leuprolide acetate during *in vitro* and *in vivo* release. This property is quite counter intuitive and unexpected. This property can be advantageously used to tailor and fine tune the formulation to prepare better and improved products.

[0016a] In one aspect, the present invention provides a pharmaceutical composition comprising: a) a combination of a strong acid salt and a weak acid salt of a LHRH agonist selected from a group consisting of leuprolide, triptorelin, and goserelin, wherein the molar ratio of (strong acid anion + weak acid anion) to the LHRH agonist is ≤ 2:1 and the molar ratio of the strong acid anion to the LHRH agonist is from 1:1 to less than 2:1; b) a biodegradable polymer selected from the group of a homopolymer polylactide or polylatic acid, and a copolymer poly (lactic acid-co-glycolic acid) or poly (lactide-co-glycolide), wherein the ratio of lactide:glycolide (or lactic acid:glycolic acid) of the copolymer is from 50:50 to less than 100:0; and c) N-methyl-2-pyrrolidone (NMP), wherein the pharmaceutical composition having a selected release duration ranging from one month to 6 months can be prepared by varying the ratios of a strong acid salt and a weak acid salt of the LHRH agonist .

[0016b] In another aspect, the present invention provides a pharmaceutical composition comprising: a) a combination of leuprolide mesylate and leuprolide acetate, wherein the molar ratio of (mesylate + acetate) to leuprolide is ≤ 2:1 and the molar ratio of mesylate anion to leuprolide is from 1:1 to less than 2:1; b) a biodegradable polymer selected from the group of a homopolymer polylactide or polylatic acid, and a copolymer poly (lactic acid-co-glycolic acid) or poly (lactide-co-glycolide), wherein the ratio of lactide:glycolide (or lactic acid:glycolic acid) of the copolymer is from 50:50 to less than 100:0; and c) N-methyl-2-pyrrolidone (NMP); wherein the pharmaceutical composition having a selected release duration ranging from one month to 6 months can be prepared by varying the ratios of mesylate to leuprolide.

[0016c] In another aspect, the present invention provides a pharmaceutical composition comprising: a) a combination of leuprolide mesylate and leuprolide formate, wherein the

molar ratio of (mesylate + formate) to leuprolide is ≤ 2:1 and the molar ratio of mesylate anion to leuprolide is from 1:1 to less than 2:1; b) a biodegradable polymer selected from the group of a homopolymer polylactide or polylatic acid, and a copolymer poly (lactic acid-co-glycolic acid) or poly (lactide-co-glycolide), wherein the ratio of lactide:glycolide (or lactic acid:glycolic acid) of the copolymer is from 50:50 to less than 100:0; and c) N-methyl-2-pyrrolidone (NMP); wherein the pharmaceutical composition having a selected release duration ranging from one month to 6 months can be prepared by varying the ratios of mesylate to leuprolide.

[0017] Accordingly, the present disclosure provides a stabilized injectable biodegradable polymeric composition for forming an economical, practical, and efficient controlled release delivery system for a LHRH agonist or antagonist. The present disclosure also provides a method of manufacturing and a method of use thereof. According to the present disclosure, the drug delivery system is produced easily and delivered conveniently to a subject such as a mammal or human. The compositions deliver a therapeutic amount of peptide over a desired, extended period of time, based on the specific composition of the biodegradable polymer used in the composition with the salt of a peptide formed from a strong acid. The compositions are both biocompatible and biodegradable, and disappear harmlessly after delivering the dose of the peptide agents.

[0018] The compositions in accordance with the present disclosure comprise a) a salt of a LHRH agonist or antagonist formed with a strong acid that minimizes or prevents the interaction/reaction between the peptide and the polymer in an organic solution; b) a biodegradable polymer; c) a pharmaceutically acceptable organic solvent, that when formulated together can deliver the LHRH agonist or antagonist over a 1-, 3-, 4- or 6-month period. According to the disclosure, the pharmaceutical composition may optionally include excipients to achieve optimal delivery of the peptide agent. The

diffuses/dissipates from the inventive composition, which causes the coagulation of the polymer to form a gel, or solid matrix encapsulating the peptide agent. According to the present disclosure the biodegradable polymer may be a linear polymer, or a branched polymer, or a mixture of the two. Preferably, the polymer is a lactate-based polymer. The lactate-based polymer includes homopolymers of lactic acid or lactide monomers (poly(lactic acid) or polylactide, PLA), and copolymers of lactic acid (or lactide) with other monomers (for example, glycolic acid, glycolide (poly(lactide-co-glycolide), PLG or PLGA) and the like). Examples of the polymers suitable for the present composition includes, without limitation, polylactides, polyglycolides, polycaprolactones, polyanhydrides, polyurethanes, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyorthocarbonates, polyphosphazenes, polyhydroxybutyrates, polyhydroxyvalerates, polyalkylene oxalates, polyalkylene succinates, poly(malic acid), poly(maleic anhydride), and copolymers, terpolymers, or combinations or mixtures therein. Lactic acid-based polymers, and copolymers of lactic acid and glycolic acid (PLGA), including poly(D,L-lactide-co-glycolide) and poly(L-lactide-co-glycolide) are preferably used in the present disclosure. In some examples, the PLGA polymers have weight average molecular weights of between about 2,000 to about 100,000 and monomer ratios of lactic acid to glycolic acid of between about 50:50 to about 100:0. The preferred polymers of the present disclosure are PLA with molecular weight of between 11,000 and about 18,000 for a controlled delivery of 6 months, and a PLGA with molecular weight of between 10,000 and 25,000 dalton having a lactide content of 80-90% for a 3- or 4-month delivery.

[0024] The pharmaceutically acceptable organic solvents may be selected from a group consisting of N-methyl-2-pyrrolidone, dimethylacetamide, methoxypolyethylene glycol, alkoxypolyethylene glycol, polyethylene glycol esters, glycofurol, glycerol formal, methyl acetate, ethyl acetate, methyl ethyl ketone, dimethylformamide, dimethyl sulfoxide,

What is claimed is:

1. A pharmaceutical composition comprising:

    a) a combination of a strong acid salt and a weak acid salt of a LHRH agonist selected from a group consisting of leuprolide, triptorelin, and goserelin, wherein the molar ratio of (strong acid anion + weak acid anion) to the LHRH agonist is ≤ 2:1 and the molar ratio of the strong acid anion to the LHRH agonist is from 1:1 to less than 2:1;

    b) a biodegradable polymer selected from the group of a homopolymer polylactide or polylatic acid, and a copolymer poly (lactic acid-co-glycolic acid) or poly (lactide-co-glycolide), wherein the ratio of lactide:glycolide (or lactic acid:glycolic acid) of the copolymer is from 50:50 to less than 100:0; and

    c) N-methyl-2-pyrrolidone (NMP);

    wherein the pharmaceutical composition having a selected release duration ranging from one month to 6 months can be prepared by varying the ratios of a strong acid salt and a weak acid salt of the LHRH agonist.

2. The pharmaceutical composition of claim 1 wherein the LHRH agonist is leuprolide.

3. The pharmaceutical composition of claim 1 wherein the strong acid is selected from a group consisting of methanesulfonic acid, HCl, and sulfuric acid.

4. The pharmaceutical composition of claim 1 wherein the strong acid is sulfuric acid and the molar ratio of the sulfate anion to the LHRH agonist is from 0.5:1 to 1:1.

5. The pharmaceutical composition of claim 1 wherein the weak acid is selected from a group consisting of acetic acid and formic acid.

6. A pharmaceutical composition comprising:

   a) a combination of leuprolide mesylate and leuprolide acetate, wherein the molar ratio of (mesylate + acetate) to leuprolide is ≤ 2:1 and the molar ratio of mesylate anion to leuprolide is from 1:1 to less than 2:1;

   b) a biodegradable polymer selected from the group of a homopolymer polylactide or polylatic acid, and a copolymer poly (lactic acid-co-glycolic acid) or poly (lactide-co-glycolide), wherein the ratio of lactide:glycolide (or lactic acid:glycolic acid) of the copolymer is from 50:50 to less than 100:0; and

   c) N-methyl-2-pyrrolidone (NMP);

   wherein the pharmaceutical composition having a selected release duration ranging from one month to 6 months can be prepared by varying the ratios of mesylate to leuprolide.

7. A pharmaceutical composition comprising:

   a) a combination of leuprolide mesylate and leuprolide formate, wherein the molar ratio of (mesylate + formate) to leuprolide is ≤ 2:1 and the molar ratio of mesylate anion to leuprolide is from 1:1 to less than 2:1;

b) a biodegradable polymer selected from the group of a homopolymer polylactide or polylatic acid, and a copolymer poly (lactic acid-co-glycolic acid) or poly (lactide-co-glycolide), wherein the ratio of lactide:glycolide (or lactic acid:glycolic acid) of the copolymer is from 50:50 to less than 100:0; and

c) N-methyl-2-pyrrolidone (NMP);

wherein the pharmaceutical composition having a selected release duration ranging from one month to 6 months can be prepared by varying the ratios of mesylate to leuprolide.

8. The pharmaceutical composition of claims 6 and 7 wherein the molar ratio of mesylate anion to leuprolide is from 1.4:1 to less than 2:1.

9. The pharmaceutical composition of claims 6 and 7 wherein the molar ratio of mesylate anion to leuprolide is from 1.5:1 to 1.8:1.

10. The pharmaceutical composition of claims 1, 6 and 7 wherein the biodegradable polymer has at least one hydroxyl terminal group.

11. The pharmaceutical composition of claims 1, 6 and 7 wherein the biodegradable polymer has 30 – 60% of the composition by weight, has an average molecular weight of 8,000 to 50,000, and has a polydispersity less than or equals to 2.5.