ejpmr, 2018,5(6), 376-380

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

ENHANCEMENT OF BIOAVAILABILITY OF IBUPROFEN BY USING SOLID DISPERSION TECHNIQUE

Mali Alpesh Mahadeo*, Ghodake Ganesh, Gharge Varsha

Gourishankar Institute of Pharmaceutical Education & Research, Limb, Satara, Maharashtra, India-415015.

***Corresponding Author: Mali Alpesh Mahadeo**

Gourishankar Institute of Pharmaceutical Education & Research, Limb, Satara, Maharashtra, India-415015.

Article Received on 25/03/2018 **Article Revised on 15/04/2018** **Article Accepted on 05/05/2018**

ABSTRACT

In this study of Ibuprofen it is an (NSAIDs) 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 dysmenorrheal. 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, hydro trophy. nano- technology approach. In this study, the dissolution rate of poorly soluble drug was increased by preparing solid dispersion with PEG-4000 in ratio of (1:1), (1:3) &,(1:5) by using melt dispersion and solvent evaporation method. The rate of dissolution was increased with the proportion of (1:5) when compared to the other formulations.

KEYWORDS: Ibuprofen, PEG-4000, PVP k30,Solid dispersion, Dissolution Rate.

INTRODUCTION

Ibuprofen is an essential non-steroidal anti-inflammatory drug it has poor aqueous solubility. Dissolution of ibuprofen is a rate limiting step that sometimes results in incomplete absorption due to poor dissolution and.[1] but rapid onset of action is vital for pain situations particularly in dental pain, rheumatoid and osteoarthritis and breast cancers. Moreover, ibuprofen has been rated as the safest conventional NSAID by spontaneous adverse drug reaction reporting systems in the UK.[2] Again Ibuprofen is the most commonly used and most frequently prescribed NSAID.[3]To improve solubility characteristics followed by dissolution of such drug is challenging and rational. Among the various approaches, the solid dispersion technique has been proved to be the most successful in improving the dissolution and bioavailability particularly of drugs having poor aqueous solubility.[4] it has become popular because of its simplicity, cost effectiveness and advantages over other techniques. Solid dispersion is a mean of reducing particle size and the drug can be dispersed molecularly in amorphous particles (clusters) or in crystalline particles.[5] it allows distribution of carrier component in between and around the drug and thus offers better surface characteristics and wetting. The poor dissolution characteristics of poorly water soluble drugs is a problem to the pharmaceutical industry because the dissolution rate of poorly water soluble drugs could be the rate limiting process in the absorption of a drug from a solid dosage form.[6,7] Solubilization is the process by which the apparent solubility of a poorly water soluble drug is increased. Solubilization techniques include addition of a cosolvent, salt formation, prodrug design, complexation, particle size reduction and the use of surface active agents (micellization).[8] Use of solvate and hydrates, polymorphs, hydrotrophy, absorbents, pH adjustment, solubilizing vehicles, etc. are the some other physico-chemical approaches to enhancing oral absorption of poorly water soluble drugs.[9-11]

MATERIALS AND METHOD

Materials

Ibuprofen was obtained from Alembic Pvt. Ltd; Vadodara. PEG-4000, PVP k30 & Ethanol Loba Chemic Mumbai. All other chemicals and ingredients were used for study are of Analytical grade.

METHODS[12,13]

The methods used for preparation of solid dispersions of Ibuprofen with carrier PEG 4000 & PVP k30 were Fusion method and solvent evaporation.

Fusion method

Solid dispersion were prepared by melting the accurately weigh amount of PEG 4000 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, 1:3, 1:5.

b) Solvent evaporation method

Solid dispersions were prepared by dissolving accurately weighed amounts (according to their w/w ratio respectively) of Ibuprofen with carrier PVP k30 in

methanol. After complete dissolution, solvent was evaporated under reduced pressure at room temperature. Subsequently, the solid mass was ground and prepared solid mass stored in desiccators for further use.

Evaluation Parameters
Preformulating studies of Ibuprofen
Characterization of Ibuprofen: Description
Ibuprofen was found to be colour, odour, nature & taste.

Melting point of drug
The melting point of Ibuprofen was carried out.

Standard curve of Ibuprofen
Standard curve of ibuprofen in phosphate buffer pH 7.2 at 221 nm was plotted using various concentrations against the absorbance values found at respective concentrations. The standard curve of ibuprofen was found to be linear in the range of 5-30 µg/ml, which means that present drug sample was obeying Beers-Lamberts range (5-30 µg/ml) and coefficient of correlation was found to be 0.999. The observations of calibration curve are shown in table 6, the plot of calibration curve is shown in figure 4 and the parameters from the calibration curve are mentioned in the table no. 7.

Fourier Transform Infrared Spectroscopy[14]
The fourier transform infra-red analysis was conducted for the structure characterization FTIR spectra of the pure drug Nimesulide. Approximately 5mg of samples were mixed with 50mg of spectroscopic grade KBr, samples were scanned in the IR ranges found 500 to 2000 cm-1, with a resolution of 4 cm-1.

Evaluation of solid dispersion[15,16,17]
Solubility Studies
Solubility studies were performed in triplicate according to the method reported by Higuchi and Connors. Excess of pure drug physical mixture or solid dispersion were added to 20ml distilled water in a screw- cap to and shake in a rotary flask shaker at room temp.(25 0c)for 24 hr. Once equilibrium had been achieved, appropriate aliquots were withdrawn and filtered through Whitman filter paper no.41 and a filtrate analysed spectrophotometrically at221nm.

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 221 nm.

Dissolution Studies
The dissolution studies of Ibuprofen alone, physical mixture and solid dispersions were performed in triplicate by using USP dissolution apparatus XXIV-Type II (Electro Lab, Mumbai). Dissolution studies were carried out using 900ml of phosphate buffer (ph-7.2) at 37 +-0.5 0c at 100 rpm. 400 mg of Ibuprofen of its equivalent amount of solid dispersions was added to 900ml phosphate buffer (pH 7.2). Samples of 5ml were withdrawn at time intervals of 10, 20, 30,40,50,60 min.The volume of dissolution medium was adjusted to 900 ml by replacing each 5ml aliquot withdrawn with 5ml of fresh phosphate buffer (pH 7.2). The solutions were immediately filtered through 0.45um membrane filter, suitably diluted and the conc. of Ibuprofen in samples was determined spectrophotometrically at 221nm.

RESULTS AND DISCUSSION

Preformulating studies of Ibuprofen
Characterization of Ibuprofen: Description
Ibuprofen was found to be white, odourless, amorphous powder having slight bitter taste.

Solubility of drug
Ibuprofen was found to be slightly soluble in water and freely soluble in methanol.

Melting point of drug
The melting point of Ibuprofen was found to be in the range of 74-76^{0}C.

Standard curve of Ibuprofen
Table No 1: Observations for standard curve of ibuprofen

Sr. no.	Concentration (µg/ml)	Absorbance
1	0	0.0000
2	5	0.193
3	10	0.244
4	15	0.316
5	20	0.416
6	25	0.520
7	30	0.594

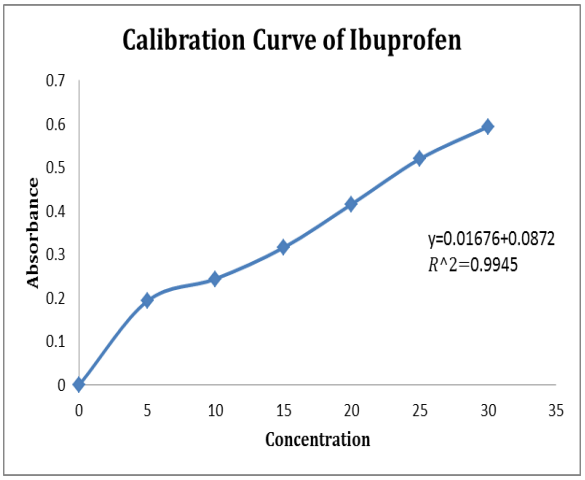


Fig. 1: calibration curve of Ibuprofen.

Table No 2: Parameters from the calibration curve.

Sr.No.	Parameters	Observation
1	Slope	0.01676
2	Intercept	0.0872
3	Coefficient of correlation (r2)	0.9945

For determination of unknown concentration of Ibuprofen following equation of straight line was used,
Y = Absorbance,
m = Slope,
C = Intercept.
Thus, from the calibration curve following equation was used.

FTIR

I) IBUPROFEN

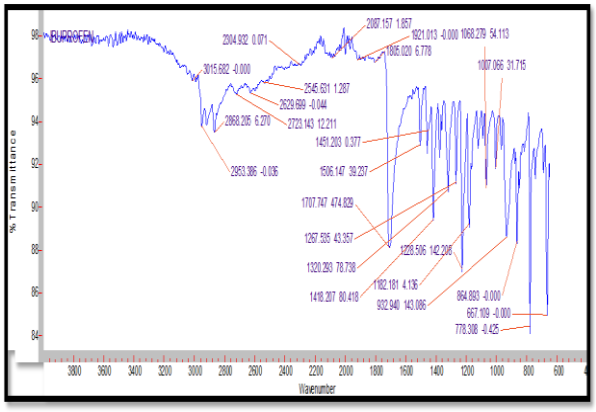
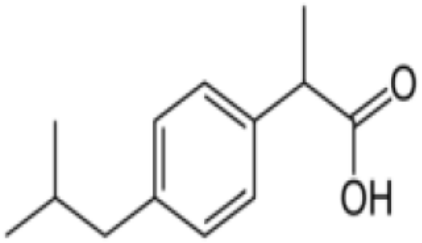


Fig. 2: FTIR Study of Ibuprofen.



(*RS*)-2-(4-(2-methylpropyl) phenyl propanoic acid

Table No 3: IR Interpretation value of Ibuprofen.

FUNCTIONAL GROUP	STANDARD WAVENUMBER RANG (Cm-1)	OBSERVED WAVENAMBER(Cm-1)
Aromatic C-H (stretch)	3000-3100	3015.68
Aromatic C=C (stretch)	1400-1600	1418.20,1451.20,1508.14
Acid i)C=O (stretch) ii)O-H (stretch) iii)C-O (stretch)	 1700-1725 2500-3300 1210-1320	 1707.74 2723.14,2888.20,2963.38,3015.68 1320
Alkane i) C-H (stretch)	 2850-3000	 2868.20,2963.36

PHASE SOLUBILITY

Stability study=K 1:1 = Slope/Intercept*(1-Slope)

Table No 4: Observation table of conc of PEG-4000 of ibuprofen.

Conc. of PEG-4000	Conc. of Ibuprofen
0	4.03
2	5.15
4	6.5
6	7.5
8	8.8
10	10

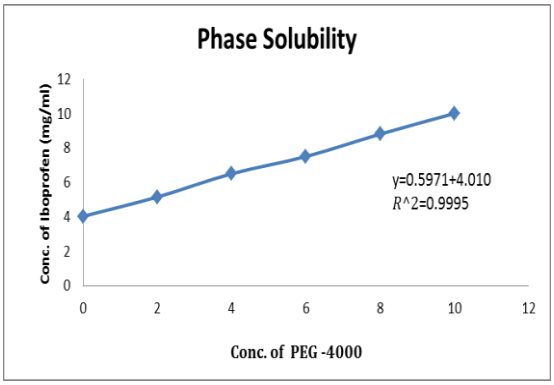


Fig. 3: Phase Solubility Study of Ibuprofen solid dispersion.

DRUG CONTENT

Drug content of Ibuprofen: PEG-4000 formulation was found in the range of 97.5±1.1 to 99.58±0.74%w/w.

DISSOLUTION PROFILE

Table No 5: In- Vitro dissolution Study Ibuprofen: PEG-4000 Solid Dispersion.

TIME	IBUPROFEN	F1[1:1]	F2[1:3]	F3[1:5]
0%	0%	0%	0%	0%
10	24.25%	45.08%	56.36%	62.36%
20	36.38%	49.02%	61.20%	69.35%
30	36.70%	57.32%	68.36%	76.29%
40	37.03%	57.86%	73.25%	84.56%
50	43.58%	67.53%	78.45%	89.75%
60	47.87%	70.21%	82.56%	92.86%

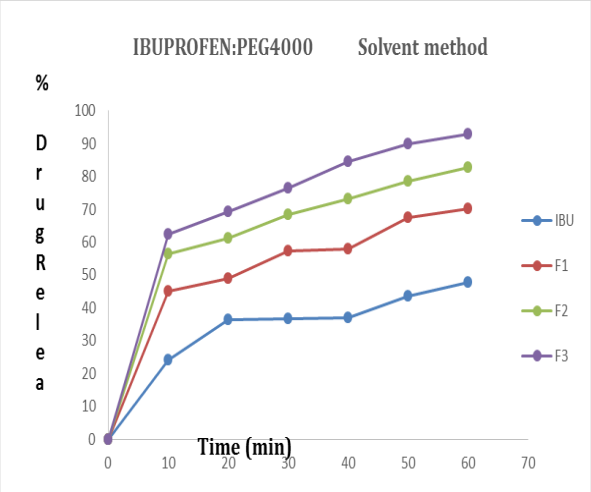


Fig. 4: In- Vitro dissolution Study of Ibuprofen solid dispersion PEG-4000.'

Table No 6: In- Vitro dissolution Study Ibuprofen: PEG-4000 Solid Dispersion.

Time	Ibuprofen	F1[1:1]	F2 [1:3]	F3 [1:5]
0	0%	0%	0%	0%
10	24.25%	44.81%	56.06%	72.56%
20	36.38%	46.12%	58.31%	74.62%
30	36.70%	47.43%	60.37%	77.06%
40	37.03%	48.93%	62.81%	79.05%
50	43.58%	51.37%	64.12%	82.13%
60	47.87%	53.25	66.75%	85.12%

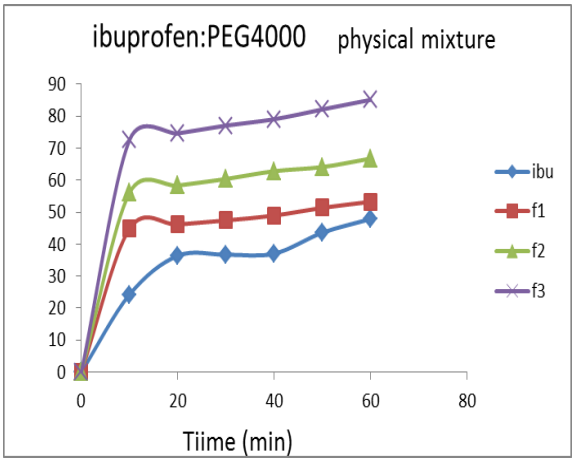
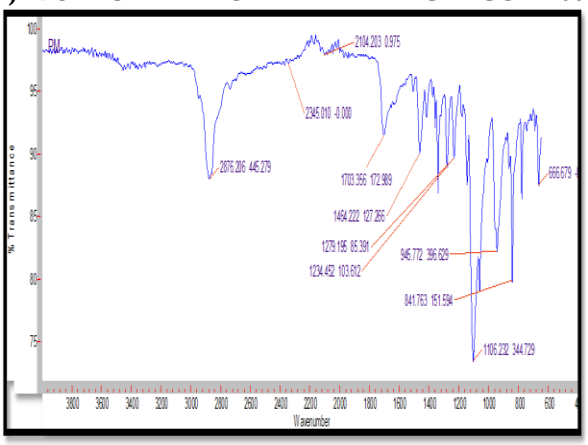
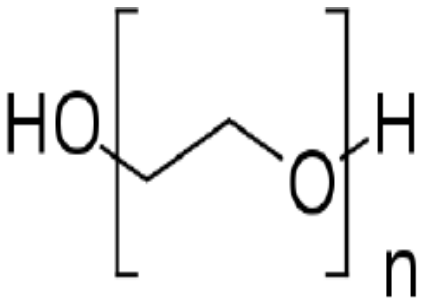


Fig. 5: In- Vitro dissolution Study of Ibuprofen solid dispersion PVA 30

II) IBUPROFEN + POLYEHYLENE GLYCOL-4000





Poly (ox ethylene) {structure-based}, poly (ethylene oxide) {source-based}

Fig. 6: IR Interpretation value of Ibuprofen + Polyethylene glycol-4000.

Table No 1: IR Interpretation value of Ibuprofen Solid Dispersion (Ibuprofen + Polyethylene glycol-4000).

FUNCTIONAL GROUP.	STANDARD WAVENUMBER RANG. (Cm-1)	OBSERVED WAVENAMBER (Cm-1)
Aromatic C-H (stretch)	3000-3100	-
Aromatic C=C (stretch)	1400-1600	1464.22
Acid i)C=O (stretch) ii)O-H (stretch) iii)C-O (stretch)	 1700-1725 2500-3300 960-1310	 1703.35 2876.20, 945.77,1106.23,1234.45
Alkane i) C-H (stretch)	2850-3000	2876.20
Ether i)C-O (stretch)	1000-1300(1070-	1106.23,1234.45

CONCLUSION

Solid dispersion of ibuprofen was prepared by solvent evaporation and melt dispersion method by using PEG-4000 as dispersing agent. In saturation solubility and phase – solubility studies, it was found that the solubility was increased with increasing the proportion of PEG-4000 in the formulation. The highest solubility was shown when the ratio of drug &PEG-4000 was 1:5 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 rate then pure drug.

The dissolution study was carried out in phosphate buffer (pH7.2) at 37+0.5^{0}C up 60 min and it was found that the rate of dissolution was increased in solid dispersion as compare to pure drug. The dissolution rate increased about fold to the pure drug when solid dispersion in the ratio of 1:5 (Drug: PEG-4000). 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 solid dispersion methods.

ACKNOWLEDGEMENT

The authors are sincerely thanks to the Gourishankar Institute of Pharmaceutical Education & Research, Limb, Satara, India for providing the facilities to complete this research work.

REFERANCES

1. Mohammad AD, Investigation of solid dispersion technique in improvement of physicochemical characteristics of ibuprofen powder. Iranian J. Pharm. Sci., 2007; 3: 69-76.
2. Rabia B, An overview of clinical pharmacology of ibuprofen. Oman Med. J., 2010; 25: 155-161.
3. Tripathi KD, Non steroidal anti inflammatory drugs and anti pyretic analgesics. Essentials of medical pharmacology. (5th ed.), Jaypee Brothers, New Delhi, 2003; 176.
4. Ruchi T, Solid Dispersions: An Overview to Modify Bioavailability of poorly Water Soluble Drugs. Int. J. PharmTech Res., 2009; 1: 1338- 1349.
5. Pouton CW, Lipid formulations for oral administration of drugs: non-emulsifying, self-emulsifying and 'self-microemulsifying' drug delivery systems. Eur. J. Pharm. Sci., 2000; 2: 93-98.
6. Patidar K, Solid Dispersion: Approaches, Technology involved, Unmet need & Challenges. Drug Invention Today., 2010; 2: 349-357.
7. Leuner C, Improving drug solubility for oral delivery using solid dispersions. Eur. J. Pharm. Biopharm. 2000; 50: 47-60.
8. James S. Encyclopedia of Pharmaceutical Technology. (2nd Edition), Marcel Dekker Inc., New York Basel, 2002; 2: 1676-1685.
9. Satinder A, Handbook of Modern Pharmaceutical Analysis, Academic Press, San Diego USA, London UK, 2001; 3: 202-203.
10. Carter SJ, Cooper and Gunn's Tutorial Pharmacy. (6th Edition), CBS Publishers and Distribotors, New Delhi., 2002; 13
11. Rasool AA, Solubility enhancement of some water insoluble drugs in the presence of nicotinamide and related compounds. J. Pharm. Sci., 1991; 80: 387-393.
12. Md Abdullah, Enhancement of Solubility and Dissolution Characteristics of Ibuprofen by Solid Dispersion Technique J. Pharm. Sci., 2012; 11(1): 1-6,
13. Tagalpallewar VR, Enhancement of Dissolution of Poorly Water Soluble Drug by Solid Dispersion Technique Int. J. Pharm. Sci. Rev. Res., 2017; 43(1): 155-160.
14. Gharge VG, Comparative Evaluation Of Disintegtrant Properties In Nimesulide Tablet Formulation By Using Natural And Synthetic Superdisintegrant, International Journal of Research in Pharmaceutical and Nano Sciences., 2017; 6(1): 1 - 9.
15. Gupta MM, Enhancement of dissolution rate of ibuprofen by preparing solid dispersion using different methods, international journal of pharmacy and pharmaceutical sciences, 2011; 3(3): 0975-1491.
16. Hasnain M, Solubility and dissolution enhancement of ibuprofen by solid dispersion technique using PEG 6000- PVP K 30 combination carrier, Bulgarian journal of science education, 2012; 21: 118-129.
17. Sachin KG, In Vivo-In Vitro Evaluation of Solid Dispersion Containing Ibuprofen AJADD, 2013; 1(1): 066-072.