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(54) **COMBINED NSAID AND ACETAMINOPHEN
FORMULATION AND METHOD**

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(57) **ABSTRACT**

The present invention is directed to co-administration of a non-steroidal anti-inflammatory agent (NSAID) and acetaminophen for the treatment of pain and inflammation with reduced gastrointestinal irritation. A pharmaceutical composition suitable for the co-administration contains a therapeutically effective amount of at least one non-steroidal anti-inflammatory agent, and a therapeutically effective amount of acetaminophen or a pharmaceutically acceptable salt thereof. A ratio of the non-steroidal anti-inflammatory agent to acetaminophen in the composition is within a range that provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by the administration of the non-steroidal anti-inflammatory agent or acetaminophen alone. Examples of pharmaceutical compositions for co-administration of the agents are those containing ibuprofen in combination with the acetaminophen.

**COMBINED NSAID AND ACETAMINOPHEN
FORMULATION AND METHOD****CROSS-REFERENCE TO RELATED
APPLICATIONS**

[0001] Not Applicable.

**STATEMENT RE: FEDERALLY SPONSORED
RESEARCH/DEVELOPMENT**

[0002] Not Applicable

BACKGROUND OF THE INVENTION

[0003] 1. Technical Field

[0004] The invention generally relates to pharmaceutical compositions for the treatment of pain and inflammation, and methods of treatment with the pharmaceutical compositions.

[0005] 2. Related Art

[0006] Pain-relief compounds and methods for their use have been developed for the treatment of various different painful conditions, such as conditions involving acute and/or chronic pain. Categories of compounds known to be useful for such treatment include steroidal and non-steroidal anti-inflammatory compounds (NSAIDs), opioids, NMDA antagonists, and other analgesic agents. Non-steroidal anti-inflammatory drugs in particular have been found to be useful in the treatment of pain associated with inflammation, such as rheumatoid arthritis, osteoarthritis, headache and migraine pain, post-operative pain, tissue injury, gout, ileus and other painful inflammatory disorders. The non-steroidal anti-inflammatory drugs are widely-used because they are non-narcotic and typically relatively safe, with certain NSAIDs even being available over-the-counter without a prescription. Examples of popular NSAIDs include aspirin, ibuprofen and naproxen.

[0007] However, a problem with the use of NSAIDs is that they have been discovered to cause significant adverse drug reactions in the form of severe gastrointestinal irritation in certain circumstances, such as with very high doses or prolonged administration of the NSAIDs. The gastrointestinal irritation can be serious enough to cause gastric injury, including serious ulcers and gastrointestinal bleeding, even resulting in death. Certain precautions can be taken to reduce the chances of gastric injury, such as by advising patients to take NSAIDs only after consuming a meal and/or drinking water, and by limiting the dose of the NSAID and duration over which it is administered. However, the risk of gastric injury continues to limit the use of NSAID compounds to lower doses and shorter durations of administration than what may otherwise be desired to achieve pain relief. Also, some patients and physicians avoid taking and/or prescribing NSAIDs altogether out of concern for the potential gastrointestinal risks. The limitations of NSAIDs are especially concerning for chronic conditions such as rheumatoid arthritis, which require long-term therapy.

[0008] Accordingly, there remains a need for pharmaceutical compositions and methods capable of providing pain relief without causing adverse gastrointestinal side effects. There is also a need for pharmaceutical compositions and methods including NSAIDs that provide satisfactory pain relief without gastrointestinal irritation. Furthermore, there is a need for compositions and methods that allow for the rela-

tively safe administration of increased doses of NSAIDs and/or increased administration duration to provide desired pain treatment.

BRIEF SUMMARY OF THE INVENTION

[0009] The present invention is directed to co-administration of a non-steroidal anti-inflammatory agent (NSAID) and acetaminophen or pharmaceutically acceptable salt thereof for the treatment of pain and inflammation with reduced gastrointestinal irritation. In one version, a pharmaceutical composition suitable for the co-administration contains a therapeutically effective amount of at least one non-steroidal anti-inflammatory agent, and a therapeutically effective amount of the acetaminophen or pharmaceutically acceptable salt thereof. A ratio of the non-steroidal anti-inflammatory agent to acetaminophen in the composition is within a range that provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by the administration of the non-steroidal anti-inflammatory agent or acetaminophen alone.

[0010] In one embodiment of the invention, a method for treating at least one of pain and inflammation in a patient in need thereof is provided that results in reduced gastrointestinal irritation. The method involves administering to the patient a therapeutically effective amount of at least one non-steroidal anti-inflammatory (NSAID) agent, and a therapeutically effective amount of acetaminophen or a pharmaceutically acceptable salt thereof. The ratio of the non-steroidal anti-inflammatory agent to acetaminophen administered to the patient is maintained in a range that provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by administration of the non-steroidal anti-inflammatory agent or acetaminophen alone.

[0011] In an embodiment of a pharmaceutical composition for co-administration of the NSAID and acid blocking agent, the pharmaceutical composition contains a non-steroidal anti-inflammatory agent (NSAID) that is ibuprofen or a pharmaceutically acceptable salt thereof in an amount of from about 100 mg to about 800 mg, and acetaminophen or a pharmaceutically acceptable salt thereof in an amount of from about 250 mg to 750 mg. In this embodiment, a ratio of the non-steroidal anti-inflammatory agent to the acetaminophen can be selected to be within a range of from about one part by weight of the non-steroidal anti-inflammatory agent to about one-fifth to about one-half parts by weight of the acetaminophen, such that the composition provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by administration of the non-steroidal anti-inflammatory agent or acetaminophen alone.

[0012] The present invention is best understood by reference to the following detailed description.

DETAILED DESCRIPTION OF THE INVENTION

[0013] The detailed description set forth below is intended as a description of the presently preferred embodiments of the invention, and is not intended to represent the only form in which the present invention may be prepared or utilized. The description sets forth the functions and sequences of steps for preparing and using the invention. It is to be understood, however, that the same or equivalent functions may be accomplished by different embodiments and that they are also intended to be encompassed within the scope of the invention.

[0014] The expression "pharmaceutically acceptable salt" as used herein is meant to refer to those salts of biological compounds which retain the biological effectiveness and

properties of the free compound (i.e. free bases and/or acids), and can include, but are not limited to, pharmaceutically acceptable acid and/or base addition salts, as well as pharmaceutically acceptable cationic and/or anionic salts. Examples of pharmaceutically acceptable salts include, for example, acid addition salts, such as hydrochloride salts, alkali metal salts, such as sodium and potassium, alkaline earth salts, ammonium salts, and the like.

[0015] It should also be understood that the compounds and/or pharmaceutically acceptable salts thereof as described herein may be provided in their hydrate and/or solvate forms.

[0016] The expression “therapeutically effective amount” as used herein is meant to refer to an amount of a compound or composition effective to result in the amelioration of symptoms associated with a condition, or to provide a beneficial therapeutic effect, such for example including, but not limited to, at least partial pain relief, reduction of inflammation, reduction in gastrointestinal irritation, and/or protection of the stomach lining.

[0017] The expression “gastrointestinal irritation” as used herein is meant to refer to at least one of dyspeptic symptoms, gastroduodenal ulcers, peptic ulcers, perforation of ulcers, gastropathy, upper and/or lower gastrointestinal hemorrhaging, gastroduodenal damage, ulcer complications, stomach erosions and the like.

[0018] The expression “co-administration” as used herein is meant to refer to the administration of at least two compounds within the same time frame, such as substantially simultaneously. The expression can refer to the administration of at least two compounds in the same dosage form, substantially simultaneous administration in separate dosage forms, or sequential administration of the compounds within a timeframe selected such that the therapeutic effects of the compounds temporally overlap.

[0019] The term “patient” as used herein is meant to refer to a human or non-human mammal capable of receiving treatment with the compositions and methods taught herein.

[0020] The term “synergistic effect” as used herein is meant to refer to a therapeutic or other effect achieved by the co-administration of two or more compounds that exceeds a mere additive effect of the compounds.

[0021] It has been surprisingly discovered that the gastrointestinal irritation caused by NSAIDs can be reduced by co-administration of the NSAID with acetaminophen or a pharmaceutically acceptable salt thereof, thereby allowing for improved treatment of painful and inflammatory conditions. The break-down of the gastric mucosa and stomach lining has been discovered to be decreased by taking the two compounds together, thereby providing gastric protection and reducing gastric irritation, gastric erosion, and lessening the incidence of gastrointestinal ulcers and bleeding. Also, the co-administration of the compounds can provide for synergistic results in the treatment of pain, as the reduction in pain levels can exceed a mere additive contribution from each of the compounds. In particular, it has been discovered that the NSAID and acetaminophen can be co-administered in a ratio that is within a range that provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by the administration of either of the NSAID or acetaminophen alone. Thus, adverse side effects normally associated with NSAIDs are decreased by administering the NSAID and acetaminophen together, resulting in improved treatment of pain and inflammation, and also improved patient compliance.

[0022] The NSAID used for co-administration with the acetaminophen can be selected in relation to the particular condition being treated, and preferably has proven efficacy in

the treatment of pain and/or inflammation. Examples of NSAIDs (and their brand-names) suitable for co-administration with the acid blocking agent include, but are not limited to, at least one of diclofenac (Cataflam®, Voltaren®, Voltaren SR®), etodolac (Lodine®, Lodine XL®), ibuprofen (Motrin®), fenoprofen (Nalfon®), indomethacin (Indocin®), ketoprofen (Orudis®, Oruvail®), nabumetone (Relafan®), naproxen (Naprosyn®), oxaprozin (Daypro®), sulindac (Clinoril®) and tolmetin (Tolectin®), as well as pharmaceutically acceptable salts of these compounds. In one version, the NSAID co-administered with the acetaminophen comprises ibuprofen or a pharmaceutically acceptable salt thereof, which drug is both systemically and locally acting and has high efficacy in controlling pain in humans and animals. Ibuprofen corresponds to the chemical formula 2-(4-isobutylphenyl)propionic acid, and is described in further detail together with its pharmaceutically acceptable salts in, for example, U.K. Patent No. 971,700, which is herein incorporated by reference in its entirety. Acetaminophen, also sometimes called paracetamol, corresponds to the formula N-(4-hydroxyphenyl)acetamide, and is a compound that is capable of providing pain relief, although it has minimal anti-inflammatory effects as compared to NSAIDs. Acetaminophen and pharmaceutically acceptable salts thereof are further described in U.S. Pat. No. 6,126,967 to Clemente et al, issued Oct. 3, 2000, which is herein incorporated by reference in its entirety. It should be understood that the term “acetaminophen” as used herein is intended to encompass not only the free acetaminophen compound (non-salt form), but also pharmaceutically acceptable salts thereof.

[0023] The relative amounts of the NSAID and acetaminophen administered to the patient are selected according to criteria such as the condition to be treated, the particular NSAID being administered, the extent of gastric protection desired, the chronic or acute nature of the condition, and other similar criteria. Generally speaking, a ratio of the NSAID to the acetaminophen is within a range of from about one part by weight of the NSAID to about one-fifth to about one part by weight of the acetaminophen, such as from about one-half to about one part by weight of the acetaminophen. While this ratio is calculated with respect to the free compound (non-salt form), it should be understood that the equivalent ratio can also readily be determined for pharmaceutically acceptable salts of the compounds by using a ratio of the molecular weights of the salts, as known by those of ordinary skill in the art. This range has been discovered to provide greater pain relief and reduction of inflammation, with less gastrointestinal irritation, than what would otherwise be obtainable by the administration of either the NSAID or acetaminophen alone. In other words, the administration of these compounds exhibits synergistic effects that exceed the mere additive contribution of the individual components.

[0024] Suitable dosages of the NSAID and acetaminophen for co-administration are similarly selected according to the painful and/or inflammatory condition to be treated, as well as to provide for the synergistic effects in terms of pain relief, reduction in inflammation and reduced gastrointestinal irritation. Generally, a suitable dosage of the NSAID may range from about 50 mg to about 1000 mg, whereas a suitable dosage of the acetaminophen for co-administration with the NSAID may range from about 200 mg to about 800 mg. For example, a suitable treatment regimen can comprise co-administering ibuprofen or a pharmaceutically acceptable salt thereof in a dosage of from 100 mg to about 800 mg, such as from about 200 mg to about 400 mg, with acetaminophen or a pharmaceutically acceptable salt thereof in a dosage of from about 250 mg to about 750 mg, such as about 250 mg.

[0025] The NSAID and acetaminophen are co-administered to treat patients suffering from any of a variety of different painful and/or inflammatory conditions, including but not limited to acute as well as chronic pain conditions. For example, the compounds can be co-administered to treat pain associated with inflammation in arthritic conditions, including but not limited to at least one of rheumatoid arthritis, Still's disease, osteoarthritis, other arthritic conditions. The compounds can also be co-administered to treat pain and/or inflammation associated with non-arthritic conditions, including but not limited to at least one of musculo-skeletal injury, soft tissue injury, dental pain, post-operative pain, port partum pain, surgical pain, dysmenorrhea, migraine, tension headache, sinus headache and neuralgia. Patients treatable by co-administration of the compounds include human patients suffering from these and other painful and/or inflammatory conditions. Veterinary patients suffering from painful conditions, such as for example any of dogs, cats, horses, livestock and the like, may also benefit from the NSAID and acetaminophen co-administration treatment.

[0026] In one version, co-administration of the NSAID and acetaminophen is achieved by formulating the compounds into a pharmaceutical composition. The pharmaceutical composition comprises a dosage form suitable for any of a number of different means of administration, including but not limited to oral, buccal, parenteral, topical, transdermal, rectal, intravenous, intraperitoneal and inhalable dosage forms. For example, the dosage forms can comprise solid dosage forms, such as at least one of powders, granules, tablets, capsules (e.g. hard and soft gelatin capsules), caplets, cachets, suppositories and pessaries. The dosage forms can also be provided in liquid form, such as for example as solutions, suspensions, emulsions, syrups, elixirs and even pressurized compositions. Other dosage forms can include transdermal forms, such as transdermal patches, as well as aerosolizable forms suitable for pulmonary administration. Sustained release dosage forms can also be provided. The dosage forms typically comprise dosage units, such as tablets or caplets, which contain the appropriate dosage of the NSAID and acetaminophen for administration to the patient. Each unit dosage form can comprise up to about 99% by weight of the combined NSAID and acetaminophen, such as from about 0.03% to about 99% by weight, and even from about 1 to about 80% by weight.

[0027] Examples of solid dosage forms of the pharmaceutical composition are those including a pharmaceutically acceptable carrier, which can optionally also include other substances such as at least one of a flavoring agent, filler, compression aid, binders, disintegrants and encapsulating materials. Suitable carriers and/or ingredients suitable for solid dosage forms can include, but are not limited to, at least one of calcium phosphate, magnesium stearate, talc, sugars, hydrous lactose, anhydrous lactose, ribose, dextrin, starch, gelatin, cellulose, methyl cellulose, carboxymethyl cellulose, microcrystalline cellulose, starch glycolate, polyvinylpyrrolidone, polymers of methacrylic acid and divinylbenzene, waxes and ion exchange resins, among others. In the formulation of powder solid dosage forms, the carrier and active ingredients are finely divided and mixed together, and used to fill capsules, sachets, and the like. In the formulation of tablet solid dosage forms, the active ingredients are mixed with a carrier having suitable compression properties, and then compressed into a desired tablet shape and size. Spray-drying techniques can also be used to provide granules suitable for incorporation into capsules or compression into tablets.

[0028] Examples of liquid forms of the pharmaceutical composition are those comprising liquid carriers, including but not limited to water, organic solvents, pharmaceutically

acceptable oils and/or fats, and combinations thereof, in which one or more of the active agents are dissolved or suspended. The liquid forms optionally further comprise other suitable pharmaceutically acceptable additives such as solubilizers, emulsifiers, buffering agents, preservatives, sweeteners, flavoring agents, suspending agents, thickening agents, coloring agents, viscosity regulators, stabilizers, osmoregulators, and the like. Some examples of liquid forms suitable for oral administration include but are not limited to: liquid compositions having water as a carrier and including additives such as cellulose derivatives, including carboxymethyl cellulose solutions; compositions having an alcoholic carrier and including mono and polyhydric alcohols, such as glycerin and non-toxic glycols; and also liquid forms comprising pharmaceutically acceptable oils as a carrier, such as coconut oil, safflower oil and/or arachis oil.

[0029] The dosage form can be provided in a regimen as prescribed by a physician or veterinarian depending upon the needs of the patient. As an example, a suitable regimen may comprise the administration of one dosage unit (e.g. a tablet and/or capsule) two to four times per day according to the severity of the pain and/or inflammation and the responsiveness of the patient to the medication.

[0030] While formulation of the NSAID and acetaminophen has been described with regards to the combination of the compounds into a single formulation, it should also be understood that the compounds could be co-administered in separate preparations, such as a first unit dosage form comprising the NSAID, and a second unit dosage form suitable for co-administration with the first unit dosage form comprising the acetaminophen. Other methods or modes of co-administration not specifically described herein should also be understood to be encompassed by the instant invention.

EXAMPLES

[0031] Preferred embodiments of pharmaceutical compositions suitable for co-administration of the NSAID with the acetaminophen are described in more detail in the following examples. It should be understood that these examples are meant for illustrative purposes only, and are in no way intended to limit the scope of the invention thereto.

Example 1

[0032] Tables I-IV illustrate tablet formulations that provide for co-administration of the NSAID ibuprofen with acetaminophen. The tablets were prepared by mixing batches of the ingredients and compressing into the tablet unit dosage forms.

TABLE I

Tablet Ingredient	Amount
Ibuprofen	250 mg
Acetaminophen	250 mg
Avicel® PH-101 ^(a)	60.5 mg
Lactose hydrous USP	20 mg
Explotab® ^(b)	10 mg
Magnesium Stearate USP	2 mg

^(a)microcrystalline cellulose;

^(b)starch, glycolate USP

TABLE II

Tablet Ingredient	Amount
Ibuprofen	200 mg
Acetaminophen	250 mg
Avicel® PH-101 ^(a)	247 mg
Anhydrous Lactose USP	227 mg
Amberlite® IRP 88 ^(b)	16 mg
Magnesium Stearate USP	4 mg

^(a)microcrystalline cellulose;^(b)methacrylic acid and divinylbenzene polymer

TABLE III

Tablet Ingredient	Amount
Ibuprofen	400 mg
Acetaminophen	500 mg
Avicel® PH-101 ^(a)	228 mg
Anhydrous Lactose USP	100 mg
Amberlite® IRP 88 ^(b)	6 mg
Magnesium Stearate USP	3 mg

^(a)microcrystalline cellulose;^(b)methacrylic acid and divinylbenzene polymer

TABLE IV

Tablet Ingredient	Amount
Ibuprofen	800 mg
Acetaminophen	750 mg
Avicel® PH-101 ^(a)	60 mg
Anhydrous Lactose USP	100 mg
Explotab® ^(b)	10 mg
Talc USP	10 mg
Magnesium Stearate USP	3.5 mg

^(a)microcrystalline cellulose;^(b)starch, glycolate USP

Example 2

[0033] Table V illustrates capsule formulations 1-3 that provide for co-administration of the NSAID ibuprofen with the acetaminophen. The capsules were prepared by mixing batches of the ingredients and filling hard gelatin capsules with unit dosages of the mixture.

TABLE V

Ingredient	Formulation 1	Formulation 2	Formulation 3
Ibuprofen	200 mg	400 mg	800 mg
Acetaminophen	250 mg	500 mg	750 mg
Lactose hydrous USP	61.5 mg	163 mg	190 mg
Maize starch dried USP	20 mg	20 mg	20 mg
Talc USP	10 mg	20 mg	10 mg
Magnesium stearate	1 mg	1 mg	1 mg

Example 5

[0034] In this example, a method of preparing capsule formulations for the co-administration of ibuprofen and acetaminophen is described. A batch of the formulation is prepared by providing 20 grams of ibuprofen, USP powder, 25 grams of acetaminophen, USP powder, and 13.7 grams of lactose monohydrate spray dried powder. The ingredients are

combined in a mortar using the principles of geometric dilution, and triturated well to reduce particle size. Once the ingredients have been combined and reduced to the desired particle size, the mixture is poured evenly into 100 separate capsules, resulting in capsule unit dosage forms each having 200 mg of ibuprofen and 250 mg of acetaminophen.

Example 6

[0035] In this example, a method of preparing yet another capsule formulation for the co-administration of ibuprofen and acetaminophen is described. A batch of the formulation is prepared by providing 20 grams of ibuprofen, USP powder, 20 grams of acetaminophen, USP powder, 6.7667 grams of lactose monohydrate spray dried powder, and 0.6 grams of riboflavin (vitamin B2), USP powder. The ingredients are combined in a mortar using the principles of geometric dilution, and triturated well to reduce particle size. Once the ingredients have been combined and reduced to the desired particle size, the mixture is poured evenly into 100 separate capsules, resulting in capsule unit dosage forms each having 200 mg of ibuprofen and 200 mg of acetaminophen.

[0036] Additional modifications and improvements of the present invention may also be apparent to those of ordinary skill in the art. Thus, the particular combination of compounds and methods of administration described and illustrated herein is intended to represent only certain embodiments of the present invention, and is not intended to serve as limitations of alternative devices and methods within the spirit and scope of the invention. Along these lines, it should be understood that other combinations of NSAIDs other than those specifically described can also be used. Also, a pharmaceutical composition used for co-administration of the agents may take any of a variety of dosage forms that are known or later developed in the art. Also, it should be understood that different dosages and/or ratios of the NSAID and acetaminophen other than those specified may be used depending on the nature and synergistic potential with acetaminophen of each particular NSAID being used.

What is claimed is:

1. A pharmaceutical composition for the treatment of pain and inflammation with reduced gastrointestinal irritation, the composition comprising:

- (a) a therapeutically effective amount of at least one non-steroidal anti-inflammatory (NSAID) agent; and
- (b) a therapeutically effective amount of acetaminophen or a pharmaceutically acceptable salt thereof,

wherein a ratio of the non-steroidal anti-inflammatory agent to acetaminophen or pharmaceutically acceptable salt thereof in the composition is within a range that provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by the administration of the non-steroidal anti-inflammatory agent or acetaminophen or pharmaceutically acceptable salt thereof alone.

2. The pharmaceutical composition of claim 1 wherein the non-steroidal anti-inflammatory agent comprises at least one of diclofenac, etodolac, fenoprofen, ibuprofen, indomethacin, ketoprofen, nabumetome, naproxen, oxaprozin, sulindac, tolmetin, and pharmaceutically acceptable salts thereof.

3. The pharmaceutical composition of claim 2 wherein the non-steroidal anti-inflammatory agent comprises ibuprofen or a pharmaceutically acceptable salt thereof.

4. The pharmaceutical composition of claim 1 comprising the non-steroidal anti-inflammatory agent and acetaminophen or pharmaceutically acceptable salt thereof in relative amounts of from about one part by weight of the non-steroidal

anti-inflammatory agent and from about one-fifth to about one parts by weight of the acetaminophen or pharmaceutically acceptable salt thereof.

5. The pharmaceutical composition of claim 4 comprising the non-steroidal anti-inflammatory agent and acetaminophen or pharmaceutically acceptable salt thereof in relative amounts of from about one part by weight of the non-steroidal anti-inflammatory agent and from about one-half to about one parts by weight of the acetaminophen or pharmaceutically acceptable salt thereof.

6. The pharmaceutical composition of claim 1 comprising from about 100 mg to about 800 mg of ibuprofen or a pharmaceutically acceptable salt thereof, and from about 250 mg to about 750 mg of acetaminophen or a pharmaceutically acceptable salt thereof.

7. The pharmaceutical composition of claim 6 comprising from about 200 mg to about 400 mg of ibuprofen or a pharmaceutically acceptable salt thereof, and about 250 mg of acetaminophen or a pharmaceutically acceptable salt thereof.

8. The pharmaceutical composition of claim 1, wherein the composition is in a dosage form that comprises at least one of oral, buccal, parenteral, topical, transdermal, rectal, intravenous, intraperitoneal and inhalable form.

9. The pharmaceutical composition of claim 8 wherein the dosage form comprises from 0.03% to 99% by weight of the non-steroidal anti-inflammatory agent and acetaminophen or pharmaceutically acceptable salt thereof.

10. The pharmaceutical composition of claim 8 wherein the composition is in a solid dosage form, and comprises a pharmaceutically acceptable carrier comprising at least one of calcium phosphate, magnesium stearate, talc, sugars, hydrous lactose, anhydrous lactose, ribose, dextrin, starch, gelatin, cellulose, methyl cellulose, carboxymethyl cellulose, microcrystalline cellulose, starch glycolate, polyvinylpyrrolidone, polymers of methacrylic acid and divinylbenzene, waxes and ion exchange resins.

11. The pharmaceutical composition of claim 10 wherein the solid dosage form comprises at least one of a powder, granules, tablet, capsule, suppository and pessary.

12. A method for treating at least one of pain and inflammation in a patient in need thereof with reduced gastrointestinal irritation, the method comprising:

administering to said patient:

- (i) a therapeutically effective amount of at least one non-steroidal anti-inflammatory (NSAID) agent; and
- (ii) a therapeutically effective amount of acetaminophen or a pharmaceutically acceptable salt thereof,

wherein the ratio of the non-steroidal anti-inflammatory agent to acetaminophen or pharmaceutically acceptable salt thereof is in a range that provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by administration of the non-steroidal anti-inflammatory agent or acetaminophen or pharmaceutically acceptable salt thereof alone.

13. The method of claim 12, wherein the patient is suffering from at least one of rheumatoid arthritis, Still's disease, osteoarthritis, other arthritic conditions, pain associated with

musculo-skeletal injury, soft tissue injury, dental pain, post-operative pain, post partum pain, surgical pain, dysmenorrhea, migraine, tension headache, sinus headache and neuralgia.

14. The method of claim 12, wherein the non-steroidal anti-inflammatory agent comprises at least one of diclofenac, etodolac, fenoprofen, ibuprofen, indomethacin, ketoprofen, nabumetone, naproxen, oxaprozin, sulindac, tolmetin, and pharmaceutically acceptable salts thereof.

15. The method of claim 14, wherein the pharmaceutical composition comprises a non-steroidal anti-inflammatory agent that is ibuprofen or a pharmaceutically acceptable salt thereof.

16. The method of claim 12 comprising administering the non-steroidal anti-inflammatory agent and acetaminophen or pharmaceutically acceptable salt thereof in relative amounts of from about one part by weight of the non-steroidal anti-inflammatory agent and from about one-fifth to about one parts by weight of the acetaminophen or pharmaceutically acceptable salt thereof.

17. The method of claim 16 comprising administering from about 100 mg to about 800 mg of ibuprofen or a pharmaceutically acceptable salt thereof, and from about 250 mg to about 750 mg of acetaminophen or a pharmaceutically acceptable salt thereof.

18. The method of claim 17 comprising administering from about 200 mg to about 400 mg of ibuprofen or a pharmaceutically acceptable salt thereof, and about 250 mg of acetaminophen or a pharmaceutically acceptable salt thereof.

19. The method of claim 12 comprising administering the NSAID and acetaminophen or pharmaceutically acceptable salt thereof by at least one of oral, buccal, parenteral, topical, transdermal, rectal, intravenous, intraperitoneal and inhalable route.

20. A pharmaceutical composition for the treatment of pain and inflammation with reduced gastrointestinal irritation, the composition comprising:

- (a) a non-steroidal anti-inflammatory agent (NSAID) comprising ibuprofen or a pharmaceutically acceptable salt thereof in an amount of from about 100 mg to about 800 mg; and
- (b) acetaminophen or a pharmaceutically acceptable salt thereof in an amount of from about 250 mg to about 750 mg,

wherein a ratio of the non-steroidal anti-inflammatory agent to the acetaminophen or pharmaceutically acceptable salt thereof is within a range of from about one part by weight of the non-steroidal anti-inflammatory agent to about one-fifth to about one parts by weight of the acetaminophen or pharmaceutically acceptable salt thereof, and wherein the composition provides greater pain relief and reduction of inflammation with less gastrointestinal irritation than that obtainable by administration of the non-steroidal anti-inflammatory agent or acetaminophen or pharmaceutically acceptable salt thereof alone.

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