Available online on 15.06.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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Solubility Enhancement of Sulfamethoxazole by Solid Dispersion using Spray Dryer Technique

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ABSTRACT

The aim of this study was to enhance the solubility of SMZ by preparing solid dispersion using a spray dryer. Different polymers were used to study their effect on the solubility of SMZ. Effect of polymer on solubility of drug in the form of solid dispersion was studied by determining the solubility of each solid dispersion separately. It was observed that solubility of drug changes with change in the polymer. As a result of this study, it was found that solubility of SMZ was significantly enhanced by solid dispersion with the polymers especially with the PVP K30 and HPMC E15.

Keywords SMZ, Solubility, Solid dispersion, Spray dryer.

Article Info: Received 18 April 2019; Review Completed 21 May 2019; Accepted 25 May 2019; Available online 15 June 2019

Cite this article as:

Gadakh P, Valvi SS, Jagatp S, Gomase A, Solubility Enhancement of Sulfamethoxazole by Solid Dispersion using Spray Dryer Technique, Journal of Drug Delivery and Therapeutics. 2019; 9(3-s):76-79 **http://dx.doi.org/10.22270/jddt.v9i3-s.2796**

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INTRODUCTION

Sulfonamides are bacteriostatic agents which are used to treat bacterial infection. SMZ is a derivative of sulfonamide which inhibits synthesis Folic acid which is metabolite of bacteria for DNA synthesis[1]. Sulfonamides are poorly water soluble drugs, not well absorbed after oral administration[2]. SMZ is an antibacterial drug which has been used in treatment of various systemic infections in human and other species[3]. SMZ is absorbed from gastrointestinal area however; its absorption and bioavailability are limited with its solubility like all other sulfonamide groups[1].The aqueous solubility of drug molecule is major pharmaceutical challenge as it is critical for achieving optimal oral bioavailability. Modification of physicochemical properties of molecule, the use of surfactant, solubilizer are the some approaches used to improve solubility of poorly aqueous soluble drug molecule[4]. Solid dispersion is a promising approach to enhance the aqueous solubility of drugs.

Solid Dispersion Technique

Solid dispersion has been widely used to improve the solubility and oral absorption of poor water soluble drugs[5]. Solid dispersion is defined as dispersion involving the formation of complex of drug with water soluble carrier by solubilizing of their physical mixture[4]. solid dispersion refer to a group of solid product consisting of at least two different components generally hydrophilic and hydrophobic drug[5].Once the solid dispersion was exposed to aqueous media and carrier dissolved the drug was released as very fine colloidal particles. Because of greatly enhanced surface area obtained in this way the solubility and bioavailability of poorly water soluble drugs were expected to be high[4].

MATERIALS AND METHODS

Materials

Following were used in the study. SMZ, HPMC E15, PVP K30, Mannitol were obtained from Merck. All chemicals used were of analytical grade.

Apparatus

UV Spectrophotometer (Shimadzu UV 1800), IR Spectrophotometer (FTIR Bruker), Spray Dryer, Bulk density apparatus, Moisture analyzer, Motic microscope (Motic DMWB1-223ASC)

Method

The solid dispersion was prepared by spray dryer technique. The drug polymer was mixed separately in given ratio(Table-1).The polymer solutions were prepared by adding given quantity of polymer in methanol. The given quantity of SMZ was added to the polymer solutions and resulting mixtures

were spray dried. Spray drying parameters are described in Table-2.

Table 1: Different drug and polymers ratio.

Polymers	Drug polymer ratio
HPMC E15	1:1
PVP K30	1:1
Mannitol	1:1

Table 2: Spray-Drying parameters

Inlet temperature(°c)	Outlet temperature(°c)	Feed pump rate	Aspiration flow rate
120°c	80°c	1ml/min	40mm³/hr

Evaluations

Micromeritic properties

Micromeritic properties of solid dispersion studied were Bulk density, Tapped density, Compressibility index, Hausner ratio and Angle of repose. The results are reported in Table no-3

Table 3: Micromeretic properties of solid dispersion

Parameters	SD SMZ+HPMC E15	SD SMZ+PVP K30	SD SMZ+MANNITOL
Bulk density (gm/ml)	0.224	0.256	0.392
Tapped density (gm/ml)	0.344	0.392	0.512
Hausner ratio	1.53	1.531	1.306
Carrs index	29.06	34.69	23.43
Angle of repose	33.69	37.69	32.01
Particle Size(µm)	3-6	2-5	5-9
Moisture content(%)	1%	0.5%	1%

Solubility study

Solubility of SMZ was studied in water. Drug solubility was determined by adding excess amount of SMZ and solid dispersion in 50ml distilled water separately at 37°c ±3°c respectively. The solution formed were equilibrated under continuous agitation on mechanical stirrer for 24hrs and then solution was filtered through 0.45µm filter paper to obtain clear solution. Then suitable dilutions were prepared and absorbance of the sample was measured using UV spectrophotometer at 256nm and concentration in µm/ml was determined. The results are reported in Table no-4

Table 4: Solubility of SMZ and solid dispersion in water (µm/ml)

SMZ	Solid dispersion DRUG+HPMC E15	Solid dispersion DRUG+PVP K30	Solid dispersion MANNITOL
18.62µm/ml	94.67µm/ml	95.80µm/ml	45.08µ/ml

Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectral measurements were taken at ambient temperature using a FTIR Bruker Model 9003 5239.FTIR spectra were obtained by powder diffuse reflectance on FTIR spectrophotometer.

Figure 1 shows molecular interaction between SMZ and polymers used in solid dispersion was investigated by FT-IR spectroscopy. The spectral differences between the solid dispersion and SMZ are seen at wavenumber 3370cm^{-1} to 4000cm^{-1}. The spectrum is particularly noticed at wave numbers 3400cm^{-1} in which the N-H strain is shifted to a lower wave number.

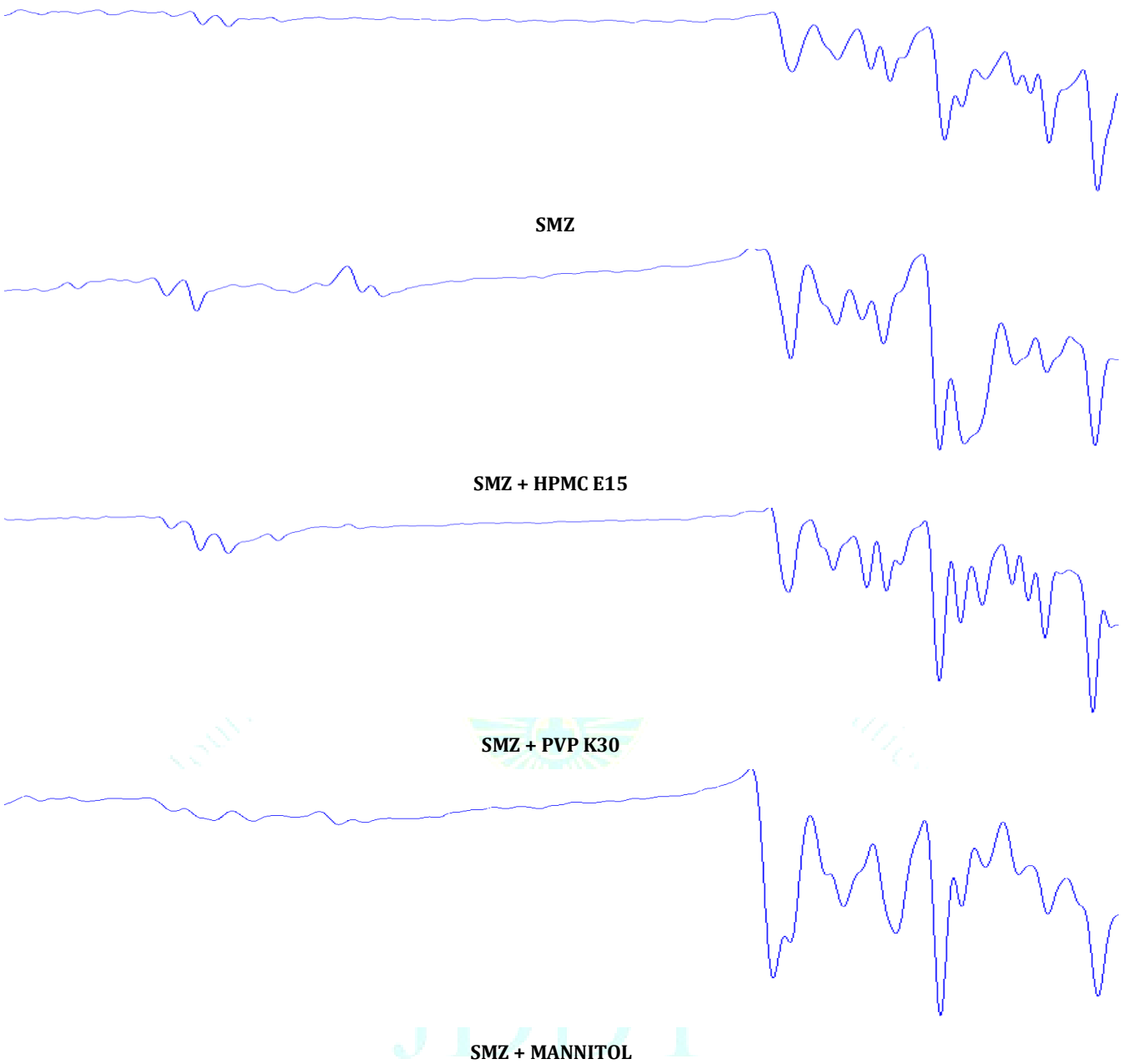

Figure 1: FT-IR Spectra of Solid dispersion

RESULT AND DISCUSSION

The closeness of values of bulk density and tapped density indicates the free flowing property of solid dispersion. The values of compressibility index, Hausner ratio and angle of repose indicate that the flow character of solid dispersion is fair and no aid is needed to increase the flow properties. Particle size varies according to the polymer. Moisture presence may aggregate the solid dispersion. Moisture found in solid dispersion was within limit(≤1).

From this study an increased in solubility of SMZ was achieved by preparing solid dispersion of SMZ using spray dryer technique. Solubility of SMZ was found to be increased in its solid dispersion forms significantly compare to its aqueous solubility. About 3-5 folds solubility of SMZ was enhanced using the solid dispersion. Solid dispersion with PVP K30 and HPMC E15 (95.80µm/ml and 94.67µm/ml respectively) shows greater solubility enhancement compare to Mannitol.

FT-IR spectroscopy analysis is used to characterize the complex of two compounds in solid dispersion which can be linked by hydrogen bond. As seen in fig 1 there is shift of N-H strain which indicates the formation of hydrogen bond as a consequence of solid dispersion phase formation between SMZ and polymers.

CONCLUSION

It can be concluded that solid dispersion technique is novel technique for solubility enhancement of poorly aqueous soluble drugs. Enhancement in solubility of SMZ is an indication that Solid dispersion using spray dryer can be used in future for solubility enhancement of poorly water soluble drugs in which low bioavailability is concern.

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