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AN APPROACH FOR IMPROVEMENT OF THE WATER SOLUBILITY OF NIMESULIDE IN SOLID DISPERSION WITH PEG 4000

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INTRODUCTION

Many drugs show bioavailability problems due to their low water solubility, slow dissolution rate, and instability in the gastrointestinal tract. Nimesulide is a non-steroidal anti-inflammatory, analgesic and antipyretic agent, chemically is N-(4 nitro-2-phenoxyphenyl) methane sulfonamide. It is poorly soluble in water and irregularly absorbed by gastrointestinal tract. Among the various approaches to improve the dissolution of poorly soluble drugs, the preparation of solid dispersions has often to be successful [1]. Solid dispersion (SD) is defined as the dispersion of one or more active ingredients in inert carriers at solid state prepared by fusion, solvent, or solvent-fusion methods. In solid dispersions, the particle size of the drugs was reduced, wettability and the dispersibility of the drugs were enhanced; therefore, drug dissolution was improved markedly. Solid dispersion is a promising approach to improve the dissolution and bioavailability of drugs [2]. The methods utilized in the preparation of solid dispersion include melting, use of common solvent and a combination of melting and solvent approach[1,6]. Various hydrophilic carriers, such as polyethylene glycols, polyvinyl pyrrolidone, and hydroxyl propyl methylcellulose have been
Investigated as carriers for solid dispersions, improvement of dissolution characteristics and
bioavailability of poorly aqueous-soluble drugs[1,6]. Solid dispersion prepared from soluble carriers such as polyethylene glycol, usually have the disadvantage of being tacky and therefore difficult to subdivide and handle. PEG solid dispersions were formulated using combinations of melting and solvent approach in which the melted drug and carrier mixture were granulated with excipients that result less tacky granulation.

MATERIALS AND METHODS

Preparation of Solid Dispersions

Solid dispersions were prepared by taking different ratios of nimesulide, PEG 4000 calculated on the weight basis by the melting and solvent approach method. The solid dispersions were prepared by a solvent-melting method using different concentrations (0-20%w/v) of PEG 4000. In the solvent-melting method, the required amount of PEG 4000 was melted in a glass container on a heating mental maintained at a temperature of about 50–60°C. The required amount of nimesulide (1%w/v) solution in chloroform was prepared and added to the molten PEG 4000 and mixed thoroughly with a glass rod for 15 min. The glass container was placed in deep freezer at -70°C for 1 day; the mixture cooled rapidly and solidified. The solidified mixture was then powdered in a mortar, sieved through an 85-mesh screen, and stored in a screw-cap vial at room temperature until use [3].

Solubility determinations of nimesulide

Solubility determinations were performed in triplicate according to the method of Higuchi and Connors[8]. An excess amount of nimesulide and solid dispersion of different concentration of PEG 4000 was placed in a separate glass beaker, which contain 10 mL of an aqueous solution, until saturation. The samples were shaken at 37 ± 0.5 °C for 24 h in a shaking incubator (Lab tech, Daihan Labtech Co., Ltd.) at 100 rpm. After 24 h, the samples were filtered through a filter paper. The filtrate was suitably diluted and analyzed spectrophotometrically at 296 nm using a UV-vis spectrophotometer (Shimadzu UV-1700, Pharm Spec).

RESULT AND DISCUSSION

Solubility Studies

The solubility behaviour of nimesulide from solid dispersion, which have 0-20% (w/v) PEG 4000 compositions, showed an increased solubility (**Table 1**). Maximum solubility of nimesulide 360µg/ml was observed at 20%w/v PEG 4000 concentration (**Figure 1**)

TABLE 1: EFFECT OF PEG 4000 CONCENTRATION ON NIMESULIDE SOLUBILITY

Concentration of drug(%w/v)	Concentration of polymer(PEG4000) (%w/v)	Physical appearance of product	Solubility (µg/ml)
1	0	Yellow –white crystalline powder	10.9
1	2	Yellow –white crystalline powder	75.1
1	4	Yellow –white crystalline powder	120.2
1	6	Yellow –white crystalline powder	160.5
1	8	Yellow –white crystalline powder	178.1
1	10	Yellow –white crystalline powder	192
1	12	Yellow –white crystalline powder	240.2
1	14	Yellow –white crystalline powder	262.6
1	16	Yellow –white crystalline powder	292
1	18	Yellow –white crystalline powder	332
1	20	Yellow –white crystalline powder	360

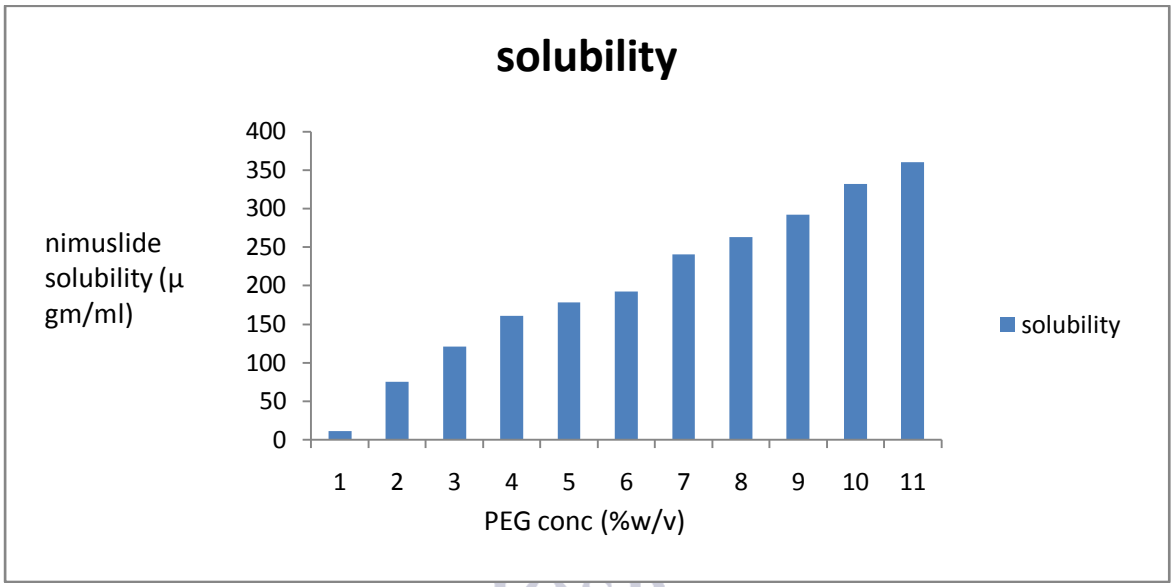

FIG. 1: EFFECT OF PEG 4000 CONCENTRATION ON NIMUSLIDE SOLUBILITY

CONCLUSION AND DISCUSSION

The solubility of nimesulide can be enhanced in Solid Dispersion with PEG 4000. The solubilization effect of PEG 4000, reduction of particle aggregation of the drug, absence of crystallinity, increased wettability and dispersibility,and alteration of surface properties of the drug particles may be responsible for the enhanced solubility of nimesulide from its Solid dispersion. It can be concluded that nimesulide SDs with PEG 4000 provide a promising way to enhance its solubility.

REFERENCES

1. J.E.F. Reynolds, Martindale: The Extra Pharmacopoeia XXX, Pharmaceutical Press: London,30, 1993,279–280.
2. M. Moneghini, Characterisation of nimesulide–betacyclodextrins systems prepared by supercritical fluid impregnation, European Journal of Pharmaceutics and Biopharmaceutics,58,2004, 637-644.
3. N.R. Saha, Solubility enhancement of nimesulide and ibuprofen by solid dispersion technique, Indian j.pharm.sci.,64(6),529-534.