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Research Article

# ENHANCEMENT OF DISSOLUTION RATE OF IBUPROFEN BY PREPARING SOLID DISPERSION USING DIFFERENT METHODS

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**ABSTRACT**

Ibuprofen is (NSAID) non-steroidal anti-inflammatory drug and used as analgesic & anti-inflammatory drug. It can be also used in the treatment of rheumatoid arthritis, osteoarthritis, and primary dysmenorrhea. Ibuprofen is absorbed rapidly, bound avidly to protein, but it has low aqueous solubility so, it also lowers the dissolution profile of drug. To overcome this problem, various techniques are used, like solid dispersion, complexation, co-solvency, hydrotrophy, nano technology approach.

In this study, the dissolution rate of poorly soluble drug Ibuprofen was increased by preparing solid dispersion with urea in ratio of (1:1), (1:3) & (1:5) by using melt dispersion method & solvent evaporation method. The rate of dissolution of Ibuprofen was increased with the proportion of (1:5) when compared to the other formulations.

**Keywords:** Ibuprofen, Urea, Solid dispersions, Dissolution Rate.

## INTRODUCTION

Solid dispersion technique can be used to enhance the solubility, dissolution rate and absorption of several insoluble drugs [1].Though ibuprofen is absorbed rapidly and bound avidly to protein, it is not showing complete therapeutic effect because of their poor solubility and dissolution, which leads to poor bioavailability of the drug [2,3].Now a days, the most importance is given to enhance the dissolution rate of the poorly soluble drugs, so, it increases the bioavailability of drug.

Solid dispersion is one of the techniques used to increase the dissolution rate of the lipophilic drugs [4, 5, 6]. Solid dispersions are prepared by solvent or co-precipitation method where both guest solute and solid carrier solvent are dissolved in a common volatile solvent such as alcohol. The liquid solvent is removed by evaporation under reduced pressure or by freeze drying which results in amorphous precipitation of guest in a crystalline carrier [7, 8]. Solid dispersions are two-component systems which consist of a hydrophilic carrier in which the drug is incorporated. The drug is incorporated in the hydrophilic carrier which may be molecularly dispersed or may occur as Nano crystals or amorphous nanoparticles. The enhancement in dissolution rate of the drug can be ascribed to-

(a) An increasing solubility of the drug because of its amorphous state or small particle size (Kelvin's law) [9- 12]

(b) An increased surface area available for drug dissolution because of the small size of the drug particles [13, 14]

(c) An improvement in wetting of the drug caused by the hydrophilic carrier [15, 16].

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID and used to relieve the pain, tenderness, inflammation and stiffness caused by arthritis and gout. It is also used to reduce fever and to relieve headaches, muscle aches, menstrual pain, aches and pains from the common cold, backache and pain after surgery or dental work. Ibuprofen is a core medicine in the World Health Organization's "Essential Drugs List", that means it is in list of minimum medical needs for a basic health care system [17]. Ibuprofen is a non-selective COX inhibitor that inhibits two iso forms of cyclooxygenase, COX-1 and COX-2. The analgesic, antipyretic, and anti-inflammatory activity of NSAIDs are mainly achieved through inhibition of COX-2, whereas inhibition of COX-1 is responsible for unwanted effects on the gastrointestinal tract and platelet aggregation. However, the role of the individual COX iso forms in the analgesic, antipyretic, anti-inflammatory, and gastric damage effects of NSAIDs is uncertain and different compounds which cause different degrees of analgesia and gastric damage [18].

## MATERIALS

Ibuprofen pure drug obtanes as gift sample from Sun Pharmaceuticals, Ahemadabad, Mannitol. Methanol, dichloromethane, urea were of analytical grade.

## METHODS

### Solvent evaporation method

Ibuprofen was dissolved in a solvent blend of methanol and dichloro methane (1:1) to get a clear solution in a 100ml round bottom flask. The excipient (urea) was then added and dispersed. The solvent from the mixture was removed by evaporation at 50º C under pressure while mixing the contents. The mass obtained was pulverized, mixed and passed through mesh no#60 co-evaporates were prepared in various ratios of drug: excipient such as 1:1, 1:3, and 1:5.

### Melt dispersion method

500mg of ibuprofen and 500mg of urea (1:1) were melt together in a china dish and mixed thoroughly both ingredients. After mixing the china dish was put on ice bath for cooling, and then resulted in damp mass. The damp mass passed through mesh no #60 and like this, other formulations with different proportion were prepared.

**Table 1: Formulation of Ibuprofen:urea solid dispersion by different methods & different ratio**

| Batch code | Method | Ratio |
|---|---|---|
| F1 | Solvent Evaporation Method | 1:1 |
| F2 | Solvent Evaporation Method | 1:3 |
| F3 | Solvent Evaporation Method | 1:5 |
| F4 | Melt Dispersion Method | 1:1 |
| F5 | Melt Dispersion Method | 1:3 |
| F6 | Melt Dispersion Method | 1:5 |

## EVALUATION

### Saturation solubility and phase-solubility studies

A modified method of solubility determination was used to determine the solubility of different ibuprofen solid dispersions [21]. Weighed amounts of ibuprofen (pure drug), solid dispersions, and physical mixture, each sample equivalent to 0.5 g of ibuprofen, were

separately introduced into 15 ml stopper conical flasks containing 5 ml of phosphate buffer solution (pH 7.4). The sealed flasks were agitated on a rotary shaker for 72 hr at 37 °C. The supernatant solution was filtered through 0.45 µm membrane filter, and the filtrate was suitably diluted and analyzed on a UV-Visible spectrophotometer (Shimadzu 1800) at 221 nm. Determinations were carried out in triplicate.

**Table 2: Saturation solubility and phase-solubility studies**

| Composition | Method | Ratio | Batch code | Saturated solubility(mg/ml) |
|---|---|---|---|---|
| Ibuprofen pure drug | - | -- | -- | 1.78 ± 0.04 |
| Drug : Urea | Solvent Evaporation | 1:1 | F1 | 4.11 ± 0.18 |
| | | 1:3 | F2 | 4.48 ± 0.03 |
| | | 1:5 | F3 | 4.51 ± 0.22 |
| Drug : Urea | Melt Dispersion | 1:1 | F4 | 3.64 ± 0.31 |
| | | 1:3 | F5 | 3.95 ± 0.12 |
| | | 1:5 | F6 | 4.01 ± 0.29 |

**Dissolution test**

Dissolution rate of Ibuprofen was studied using USP-II (paddle Type) dissolution test apparatus. The quantity of dissolution medium was 900ml of phosphate buffer (pH 6.8), with the speed of rotation at 75 rpm and the temperature was set at 37+ 0.5°C. The sample was withdrawn at different time intervals. The withdrawn samples were suitably diluted with more quantity of dissolution medium and the same volume was replaced with fresh dissolution medium. The samples were then studied in UV-Visible Spectrophotometer at 221 nm for Ibuprofen content. The release rate at different time intervals were then determined.

**Table 3: Comparison of dissolution study between drug and solid Dispersion (Solvent evaporation method)**

| Time (Minute) | Cumulative drug release (%) | | | |
|---|---|---|---|---|
| | Drug ((Ibuprofen) | Solid dispersion | | |
| | | Drug : urea (1:1) batch F1 | Drug : urea (1:3) batch f2 | Drug : urea (1:5) batch f3 |
| 0 | 0 | 0 | 0 | 0 |
| 5 | 12.19 | 12.69 | 15.61 | 16.41 |
| 10 | 14.62 | 22.18 | 18.93 | 28.82 |
| 15 | 20.09 | 27.33 | 31.12 | 34.71 |
| 30 | 24.36 | 41.04 | 33.63 | 47.07 |
| 45 | 26.13 | 50.52 | 46.15 | 54.09 |
| 60 | 30.96 | 58.61 | 52.60 | 67.12 |
| 75 | 33.77 | 69.72 | 70.72 | 76.56 |
| 90 | 37.08 | 76.72 | 78.81 | 88.33 |

**Table 4: Comparison of dissolution study between drug and solid dispersion (Melt dispersion method)**

| Time ((Minute) | Cumulative drug release (%) | | | |
|---|---|---|---|---|
| | Drug (Ibuprofen) | Solid dispersion | | |
| | | Drug : urea (1:1) batch f4 | Drug : urea (1:3) batch f5 | Drug : urea (1:5) batch f6 |
| 0 | 0 | 0 | 0 | 0 |
| 5 | 12.19 | 12.32 | 13.32 | 18.21 |
| 10 | 14.62 | 20.48 | 25.16 | 24.22 |
| 15 | 20.09 | 27.18 | 29.12 | 34.86 |
| 30 | 24.36 | 36.72 | 46.42 | 49.52 |
| 45 | 26.13 | 43.04 | 51.17 | 58.67 |
| 60 | 30.96 | 56.51 | 58.61 | 66.92 |
| 75 | 33.77 | 61.18 | 66.24 | 76.86 |
| 90 | 37.08 | 69.33 | 71.79 | 82.31 |

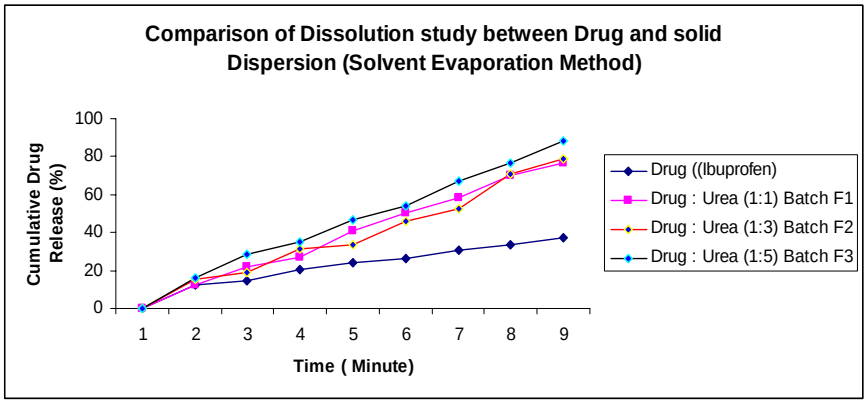


**Fig. 1: Comparison of dissolution study between drug and solid dispersion (solvent evaporation method)**

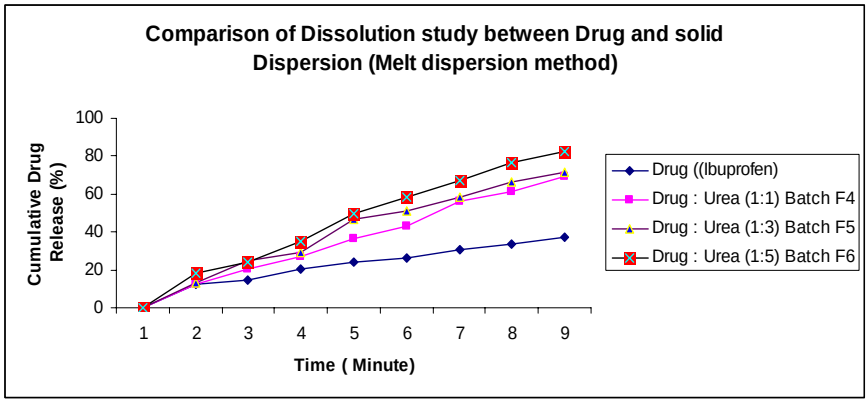


**Fig. 2: Comparison of dissolution study between drug and solid dispersion (Melt dispersion method)**

## RESULTS AND DISCUSSION

Solid dispersions of Ibuprofen was prepared by solvent evaporation and melt dispersion method by using urea as dispersing agent.. In Saturation solubility and phase-solubility studies, it was found that the solubility was increased with increasing the proportion of urea in the formulation. The highest solubility was shown when the ratio of drug & urea was 1:5 f prepared by solvent evaporation method. It was found that dissolution rate of poorly soluble drug Ibuprofen can be increased by forming into solid dispersions; solid dispersions demonstrated a higher dissolution rate than pure drug.

The dissolution study was carried out in phosphate buffer (pH 7.4) at 37+ 0.5°C up 90 minute and it was found that the rate of dissolution was increased in solid dispersion as compare to pure drug. The dissolution rate is increased about the double fold to the pure drug when solid dispersion in the ratio of 1:5 (Drug: Urea). When the dissolution profiles compare between the solvent evaporation and melt dispersion method then it was found that dissolution rate is better in solvent evaporation method so it was concluded that dissolution of poorly soluble drug can be effectively increased by the solid dispersion methods

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