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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF SOLID DISPERSIONS OF NABUMETONE

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ABSTRACT

Solid dispersions are an effective method of increasing the solubility and bioavailability of poorly soluble drugs. In the present study it is aimed at to enhance solubility of Nabumetone a poorly soluble anti-inflammatory drug by solid dispersion technique by employing solvent evaporation technique using PEG 4000 And PEG 6000 as carriers. The formulations were prepared in ratios of 1:1, 1:2 , 1:3, 1:4 and characterized by FTIR, XRD, and dissolution studies. The prepared solid dispersions showed excellent improvement of drug solubility due to mean drug particle size reduction which lead to increase drug dissolution and bioavailability.

Key words: Nabumetone, PEG4000, PEG6000, FTIR, XRD.

INTRODUCTION:

Nabumetone is a non-steroidal anti-inflammatory drug used to treat pain or inflammation caused by arthritis. It has poor oral absorption due to poor solubility and low dissolution rate.[1] Therefore a strategy was developed pharmaceutically to increase its solubility and dissolution by the method of solid dispersions. Solid dispersions is the most popularly employed techniques which could improve dissolution rate and solubility of poorly water soluble drugs by reducing particle size, fractionating to amorphous form and improving the wettability. [2]This transformation to amorphous to amorphous form of drug from crystalline state attributes to increase in solubility and improves bioavailability.[3]

As reported even hydrogen bonding formed between drug and carriers is another reason for improved solubility and decreased crystallinity of drug in solid dispersions.[4,5] The formulations were prepared by solvent evaporation technique and later subjected to various evaluation tests like FTIR,XRD and dissolution studies and compared to pure drug. Comparison of results with those for pure drug powder and physical mixtures of the drug and carrier can help to indicate the mechanism by which the carrier improves dissolution: via solubilization and wetting effects which could be affected by a simple mixture of the components, or by formation of a solid dispersion/solution. [6,7]A well-designed release experiment will show whether the solubility of the drug and its dissolution rate has been enhanced, and also whether the resulting supersaturated solution is stable or tends to precipitate quickly.[8,9,10]

MATERIALS AND METHODS

Solvent evaporation technique:[11,12]

Solid dispersions were prepared by solvent evaporation method. The carrier PEG 4000 and PEG 6000 are used by adding amounts of nabumetone corresponding the ratio 1:1;1:2,1:3 and 1:4 was accurately weighed and mixed properly. This physical mixture was solubilised in common solvent that is in methanol (5ml). The solvent was allowed to evaporate in hot air oven at 45C±10c. The process of evaporation was opted until the constant weight was obtained. The formulation was kept in desiccators for 24hrs under vacuum. Then, solid dispersion formulation was pulverized using a porcelain mortar and pestle. The pulverized powder was classified using the sieves (size 60#) and the powder was used for study.

Evaluation of prepared solid dispersions:

Drug content

The dispersion system equivalent to 10mg of Nabumetone Phosphate Buffer was taken in 100ml vol. Flask and dissolved in methanol. The volume was made up to mark with buffer and filtered. One ml of filtrate was further diluted to 10ml with methanol and absorbance was recorded at 271nm. The amount of drug in each dispersion system was determined spectrophotometrically. The results were shown in table 2

In Vitro drug release

In Vitro drug release rate of Nabumetone Phosphate Buffer solid dispersion of different samples was determined using USP dissolution test apparatus. The dissolution medium consisted of 6.8 Phosphate Buffer. Samples of drug, solid dispersion equivalent to 100mg of drug was spread onto the surface of 900ml of preheated dissolution medium at 37 C. Aliquots of 5ml were withdrawn at regular intervals of time(5,10,15,20,upto 120min)and the same is replaced with fresh dissolution medium each time. The samples were measured for absorbance at 271nm. The graph is plotted by taking percentage drug release on Y-axis and time on X-axis[16]. The results are shown in table 3&4, graphs in fig 8&9.

Fourier transforms Infrared spectroscopy

FT-IR spectra:[13]

FT-IR spectra were recorded using an FT-IR spectrophotometer (shimadzu).The samples (nabumetone PHOSPHATE BUFFER, PEG6000, and solid dispersions) were previously ground and mixed thoroughly with potassium bromide .Forty scans were obtained at a

resolution of 4/cm from 4500/cm.The corresponding graphs are shown in fig 1,2,3&4.

X-ray diffraction:[14,15]

The crystalline state of different samples was evaluated with X-ray powder diffraction. Diffraction patterns were obtained using an XPERT-PRO diffract meter (PAN atypical) with a radius of 240nm. The Cu Kα radiation (K α 1.54060A°) was Ni filtered. A system of diverging and receiving slits of 1° and 0.1mm respectively was used. The pattern was collected with 40kv of tube voltage and 30 mA of tube current and scanned over the 2_{φ} range of 5-60°. The corresponding results were shown in fig 5, 6 & 7.

RESULTS:

Table 1: Formulation of solid dispersions in various ratios:

Contents	F1	F2	F3	F4	F5	F6	F7	F8
Nabumetone	1	1	1	1	1	1	1	1
PEG 4000	1	2	3	4	-	-	-	-
PEG 6000	-	-	-	-	1	2	3	4

Table 2: Drug content

Formulation	Drug content (%)
F1	9869
F2	89.78
F3	88.53
F4	99.67
F5	95.56
F6	92.67
F7	96.34
F8	95.23

Table 3: Dissolution studies of formulations with PEG 4000.

Time	F1	F2	F3	F4	Pure Drug
0	0	0	0	0	0
10	12.34	14.4	32	44	9.12
20	20.12	34.2	34	56	15.02
30	29.34	39.6	48	67	21.21
40	32.34	44.3	55	79	25.05
50	40.12	51.2	62	95	32.23
60	52.23	63	70	98	39.01

Table 4: Dissolution studies of formulations with PEG6000.

Time	F1	F2	F3	F4	Pure Drug
0	0	0	0	0	0
10	10.56	12.23	15.56	20.12	9.12
20	15.12	20.34	24.34	30.23	15.02
30	26.23	33.23	35.56	41.23	21.21
40	30.34	44.56	46.34	52.34	25.05
50	35.54	49.23	51.23	60.43	32.23
60	40.12	51.43	60.23	74.45	30.01

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Figure 1: FTIR spectra of pure drug

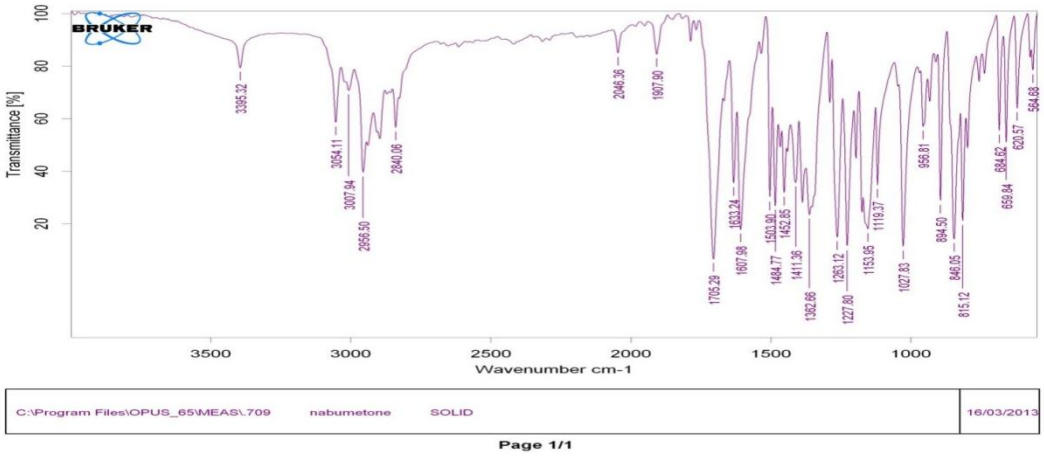

Figure 2: FTIR SPECTRA of PEG 4000

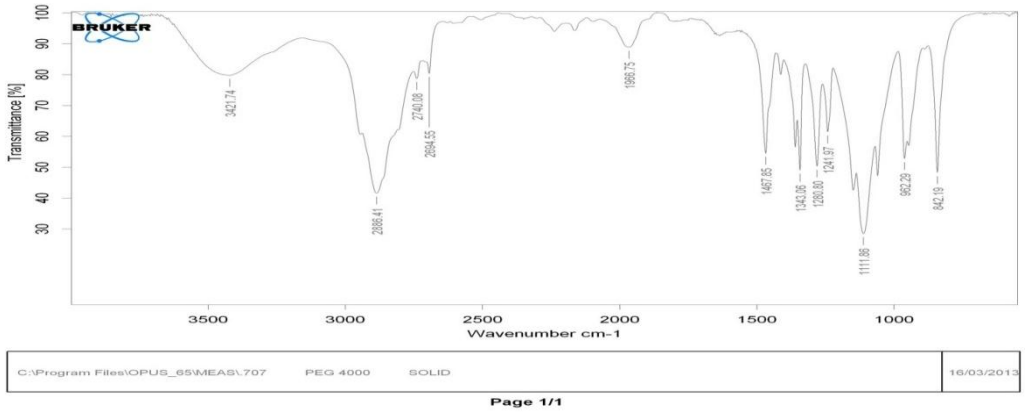

Figure 3: FTIR SPECTRA OF PEG 6000

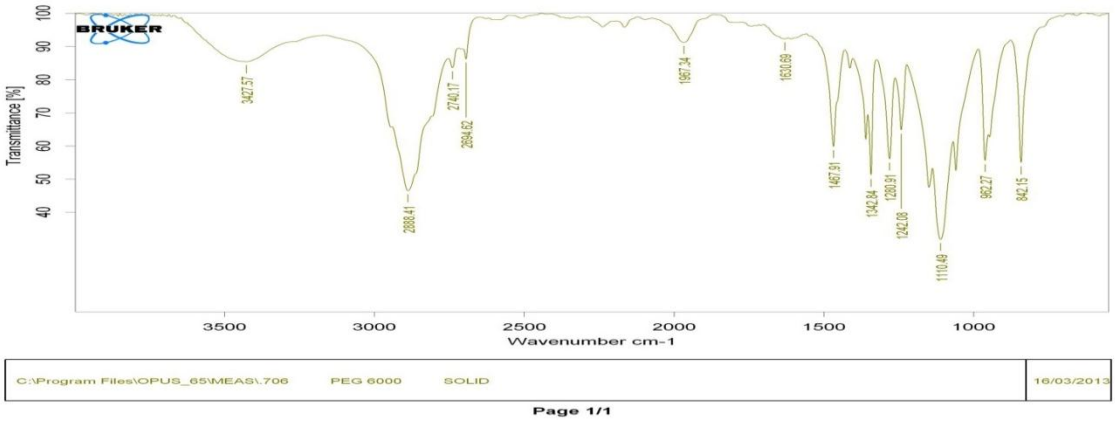

Figure 4: FTIR Spectra of solid dispersion

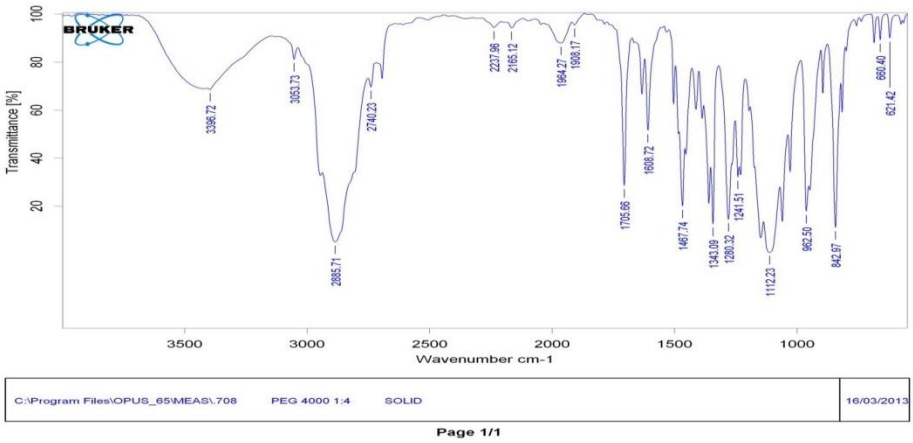

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Figure 5: XRD spectra of nabumetone:

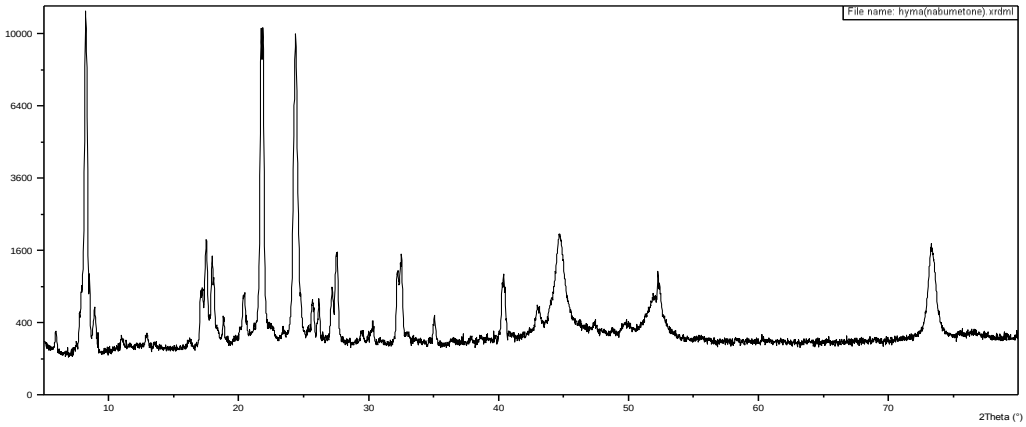


Figure 6: XRD spectra of PEG 4000

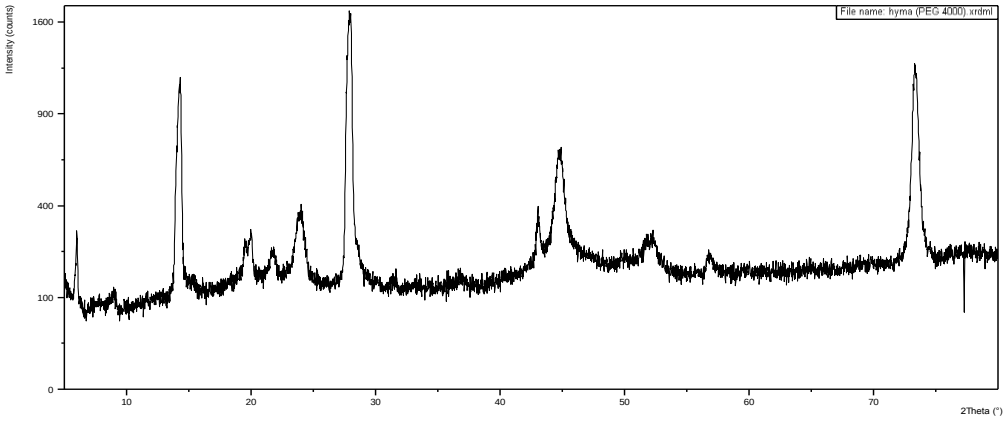


Figure 7: XRD spectra of solid dispersion

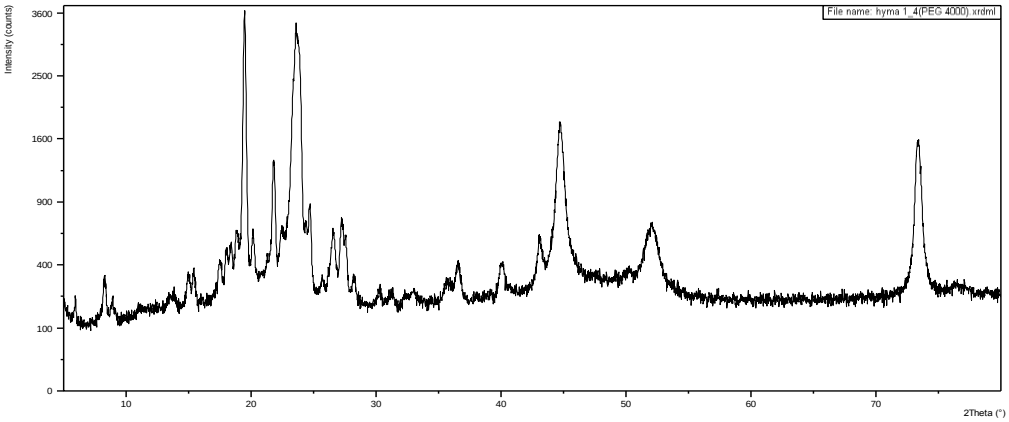


Figure 8: Dissolution profile of solid dispersions with PEG 4000

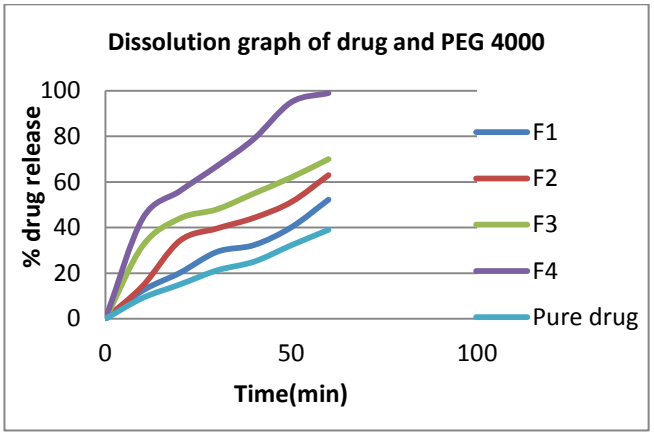
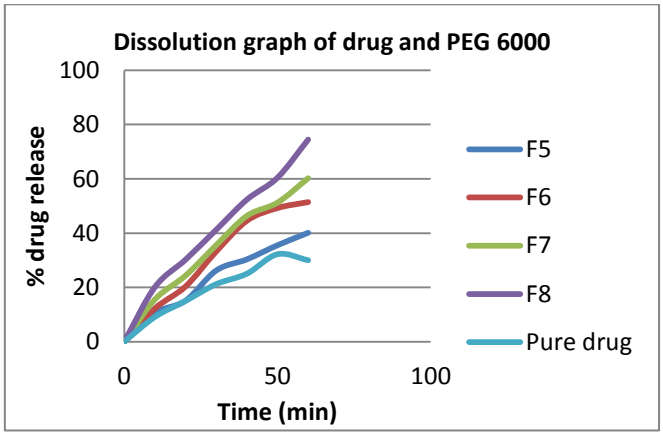


Figure 9: Dissolution profile of solid dispersions with PEG 6000



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DISCUSSION:

FTIR spectra:

As can be seen, a strong absorption band of c=0 stretching at 1705 and C=C ring stretching at 1607; 1633; 1484; 150cm-1. Occurs int the IR spectrum of Nabumetone. The same absorption bands at 1705 & 1605 cm-1 are present in the spectra of SOLID DISPERSION of Nabumetone and PEG 4000.The absence of any shift of carbonyl stretching band and alkenes ring stretching band suggested that know chemical interaction occurs between Nabumetone and PEG 4000[14].

Dissolution Studies

Invitro Drug Release:-Dissolution profiles of pure drug and solid dispersions show that improved dissolution rate is proportional with carrier and drug ratio. The influence of PEG 6000 & PEG 4000 on the dissolution of can be explained by the formation of region of high concentration of dissolved polymer at the surface of drug crystals in which the drug can solublise and subsequently diffuse and dilute in the bulk of the solution. At the end of I hour, F1 is 90, F2 is 92, F3 is 95, F4 is 101.12, F5 is 100.09, F6 is 99.14, F7 is 99 and F8 is 98.Based on dissolution studies the optimized formula was found to be which released 99 % at the end of 1 hour compared to pure drug releasing 39.01 at the end of one hour. Therefore f4 was further investigated for further evaluation[17].

XRD studies:

1n XRD study, characteristic peak of drug appeared in 20 range of 10°-30° indicating that the unprocessed drug was a crystalline material. The pure drug exhibit, its characteristic diffraction peaks at various diffraction angles indicating the presence of crystallinity. The X-Ray diffraction study of solid dispersion showed broadening and reduction of major drug peaks indicating that mostly an amorphous form existed in solid dispersion. These results could explain the observed enhancement of solubility and rapid dissolution of drug in solid dispersion.

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