycerides; modified triglycerides; fractionated triglycerides; and mixtures thereof.

64. The pharmaceutical composition of claim 60, wherein the triglyceride is selected from the group consisting of a medium chain triglyceride, a long chain triglyceride, a modified triglyceride, a fractionated triglyceride, and mixtures thereof.

65. The pharmaceutical composition of claim 60, wherein the hydrophilic surfactant comprises at least one non-ionic hydrophilic surfactant having an HLB value greater than or equal to about 10.

66. The pharmaceutical composition of claim 60, wherein the hydrophilic surfactant comprises at least one ionic surfactant.

67. The pharmaceutical composition of claim 65, which further comprises at least one ionic surfactant.

68. The pharmaceutical composition of claim 65, wherein the non-ionic surfactant is selected from the group consisting of alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl macrogolglycerides; polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acid esters; polyethylene glycol

glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; sugar esters, sugar ethers; sucroglycerides; and mixtures thereof.

69. The pharmaceutical composition of claim 65, wherein the non-ionic hydrophilic surfactant is selected from the group consisting of polyoxyethylene alkylethers; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

70. The pharmaceutical composition of claim 65, wherein the glyceride is selected from the group consisting of a monoglyceride, diglyceride, triglyceride, and mixtures thereof.

71. The pharmaceutical composition of claim 69, wherein the reaction mixture comprises the transesterification products of a polyol and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

72. The pharmaceutical composition of claim 69, wherein the polyol is selected from the group consisting of glycerol, ethylene glycol, polyethylene glycol, sorbitol, propylene glycol, pentaerythritol, a saccharide, and mixtures thereof.

73. The pharmaceutical composition of claim 65, wherein the hydrophilic surfactant is selected from the group consisting of PEG-10 laurate, PEG-12 laurate, PEG-20 laurate, PEG-32 laurate, PEG-32 dilaurate, PEG-12 oleate, PEG-15 oleate, PEG-20 oleate, PEG-20 dioleate, PEG-32 oleate, PEG-200 oleate, PEG-400 oleate, PEG-15 stearate, PEG-32 distearate, PEG-40 stearate, PEG-100 stearate, PEG-20 dilaurate, PEG-25 glyceryl trioleate, PEG-32 dioleate, PEG-20 glyceryl laurate, PEG-30 glyceryl laurate, PEG-20 glyceryl stearate, PEG-20 glyceryl oleate, PEG-30 glyceryl oleate, PEG-30 glyceryl laurate, PEG-40 glyceryl laurate, PEG-40 palm kernel oil, PEG-50 hydrogenated castor oil, PEG-40 castor oil, PEG-35 castor oil, PEG-60 castor oil, PEG-40 hydrogenated castor oil, PEG-60 hydrogenated castor oil, PEG-60 corn oil, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, polyglyceryl-10 laurate, PEG-30 cholesterol, PEG-25 phyto sterol, PEG-30 soya sterol, PEG-20 trioleate, PEG-40 sorbitan oleate, PEG-80 sorbitan laurate, polysorbate 20, polysorbate 80, POE-9 lauryl ether, POE-23 lauryl ether, POE-10 oleyl ether, POE-20 oleyl ether, POE-20 stearyl ether, tocopheryl PEG-100 succinate, PEG-24 cholesterol, polyglyceryl-10 oleate, Tween 40, Tween 60, sucrose monostearate, sucrose monolaurate, sucrose monopalmitate, PEG 10-100 nonyl phenol series, PEG 15-100 octyl phenol series, a poloxamer, and mixtures thereof.

74. The pharmaceutical composition of claim 65, wherein the hydrophilic surfactant is selected from the group consisting of PEG-20 laurate, PEG-20 oleate, PEG-35 castor oil, PEG-40 palm kernel oil, PEG-40 hydrogenated castor oil, PEG-60 corn oil, PEG-25 glyceryl trioleate, polyglyceryl-10 laurate, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, PEG-30 cholesterol, polysorbate 20, polysorbate 80,

POE-9 lauryl ether, POE-23 lauryl ether, POE-10 oleyl ether, PEG-24 cholesterol, sucrose monostearate, sucrose monolaurate, a poloxamer, and mixtures thereof.

75. The pharmaceutical composition of claim 65, wherein the hydrophilic surfactant is selected from the group consisting of PEG-35 castor oil, PEG-40 hydrogenated castor oil, PEG-60 corn oil, PEG-25 glyceryl trioleate, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, polysorbate 20, polysorbate 80, tocopheryl PEG-1000 succinate, PEG-24 cholesterol, a poloxamer, and mixtures thereof.

76. The pharmaceutical composition of claim 66, wherein the ionic surfactant is selected from the group consisting of alkyl ammonium salts; bile salts; fusidic acid; fatty acid conujugates of amino acids, oligopeptides, and polypeptides; glyceride esters of amino acids, oligopeptides, and polypeptides; acyl lactylates; mono- and diacetylated tartaric acid esters of mono- and diglycerides; succinylated monoglycerides; citric acid esters of mono- and diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids and derivatives thereof; carnitine fatty acid ester salts; phospholipids and derivatives thereof; salts of alkylsulfates; salts of fatty acids; sodium docusate; and mixtures thereof.

77. The pharmaceutical composition of claim 66, wherein the ionic surfactant is selected from the group consisting of bile salts; lecithins, lysolecithin, phospholipids, lysophospholipids and derivatives thereof; carnitine fatty acid ester salts; salts of alkylsulfates; salts of fatty acids; sodium docusate; acyl lactylates; mono- and diacetylated tartaric acid esters of mono- and diglycerides; succinylated monoglycerides; citric acid esters of mono- and diglycerides; and mixtures thereof.

78. The pharmaceutical composition of claim 66, wherein the ionic surfactant is selected from the group consisting of lecithin, lysolecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, phosphatidic acid, phosphatidylserine, lysophosphatidylcholine, lysophosphatidylethanolamine, lysophosphatidylglycerol, lysophosphatidic acid, lysophosphatidylserine, PEG-phosphatidylethanolamine, PVP-phosphatidylethanolamine, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, cholate, chenodeoxycholate, lithocholate, ursodeoxycholate, taurocholate, glycocholate, deoxycholate, taurodeoxycholate, chenodeoxycholate, glycodeoxycholate, glycochenodeoxycholate, taurochenodeoxycholate, ursodeoxycholate, lithocholate, tauroursodeoxycholate, glycoursodeoxycholate, cholylsarcosine, N-methyl taurocholate, caproate, caprylate, caprate, laurate, myristate, palmitate, oleate, ricinoleate, linoleate, linolenate, stearate, lauryl sulfate, tetraacetyl sulfate, docusate, lauroyl carnitine, palmitoyl carnitine, myristoyl carnitine, and salts and mixtures thereof.

79. The pharmaceutical composition of claim 66, wherein the ionic surfactant is selected from the group consisting of lecithin, lysolecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, lysophosphatidylcholine, PEG-phosphatidylethanolamine, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, cholate, taurocholate, glycocholate, deoxycholate, taurodeoxycholate, chenodeoxycholate, lithocholate, ursodeoxycholate, glycodeoxycholate, cholylsarcosine, caproate, caprylate, caprate, laurate oleate, lauryl sulfate, docusate, lauroyl carnitine, palmitoyl carnitine, myristoyl carnitine, and salts and mixtures thereof.

80. The pharmaceutical composition of claim 66, wherein the ionic surfactant is selected from the group consisting of lecithin, lactylic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, chenodeoxycholate, lithocholate, ursodeoxycholate, taurocholate, caprylate, caprate, oleate, lauryl sulfate, docusate, lauroyl carnitine, palmitoyl carnitine, myristoyl carnitine, and salts and mixtures thereof.

81. The pharmaceutical composition of claim 60 wherein the hydrophobic surfactant is a compound or mixture of compounds having an HLB value less than about 10.

82. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is selected from the group consisting of alcohols; polyoxyethylene alkylethers; fatty acids; bile acids; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lower alcohol fatty acid esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid esters of mono/diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; transesterified vegetable oils; sterols; sugar esters; sugar ethers; sucroglycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

83. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is selected from the group consisting of fatty acids; bile acids; lower alcohol

fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lactic acid esters of mono/diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

84. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is selected from the group consisting of bile acids; lower alcohol fatty acid esters; polypropylene glycol fatty acid esters; propylene glycol fatty acid esters; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lactic acid derivatives of mono/diglycerides; sorbitan fatty acid esters; polyoxyethylene vegetable oils; and mixtures thereof.

85. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is selected from the group consisting of a glycerol fatty acid ester, an acetylated glycerol fatty acid ester, and mixtures thereof.

86. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is a reaction mixture of a polyol and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

87. The pharmaceutical composition of claim 86, wherein the reaction mixture is a transesterification product of a polyol and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols.

88. The pharmaceutical composition of claim 86, wherein the polyol is selected from the group consisting of polyethylene glycol, sorbitol, propylene glycol, pentaerythritol, a saccharide, and mixtures thereof.

89. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is selected from the group consisting of myristic acid; oleic acid; lauric acid; stearic acid; palmitic acid; PEG 1-4 stearate; PEG 2-4 oleate; PEG-4 dilaurate; PEG-4 dioleate; PEG-4 distearate; PEG-6 dioleate; PEG-6 distearate; PEG-8 dioleate; PEG 3-16 castor oil; PEG 5-10 hydrogenated castor oil; PEG 6-20 corn oil; PEG 6-20 almond oil; PEG-6 olive oil; PEG-6 peanut oil; PEG-6 palm kernel oil; PEG-6 hydrogenated palm kernel oil; PEG-4 capric/caprylic triglyceride, mono, di, tri, tetra esters of vegetable oil and sorbitol; pentaerythrityl di, tetra stearate, isostearate, oleate, caprylate, or caprate; polyglyceryl 2-4 oleate, stearate, or isostearate; polyglyceryl 4-10 pentaoleate; polyglyceryl-3 dioleate; polyglyceryl-6 dioleate; polyglyceryl-10 trioleate; polyglyceryl-3 distearate; propylene glycol mono- or diesters of a C_6 to C_{22} fatty acid; monoglycerides of a C_6 to C_{22} fatty acid; acetylated monoglycerides of C_6 to C_{22} fatty acid; diglycerides of C_6 to C_{22} fatty acids; lactic acid esters of monoglycerides; lactic acid esters of diglycerides; cholesterol; phytosterol; PEG 5-20 soya sterol; PEG-6 sorbitan tetra, hexastearate; PEG-6 sorbitan tetraoleate; sorbitan monolaurate; sorbitan monopalmitate; sorbitan mono, trioleate; sorbitan mono, tristearate; sorbitan monoisostearate; sorbitan sesquioleate; sorbitan sesquistearate; PEG 2-5 oleyl ether; POE 2-4 lauryl ether; PEG-2 cetyl ether; PEG-2 stearyl ether; sucrose distearate; sucrose dipalmitate; ethyl oleate; isopropyl myristate; isopropyl palmitate; ethyl linoleate; isopropyl linoleate; poloxamers; cholic acid; ursodeoxycholic acid; glycocholic acid; taurocholic acid; lithocholic acid; deoxycholic acid; chenodeoxycholic acid; and mixtures thereof.

90. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is selected from the group consisting of oleic acid; lauric acid; glyceryl monocaprate; glyceryl monocaprylate; glyceryl monolaurate; glyceryl monooleate; glyceryl dicaprate; glyceryl dicaprylate; glyceryl dilaurate; glyceryl dioleate; acetylated monoglycerides; propylene glycol oleate; propylene glycol laurate; polyglyceryl-3 oleate; polyglyceryl-6 dioleate; PEG-6 corn oil; PEG-20 corn oil; PEG-20 almond oil; sorbitan monooleate; sorbitan monolaurate; POE-4 lauryl ether; POE-3 oleyl ether; ethyl oleate; poloxamers; cholic acid; ursodeoxycholic acid; glycocholic acid; taurocholic acid; lithocholic acid; deoxycholic acid; chenodeoxycholic acid; and mixtures thereof.

91. The pharmaceutical composition of claim 60, wherein the therapeutic agent is selected from the group consisting of a drug, a vitamin, a nutritional supplement, a cosmeceutical, and mixtures thereof.

92. The pharmaceutical composition of claim 60, wherein the therapeutic agent is a hydrophobic drug.

93. The pharmaceutical composition of claim 92, wherein the hydrophobic drug has a molecular weight of less than about 1000 g/mol.

94. The pharmaceutical composition of claim 60, wherein the therapeutic agent is a hydrophilic drug.

95. The pharmaceutical composition of claim 94, wherein the hydrophilic drug is selected from the group consisting of a peptidomimetic, a peptide, a protein, an

oligonucleotide, an oligodeoxynucleotide, RNA, DNA, genetic material, and mixtures thereof.

96. The pharmaceutical composition of claim 94, wherein the hydrophilic drug has a molecular weight of less than about 1000 g/mol.

97. The pharmaceutical composition of claim 60, wherein the surfactants are present in amounts such that the triglyceride can be present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous dispersion of the triglyceride and a carrier having a hydrophilic surfactant but not having a hydrophobic surfactant, and having the same total surfactant concentration.

98. The pharmaceutical composition of claim 60, wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 10:1 by weight, the composition forms a clear aqueous dispersion.

99. The pharmaceutical composition of claim 60, wherein the absorbance is less than about 0.2.

100. The pharmaceutical composition of claim 60, wherein the absorbance is less than about 0.1.

101. The pharmaceutical composition of claim 60 in the form of a preconcentrate in a liquid, semi-solid, or solid form, or as an aqueous or organic diluted preconcentrate.

102. A dosage form comprising the pharmaceutical composition of claim 75 processed by a technique selected from the group consisting of lyophilization, encapsulation, extruding, compression, melting, molding, spraying, coating, comminution, mixing, homogenization, sonication, granulation, and combinations thereof.

103. A dosage form comprising the pharmaceutical composition of claim 60, wherein the dosage form is selected from the group consisting of a pill, capsule, caplet, tablet, granule, bead and powder.

104. The dosage form of claim 103, which further comprises an enteric coating, a seal coating, or both.

105. A dosage form comprising the pharmaceutical composition of claim 60, wherein the dosage form is selected from the group consisting of a solution, suspension, emulsion, cream, ointment, lotion suppository, spray, aerosol, paste, gel, drops, douche, ovule, wafer, troche, cachet, syrup and elixir.

106. A dosage form comprising a multiparticulate carrier coated onto a substrate with the pharmaceutical composition of claim 60.

107. The dosage form of claim 106, wherein the substrate is selected from the group consisting of a particle, a granule and a bead, and is formed of the therapeutic agent, a pharmaceutically acceptable material, or a mixture thereof.

108. The dosage form of claim 106, wherein the multiparticulate carrier is selected from the group consisting of an enteric coating, seal coating, and a mixture thereof.

109. The pharmaceutical composition of claim 60, which further comprises an additional amount of the therapeutic agent, said additional amount not solubilized in the composition.

110. The dosage form of claim 106, wherein the dosage form is further processed by a technique selected from the group consisting of encapsulation, compression, extrusion or molding.

111. The dosage form of claim 106, wherein the dosage form is encapsulated in a capsule selected from the group consisting of a starch capsule, a cellulosic capsule, a hard gelatin capsule, and a soft gelatin capsule.

112. The dosage form of claim 106, wherein the dosage form is encapsulated in a capsule selected from the group consisting of a starch capsule, a cellulosic capsule, and a soft gelatin capsule.

113. A pharmaceutical composition consisting of:

(a) a triglyceride;

(b) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic, wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm;

(c) a first amount of a therapeutic agent, said first amount being solubilized in the triglyceride, the carrier, or both the triglyceride and the carrier; and

(d) a second amount of a therapeutic agent, said second amount not solubilized in the triglyceride or the carrier.

114. A pharmaceutical composition comprising:

(a) a triglyceride; and

(b) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm, and wherein the triglyceride is present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous dispersion of the triglyceride and a carrier having only one surfactant, the surfactant being hydrophilic, and having the same total surfactant concentration.

115. The composition of claim 114, wherein the triglyceride comprises a digestible oil.

116. The pharmaceutical composition of claim 114, wherein the triglyceride is selected from the group consisting of vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, synthetic triglycerides, and mixtures thereof.

117. The pharmaceutical composition of claim 114, wherein the triglyceride is selected from the group consisting of almond oil; babassu oil; borage oil; blackcurrant seed oil; canola oil; castor oil; coconut oil; corn oil; cottonseed oil; evening primrose oil;

grapeseed oil; groundnut oil; mustard seed oil; olive oil; palm oil; palm kernel oil; peanut oil; rapeseed oil; safflower oil; sesame oil; shark liver oil; soybean oil; sunflower oil; hydrogenated castor oil; hydrogenated coconut oil; hydrogenated palm oil; hydrogenated soybean oil; hydrogenated vegetable oil; hydrogenated cottonseed and castor oil; partially hydrogenated soybean oil; partially hydrogenated soy and cottonseed oil; glyceryl tricaproate; glyceryl tricaprylate; glyceryl tricaprate; glyceryl triundecanoate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl trilinolenate; glyceryl tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; glyceryl tricaprylate/caprate/stearate; saturated polyglycolized glycerides; linoleic glycerides; caprylic/capric glycerides; and mixtures thereof.

118. The pharmaceutical composition of claim 114, wherein the triglyceride is selected from the group consisting of coconut oil; corn oil; olive oil; palm oil; peanut oil; safflower oil; sesame oil; soybean oil; hydrogenated castor oil; hydrogenated coconut oil; partially hydrogenated soybean oil; glyceryl tricaprate; glyceryl trilaurate; glyceryl trioleate; glyceryl trilinoleate; glyceryl tricaprylate/caprate; glyceryl tricaprylate/caprate/laurate; glyceryl tricaprylate/caprate/linoleate; glyceryl tricaprylate/caprate/stearate; saturated polyglycolized glycerides; linoleic glycerides; caprylic/capric glycerides; and mixtures thereof.

119. The pharmaceutical composition of claim 114, wherein the triglyceride is selected from the group consisting of a medium chain triglyceride, a long chain triglyceride, and mixtures thereof.

120. The pharmaceutical composition of claim 114, which further comprises a therapeutic agent.

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121. A method of treating an animal with a therapeutic agent, the method comprising:

(a) providing a dosage form of a pharmaceutical composition consisting of:

(i) a triglyceride; and

(ii) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm;

(b) providing a therapeutic agent; and

(c) administering said dosage form to said animal.

122. The method of claim 121, wherein the dosage form is processed by a technique selected from the group consisting of lyophilization, encapsulation, extruding, compression, melting, molding, spraying, coating, comminution, mixing, homogenization, sonication, granulation, and combinations thereof.

123. The method of claim 121, wherein the dosage form is selected from the group consisting of a pill, capsule, caplet, tablet, granule, bead and powder.

124. The method of claim 123, wherein the capsule further comprises a coating selected from the group consisting of an enteric coating, a seal coating, and a combination thereof.

125. The method of claim 121, wherein the dosage form is selected from the group consisting of a solution, suspension, emulsion, cream, ointment, lotion, suppository, spray, aerosol, paste, gel, drops, douche, ovule, wafer, troche, cachet, syrup and elixir.

126. The method of claim 121, wherein the dosage form comprises a multiparticulate carrier coated onto a substrate with the pharmaceutical composition.

127. The method of claim 126, wherein the substrate is selected from the group consisting of a particle, a granule and a bead, and is formed of a material selected from the group consisting of the therapeutic agent, a pharmaceutically acceptable material and a mixture thereof.

128. The method of claim 126, wherein the multiparticulate carrier is coated with a coating selected from the group consisting of an enteric coating, seal coating, and a combination thereof.

129. The method of claim 126, wherein the dosage form is further processed by encapsulation, compression, extrusion or molding.

130. The method of claim 126, wherein the capsule is a starch capsule, a cellulosic capsule, a hard gelatin capsule, or a soft gelatin capsule.

131. The method of claim 126, wherein the capsule is a starch capsule, a cellulosic capsule, or a soft gelatin capsule.

132. The method of claim 121, wherein the therapeutic agent is provided by solubilizing the therapeutic agent in the triglyceride, in the carrier, or in both the triglyceride and the carrier.

133. The method of claim 121, wherein the therapeutic agent is provided separately from the dosage form of the pharmaceutical composition.

134. The method of claim 121, wherein the dosage form is administered by a route selected from the group consisting of an oral, parenteral, buccal, topical, transdermal, ocular, pulmonary, vaginal, rectal and transmucosal.

135. The method of claim 121, wherein the animal is a mammal.

136. The method of claim 135, wherein the mammal is a human.

137. A method of increasing the amount of a triglyceride that can be solubilized in a clear aqueous dispersion, the method comprising:

(a) providing a composition comprising a triglyceride and a carrier, the carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic; and

(b) dispersing the composition in an aqueous solution,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm, and wherein the triglyceride is present in an amount greater than the amount of the triglyceride that remains solubilized in an aqueous

dispersion of the triglyceride and a carrier having only one surfactant and having the same total surfactant concentration.

138. The method of claim 137, wherein the step of dispersing the composition comprises mixing the composition with an aqueous solution *in vitro*.

139. The method of claim 137, wherein the step of dispersing the composition comprises allowing the composition to contact an aqueous biological solution *in vivo* upon administering the composition to an animal.

140. A method of treating an animal with a therapeutic agent, the method comprising:

(a) providing a dosage form of a pharmaceutical composition consisting of:

(i) an effective amount of a triglyceride; and

(ii) a carrier comprising at least two surfactants, at least one of the surfactants being hydrophilic,

wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous solution in an aqueous solution to composition ratio of about 100:1 by weight, the composition forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400 nm; and

(iii) said therapeutic agent; and

(b) administering said dosage form to said animal.

141. The method of claim 140, wherein the effective amount of the triglyceride is a nutritionally effective amount of a digestible oil.

142. The method of claim 140, wherein the effective amount of the triglyceride is an amount sufficient to improve the bioabsorption of a therapeutic agent co-administered with the dosage form of the pharmaceutical composition.

143. The dosage form of claim 50, comprising a capsule.

144. The pharmaceutical composition of claim 81, wherein the hydrophobic surfactant is a glycerol fatty acid ester.

145. The dosage form of claim 103, comprising a capsule.

146. The method of claim 123, wherein the dosage form comprises a capsule.

147. The dosage form of claim 143, wherein the capsule id selected from the group consisting of a starch capsule, a cellulosic capsule, a hard gelatin capsule and a soft gelatin capsule.

148. The dosage form of claim 147, wherein the capsule is selected from the group consisting of a starch capsule, a cellulosic capsule, and a soft gelatin capsule.

149. The pharmaceutical composition of claim 144, wherein the glycerol fatty acid ester is selected from the group consisting of a monoglyceride, a diglyceride, and mixtures thereof.

150. The pharmaceutical composition of claim 149, wherein the fatty acid of the glycerol fatty acid ester is a C_6 to C_{22} fatty acid or a mixture thereof.

151. The dosage form of claim 145, wherein the capsule is selected from the group consisting of a starch capsule, a cellulosic capsule, a hard gelatin capsule and a soft gelatin capsule.

152. The dosage form of claim 151, wherein the capsule is selected from the group consisting of a starch capsule, a cellulosic capsule, and a soft gelatin capsule.

153. The dosage form of claim 145, wherein the capsule is selected from the group consisting of a starch capsule, a cellulosic capsule, a hard gelatin capsule and a soft gelatin capsule.

154. The dosage form of claim 151, wherein the capsule is selected from the group consisting of a starch capsule, a cellulosic capsule, and a soft gelatin capsule.

155. A pharmaceutical composition substantially as hereinbefore described with reference to the examples and/or the preferred embodiments and excluding, if any, comparative examples.

156. A method of treating an animal with a therapeutic agent substantially as hereinbefore described with reference to the examples and/or the preferred embodiments and excluding, if any, comparative examples.

Dated this twenty-ninth day of July 2005

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