(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 September 2009 (17.09.2009)

PCT

(10) International Publication Number
WO 2009/113086 A2

(51) International Patent Classification:
A61K 9/48 (2006.01) *A61K 31/192* (2006.01)

(21) International Application Number:
PCT/IN2009/000010

(22) International Filing Date:
5 January 2009 (05.01.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
45/MUM/2008 7 January 2008 (07.01.2008) IN

(71) Applicant *(for all designated States except US)*: **ALKEM LABORATORIES LTD.** [IN/IN]; Devashish, Alkem House, Senapati Bapat Marg, Lower Parel, Mumbai 400 013, Maharashtra (IN).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **VIJAY, V.** [IN/IN]; House No. 10-11, Yadav Nagar, Kodad, Nalgonda (Dist.) 508 206, Andra Pradesh (IN). **RAGHUPATI, Srinivas** [IN/IN]; Plot #22, A-Wing #402, Sai Savli Apartment, Sector 19, Kharghar, Navi Mumbai (IN). **PRASAD, M., Krishna** [IN/IN]; 7-4-2, Ferozguda, Bowenpalli (PO), Secundrabad 500 011, AP (IN). **SATYANARAYANA, V.** [IN/IN]; 1004, Iris, Kesar Garden, Sector 20, Kharghar, Navi Mumbai 410 210, Maharashtra (IN). **RAMPAL, Ashok** [IN/IN]; C-943, Sushant Lok, -1, Gurgaon 122 002, Haryana (IN).

(74) Agent: **KHER, SANJAY**; Clover Consulting, Clover House, 176-A, Vaishali, Sir Bhalchandra Road, Hindu Colony, Dadar, Mumbai 400 014 (IN).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

WO 2009/113086 A2

(54) **Title**: IBUPROFEN LIQUID FILL FORMULATION, DOSAGE FORM THEREOF AND A PROCESS FOR ITS PREPARATION

(57) **Abstract**: The present invention relates to an ibuprofen liquid fill formulation, wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0 1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

IBUPROFEN LIQUID FILL FORMULATION, DOSAGE FORM THEREOF AND A PROCESS FOR ITS PREPARATION

The present invention relates to oral compositions of ibuprofen. More specifically the present invention relates to oral compositions of ibuprofen liquid fill formulations, dosage forms thereof and process for their preparation.

BACKGROUND OF THE INVENTION

Soft gelatin capsules has been around in the pharmaceutical industry for many years and have become increasingly important as a medical dosage form since it became feasible, in the 1930's, to manufacture them by making and filling the capsules in one operation. A soft gelatin capsule, also called softgel is a solid capsule (outer shell) surrounding a liquid or semi solid center (inner fill). An active ingredient can be incorporated into the outer shell, the inner fill, or both. Compared to other medical dosage forms soft gelatin capsules show many advantages like ease of use; easy of swallowing; lack of obnoxious taste; convenience of unit dose delivery; tamper-proof nature; versatile wide variety of colors, shapes, and sizes; ability to accommodate a wide variety of therapeutic compounds filled as a semi-solid, liquid, gel or paste; possible use as immediate or delayed drug delivery; and possible usage to improve bioavailability of therapeutic compounds by delivering the therapeutic compounds in solution or other absorption enhancing media.

Soft gelatin capsules offer the possibility of delivering a liquid in a solid oral dosage form. The soft gelatin capsules can therefore contain the active ingredient in solution, suspension or emulsion, which will inherently lead to better absorption of the active ingredient as compared with delivery in a tablet or as a powder. Softgels are therefore the ideal solution and sometimes the only solution for delivery of compounds with poor oral bioavailability. Other properties that make softgels a useful and frequently applied dosage form include their aesthetic properties and 'swallowability', their tamper-resistance, their protection of the

active ingredient from light and oxidation, their taste-masking of ingredients and their masking of unpleasant odours of ingredients.

Soft gelatin technology can be used for liquid and suspension fills encapsulated with a compatible gelatin shell formulation for the insoluble compounds, highly potent compounds, oxygen-sensitive materials, taste masking products, topical applications etc.

Ibuprofen is generally known as non steroidal anti-inflammatory substance having analgesic, anti-inflammatory and antipyretic action.

United States Patent No. 5,071,643 and 5,360,615 disclose a pharmaceutically acceptable highly concentrated solution of an acidic pharmaceutical agent suitable for filling softgels or for two-piece encapsulation or for tablet formation for subsequent oral administration, comprising the acidic pharmaceutical agent and a solvent system, the solvent system comprising 10% to 80% polyethylene glycol by weight of the solvent system, 1% to 20% water by weight of the solvent system and a hydroxide species such as potassium hydroxide partially ionizing the acidic pharmaceutical agent such that the acidic pharmaceutical agent is present in a dissolved state in the solution as both a free acid and a cationic salt in a total amount of 20% to 80% by weight of the solution. The patents further exemplify the preparation of liquid fill compositions by dispersing the acidic pharmaceutical agent in polyethylene glycol or polyethylene glycol and glycerin or polyethylene glycol and polyvinylpyrrolidone or polyethylene glycol, glycerin, and polyvinylpyrrolidone. Aqueous solutions of hydroxide were then added and the mixtures were warmed to 60° C and permitted to cool to the required temperature, (room temperature or 4° C.), and occasionally mixed for the next 2-7 days.

Though the prior art composition disclosed in United States Patent No. 5,071,643 and 5,360,615 is of immense value for liquid fill compositions of acidic drugs like ibuprofen, the process of preparation of these formulations as given in the prior art is too time consuming. It would be desirable to have liquid fill compositions of ibuprofen which can be quickly

prepared. We have surprisingly found that when ibuprofen of a particular particle size is used, the process time of preparing the liquid fill composition can be drastically reduced.

OBJECT OF THE INVENTION

It is the object of the present invention to provide an ibuprofen liquid fill formulation, which can be prepared with a reduced process time as compared to prior art process.

It is the object of the present invention to provide an ibuprofen dosage form comprising a drug delivery device and liquid fill formulation, wherein the said liquid fill can be prepared with a reduced process time as compared to prior art process.

It is the object of the present invention to provide an ibuprofen capsule comprising a liquid fill wherein the said liquid fill can be prepared with a reduced process time as compared to prior art process.

It is the object of the present invention to provide a process of preparing ibuprofen liquid fill formulation, wherein the said liquid fill can be prepared with a reduced process time as compared to prior art process.

It is the object of the present invention to provide a process of preparing an ibuprofen dosage form comprising preparing a liquid fill formulation in a reduced process time as compared to prior art process, and incorporating the said liquid fill formulation in a drug delivery device.

At least one of the preceding objects is met, in whole or in part, by the present invention, in which is provided an ibuprofen liquid fill formulation, wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

SUMMARY OF THE INVENTION

According to one aspect of the present invention, an ibuprofen liquid fill formulation is provided, wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

According to another aspect of the present invention, ibuprofen dosage form comprising a drug delivery device and liquid fill formulation is provided wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

According to another aspect of the present invention, ibuprofen capsule is provided comprising a liquid fill comprising ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

According to another aspect of the present invention, a process of preparing ibuprofen liquid fill formulation comprising mixing ingredients comprising ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species is provided.

According to another aspect of the present invention, a process of preparing an ibuprofen dosage form comprising mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system

comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species to form a liquid fill formulation, and incorporating the said liquid fill formulation in a drug delivery device, is provided.

The invention may be summarized as given below:

A. An ibuprofen liquid fill formulation, wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

B. An ibuprofen liquid fill formulation as in A above, wherein polyethylene glycol has an average molecular weight from about 200 to about 100,000.

C. An ibuprofen liquid fill formulation as in A above, wherein hydroxyl ion source is selected from the group comprising sodium hydroxide, ammonium hydroxide, potassium hydroxide and the like or a mixture thereof.

D. An ibuprofen dosage form comprising a drug delivery device and the ibuprofen liquid fill formulation as in A above.

E. An ibuprofen dosage form as in D above, wherein the drug delivery device is a capsule.

F. An ibuprofen dosage form as in E above, wherein said capsule comprises a soft gelatin capsule.

G. An ibuprofen dosage form as in E above, wherein said capsule comprises a hard gelatin capsule.

H. A process of preparing an ibuprofen liquid fill formulation comprising mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

I. A process of preparing an ibuprofen dosage form comprising mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species to form a liquid fill formulation wherein the said liquid fill formulation is incorporated in a drug delivery device.

J. The process as in I above, wherein the drug delivery device is a capsule.

DETAILED DESCRIPTION OF THE INVENTION

Before the present formulations and methods are described, it is to be understood that this invention is not limited to particular compounds, formulas or steps described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

Though the prior art composition disclosed in United States Patent No. 5,071,643 and 5,360,615 is of immense value for liquid fill compositions of acidic drugs like ibuprofen, the process of preparation of these formulations as given in the prior art is too time consuming. This invention is based on the surprising finding that when ibuprofen of a particular particle size is used, the process time of preparing the liquid fill composition is drastically reduced.

The present invention relates to an ibuprofen liquid fill formulation, wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of

the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

The present invention also relates to an ibuprofen dosage form comprising a drug delivery device and liquid fill formulation, wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

The present invention also relates to an ibuprofen capsule comprising a liquid fill comprising ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

The present invention also relates to a process of preparing ibuprofen liquid fill formulation comprising mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

The present invention also relates to a process of preparing an ibuprofen dosage form comprising mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species to form a liquid fill formulation, and incorporating the said liquid fill formulation in a drug delivery device.

As used herein, the term "dosage form" is intended to encompass any drug delivery device which can be used to incorporate the ibuprofen liquid fill formulation of the invention. Any drug delivery device known in the art may be used but capsules are the preferred drug delivery devices.

As used herein, the term "capsule" is intended to encompass all kinds of capsules such as soft gelatin capsules and hard gelatin capsules which employ gelatin or gelatin- like casing. Numerous casing materials have been proposed for soft capsules including gums, carrageenans, hydroxypropylated starches, celluloses, and the like. The capsules may be two piece capsule or a one-piece, hermetically sealed capsule, which can be made by techniques known to the person skilled in the art.

The present invention provides a dosage form of an anti-inflammatory therapeutic agent like ibuprofen. The ibuprofen is used in the liquid fill formulation of the dosage form in amounts ranging from about 20% w/w to about 70% w/w. It is preferred that the ibuprofen in the liquid fill formulation is used in amounts ranging from about 30% w/w to about 50% w/w. In a preferred embodiment, the ibuprofen is used in amounts of about 200mg. The ibuprofen used in the liquid fill formulation of the present invention is of a particle size such that 50% of the particles are not more than 50 microns and/or 90% of the particles are not more than 100 microns, when determined by Malvern analyzer with dry dispersion technique.

The present invention provides a liquid fill formulation comprising a solvent system comprising polyethylene glycol, water and hydroxide species.

The present invention uses polyethylene glycol (PEG) as a part of the solvent system, preferably having an average molecular weight between about 200-100,000, and most preferably having an average molecular weight between about 400-600 for liquid fills, between about 800-10,000 for semi-solid fills, and between 10,000-100,000 for solid fills. Non-ionized acidic pharmaceutical agents have some solubility in polyethylene glycol, utilizing the solvents hydrophobic binding sites. However, this solubility alone is insufficient to produce a highly concentrated solution which would permit encapsulation of a unit dose in

a softgel that would be small enough to permit easy swallowing. The polyethylene glycol may be used in amounts ranging from about 1% w/w to about 80% w/w polyethylene glycol,

The present invention may optionally use a hydroxyl ion source known in the art, in the liquid fill formulation of the dosage form of the invention. The hydroxyl ion source may be preferably selected from the group comprising of sodium hydroxide, ammonium hydroxide, potassium hydroxide and the like or a mixture thereof. The hydroxyl ion source may be used in amounts ranging from about 0.1% w/w to about 20% w/w. Potassium hydroxide is a preferred hydroxyl ion source in the composition of this invention. The potassium hydroxide may be used in amounts ranging from about 0.1% w/w to about 20% w/w. The potassium hydroxide is preferably used in amounts ranging from about 1% w/w to about 5% w/w.

An aqueous solution known in the art may be optionally used as a vehicle in the liquid fill formulation of the dosage form of the invention. It is preferred that the aqueous solution is purified water. The aqueous solution may be used in amounts ranging from about 0.1% w/w to about 15% w/w.

The liquid fill formulation of the dosage form of the invention may have other excipients known in the art such as propylene glycol, ethanol, wetting agents such as Tween 80 and the like.

The liquid fill formulation is encapsulated or incorporated into drug delivery device to form the dosage form of the invention. The drug delivery device is preferably a capsule dosage form. The capsule may be a soft gelatin capsule or a hard gelatin capsule. The hard gelatin capsule can be a two-piece, standard gelatin capsule which typically includes a first capsule half and a second capsule half which is well known to those of ordinary skill in the art. The soft gelatin capsule can be a two-piece capsule wherein the two parts are sealed together or a one-piece, hermetically sealed capsule. More preferably, the drug delivery device is a soft gelatin capsule which is a one-piece, hermetically sealed gelatin based capsule which can be made by techniques known to those skilled in the art. However, the soft gelatin capsule is preferred to the conventional two-piece type capsule as the soft gelatin capsule does not

require any additional sealing of the capsule halves as would be required with the liquid filled two-piece type capsule, and commensurately, is less prone to deliberate tampering or contamination. The soft gelatin capsule includes a plasticizer to control the softness and flexibility of the sheath, water, and optionally, other additives such as flavorants, colorants, opacifiers, etc. The soft gelatin capsules may be produced in a known manner with a rotary die process in which a molten mass of a gelatin sheath formulation is fed from a reservoir onto drums to form two spaced sheets or ribbons of gelatin in a semi-molten sate. These ribbons are fed around rollers and brought together at convergent angle into the nip of a pair of roller dies that include opposed die cavities. A fill formulation to be encapsulated is fed into the wedge-shaped joinder of the ribbons. The gelatin ribbons are continuously conveyed between the dies, with portions of the fill formulation being trapped between the sheets inside the die cavities. The sheets are then pressed together, and severed around each die so that opposed edges of the sheet flow together to form a continuous gelatin sheath around the entrapped therapeutic agent. The part of the gelatin sheet that is severed from the segments forming the capsules is then collected for recycling, and the soft capsules are dried. Various gelatin capsule formulations known in the prior art may be used to encapsulate the liquid fill formulations of the present invention. For example, suitable gelatin capsule may include from about 30% w/w to about 50% w/w gelatin; about 15% w/w to about 40% w/w of one or more plasticizer; and from 25% w/w to about 50% w/w of water. These formulations when formed into capsules and dried will result in capsule sheaths. The gelatin will normally have a bloom in the rage of about 150 to about 275, and may be Type A or B gelatins or mixture thereof. The sheath plasticizer may be selected from sorbitol, sorbitol special (mixture of sorbital and sorbitan), maltitol or a mixture thereof. The gelatin capsule formulations may also contain other ingredients, such as taste modifiers, coloring agents, and moisture retaining agents.

Typically the process of preparing ibuprofen liquid fill formulation comprises mixing ingredients comprising ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

Typically the process of preparing an ibuprofen dosage form comprises mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species to form a liquid fill formulation, and incorporating the said liquid fill formulation in a drug delivery device.

According to another aspect, the present invention relates to methods of treating pain, inflammation, fever and other related such conditions. The methods comprise administering to the patient a therapeutically effective amount of a composition according to the present invention. The frequency and amount of dosage will be determined by the clinician based on various clinical factors. The methods will typically comprise administration of the unit dosage form of the present invention to the patient or the person in need thereof. The present invention is further directed to the use of a therapeutically effective amount of the compositions as described for the manufacture of medicament for treating pain, inflammation, fever and other related such conditions.

According to still another aspect, the present invention relates to articles of manufacture which include compositions of the invention packaged for distribution in conjunction with labeling or package inserts describing indications and giving dosage instructions. Packaging can be accomplished by any conventional methods utilized in the pharmaceutical industry. Examples of such packaging are: individual packs or blister packs or bottles or enclosed in a box or container along with package inserts and the like. Other modes of packaging would be readily apparent to one skilled in the pharmaceutical packaging arts.

The following examples are intended to illustrate the scope of the present invention in all its aspects but not to limit it thereto.

EXAMPLE 1

The composition of ibuprofen dosage form as per the invention was prepared as described in Table 1 below.

Table 1

Name of Ingredients	Category	Quantity (mg/Cap)	% w/w
Liquid fill formulation			
Ibuprofen *50% of particles NMT 50 microns* *90% of particles NMT 100 microns*	Active	200	40.00
Polyethylene glycol 400/600	Vehicle	245	49.00
Potassium hydroxide	Solubiliser	20	4.00
Purified water	Vehicle	35	7.00
Total		**500**	**100**
Gel mass composition of the soft gelatin capsule			
Name of Ingredients	**Category**	**Kg/50 Kg gel mass**	**% w/w**
Gelatin Type A 200 bloom	Shell forming agent	21.0	42.02
Liquid Sorbitol (Polysorb)	Plasticizer	7.5	15.01
Maltitol Syrup (Maltisorb)	Plasticizer	2.5	5.00
FD&C Green # 3	Color	0.002	0.004
Purified water	Vehicle	18.98	37.98

Soft gelatin capsule preparation:

The gelatin was soaked in the mixture of maltisorb, polysorb and water for 1hr with the temperature of the mixture maintained at 4°C to 15°C. The soaked gelatin mass was transferred into a reactor and subjected to a melting process for 3-4 hrs with the temperature not exceeding more than 58°C. The gelatin mass was deaerated for 45 min. FD&C Green no # 3 was added in required quantity of water and added to the gelatin mass and mixed for 15 min. The above mass was deaerated for 45 min.

Liquid fill formulation

The required quantity of polyethylene glycol was taken in a SS Vessel and ibuprofen of the specified particle size was added to this vessel under stirring at room temperature. In another

vessel, potassium hydroxide was dissolved in required quantity of water. The solution of the potassium hydroxide was added to the mixture of ibuprofen and polyethylene glycol under stirring to get clear solution. The whole process of preparing the liquid fill formulation was completed in a time period of not more than 4 hours unlike the prior art processes which took days together.

The above liquid fill formulation was encapsulated using 10 minim oblong die role and subjected to drying to obtain ibuprofen soft gelatin capsules.

Although the invention has been described in terms of particular embodiments and applications, one of ordinary skill in the art, in light of this teaching, can generate additional embodiments and modifications without departing from the spirit of or exceeding the scope of the claimed invention. It should be emphasized that the above-described embodiments of the present invention, particularly any "preferred" embodiments, are merely possible examples of the invention of implementations, merely set forth for a clear understanding of the principles of the invention. Accordingly, it is to be understood that the drawings and descriptions herein are proffered by way of example to facilitate comprehension of the invention and should not be construed to limit the scope thereof.

Claims:

1. An ibuprofen liquid fill formulation, wherein the said liquid fill comprises ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

2. An ibuprofen liquid fill formulation according to claim 1, wherein polyethylene glycol has an average molecular weight from about 200 to about 100,000.

3. An ibuprofen liquid fill formulation according to claim 1, wherein hydroxyl ion source is selected from the group comprising sodium hydroxide, ammonium hydroxide, potassium hydroxide and the like or a mixture thereof.

4. An ibuprofen dosage form comprising a drug delivery device and the ibuprofen liquid fill formulation as claimed in claim 1.

5. An ibuprofen dosage form as claimed in claim 4, wherein the drug delivery device is a capsule.

6. An ibuprofen dosage form as claimed in claim 5, wherein said capsule comprises a soft gelatin capsule.

7. An ibuprofen dosage form as claimed in claim 5, wherein said capsule comprises a hard gelatin capsule.

8. A process of preparing an ibuprofen liquid fill formulation comprising mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w

polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species.

9. A process of preparing an ibuprofen dosage form comprising mixing ibuprofen with 50% of the particles not more than 50 microns and/or 90% of the particles not more than 100 microns, and a solvent system comprising about 1% w/w to about 80% w/w polyethylene glycol, about 0.1% w/w to about 15% w/w of water and about 0.1% w/w to about 20% w/w of hydroxide species to form a liquid fill formulation wherein the said liquid fill formulation is incorporated in a drug delivery device.

10. The process according to claim 9, wherein the drug delivery device is a capsule.