Journal of Applied Pharmaceutical Science Vol. 5 (Suppl 1), pp. 046-053, May, 2015
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2015.54.S8
ISSN 2231-3354

Enhancement of Simvastatin dissolution by surface solid dispersion: effect of carriers and wetting agents

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ARTICLE INFO

Article history:
Received on: 29/01/2015
Revised on: 11/03/2015
Accepted on: 07/04/2015
Available online: 15/05/2015

Key words:
Simvastatin, poor water solubility, surface solid dispersion. enhancing dissolution, solid dispersion

ABSTRACT

The aim of this work was to improve the aqueous solubility of simvastatin using the surface solid dispersion (SSD) technique. Water soluble (mannitol and lactose) and insoluble (Avecil PH101) carriers were used. The effect of the addition of polymeric wetting agents (namely PEG6000, Pluronic F68, Myrj 52 and PVP K-30) to drug/carrier composite was also investigated. SSD was prepared by solvent evaporation technique. All formulations were studied regarding the dissolution behavior and solid state characterization (DSC, FT-IR and X-ray diffraction). Both water soluble and insoluble carriers improved dissolution behaviour compared to unprocessed drug, with the former showing the best results. Addition of wetting agent to the water insoluble carrier greatly improved drug dissolution, with PVP K-30 showing better dissolution parameters that was comparable to that of marketed product. Physical state characterization using DSC indicated the marked reduction in drug crystallinity. Xray diffraction confirmed drug amorphousness. The results indicated that SSD may serve as a successful strategy for enhancing solubility of poorly water soluble drugs by proper manipulation of the used additives.

INTRODUCTION

Oral route of drug administration is the most common and accepted delivery method from the patient's prospective. Nevertheless, it is a problematic and inefficient route of delivery for many drugs specially poorly water soluble ones. The bioavailability of poorly water soluble drugs is a true challenge that faces the development of the conventional oral solid dosage forms. In consequence of the low water solubility of such drugs, bad dissolution profile and lower absorption and bioavailability are usually accompanying those drugs (Gu *et al.*, 2007). Recent advances in biotechnology, coupled with combinatorial chemistry and parallel synthesis are continuously increasing the number of lipophilic molecules which are difficult to deliver due to bioavailability issues (Varma, 2004). Although there are techniques that can resolve the bioavailability issue with poorly water-soluble drugs, these techniques involve complicated technology and sophisticated machinery which are ultimately not at all cost effective. Therefore, the improvement of drug solubility, thereby its oral bio-availability, remains one of most challenging aspects of drug development process especially for oral drug delivery system. There are numerous approaches available and reported in literature to enhance the solubility of poorly water soluble drugs. Many techniques have been adopted to improve drug solubility such as formation pharmaceutical salt pharmaceutical co-crystals, micronization and solid dispersion (Remenar *et al.*, 2003; Vogt *et al.*, 2008). Solid dispersions represent a useful pharmaceutical technique for increasing the dissolution, absorption and therapeutic efficacy of drugs in dosage forms. The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The former could be crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles or crystalline particles(Chiou and Reigelman, 1971). Formation of surface solid dispersions /disposition (SSD) is a technique by which solid dispersion is performed and precipitated over a surface of inert carrier. This strategy is used to reduce the agglomeration of the drug by increasing its exposed surface area in a way that would improve its dissolution rate.

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The technique of SSD can overcome some of the limitations of the conventional solid dispersions. SSD may be achieved by the incorporation of the drug solution into carrier forming a slurry, and the subsequent deposition of the drug solution onto adsorbent carrier (Abd Elbary *et al.,* 2011).

Many materials reported to perform as carriers in SSD are non- biodegradable, porous materials and mostly hydrophilic in nature and include such compounds as microcrystalline cellulose, sodium starch glycolate, potato starch and croscarmellose. The release of drug from the carrier material depends on the hydrophilic nature, particle size, porosity and surface area of the carrier, which means the larger the surface area available for surface adsorption of the drug, the better the release rate. They can immediately disperse upon contact with water, rendering rapid release of drug particles into the medium. The dissolution of the drug particles is facilitated by the same mechanisms exhibited by the conventional solid dispersion For carriers with a large surface area such as silicon dioxide, a smaller amount of the carrier can increase the dissolution rate significantly. SSD had been demonstrated as a successful method to improve the dissolution rate of many drugs such as Glibenclamide (Abd Elbary *et al.,* 2011), Glimepiride (Kiran *et al.,* 2009) and Nifedipine (Lilithai and Lakshmi, 2010), Telmesartan (Patel *et al.,* 2012).

The aim of this work was to increase the aqueous solubility of Simvastatin (SIM), by using the surface solid dispersion technique poorly water soluble drug,. SIM has low an aqueous solubility (1.45 µg/mL) and therefore low oral bioavailability of about 5% (Rao *et al.,* 2010). Being categorized as a Class II drug (poorly soluble, highly permeable) according to biopharmaceutical classification system (BCS), SIM often shows dissolution rate-limited oral absorption and high variability in pharmacological effect. A comparison will be made between the uses of soluble versus insoluble carrier.

MATERIALS AND METHODS

Materials

Simvastatin (SIM) was a generous gift from Sigma Egypt co. ltd, Egypt. Polyethylene glycol 6000 (PEG6000) and PLX188 (Pluronic F68) were obtained from Memphis Co. (Cairo, Egypt). Myrj 52 and Polyvinyl pyrrolidone K-30 (PVP K-30) from Himedia laboratories Pvt. Ltd (India). Other chemicals and reagents were of analytical grade. Figure 1 represents the chemical structure of the used materials.

Methods

Preparation of surface solid dispersions (SSD)

Preparation of SSD using different carriers

The SSDs of drug with different carriers, namely Avicel PH101, Lactose and Mannitol(F1, F2 and F3, respectively) were prepared using solvent deposition technique (Kiran *et al.,* 2009). The selected drug to carrier ratio was1:9 w/w respectively, so as to provide a large surface area of the carrier upon which the drug will deposit. The calculated amount of drug (100mg) was dissolved in 5 mL ethanol. The solution was added to the carrier while mixing until a homogenous mixture was attained. The obtained slurry was stirred using a magnetic stirrer (LabTech®, Model LMS-1003, Korea) at room temperature until the solvent evaporated completely. The resulting mass was then gently pulverized before passing through a No. 60 sieve and stored over anhydrous calcium chloride in a desiccator.

Insert Table I

Table 1: Key formulation characteristics of prepared formulations.

Formula	Carrier	Additive	
F1	Avicel PH 101	-----	
F2	Lactose	-----	
F3	Mannitol	-----	
F4	Avicel PH 101	Poloxamer188	1:1
F5			1:3
F6	Avicel PH101	PEG 6000	1:1
F7			1:3
F8	Avicel PH 101	Myrj 52	1:1
F9			1:3
F10	Avicel PH 101	PVP k-30	1:1
F11			1:3

Preparation of SDD using different wetting agent

The effect of various polymeric wetting agents in the dissolution of the drug from the water insoluble carrier (Avicel PH101) was studied. Avicel was selected as it is a widely used formulation filler. The idea was to deposit the drug together with the polymer as solid solution onto the carrier surface. The polymeric additives used were Polyethylene glycol 6000 (PEG6000) and Poloxamer 188 (Pluronic F68), Myrj 52 and Polyvinyl pyrrolidone K-30 (PVP K-30) giving formulation F4 through F11 (Table 1). Each additive was firstly mixed with the drug at ratios of 1:1 and1:3 w/w drug:additive ratio, and then dissolved in ethanol. Each solution was poured directly onto the carrier while mixing and preparation continued as mentioned in the previous section

Preparation of physical mixture

Physical mixture was prepared for selected formulation by simple mixing the ingredients as that in F11 in geometric proportions a mortar using spatula without applying pressure and passed through sieve No. 60.

Drug Content

An accurately weighed amounts of surface solid dispersion preparations equivalent to 20 mg of SIM were dissolved in 10 mL of ethanol. The stock solutions were diluted in distilled water and analyzed by UV-vis spectrophotometry (Shimadzu UV-160A Spectro-photometer, Shimadzu, Japan) at 240nm.

In vitro dissolution studies

In-vitro dissolution studies of samples were carried out using USP apparatus II paddle method. Accurately weighed samples equivalent to 10 mg of SIM were packed in hard gelatine capsules and placed in 900 ml of dissolution medium, maintained

at 37 ± 0.50°C rotated at 50 rpm. Drug release studies on poorly water-soluble drugs often require dissolution media encompassing small amounts of surfactants or solvents to provide sink conditions for dissolution of poorly soluble drugs (Serajuddin *et al.*, 1988). The use of surfactants in the dissolution systems has physiological significance too as natural surfactants like bile salts are usually present in the gastrointestinal tract. For this reason, 0.1% sodium lauryl sulphate w/v in distilled water was used as the dissolution media. At different time intervals, aliquots were withdrawn and filtered through 0.45 mm membrane filter. The concentration of SIM at each sampling time was analyzed spectrophotometrically by blank correction method.

Solid state characterization

Differential Scanning Calorimetry (DSC)

DSC is used to determine any physicochemical interaction between drug and excipients. DSC analysis was performed using a Model DT-60 DSC (Shimadzu). Samples weighing 3-6 mg were heated in hermetically sealed aluminum pans over a temperature range of 30°C–300°C at a constant rate of 10°C/min under a stream of nitrogen.

X-ray Powder Diffractometry (XRPD)

XRPD was used to trace any change in the crystalline state of the drug that may affect its solubility. XRPD of the drug, excipient and optimized SSD formulation were plotted using X-ray diffractometer (Mnisantis XMD-300, powder diffractometer with CuKα radiation). The scanning rate employed was 8°/min over a 2θ range of 0–80.

Fourier transform infrared spectroscopy (FTIR)

FTIR spectrum helps to determine any chemical interaction between drug and excipients. FTIR spectra of the drug, excipients, and optimized SSD formulation were conducted using FTIR spectroscopy (Tensor 37, BRUKER, Germany) in the frequency range of 4000–800/cm.

RESULTS AND DISCUSSION

Drug Content

Drug content for all SSDs were in the range of 98.77–101.3%, which is acceptable according to the United States Pharmacopeia (2007). This would indicate a homogeneous distribution of the drug in the prepared formulations.

Dissolution Studies

The dissolution profiles of different SSD formulations using Avicel, Lactose and Mannitol (F1, F2 and F3, respectively) and pure SIM as control are presented as percentage cumulative drug released versus time plots in Figure 1. Insert Figure 1 Dissolution parameters represented as the percentage drug released after 10 min (Q_{10}), and the time required for the release of 50% of the drug (t_{50}) were calculated and are shown in Table 2. Additionally, percentage dissolution efficiency (%DE) was calculated from the area under each dissolution curve at certain time (t), and measured using the trapezoidal rule and expressed as a percentage of the area of the rectangle described by 100% dissolution at the same time (Khan, 1975).

Insert Table II

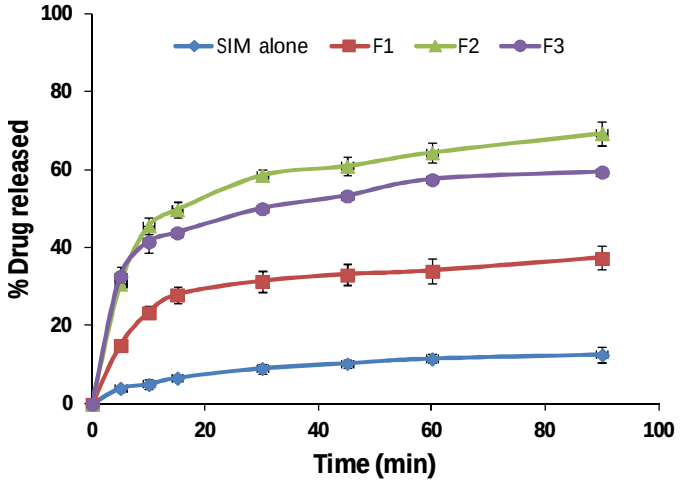

Fig. 1: Dissolution profiles of pure SIM, solid surface dispersions using Avicel (F1), Lactose (F2) and Mannitol (F3) as carriers (n=3 ±SD). Standard error bars if not shown are embedded within the symbol.

Table. 2: The dissolution parameters of SIM from different formulations and pure drug; where Q_{10} is the percentage drug released after 10 min, t_{50} is the time required for the release of 50% of the dose and %DE is the percentage dissolution efficiency.

formula	Q_{10}	t_{50}	%DE
Drug alone	5.03 ±0.64	>90	9.48
F1	23.5 ±2.1	>90	31.2
F2	45.6 ±2.6	15 ±2.1	57.4
F3	41.5 ±1.8	30 ±1.9	50.5
F4	32.0 ±1.7	90 ± 2.1	41.4
F5	26.6 ±2.0	90 ±3.6	36.1
F6	8.20 ±1.6	>90	25.0
F7	31.2 ±2.4	45 ± 2.1	46.2
F8	43.0 ±3.1	30 ±1.7	50.5
F9	52.3 ±2.8	10 ±0.66	66.2
F10	40.1 ±1.6	30 ±0.58	55.8
F11	58.7 ±3.2	<10	81.1
PM (F11)	28.3±1.7	90 ±1.5	30.3
Commercial drug	63.0 ±2.1	5.2 ±2.1	85.3

All tests were performed at least in triplicates.
PM for physical mixture.

The dissolution profile of pure SIM showed a poor dissolution profile, where the Q_{10} was only about 5% with a DE of 9%, indicating its poor solubility and wetting properties. All formulations significantly ($P < 0.05$) enhanced drug dissolution compared to pure drug. There was a rapid release of the drug (Q_{10} of 23.5±2.1, 45.6±2.6 and 41.5±1.8 for F1, F2 and F3, respectively) followed by a gradual release. The overall enhancement may be due to the SIM particles adsorbed over the carrier surface in an extremely fine state of subdivision or molecular form. The resulting decrease in particle size and the concomitant increase in the surface area increased greatly the dissolution of the drug compared to the drug alone (Abd Elbary *et al.*, 2011). Preparing SSD using the insoluble Avicel PH 101 (F1)

enhanced the dissolution parameters of SIM with about 5- and 3-folds regarding Q_{10} and %DE, respectively, compared to pure SIM. With F2 and F3, drug dissolution was greatly enhanced compared to that of F1 ($P<0.05$). With respect to the dissolution parameters, there was a comparable increase in Q_{10} of about 9-fold relative to control (Table 1). There was a rapid initial drug release of around 50% of the dose after 15 min from both formulations. Comparing the drug dissolution from F2 and F3 to that of F1, the clear superiority of the former formulations could be due to the good hydration capacity of these soluble carriers compared to the insoluble Avicel PH 101. Avicel is a widely acceptable excepient in solid dosage forms due to its free flowing properties and compactability. Therefore, trials were conducted to improve the drug dissolution from SSD using Avicel by the addition of wetting agent to the drug/carrier composite at ratios specified in Table 1. The dissolution profiles of formulations F4 through F11 are shown in Figure 2. Dissolution parameters are listed in Table 2. The dissolution results indicated that addition of a wetting agent to drug/Avicel PH101 composite significantly improved the dissolution profiles of SIM compared to control pure drug as well as F1. Enhanced dissolution may be attributed to the de-aggregation and increased wetting of drug due to the presence of the polymer. Drug and polymer co-precipitated as a solid solution at the carrier surface (see the characterization). In solid solutions, the active substance is embedded in a hydrophilic carrier. The hydrophilic polymer undergoes rapid dissolution upon exposure to the dissolution medium and attains high concentration in the diffusion layer of the drug. The dissolved polymer then increases wetting of the drug in the diffusion layer and therefore increased dissolution rate of SIM (Gines *et al.,* 1994). Insert Figure 2. The following section will discuss in details the effect of each wetting agent on the drug dissolution compared to drug alone and drug/Avicel SSD. Poloxamers (PLX) are non-ionic surfactants that have been extensively used as wetting and solubilizing agents. For SSD using PLX 188 as wetting agent (F4 and F5), the dissolution parameters were significantly ($P<0.05$) higher than that of the pure drug at the two studied drug/copolymer ratios (Figure 2A). This could be due to the solubilizing effect as a result of improving in the wetting of the hydrophobic SIM as PLX have the capability to alter physical properties such as hydrophobicity and wetting properties (Vyas *et al.,* 2009). Compared to SSD with Avicel PH101 alone (F1), both F4 and F5 didn't significantly ($P>0.05$) improved SIM dissolution parameters. This means that incorporation of PLX 188 did not add any significant advantage to drug dissolution over that of the carrier alone. It is worth noting that increasing PLX 188 concentration in F5 resulted in a decrease, rather than increase, in drug dissolution. This may be explained by considering the thermo-reversible gelation activities of the polymer, which is a known phenomena of PLX polymers (Elkordy *et al.*, 2012). The gel formation capability of the PLXs based on both critical micelle temperature (CMT) and concentration. CMT is the temperature where micelles are formed, and is reported to be about 24°C (Lin and Alexandridis, 2002). Above which the liquid-phase micelles formed by PLX copolymers undergo transition into liquid crystal gel phases in response to increased temperature (Wanka *et al.,* 1994). In this study, though the temperature of the dissolution medium was above CMT (37 °C in the dissolution medium), but the concentration of the polymer was too small to form the gel structure, as it was reported that PLX 407 forms gel above a concentration of about 15% w/v (Sharma and Bhatia, 2004; Kwon *et al.,* 2001). However, at the microenvironment level in the diffusion layer, the concentration may be at the saturation level. This may resulted in the formation of a gel microenvironment that would slow down drug diffusion through it by increasing the viscosity. This could explain why higher PLX 188 concentration showed less drug dissolution. In respect to F6 and F7, prepared using PEG6000 as wetting agent, both formulations significantly ($P<0.05$) improved drug dissolution compared to pure drug (Figure 2B). However, there was a nonsignificant improvement in drug dissolution compared to F1. Marginal enhancement in drug dissolution from the PEG SSD is suggestive of the formation of non-interacting complex. PEG6000, with its two terminal hydroxyl groups, may formed a hydrogen bonding with Avicel PH101 thus conferring cohesion to the drug carrier composite thus affecting dissolution rate (Alkinlade *et al.,* 2010). Other possible explanation could be due to increased viscosity in the diffusion layer due to the large molecular weight of PEG, resulting in slow down drug movement through it. Regarding formulations containing Myrj 52 (F8, F9) and PVP K-30 (F10, F11) as wetting agent, there was a marked enhancement in drug dissolution compared to both drug and Avicel alone (Figure 2C and D, respectively). The four formulations had a higher % DE and $Q_{10,}$ and lower t_{50} compared to F1. The % DE was increased in the following order: F11 > F9 > F10 > F8. Amongst all tested formulations in this study, F11 showed the highest %DE (81%), highest Q_{10} (about 60%) and lowest t_{50} (5-10 min) (Table 2). This implied the superiority of PVP as a wetting agent in enhancing SIM aqueous solubility. The obtained results could be due to formation of soluble complex between the polymer and SIM in the solid solution state adsorbed upon the carrier surface. In solid solution, the drug is molecularly dispersed within the hydrophilic wetting agent. The latter is now considered as a carrier for the drug. The enhancement of drug release was achieved as the drug was at its amorphous state, so no energy was required to break up the crystal lattice during the dissolution process (Taylor and Zografi, 1997). Besides being the best wetting agent for SIM, there is an additional advantage of using PVP K-30. It was stated that PVP polymers have the capability to stabilize the formed amorphous state of the drug. As the active substance in a solid solution is in an amorphous state and therefore in a more energetic form, and as its surface area is much greater in solid solutions, the question of its physical and chemical stability arises. The main criterion for physical stability is the extent of recrystallization, which can reduce the bioavailability of the active substance. A survey of publications in which recrystallization and chemical stability have been investigated revealed only relatively few cases of instability of the solid solution when using PVP polymers used as carrier (Buhler and Kollidon, 2008).

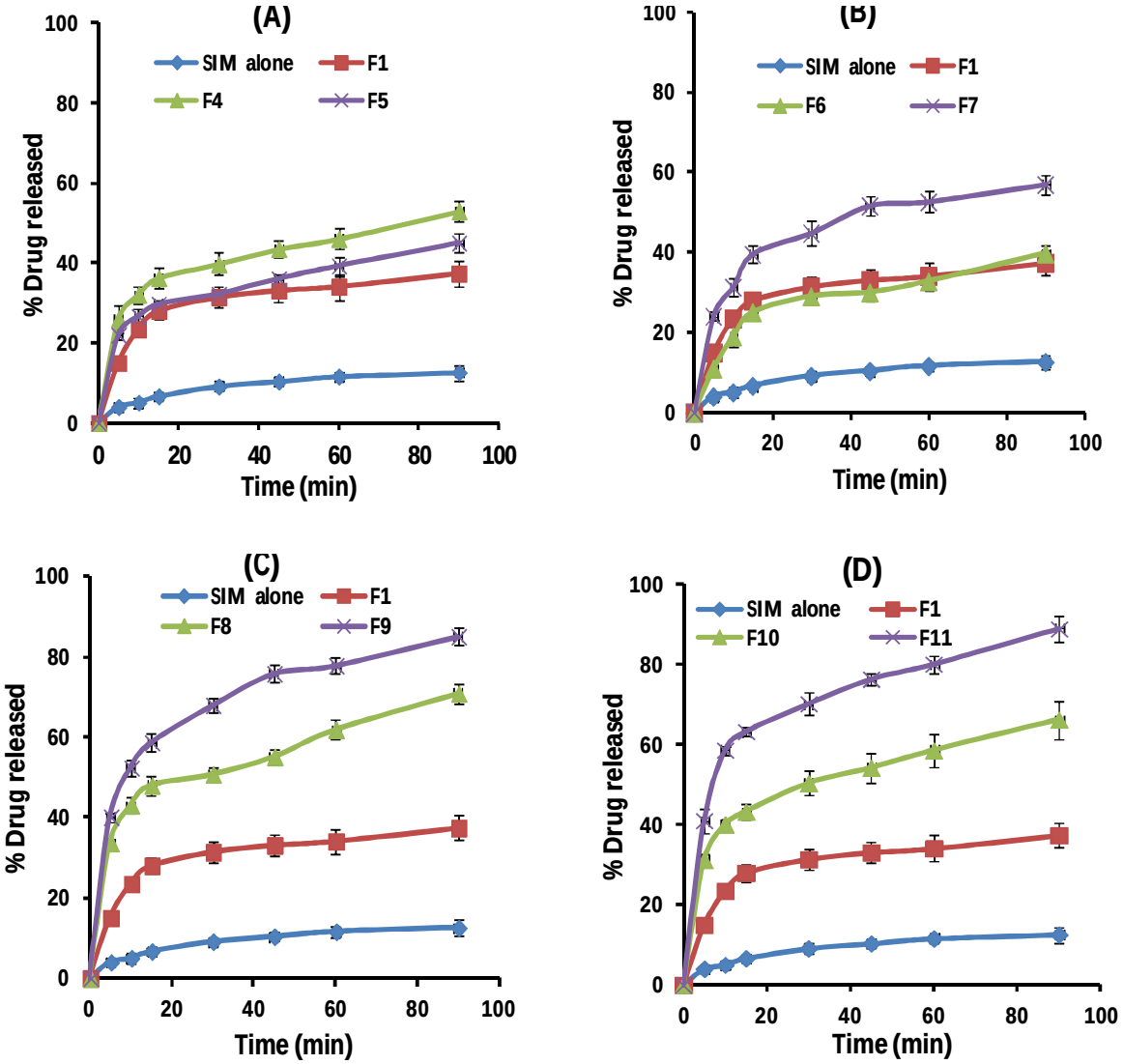

Fig. 2: Dissolution profiles of simvastatin/Avicel SSD formulations prepared using different wetting agents; Poloxamer 188 (A), PEG 6000 (B), Myrj 52 (C) and PVP (D) together with pure SIM and SIM/Avicel SSD. Standard error bars if not shown are embedded within the symbols. For details of formulations refer to Table 1.

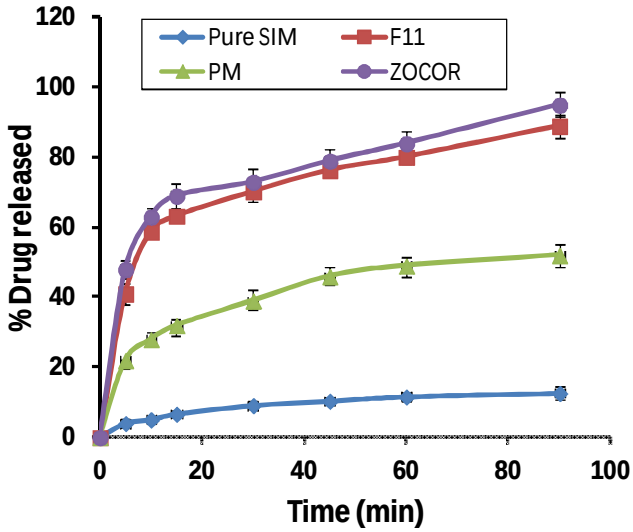

Fig. 3: Dissolution profiles of simvastatin from F11 solid surface dispersion (F11 SSD) , physical mixture (F11 PM), commercial product and simvastatin alone.

Comparison between the best formula (F11), physical mixture and commercial drug

To confirm our assumption that the obtained enhancement of drug dissolution from SSD was due to the formation of solid solution deposited at the carrier surface and to ensure the usefulness of the adopted technique, we compared the drug dissolution from the optimized SSD formula F11 to that of a physical mixture of the same ingredients of F11. The dissolution parameters were then compared to that of pure drug and F11 SSD. Figure 3 shows the obtained dissolution profiles.

Insert Figure 3

The figure illustrates that physical mixture enhanced drug dissolution compared to control drug ($P<0.05$), with a Q10 and DE of 22. and 30% , respectively. Such enhanced dissolution parameters could be due increased drug wettability by PVP. Compared to F11 SSD, drug release from SSD was much higher than that of physical mixture. This could confirms the superiority of the SSD technique to enhance drug dissolution due to increased surface area exposed to dissolution media, and also prove the role of solid solution formed during drug/PVP disposition on the carrier surface during solvent evaporation step.

To evaluate the usefulness and the applicability of our optimized formulation, commercial SIM tablets (Zocor, Merck Sharp and Dohme LTD, Cramlington, UK) was tested regarding drug dissolution and the results were compared to that of F11. The dissolution profiles and parameters are presented in Figure 3 and Table 2, respectively. There was a comparable dissolution behaviour between F3 and commercial product, with similar dissolution parameters ($P>0.05$).The study thus presented a system capable of introducing a formulation of SIM with a potential for increased drug bioavailability similar to commercial drug products.

Solid state characterization of the optimized formulation

To understand the possible mechanism of improved drug dissolution, solid state characterization of the optimized formula (F11), pure drug and individual additives were performed.

The DSC thermograms for SIM, Avicel PH 101, PVP k-30, SSD formula F11 are presented in Figure 4. The sharper the peak obtained in the DSC thermogram, the higher the melting temperature (T_m) and the higher the degree of crystallinity of the structure. Shifting of the peak to a lower T_m or peak broadening would indicate reduced drug crystallinity (Bettinetti *et al.,* 2002). For pure SIM, the DSC thermogram showed a crystalline structure with a sharp endothermic peak at 146°C (Rao *et al.,* 2010). Avicel PH 101 and PVP k-30 showed broad peaks with T_m values of about 80°C and 90°C, respectively.

These peaks are corresponding to desorption of water from the material (Balata *et al.,* 2010). For SSD formula F11, there was a complete disappearance of SIM endothermic peak, with the appearance of broad peak at 100°C could be largely due to the additives. This would indicate elimination of crystalline structure of the drug and increase amorphousness. Such finding would explain the obtained enhancement in drug dissolution.

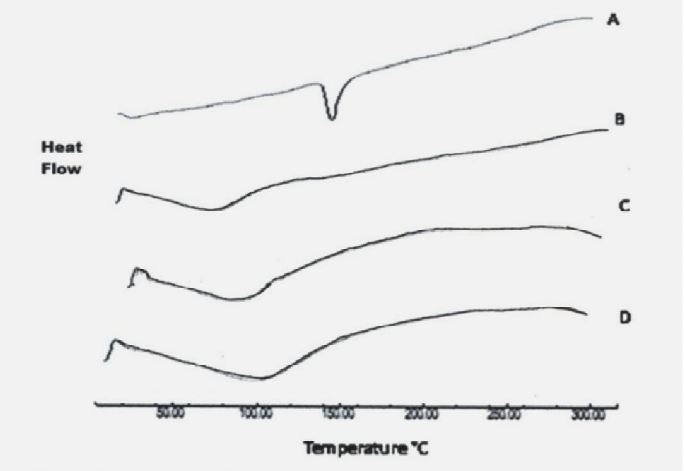

Fig. 4: DSC thermograms of simvastatin (A), Avicel PH 101 (B), PVP K-30 (C), solid surface dispersion F11 (D).

For further investigation of the drug physical characteristics, FTIR spectroscopy was used to study the possible interaction between SIM and other components in the formulation (Figure 5). Pure SIM showed the major peaks at wave-numbers of 3551 cm^{-1} (free O–H stretching vibrations); 3011, 2959, and 2884 cm^{-1} (C–H stretching vibrations); and 1698 cm^{-1} (stretching vibration of ester and lactone carbonyl functional groups).

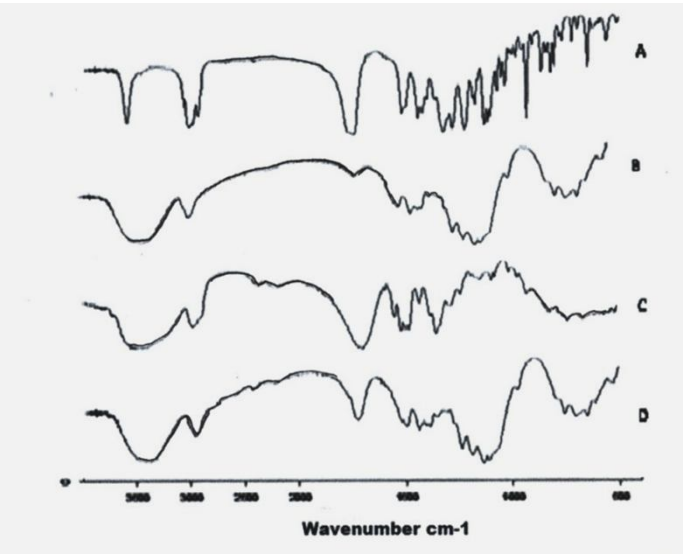

Fig. 5: FTIR spectra of simvastatin (A), Avicel PH 101 (B), PVP K-30 (C), solid surface dispersion formula F11 (D).

Avicel PH 101 showed the characteristic broad O-H stretching vibration band in the spectra which occur at 3330 cm^{-1}due to absorbed water. The FTIR spectrum of pure PVP k-30 showed –O-H stretch at 3482 cm^{-1} due to moisture absorption by the polymer (Muralidhar *et al.,* 2011). Regarding SSD, the spectra clearly show that the O-H stretching was reduced to 3349 cm^{-1}. For the carbonyl stretching there was an obvious disappearance of

some peaks with shifting of the peak to a lower value of 2901 cm^{-1}. PVP has two potential hydrogen bonding sites; one is the nitrogen of pyrrolidone moiety (C-N) and another is the carbonyl group (C=O) of pyrrolidone moiety which exhibit characteristic peaks at 1288 cm^{-1} and 1682 cm^{-1}, respectively. The shifted peak corresponding to –O-H stretch to lower wavelength suggested the formation of hydrogen bonding of drug. This hydrogen bonding could be with PVP K30 or the terminal OH groups of Avicel. The presence of hydrogen bonding in SSD suggested that the drug is present as molecular dispersion rather than clusters of drug crystalline entities. The absence of generation of new peak in any solid dispersion again confirmed absence of strong chemical interaction (Vyas *et al.,* 2009).

The PXRD patterns of pure drug, additives and solid dispersions are presented in Figure 6. The diffraction pattern of the pure drug showed a highly crystalline nature, indicated by numerous distinctive peaks at a diffraction angle of 2θ (28.0°, 22.4°, 18.0°, 17.8°, 16.9°,14.8°, 10.8°, and 9.0°) in a good agreement with previously published data (Rao *et al.,* 2010).

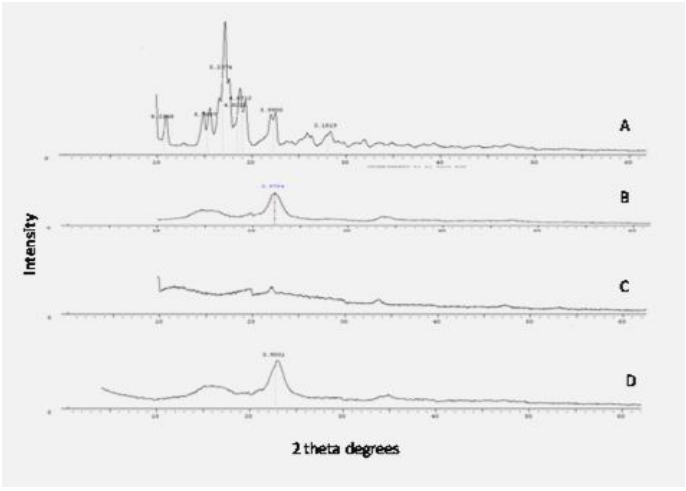

Fig. 6: XRPD of simvastatin (A), Avicel PH 101 (B), PVP K-30 (C) and solid surface dispersion formula F11.

In SSD there is a complete elimination of these peaks, with the presence of the peak corresponding to the carrier Avicel PH 101 at diffraction angle of 2θ at 22.0°. This indicates the complete disappearance of the crystalline structure of the drug and confirms the DSC and FTIR data and our previous assumption of the presence of the drug at its amorphous state due to solid solution formation with PVP K30.

CONCLUSION

Surface solid dispersion technique was a successful tool in enhancing the dissolution rate of simvastatin, a poorly water soluble drug. Both water soluble and insoluble, but hydrophilic, carriers showed a better dissolution behaviour compared to unprocessed drug. The use of wetting agents largely improved drug dissolution rate from Avicel formulation, that was comparable to that of water soluble carriers. Solid state characterization revealed that the enhanced drug dissolution was due to the presence of the drug at its amorphous state as a result of the formation of solid solution with the polymeric wetting agent at the surface of the carrier. This was augmented by the spreading of the formed solid solution as a thin film over the large surface area offered by the carrier. Thereby, a decreased drug crystallinity accompanied with increased surface area largely contributed to the enhanced drug dissolution and, consequently, with a potential to improve drug bioavailability. The study thus provides a formulation with improved drug dissolution that was comparable to marketed product of simvastatin.

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How to cite this article:

Ebtessam Ahmed Essa, Mai Dwaikat. Enhancement of Simvastatin dissolution by solid dispersion; effect of carriers and wetting agent. J App Pharm Sci, 2015; 5 (Suppl 1): 046-053.