Development of Dry Emulsion formulation of Ibuprofen and its Characterization

By

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing a degree at Brac University.

2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.

4. I have acknowledged all main sources of help.

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Approval

The thesis titled "Development of Dry Emulsion formulation of Ibuprofen and its Characterization" submitted by Jamim Bhuiyan (ID 18346057) of Summer, 2018 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of pharmacy on 30th October,2022.

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Ethics Statement

The study does not involve any kind of animal or human trial.

Abstract

Ibuprofen (IBP) is a NSAID, falls under BCS class II drug having poor aqueous solubility (21 mg/L) that may limit its biopharmaceutical behavior in clinical application. The main purpose of this study is to develop dry emulsion formulation of ibuprofen (DE-IBP). DE-IBP was prepared by evaporating a liquid O/W emulsion containing ethyl acetate polymer, polyethylene oxide 600, and medium chain triglyceride as the emulsifying agents. Physicochemical properties of DE-IBP were evaluated using various analytical techniques. The results showed reduced particle size in DE-IBP as well as the crystalline nature of IBP has reduced significantly; which might be beneficial in enhancing the solubility of IBP compared to crystalline IBP. The dissolution studies in water showed improved dissolution of DE-IBP compared to crystalline IBP, with a quick onset of drug release followed by gradual dissolution. Therefore, DE-IBP could be a promising drug delivery strategy to improve the biopharmaceutical behaviors of IBP.

Dedication

To my parents and beloved teachers who made me into the person I am today.

Acknowledgement

I am grateful to almighty Allah for providing me the opportunity to work with such wonderful people from the school of pharmacy who have always been idealistic and encouraging throughout my journey.

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List of Acronyms

NSAID	Non-Steroidal Anti-inflammatory drug
IBP	Ibuprofen
DE-IBP	Dry Emulsion Ibuprofen
DSC	Differential scanning calorimetry
XRPD	X-ray powder diffraction
SEM	Scanning electron microscope
DLS	Dynamic light scattering
FT-IR	Fourier transport infrared spectroscopy

Chapter 1 Introduction

1.1 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used as analgesics and antipyretics (Gupta & Bah, 2016; Budoff, 1979). Primarily, NSAIDs are used to treat inflammatory disorders such as rheumatoid arthritis, osteoarthritis and menstrual cramps. Nowadays, NSAIDs are considered as widely used over the counter medication in the world which stand up for 5% of all prescribed medications (Tsutsumi et al., 2004). Before the discovery and development of NSAIDs around 500 BCE, Hippocrates mentioned in his writing about willow bark and leaves which can treat pain and fever. Since then, various chemists and scientists have worked tirelessly to produce these "wonder drugs". After the discovery of aspirin in 1897 by Felix Hoffman of the Bayer industry, pharmaceutical sector gave importance to NSAIDs (Montinari et al., 2019).

1.1.1 Classification

NSAIDs are usually classified based on their chemical properties; Figure 1 illustrates the chemical classification of NSAIDs. The majority of the well-known NSAIDs have been classified as the derivatives of acetic acid, salicylic acid, anthranilic acid, enolic acid, etc. Due to scientific advancement, classification of these drugs is now based on the selectivity for inhibition of cyclooxygenase enzymes that are their primary targets. Aspirin is a nonselective and celecoxib is cyclo-oxygenase 2 (COX-2) inhibitor. Again, NSAIDs are also classified according to their plasma half-life. Aspirin, diclofenac and IBP are short acting with a plasma half-life less than 6 hours. Naproxen and celecoxib are long acting with a plasma half-life greater than 10 hours (Bindu et al.,2020).

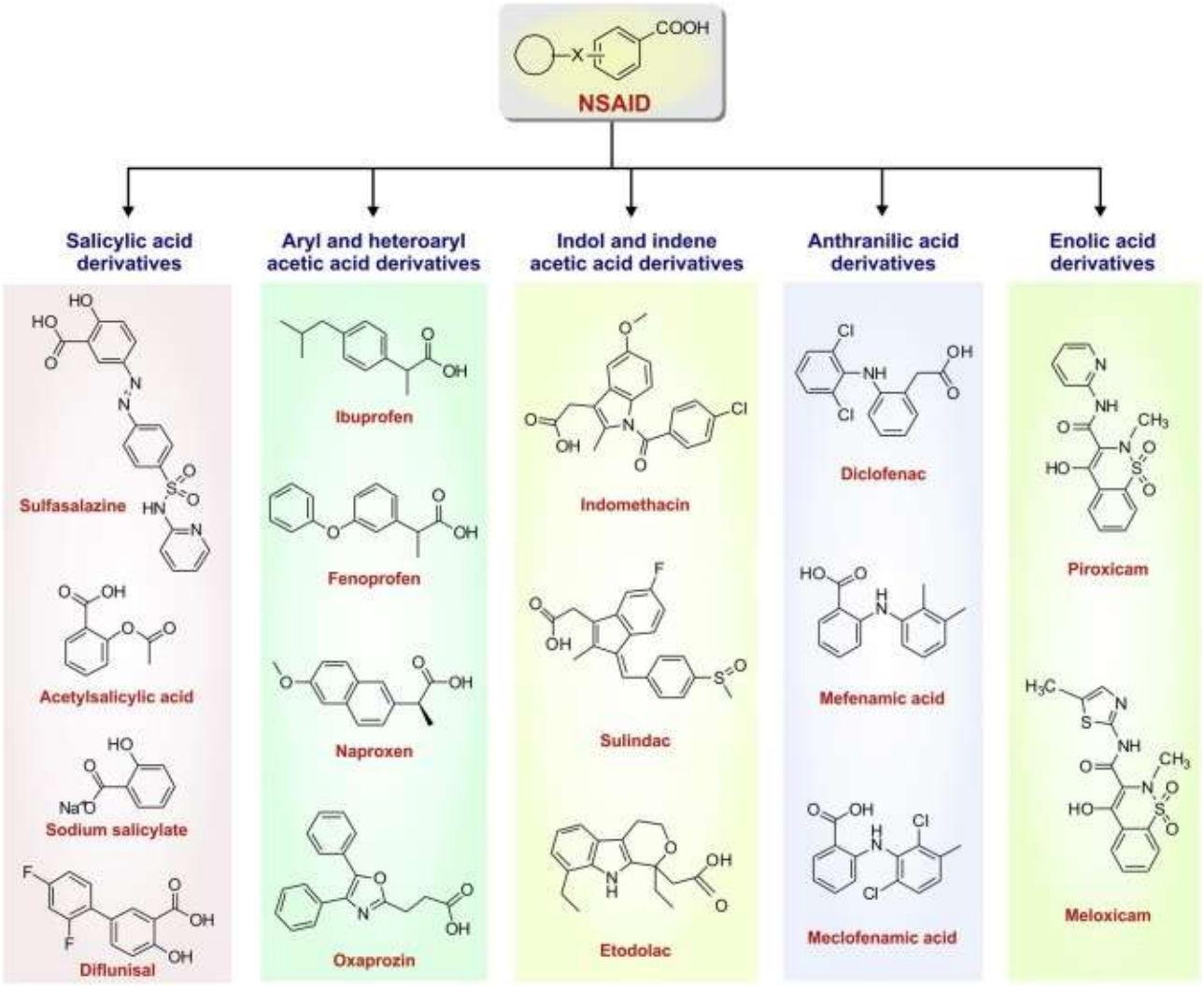

Figure 1: Chemical classification of NSAIDs.

1.1.3 Mechanism of action of NSAIDs

NSAIDs inhibit the enzyme COX which is important for converting arachidonic acid into prostacyclins, thromboxanes, and prostaglandins. Here, thromboxanes are important for platelet, adhesion, and prostaglandins are responsible for vasodilation, temperature increment in hypothalamus, anti-nociception. Among the two cyclooxygenase isoenzymes, cyclooxygenase 1

(COX-1) is constitutively expressed in the body and is important to maintain kidney function, platelet aggregation and gastrointestinal mucosa lining. Cyclooxygenase isoenzyme 2 (COX-2) is expressed while an inflammatory response occurs in the body. Mostly, NSAIDs are non-selective and inhibit both the cyclooxygenase isoenzymes but selective NSAIDs target and inhibit cyclooxygenase 2 (COX-2) so, they give therapeutic action without disturbing the gastric mucosa (Ghlichloo & Gerriets, 2022).

1.2 Effect of Solubility in Drug Development

1.2.1 Solubility

In order to get optimum drug concentration for desired pharmacological response, solubility is one of the most important factors. At the absorption site, all medication has to be in solution form for being absorbed. However, low water solubility is the main issue in developing formulations for new chemical entities as well as for generic development. Research says around 40% of the new chemical entities developed by the pharmaceutical industry are basically insoluble in water. Therefore, for formulation scientists, solubility is an obstacle. On the other hand, solubility usually happens in dynamic equilibrium which implies that it is the outcome of the opposing and simultaneous processes of dissolution and phase joining. When both processes occur at a constant rate, solubility is in equilibrium state (Savjani et al., 2012). The criteria that are set by United States Pharmacopeia (USP) for soluble drug products has been illustrated in table 1.

Table 1: Solubility criteria according to United States Pharmacopeia (USP).

Descriptive term	**Parts of solvent required for one part of solute**	**Solubility range (mg/mL)**	**Solubility assigned (mg/mL)**
Very soluble	< 1	≥ 1000	100 0
Freely soluble	From 1 to 10	100-1000	100
Soluble	From 10 to 30	33-100	33
Sparingly soluble	From 30 to 100	10-33	10
Slightly soluble	From 100 to 1000	1-10	1
Very slightly Soluble	From 1000 to 10,000	0.1-1	0.1
Practically insoluble	≥ 10,000	< 0.1	0.01

The biopharmaceutics Classification System (BCS) can be used as a guide to predict intestinal drug absorption that has been stated by the U.S. Food and Drug Administration. These drugs usually have four classes which are class I, class II, class III and class IV which correspondingly indicate high solubility and high permeability, low solubility and high permeability, high solubility and low permeability and low solubility and low permeability that has been shown in figure 2 (Absorption system, n.d.).

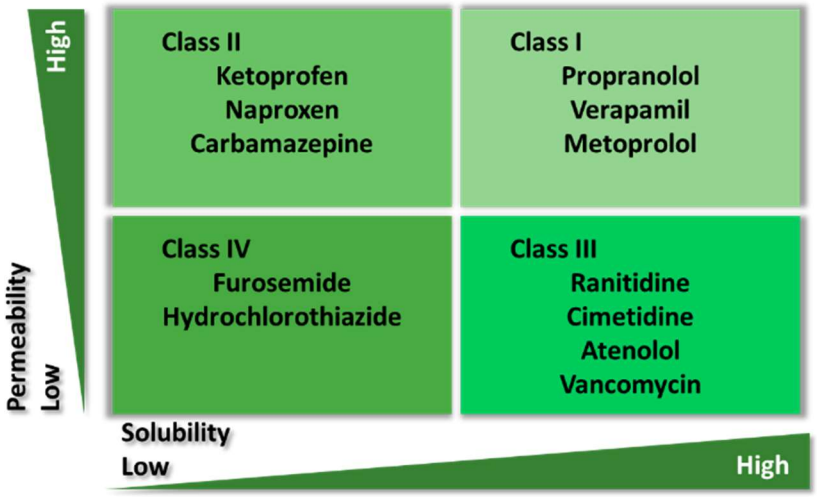

Figure 2: Biopharmaceutics Classification System (BCS).

1.2.2 Significance of solubility enhancement

The poor bioavailability is the main issue in the oral dosage form design. There are several variables such as drug permeability, aqueous solubility and dissolution rate which can affect oral bioavailability. The most common reason for low oral bioavailability is poor solubility. Solubility is one of the key factors in systemic circulation to reach the desire drug concentration and essential pharmacological response. Poorly soluble drugs when taken orally may require high dosages to attain desired therapeutic plasma concentration. Hence, low water solubility is the main challenge in formulating new chemical entities as well as generic development (Savjani et al., 2012).

1.2.3 Solubility enhancement techniques

There are several techniques to improve solubility. These are categorized into physical modification, chemical adaptation, and other techniques.

Physical modification: Micronization and nanosuspension are part of the particle size reduction technique. Furthermore, amorphous form, polymorphs and cryogenic techniquesknown for crystal habit alteration, solid dispersions, solid solutions, and drug dispersion ineutectic mixtures are some examples of drug crystallization processes.

Chemical modification: Buffer utilization, p^H change, derivatization, complexation, and salt production.

Miscellaneous techniques: Utilization of supercritical fluids, utilization of adjuvants such as surfactant, solubilizers, hydro-trophy, co-solvency, and novel excipients (Savjani et al.,2012).

1.2.3.1 Physical modification

Particle Size Reduction: As drug particles get smaller, the surface area to volume ratio rises which frequently has an intrinsic relationship with drug solubility. Increased solubility results from more contact between the surface area and the solvent. Thus, an effective, repeatable, and affordable method of improving solubility is thus made possible by particle size reduction. Another common method for reducing particle size is micronization. Micronization increases the drug's dissolution rate by increasing surface area. However, this does not result in an increase in equilibrium solubility. These drugs dissolve more quickly when their particle size is reduced which increases surface area.

Solid Dispersion: When active ingredient is dispersed in inert hydrophilic carrier matrix it is then termed as solid dispersion (Sinha et al.,2010). Polyvinyl pyrrolidone (Povidone, PVP),

polyethylene glycols (PEGs), and PlasdoneS630 are the most widely used hydrophilic carriers for solid dispersion (savjani et al.,2012).

Dry emulsion formulation of IBP (DE-IBP): When rehydrated, an O/W emulsion can be rebuilt from dry emulsions which are considered as lipid-based powder formulations (Onoue et al., 2012). Figure 3 illustrates that in dry form the lipid and the drug are separately present in formulation but when they are in the aqueous phase they are redispersed and oil in water emulsion is reconstituted.

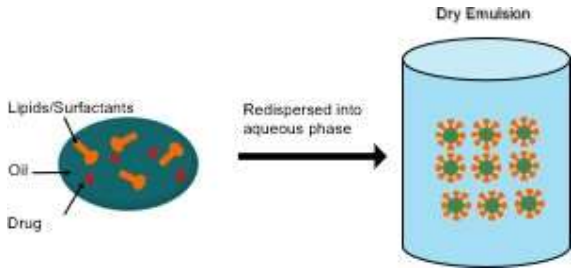

Figure 3: Redispersion of dry emulsion in the aqueous phase

Dry emulsion formulation work by providing improved bioavailability and they are more stable than other formulations of drugs. They are mainly prepared by drying the oil in water (o/w) emulsions with a solid carrier in aqueous phase and dry emulsion formulation can be prepared by lyophilization, spray drying, and rotary evaporator. We have used the rotary evaporator method in our research (Dange et al., 2015). It has been found that organic solvents and solubilizers used in liquid formulations like ethanol, castor oil create local irritation (Klyashchitsky & Owen, 1999). Besides, liquid state of emulsion formulation has several disadvantages such as few available dosages form choices, high manufacturing cost, also low stability (sato et al.,2015).

1.2.3.2 Chemical modification

***Salt Formation**:* Using salt formation technique, low water-soluble drugs' solubility can be improved. Additionally, as a function of pH, solubility is taken into account. The interrelationships between pH and solubility also reveal the counter ions which are needed to form salts, dissociation of salt into their free acid or base forms, dissolution behavior under various gastrointestinal tract pH conditions and whether common ions would affect salts' dissolution rate and solubility. Furthermore, for the selection of salt formulation techniques, drugs should have specific characteristics. Ionizable groups should be present in the salt forming drug to help with salt formation. The following criteria are used for the selection of counter ions.

a. Minimum difference between the counter ion and the drug should be 2-3pKa units.

b. Crystal lattice forces should be decreased by Counter ion.

c. FDA approval is required (Sarfraz et al.,2017).

Microemulsion: A microemulsion is an isotropic, thermodynamically stable transparent system that consists of water, surfactant and oil sometimes a co-surfactant that is utilized in different ratios (Sarfraz et al.,2017). Various drugs with poor water solubility have been made more soluble using microemulsions.

1.2.3.3 Miscellaneous techniques

Co-solvency: A drug that is poorly soluble in water can frequently have its solubility increased by adding a cosolvent which is a water-miscible solvent and in which the drug has strong solubility.

Supercritical fluid process: Another cutting-edge method that is frequently used to enhance the solubility of poorly water-soluble drugs is the supercritical fluid (SCF) process. Supercritical fluids can take on the characteristics of both a liquid and a gas because their pressure and temperature are above their critical pressure (Tp) and critical temperature (Tc).

Prodrug approach: Prodrug synthesis can be used to enhance physicochemical traits like compound lipophilicity and solubility. Additionally, this method also stops chemical degradation and presystemic drug metabolism.

Nanosuspension: These are solid colloidal dispersions with nanoscale particles (200 to 500 nm). Reducing the size of drugs improves their bioavailability and capacity to dissolve into water.

Cryogenic technologies: The use of cryogenic procedures in the pharmaceutical industry helps hydrophobic compounds to dissolve more readily because they knit together into nanoscale amorphous particles with large surface area and porosity at a lower temperature (Sarfraz et al.,2017).

1.3 Ibuprofen (IBP)

One of the safest and most potent NSAIDs available on the market is IBP (Gosh et al., 1998). In 1967, IBP was first introduced to humans as an anti-inflammatory drug in England and the United States respectively. The chemical structure of IBP is shown in Figure 4.

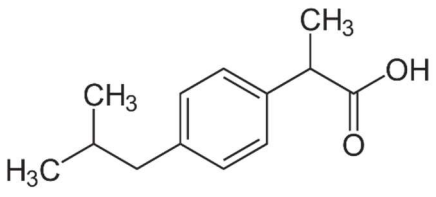

Figure 4: Ibuprofen (IBP)

It has distinct anti-inflammatory actions but much less detrimental effects on the stomach and has no impact on the adrenal-pituitary axis. In addition to treating gout syndrome, IBP is useful in treating rheumatoid arthritis and osteoarthritis (Thomas & Kantor, 2016). Further, IBP has demonstrated effectiveness in treating a variety of clinical problems including dental pain, soft tissue pain, dysmenorrhea, migraine, headache, fever, etc. For various therapeutics purposes, IBP's mechanism of action is well established. Furthermore, IBP inhibits COX-1 and COX-2 in a non-selective and reversible manner. Both COX-1 and COX-2 convert arachidonic acid into prostaglandins such as thromboxane and prostacyclin. IBP's antipyretic and analgesic effects are related to the inhibition of prostaglandins which plays a significant role in inflammation and pain sensation. Currently available dosage forms of IBP include tablets, capsules, gel formulations, injectables and metered dose inhalers. However, these have their limitations that have been demonstrated in table 2 (Irvine et al., 2017).

Table 2: Available dosage forms of IBP and their limitations

Dosage forms	**Limitations**
Oral IBP (Chewable tablets, oral suspension, capsules)	• 400 mg of IBP takes 45 minutes to give an analgesic effect that is unwanted for patients who need rapid action. • Drug is extensively metabolized in liver

Gel formulations IBP (Dermal and transdermal)	• Lack of analgesia with pH induced muscle pain because of drug clearance by plasma flow and lymphatic system • It is challenging to achieve high and prolonged permeation across skin barrier since it has poor skin permeability
Injectables of IBP(Intravenous)	• Difficult to formulate due to Low aqueous solubility • High manufacturing cost • Crystals formation after administration may generate emboli in blood vessels
Metered dose inhaler (Pulmonary delivery)	• Coordination between inhalation and drug actuation is important in order to deliver drug to deep lungs

1.4 Factors affecting bioavailability of IBP

There are several factors that affect the absorption of a drug inside the body including physicochemicalproperties like solubility, drug formulation, etc. Passive diffusion is a way of drug absorption from a highly concentrated drug area like the gastrointestinal tract to a low drug concentrated area like bloodcirculation. Passive diffusion is directly influenced by solubility. Hence, by improving the solubility, absorption and bioavailability of the drug can be readily

improved (Smith, 2019). Based on this concept, many modifications have been made to the IBP formulations shown (table 3) (Irvine et al., 2017).

Table 3: Modified formulations of available dosage forms of IBP

Dosage forms	**Modified formulations**
Oral IBP (Chewable tablets, oral suspension, liquid capsules)	• Gelatin capsules filled with solubilized IBP and salt conjugates to improve solubility • Mechanical micro-ionization • Self-emulsifying drug formulation • Use of surfactant • Block copolymers • Dendrimers • Lysinate salt form of IBP
Gel formulations IBP (Dermal and transdermal delivery)	• Liposomal IBP gel formulation with carbopol • Combination of phosphatidylcholine, cholesterol and dicetyl phosphate (7:3:1 molar ratio) as formulation • Nanoparticles and polymeric nanoparticles • Ethosomal gel with nano system had high bioavailability
Metered dose inhaler (Pulmonary delivery)	• IBP nanoparticles formulated by evaporation condensation technique • Spray drying technique to form dry emulsion • Nebulizer

1.5 Purpose of the Study

Although IBP is widely used NSAIDs but due to its low aqueous solubility it has limited therapeutic actions. Hence, the purpose of this research is to develop dry emulsion formulation of IBP that have improved biopharmaceutical behavior over conventional IBP. The objective is to increase the water solubility of IBP and hence, improve the physicochemical property of the drug.

Chapter 2 Materials and Method

2.1 Materials

IBP, kollisolv, and stearic acid have been collected from BASF, Dhaka, Bangladesh. Carbopol was collected from Evonik, Dhaka, Bangladesh and polyvinyl alcohol (PVA), polyethylene glycol (PEG) 600, aerosol 500 was collected from Beximco pharmaceutical Ltd., Dhaka, Bangladesh. All the materials and excipients used were of analytical grade.

2.2 Instrument

All the instruments that were used while performing the research has been mentioned in table 4.

Table 4: Specifications of instruments used in research

Instrument name	**Model**
UV-visible spectrophotometer	U-2910
Dissolution study	D8 USP Standard
Vortex mixture	VM-2000
Rotary evaporator	Heidolph, Gmbh
Digital analytical balance	PA213
Water bath	B120-DE
Vacuum drying oven	LVO-2030

Differential scanning calorimetry (DSC)	Q1000
X-ray powder diffraction (XRPD)	D8 ADVANCE
Scanning electron microscope (SEM)	VE-7800

2.3 Methodology

2.3.1 Construction of Calibration Curve of IBP

Preparation of stock solution required dissolving 10 mg of IBP (API) in sufficient quantity of pure methanol in a volumetric flux and the final volume was made to 100ml, hence the concentration of the stock solution was 0.1 mg/ml. Further, 1 ml of stock solution was diluted using distilled water to form primary solution of 10 µg/mL concentration. This primary solution was further diluted for preparation of solution with different concentrations of 5 µg/mL, 2.5 µg/mL and 1 µg/mL. The absorbance of the solutions was recorded in the UV-visible Spectrophotometer and were plotted against concentrations to construct calibration curve. Here, pure methanol was used as a blank.

2.3.2 Preparation of Dry Emulsion

The composition of the formulation is shown in table 5. The active pharmaceutical ingredient IBP was mixed with PVA, stearic acid, water and was kept in a water bath for around 30 minutes at 40º-50ºC. Again, carbopol and PEG600 was mixed with water and this mixture was added to the previous mixture. Further, kollisolv was added to the mixture and mixed in a vortex mixture for

30 minutes. Next, aerosil 500 was added and the formulation was placed in a rotary evaporator at 100 rpm by adding 2- 3 mL of ethanol at 45ºC for 2 hours and then placed in a dryer at 45ºC for 6 hours to get fine dry powder that has been demonstrated in figure 5. The resulting DE-IBP was found by crushing the dried particles with a mortar that was stored in a sealed container at ambient temperature away from sunlight.

Table 5: Composition of IBP loaded dry emulsion formulation

API & Excipients	**(w/w) %**	**Justification**
IBP	20	API
Ethyl acetate polymer (Carbopol® 971P NF)	20	Emulsifying agent
Polyvinyl Alcohol (PVA)	10	Stabilize the formulation
Polyethylene oxide 600 (Kollisolv® PEG 600)	15	Emulsifying agent
Stearic acid	10	Emulsion solubilizer
Medium chain triglyceride (Kollisolv® MCT 70)	25	Emulsifying agent
Aerosil 500	5	Emulsifying agent

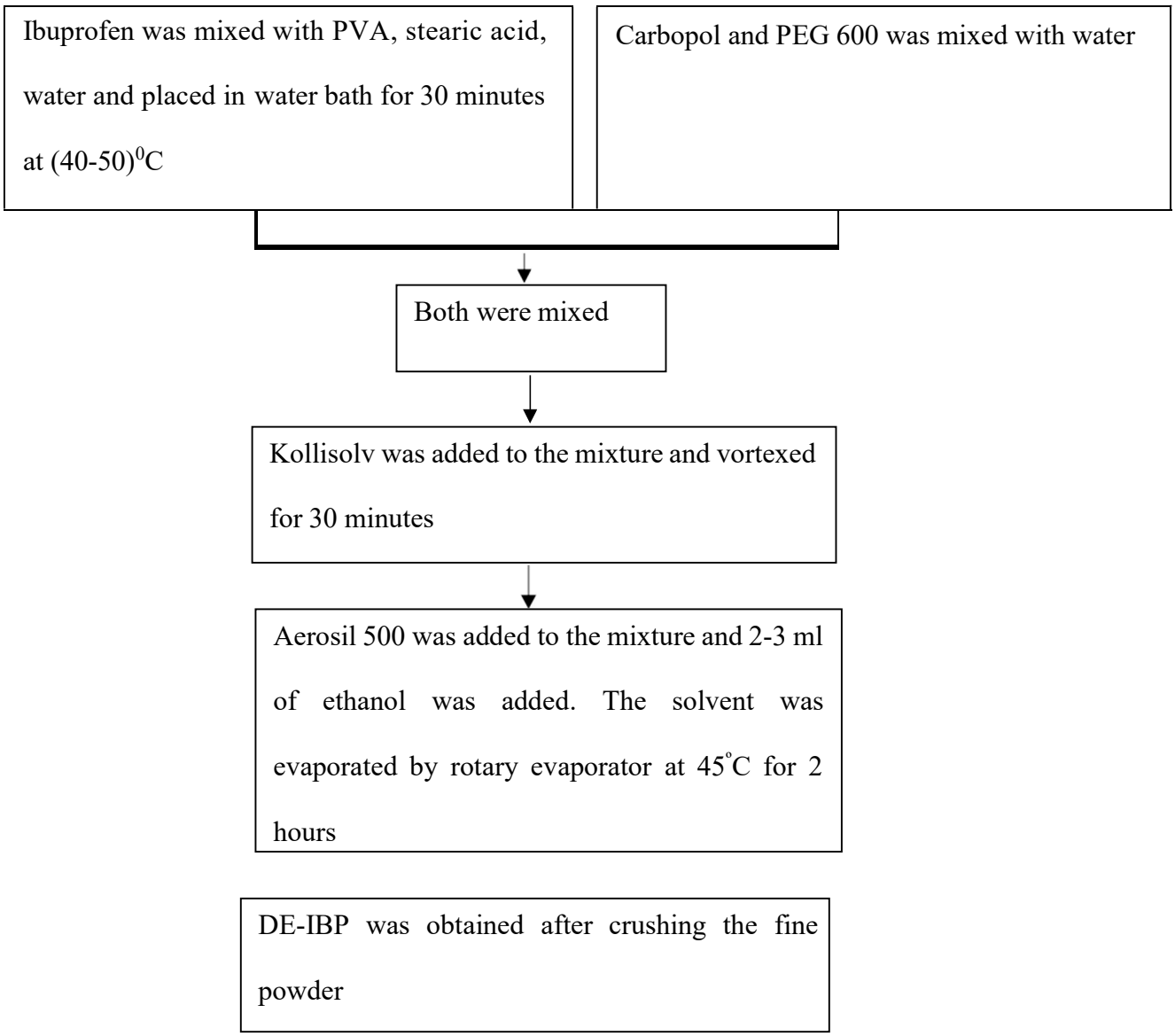

Figure 5: Flow chart for preparation of IBP loaded dry emulsion formulation

2.3.3 Dissolution Study

The DE-IBP (equivalent to 100 mg of IBP) had been added to a dissolution vessel. The dissolution study was carried out at temperature 37ºC by using USP paddle method and each vessel had 900 ml of distilled water rotating at 75 rpm. The time was recorded when paddles started to rotate. In an interval of 15 minutes, 30 minutes, 45 minutes, 60 minutes and 120 minutes, 10 ml of dissolution medium was withdrawn from each vessel and filtered. At the same time intervals, an equivalent volume of i.e., 10 ml of water was added in each vessel to maintain the original volume. Then, 2 ml of the filtered volume was taken and diluted 5 times using pure methanol. After that, the concentration of IBP-loaded dry emulsion was analyzed by a UV spectrophotometer. Here, at each time interval sample was collected thrice for each analysis.

2.4 Physicochemical Characterization

2.4.1 Particle Size Distribution

At a concentration of 0.1 mg/mL the formulations were suspended into distilled water, then they were measured in triplicate with dynamic light scattering (DLS) by using Zetasizer nano ZS (MALVERN, Worcestershire, U.K.) and these were performed at 25ºC and at a measurement angle of 90° (Sato et al., 2015).

2.4.2 Surface Morphology

To determine surface morphology microscopes like scanning electron microscopy (SEM) is used to visualize objects that cannot be seen in naked eye. A VE-7800 scanning electron microscope without Au or Pt coating was used to take SEM images of DE-IBP. Each sample was kept on a

sample holder made from aluminum which had double-sided carbon tape for SEM observation (Sato et al., 2015).

2.4.3 Differential Scanning Calorimetry (DSC)

DSC experiments were conducted using the DSC Q1000 and DSC thermograms were collected in an aluminum closed pan system which had a sample weight (ca. 3 mg) including a heating rate of 5°C/min and nitrogen purge at a rate of 70 mL/min. Furthermore, indium has been used to calibrate the temperature (5 mg, 99.999% pure, onset at 156.6°C) (Sato et al., 2015).

2.4.4 X-ray Powder Diffraction (XRPD)

The XRPD pattern was obtained from utilization of D8 ADVANCE which includes CuKα radiation produced at 40 mA and 35 kV. Data collected with a step size of 0.014º and a scanning speed of 4ºC/min (2θ) from 10º to 40º (Sato et al., 2015).

2.4.5 Fourier Transform Infrared Spectroscopy (FT-IR)

All the different polymers were analyzed by FT-IR. As different polymers or excipients have different infrared absorption spectrum they were checked for any interaction and compatibility with each other in the formulation (Arkin & Isaiah, 2013).

Chapter 3 Results and Discussion

3.1 Standardization of IBP

A linear relation has been observed between the concentration range from (1-10) µg/mL which have a correlation coefficient of (R^2) 0.9981 it is illustrated in figure 6.

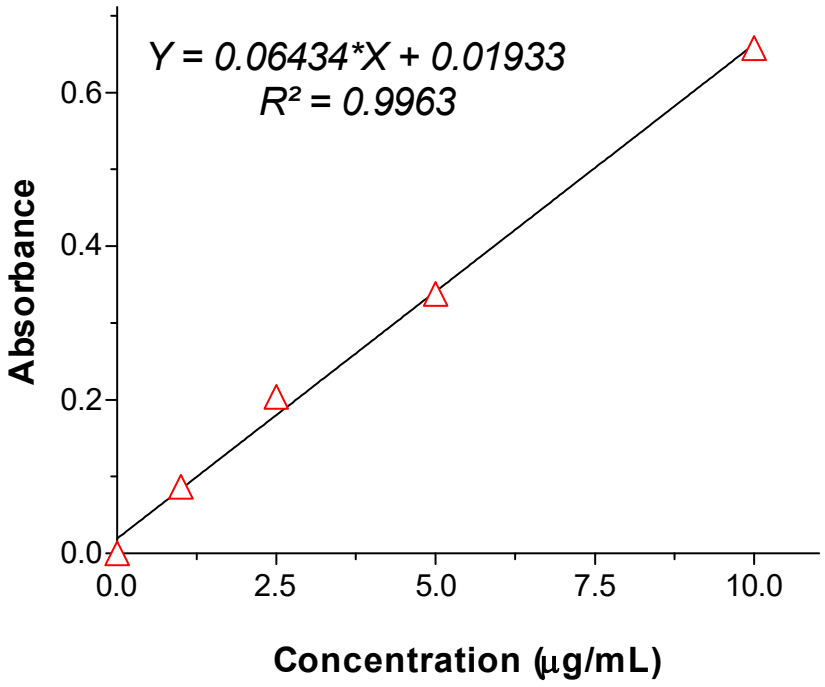

Figure 6: Calibration curve of IBP

3.2 Dissolution Study of DE-IBP

In vitro dissolution study of IBP was carried out at temperature 37ºC by using USP paddle and rotating with 75 rpm. Data represents mean and ±S.D. of 3 experiments. Released percentage of IBP verses time has been plotted in comparison with IBP to observe the dissolution rate of the DE-IBP in figure 7. At 15 minutes, approximately 39% DE-IBP was dissolved. Similarly, at the time period of 30 minutes, 45 minutes, 60 minutes and at 120 minutes DE-IBP showed approximately 37%, 42%, 45% and 50% release in comparison with non-modified IBP as given in figure 7. The prepared formulation gave a quick release of drug initially. Overall, the dissolution study showed a quicker onset of drug release in case of DE-IBP in comparison to that of non-modified IBP at 2hour period. Also, DE-IBP showed up to 50% release than IBP suggesting that DE-IBP would be a promising approach for improving the dissolution rate of IBP.

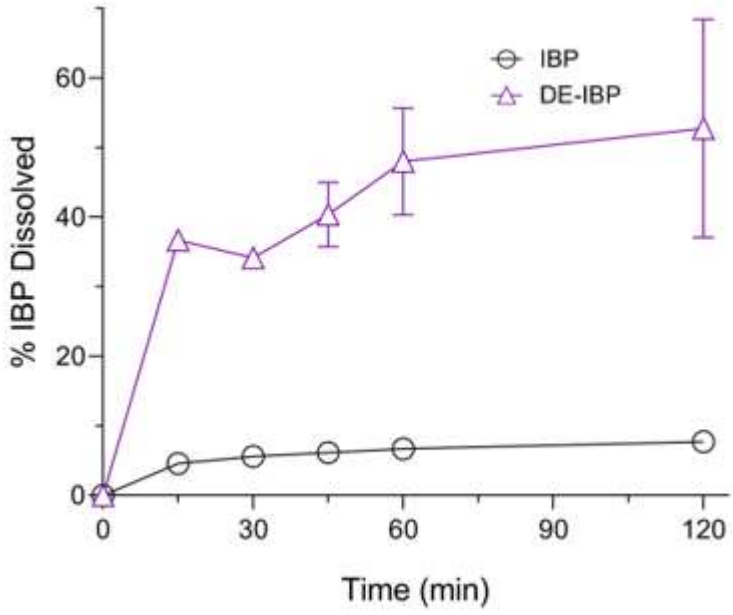

Figure 7: In vitro dissolution study of IBP and DE-IBP

3.3 Physicochemical Characterization of DE-IBP

3.3.1 Particle Size Distribution

Polydispersity index (PDI) typically represents the distribution of size populations within a particular sample and its numerical value ranges from 0.0 to 1.0. The closer to 0.0 it is an indication for a perfectly uniform sample with respect to the particle size and the closer to 1.0 that indicate for a highly polydisperse sample with multiple particle size populations (Danaei et al., 2018; Sarah & Clarke, 2013). In figure 8, D_{50}, mean particle size is 396 nm and Polydispersity index (PDI) is 0.331. Since, DE-IBP has polydispersity index is near 0 as shown in figure 8 and it forms a uniform distribution of particles in nano size in the aqueous media. Here, a dynamic light scattering (DLS) experiment was performed for the size measurement of the particles of the formulation. As, DE-IBP has reduced particle size, it will have increased aqueous solubility in comparison to IBP.

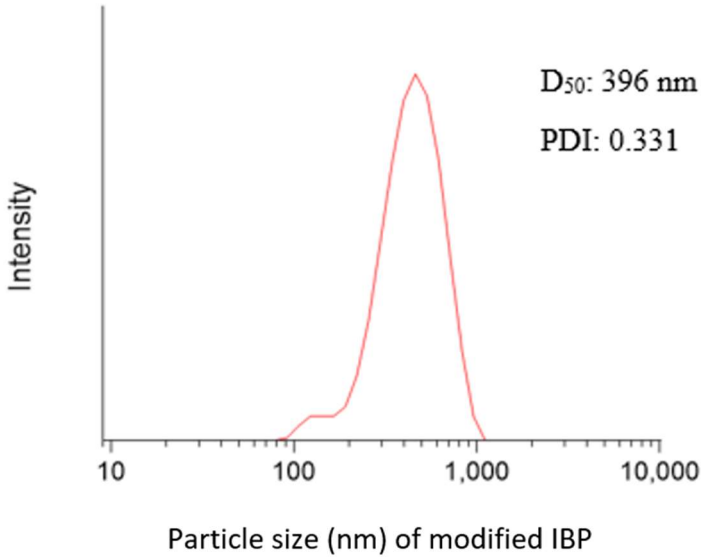

Figure 8: Particle size distribution of DE-IBP sample in water.

3.3.2 Surface Morphology

Scanning electron microscope (SEM) helps in the visualization of surface structure of IBP and DE-IBP. Figure 9 clearly illustrates that IBP has reduced surface area occupied but dry emulsion formulation has increased surface area. Each white bar represents 100 µm. Hence, DE-IBP have enhanced solubility due to increase surface area in comparison with IBP.

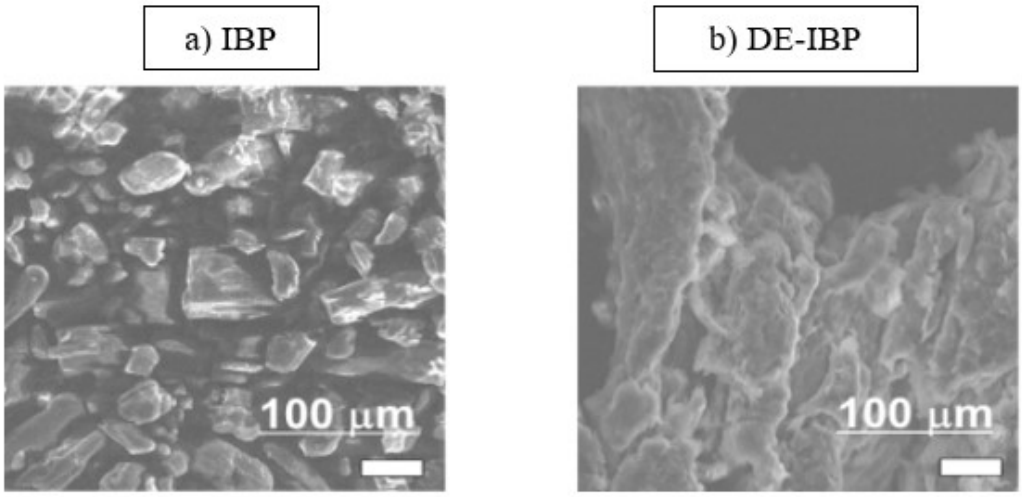

Figure 9: SEM images of a) IBP & b) DE-IBP

3.3.3 Differential Scanning Calorimetry (DSC)

In DSC analysis, crystalline IBP had a particular endothermic peak around 100°C (Figure 10), the endothermic peak in DE-IBP at the melting point of crystalline IBP was lost in DSC analysis indicating the metastable amorphous form of IBP during the preparation process. The high free energy in the amorphous state may trap the drug molecule in DE and inhibit drug precipitation or recrystallization in the supersaturated state, which would be beneficial to improving the dissolution behavior of IBP.

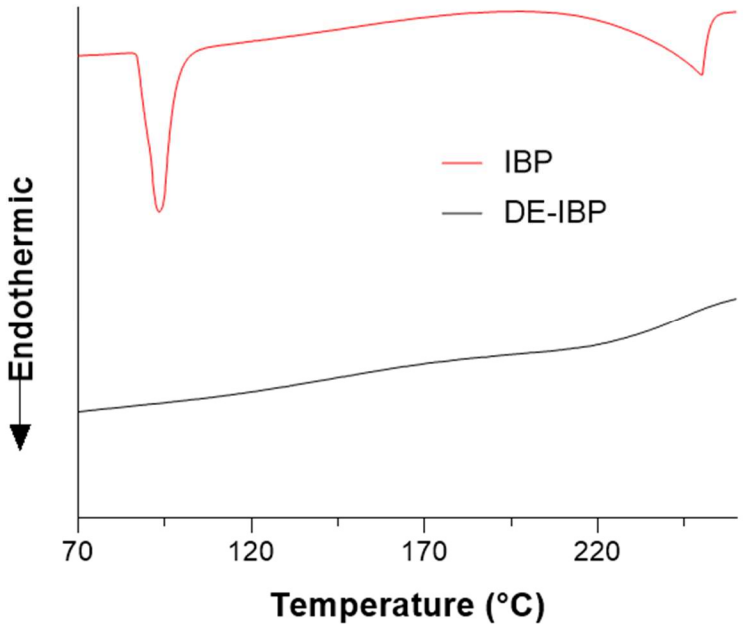

Figure 10: DSC of DE-IBP and IBP

3.3.4 X-ray Powder Diffraction (XRPD)

The XRPD pattern of crystalline IBP revealed several sharp peaks, with the strongest peak at around 20.18°, indicating the crystalline condition of IBP (Figure 11). DE-IBP, on the other hand, showed a halo diffractive pattern, and the peaks detected in crystalline IBP were minimal in the diffractogram, indicating that IBP was in an amorphous condition. Since our aim was to obtain DE with decreased crystallinity for improved solubility of the IBP, these results suggested that the release profile of IBP from the DE-IBP should be better than crystalline IBP.

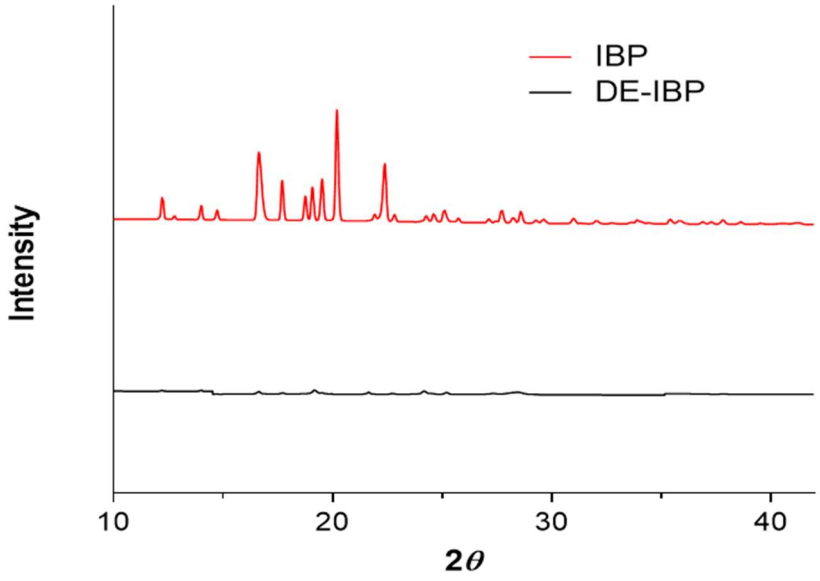

Figure 11: Crystallinity analysis of DE-IBP and IBP

3.3.5 Fourier transform infrared spectroscopy (FT-IR)

FT-IR spectroscopy experiment was performed for understanding the interaction and compatibility between the polymers and IBP as shown in figure 12. Here, Spectrum I represent DE-IBP and spectrum II-VII show individual spectrum for PVA, PEG 600, carbopol, kollisolv, stearic acid and IBP. Spectrum of each polymer is found to be different from other without having any overlap which indicates that the polymers had negligible or no interactions and are compatible with the IBP for the formulation of DE-IBP.

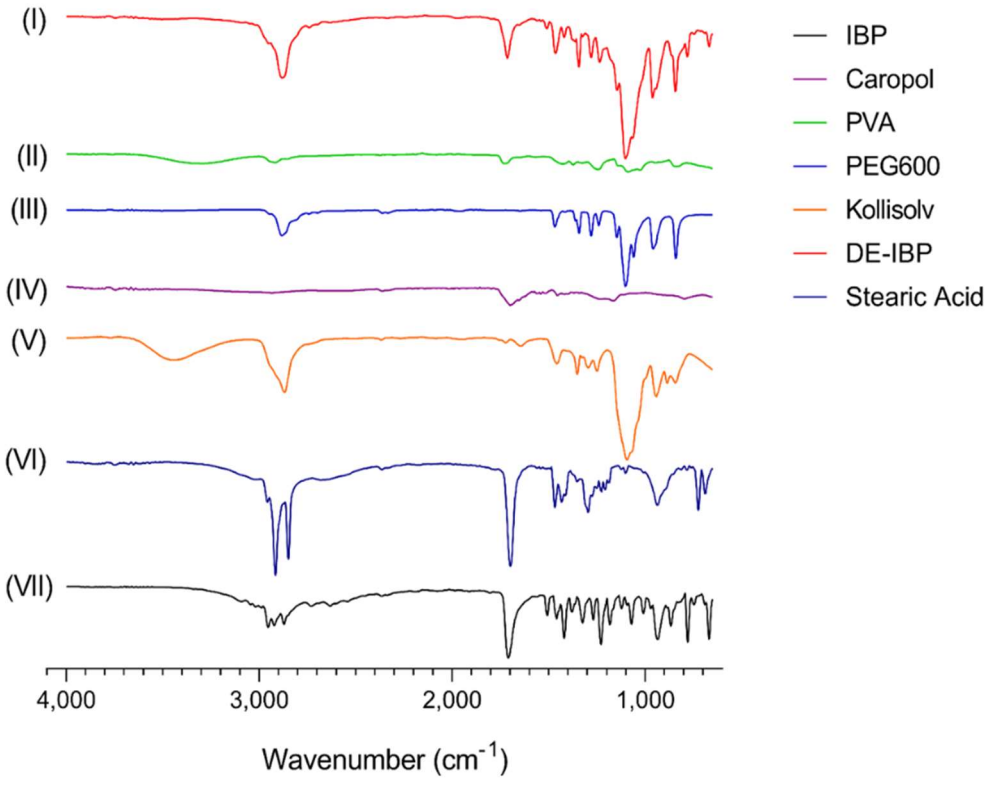

Figure 12: FT-IR analysis to determine IBP-Polymer compatibility.

Chapter 4 Conclusion

Ibuprofen has crystalline non-uniform particles which makes it difficult to be readily soluble in water and give the required therapeutic actions. On the other hand, dry emulsion formulation of Ibuprofen showed enhanced solubility due to reduced crystallinity and particle size. As a result, dissolution rate and extent of the dry emulsion formulation have also been improved suggesting better absorption and bioavailability of the drug. Dry emulsion formulation of Ibuprofen could be a promising approach to improve the biopharmaceutical behavior of Ibuprofen and could be an ideal drug for BCS class II drugs. In future dry emulsion formulation of Ibuprofen can be compared with several commercial products and *in vivo* studies can be carried out to further confirm the *in vitro* dissolution profile of the research for enhanced solubility and bioavailability of the drug product. Dry emulsion formulation can be applied to other BCS drugs to improve their physicochemical properties.

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