**In Vivo-In Vitro Evaluation of Solid Dispersion Containing Ibuprofen**

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**ABSTRACT**

Ibuprofen is a non-steroidal anti-inflammatory drug with poor water solubility. The most frequent causes of low oral bioavailability are attributed to poor solubility and low permeability. Solid dispersion technique can be used to enhance the solubility; dissolution rate and absorption of several insoluble drugs. The different solid dispersion methods were studied using PEG 6000 as carrier. Different ratio of drug-carrier was study. The all samples were characterized by FTIR study. Tests of physical evaluation, drug content, loss drying and invitro dissolution were carried out. The formulation of 1:2 ratio by fusion method was found optimized. In-vivo anti-inflammatory activity of 1:2 ratio formulation of fusion method shows highest dissolution and absorption rate than marketed preparation. The present study concluded with the importance of solid dispersion technique and their methods in enhancing the solubility of poorly water soluble drug.

**Keywords:** Solid dispersion, fusion method, solvent evaporation method, Ibuprofen, in-vivo anti-inflammatory activity.

**INTRODUCTION**

The oral bioavailability depends on several factors including aqueous solubility, drug permeability, dissolution rate, first-pass metabolism, presystemic metabolism, and susceptibility to efflux mechanisms. The most frequent causes of low oral bioavailability are attributed to poor solubility and low permeability.1 There are various techniques such as, Particle size reduction, micronization, physical modifications, nano-suspension, modification of crystal habit such as, polymorphs, pseudo polymorphs, complexation, solubilization, salt formation, and use of cyclodextrins which can enhance the solubility & dissolution rate of insoluble drug but this techniques having some practical limitations, solid dispersion technique overcome this practical limitations. However, the major challenge with the design of oral dosage forms lies with their poor bioavailability. Solid dispersion technique can be used to enhance the solubility; dissolution rate and
absorption of several insoluble drugs. The term solid dispersion refers to group of solid products consisting of at least two different components, generally a hydrophilic matrix and hydrophobic drugs.

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) and used to relieve pain, tenderness, inflammation & gout. The Ibuprofen is poorly water soluble drug and solubility of this drug was determined by different method.

MATERIALS AND METHODS

Plant Material

Ibuprofen drug obtained as a gift sample from Leben pharmaceutical pvt ltd, Akola, PEG 6000 & Ethanol was used of analytical grade and all other chemicals were procured from Ozone chemicals, Mumbai. The FT-IR Study of Ibuprofen & PEG 6000 was carried out to confirm the compatibility.

In the present study, we concentrate over different methods of solid dispersion and their comparative study was studied. The solid dispersion of ibuprofen was prepared by following methods. The table 1 contains the composition of solid dispersion.

Solvent evaporation method

Solid dispersions of Ibuprofen and carrier PEG 6000 were prepared by ratio of 1:1, 1:2, 1:3. In this technique Ibuprofen was dissolved in a ethanol solvent and obtained a clear solution. After getting a clear solution the carrier (PEG 6000) were added to that solution until the thick slurry is form and transfer it in to the petri plate & allow the solvent to evaporate and dry it.

Fusion Method

Solid dispersion were prepared by melting the accurately weigh amount of PEG 6000 in a water bath and drug were dispersed in a molten solution, & cooling immediately on ice bath with continuous stirring to dry mass. The dry mass was crushed and pulverized. The drug:carrier ratio used was 1:1, 1:2, 1:3.

Kneading Method

The weighted quantities of drug and carrier were triturated in a glass mortar with a small volume of methanol. The thick slurry was kneaded for 45 mins and then dried at 50°C to constant weight. The dried mass was pulverized properly. The solid dispersion were prepared in three proportion of Drug: PEG 6000, 1:1, 1:2, 1:3.

EVALUATION

Solubility study

The solid dispersion equivalent to 0.5 gm of Ibuprofen was introduced in to the 15 ml stopper conical flask containing 5 ml distilled water. The sealed flask was agitated on magnetic stirrer over a night. The same procedure followed for the pure ibuprofen sample. The solution was filter & the filtrate was suitably diluted and analyzed on a UV-Visible spectrophotometer at 222 nm.

Loss on Drying (LOD)

100 mg of solid dispersion was dried at a temperature of 40±2°C for 7 days and final weight was taken to Wt after drying. The LOD of solid dispersion was calculated by using following equation.

% LOD = (Weight of water in sample / Total weight of wet sample) x 100

% LOD = [(Wo − Wt) / Wo] x 100

Where,
Wo is initial weight of Sample
Wt is weight of sample after drying

Drug content

Weight amount of physical mixtures and solid dispersions, each sample equivalent to 25 mg of ibuprofen were separately taken and added to 50 ml of ethanol in stopper
conical flasks. The sealed flasks were agitated on a rotary shaker for 1 hour. The solution was diluted with ethanol and was assayed by a UV-VIS spectrophotometer (Shimadzu Corporation, Japan) for drug content at 222 nm.¹⁰

**In Vitro Dissolution study**

Dissolution studies were performed in phosphate buffer (pH 7.2, 900 ml) at 37 ± 0.5 °C, using USP XXIII apparatus with a paddle rotating at 50 rpm. The samples equivalent to 100 mg ibuprofen, were added in vessel containing phosphate buffer. At fixed time intervals, samples (5 ml) were withdrawn and equal amount of fresh dissolution medium was added. The samples were filtered through 0.45 µm membrane filter, and analyzed by UV-VIS spectrophotometer (Shimadzu Corporation, Japan) at 222 nm wavelength.¹⁰,¹¹

**In-vivo Study**

The anti-inflammatory activity of optimized preparation of solid dispersion & marketed preparation was carried out using three groups each containing two rat animals. One group for control, second group for marketed preparation & third group for optimized solid dispersion was used. 0.1 ml of 1% carageenan was injecting in the sub plantar region of left hind paw of each animal of each group. After 15 minutes of carageenan administration initial swelled area of left hind paw were measured by plethysnometer. Then marketed preparation and solid dispersion containing Ibuprofen were injected subcutaneously to second and third group respectively. The swelled area was measured by plethysnometer.¹²

**RESULTS**

The figure no1 shows the FT-IR graph of Ibuprofen, PEG 6000 and combination of both. The chemical interaction were not found hence are compatible with each other. Various ibuprofen solid dispersions were prepared using PEG 6000, as a carrier by solvent evaporation technique, Fusion method & kneading method to increase the solubility as well as dissolution of poorly aqueous soluble drug ibuprofen. All the solid dispersions (SDS) were found free flowing.

UV-VIS Spectrophotometric assay method identified the amount of drug in prepared solid dispersion Table no.2 shown the percentage of drug present in the solid dispersion. The data indicated that the drug in carrier dispersed uniformly. Pure ibuprofen showed 2.46 ± 0.40 mg/ml of saturation solubility. All the solid dispersions of ibuprofen showed an increase in drug solubility. All solid dispersion showed higher saturation solubility as compared with pure ibuprofen. This could be due to use of water soluble carrier PEG 6000 which have the good wettability increase surface area.

The all batches of solid dispersions were studied for % LOD. According the IP this procedure was followed and all batches showed the satisfactory results the data are shown in table no. 2. The loss on drying for each formulations were found less than 2 %, this could help to maintain concentration of water that helps to wet the drug particles.

Among all proportion of solid dispersion the 1:2 proportion of drug: carrier by fusion methods, solvent evaporation method and kneading method showed the greater dissolution rate and also exhibited a greater release pattern. Solid dispersion with 1:3 drugs: carrier ratio release very less concentration of drug in 10 minutes.

The solid dispersion containing 1:2 drug: carrier ratio prepared by solvent evaporation method have 97.54% drug release, while in the fusion method of 1:2 ratio, the maximum % drug release was 98.58%. This indicate that, in fusion method the and carrier get cross linked with low intermediate or bonding forces. The cumulative percent drug release of ibuprofen
from different formulations was shown in figure 2. Hence the formulation of solid dispersion of fusion method was optimized. This might be due to uniform dispersion and good wetting property of PEG 6000.

The volume of mercury measured. After administration of marketed preparation and optimized solid dispersion containing ibuprofen, the measured volumes of left paw represent in fig. no 3.

The volume of left hind paw in third group was decreased faster as compared to second group. This proved that, the dissolution and absorption rate of ibuprofen from solid dispersion was more than the marketed preparation.

**CONCLUSION**

The present study conclusively indicated that the use of various solid dispersion methods by using water soluble carrier improved the solubility of poorly water soluble drug. Among fusion, solvent evaporation, and kneading methods, fusion method of solid dispersion has best result as compared to solvent evaporation method and kneading method, because the hydrophilic carrier is uniformly mix with the drug ibuprofen in the fusion method. Hence solid dispersion is one of most promising technique used in enhancing the solubility of poorly water soluble drug.

**ACKNOWLEDGEMENTS**

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**REFERENCES**

Table 1. Composition of solid dispersion containing Ibuprofen and their evaluation

<table>
<thead>
<tr>
<th>Batch code</th>
<th>Drug : Carrier Ratio</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD1</td>
<td>1:1</td>
<td>Fusion method</td>
</tr>
<tr>
<td>SD2</td>
<td>1:2</td>
<td></td>
</tr>
<tr>
<td>SD3</td>
<td>1:3</td>
<td></td>
</tr>
<tr>
<td>SD4</td>
<td>1:1</td>
<td>Solvent evaporation method</td>
</tr>
<tr>
<td>SD5</td>
<td>1:2</td>
<td></td>
</tr>
<tr>
<td>SD6</td>
<td>1:3</td>
<td>Kneading method</td>
</tr>
<tr>
<td>SD7</td>
<td>1:1</td>
<td></td>
</tr>
<tr>
<td>SD8</td>
<td>1:2</td>
<td></td>
</tr>
<tr>
<td>SD9</td>
<td>1:3</td>
<td></td>
</tr>
<tr>
<td>Pure drug</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. % LOD Data of Solid dispersion containing Ibuprofen

<table>
<thead>
<tr>
<th>Batch code</th>
<th>Solubility (mg/ml)</th>
<th>Drug content</th>
<th>% LOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD1</td>
<td>4.77 ± 0.28</td>
<td>97.61 ± 2.92</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD2</td>
<td>5.15 ± 0.32</td>
<td>97.39 ± 2.42</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD3</td>
<td>4.95 ± 0.37</td>
<td>98.14 ± 2.56</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD4</td>
<td>4.53 ± 0.24</td>
<td>98.17 ± 2.83</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD5</td>
<td>4.78 ± 0.34</td>
<td>95.78 ± 2.88</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD6</td>
<td>5.02 ± 0.29</td>
<td>94.33 ± 3.05</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD7</td>
<td>4.45 ± 0.26</td>
<td>95.33 ± 2.90</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD8</td>
<td>4.83 ± 0.28</td>
<td>95.22 ± 2.85</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>SD9</td>
<td>4.67 ± 0.33</td>
<td>97.30 ± 2.44</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>Pure drug</td>
<td>2.46 ± 0.40</td>
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</tr>
</tbody>
</table>
Figure 1. FT-IR Graph of pure ibuprofen, PEG 6000 & physical mixture.

Figure 2. Comparative % Drug release of Ibuprofen solid dispersion.
Figure 3. In-vivo comparative anti-inflammatory activity