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Research Article

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Preparation and *In vitro* Evaluation of Solid Dispersion of Finasteride

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ABSTRACT

Solubility is an important physiochemical element that affects the absorption and effectiveness of desired drug. Failure in formulation development of the drug has been considered as the consequences of its poor aqueous solubility. The reduced solubility of and low dissolution rate in aqueous gastrointestinal tract most often lead to inadequate bioavailability of the drug. In the present study the solubility and dissolution rate of finasteride which show poor solubility has been developed by solid dispersion(SD) technique with different polymers such as polyethylene glycol 6000 (PEG6000) and Hydroxypropyl Methyl Cellulose (HPMC). SD of finasteride (FNS) was prepared by using 60,120 and 200 mg of the polymer for 200 mg of the pure FNS in each formula using solvent evaporation method. Formula containing 200mg of HPMC showed best release rather than other formulas.

Keywords: FNS; HPMC; PEG 6000; SD

INTRODUCTION

The term "Solubility" can be defined as the ability of the solid, liquid or gaseous material (solute) to be dissolute in the solvent to make a homogenous solution [1]. The solubility scope varies from the very soluble to practically insoluble. The term "insoluble" is used when the solute is poorly or very poorly soluble in solvent system [2]. Table 1 shows the main solubility description terms used by USP and BP. Biopharmaceutical Classification System (BCS) account three major factors that play significant role in controlling rate and extent of the drug absorption from the oral solid dosage forms which are the dissolution, the solubility and the intestinal permeability [3].

In view of pharmaceutical technology; particle size, molecular size, pressure, temperature, polarity and polymorph characteristics are the main factors that affect solubility [4]. Solid dispersion (SD) technique is one of the most important methods that were used to enhance water solubility of poorly soluble solid drugs in gastrointestinal fluids [5]. The term "solid dispersion" denotes the distribution of single or extra solid active substances (hydrophobic) in a solid matrix (Hydrophilic) both of them can be either in crystalline or amorphous form. Methanol, water, ethanol, chloroform and acetic acid are commonly used as solvents in solid dispersion [6]. Finasteride is synthetized 4-azasteroid compound (Figure 1). It is particular inhibitor of steroid (type II 5α- reductase) which is an endogenous enzyme convert the testosterone into 5α dihydrotestosteron (DHT). For this reason such medication can be used for treatment of prostate gland enlargement [7]. Finasteride is white to off-white, crystalline solid. Melts at about 250°C, Soluble in organic solvents especially chloroform and alcohol; very slightly soluble in aqueous media; its empirical formula is $C_{23}H_{36}N_2O_2$ with M.wt. 372.55 g/mol [8], water solubility about 0.05 mg/ml and 75 mg/ml in ethanol and soluble in methanol and chloroform. In Accordance to (BCS); FNS is a class 2 drug (having low solubility and high permeability). It is a weakly acidic drug and have (pKa) of 15.91. [9].

The main purpose of the research is to develop the aqueous solubility of finasteride by preparing it as SD with different ratios of polyethylene glycol 6000 (PEG6000) and Hydroxypropyl Methyl Cellulose (HPMC).

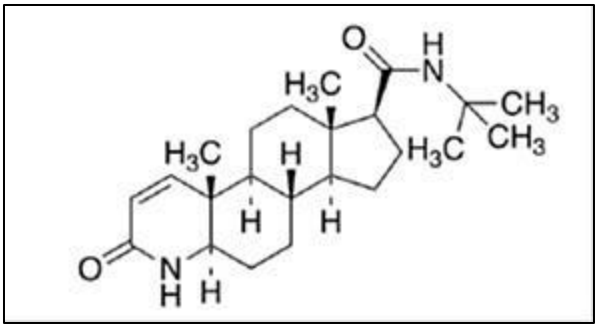

Figure 1: Finasteride chemical structure

Table 1: Solubility descriptive terms

Description	Parts of solvent required for one part of solute
Very soluble	Less than 1 portion
Freely soluble	1-10 portions
Soluble	10-30 portions
Sparingly soluble	30-100 portions
Slightly soluble	100-1000 portions
Very slightly soluble	1000-10000 portions
Practically insoluble	More than 10000

MATERIALS AND METHODS

All the materials used in this research were from laboratory grade. FNS was purchased from a local agent of Hetero Drug, India. HPMC and PEG6000 also purchased from a local agent for HiMedia, India.

Methods

Determination of FNS melting temperature*:*

Melting point of FNS was measured according to U.S.P by capillary tube procedure [10] by recording the temperature that liquefy the powder as the melting point.

Determination of FNS λmax:

Finasteride solution was prepared by dissolving 10 mg FNS in 2 ml methanol and completed with chloroform up to 100 ml which scanned by UV visible spectrophotometer(SPUV-26, Germany) from 200 to 400 nm and the maximum absorption of the drug was determined as its λmax.

Calibration curve of FNS:

It is constructed by preparing a serial of dilution of finasteride with different concentration (15, 25, 50 µg/ml) from stock solution containing 10 mg/100 ml finasteride. The absorbance was then measured at the λmax of the drug. The measured absorbances were plotted against the respective concentrations.

Solubility study*:*

Determination of the solubility is a vital factor for poor water soluble drugs formulations. The saturated solutions of FNS were prepared by adding excess of the drug in distilled water and shacked by the shaker water bath for 24 h at 30°C, filtered by Whatman filter paper, diluted and analyzed by UV spectrophotometer at its λmax. This study was done in triplicate [11]

Preparation of FNS Solid Dispersion

It is prepared by solvent evaporation method [12]. The drug and diverse polymers in dissimilar ratios were dissolved in measured volumes of water and methanol, poured into petri dish and placed in oven at 50°C overnight to complete evaporation of the solvent. The compositions of formulations are shown in Table 2.

Evaluation of Finasteride SD

Determination of production yield of SD:

It is by computing the original weight of the solid components with the ultimate weight of the gained SD as seen in the equation below:

$$SD\ yield = \frac{Practical\ weight\ of\ SD}{Theoretical\ weight\ (polymer + drug)} \times 100$$

Entrapment efficiency of finasteride SD:

Finasteride content in the SD was determined spectrophotometometrically. Saturated mixtures were prepared by addition of excess FNS formula (finasteride + polymer) in distilled water shaking by the shaker water bath for 24 h at 30°C. These solutions were clarified through filter paper then the filtrate was dried in oven at temperature 50°C overnight then added chloroform and spectrophotometric absorbance was measured at λmax of finasteride. The drug content was calculated from the calibration curve and expressed as percent entrapment efficiency ass explained in the equation below:

$$Entrapment\ efficency = \frac{Actual\ weight\ of\ Finasteride\ in\ SD}{Theoretical\ weight\ of\ Finasteride} \times 100$$

Table 2: Composition of fenasteride SD formulations

Formula code	FNS	PEG6000	HPMC
1	200	60	
2	200	120	
3	200	200	
4	200		60
5	200		120
6	200		200

RESULTS AND DISCUSSION

Determination of FNS Melting Temperature

The recorded melting point of FNS was found to be 248°C. This outcome was as the same as references value [13]; at the same time this result reflects the purity of the powder used in this study.

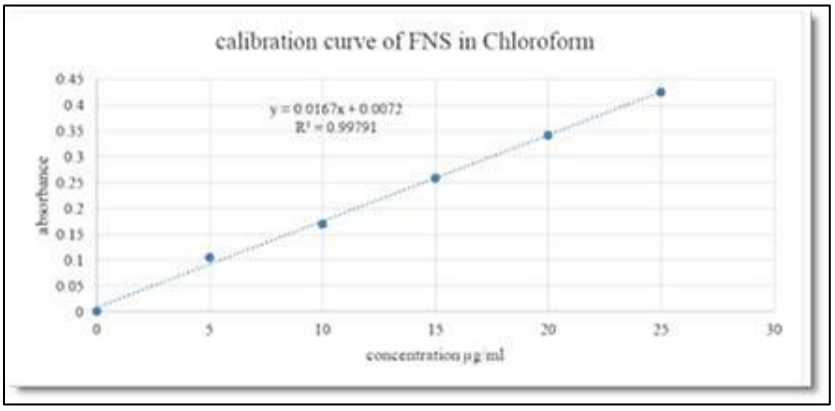

Figure 2: UV peak spectrum of finasteride

Determination λmax

It is done by scanning the solution which contains 10 µg/ml of FNS in chloroform by (UV spectrophotometer) at 200-400 nm to produce the spectrum that shown in Figure 2.

Calibration Curve of FNS

Calibration curve of FNS in chloroform is shown in Figure 3. A trend line was attained by conspiracy of the absorbance versus concentrations which specifies that the curve follows Beer's rule within the series of concentrations used.

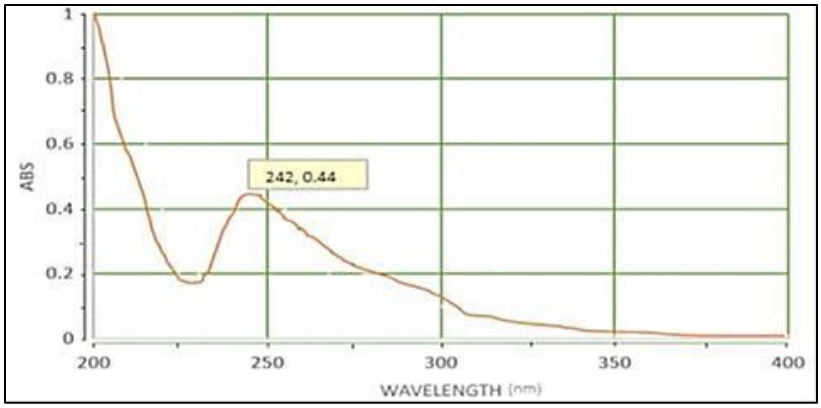

Figure 3: Calibration curve of finasteride

Solubility Study

Saturation Solubility is the extreme amount of a solute that dissolved in a specified solvent; such solution were prepared by adding extra quantities of FNS in distilled water and chloroform and shacked by shaker water bath for 10 min at 30°C. Filtration of solution was performed to exclude any unsolvable particles that might disturb the results. The results of saturation solubility study are shown in Table 3.

Table 3: Solubility data of pure FNS and finasteride SD

Formula code	Solubility (µg/ml)
Pure drug	11.7
1	27.425
2	43.05
3	48.48
4	30.675
5	41.86
6	55.36

Entrapment Efficiency

The Entrapment efficiency is an important measure for nano-particulate system. They give an impression about the %drug that successfully entrapped/absorbed in to nanoparticles and idea about production and scale-up capabilities and the encapsulation power of that particular technique. The solid dispersion method has good or excellent entrapment efficiency. The entrapment efficiency was measured to determine exactly how much FNS was entrapped in SD formula which is necessary to calculate the equivalent weight of FNS SD to that of marked product. The result is shown in Table 4.

Table 4: Percentage yield and entrapment efficiency of FNS SD formula

Formula	Yield %	Entrapment efficiency%
1	42.3	13.3
2	58	21
3	60	23.65
4	48	15.33
5	61.25	20.93
6	76.25	27.68

CONCLUSION

Preparation of FNS solid dispersion has been successfully achieved by using HPMC for enhancement the solubility of drug. *In vitro* solubility studies reveal that there is marked increased in the dissolution profile of F6 when compared to pure FNS.

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