Vol 10 | Issue 1 | 2020 | 6-10.

International Journal of Advanced Pharmaceutics

e-ISSN 2249 – 7706
print-ISSN 2249– 7714

www.ijapjournal.com

Research Article

FORMULATION AND CHARACTERIZATION OF PRAVASTATIN SODIUM SOLID DISPERSION FOR SOLUBILITY ENHANCEMENT

Kapil Gupta*, R.S. Kushwaha, Vishal Kapoor, Shailesh Jain

Patel College of Pharmacy, Ratibad-462044, Bhopal, Madhya Pradesh. India.

Access this article online

Home page: http://ijapjournal.com/

DOI: http://dx.doi.org/10.21276/ijap.2020.10.1.2

Quick Response code

Received:25.11.19 **Revised**:12.12.19 **Accepted**:15.12.19

Corresponding Author

Kapil Gupta
Email:- guptakapil1994@gmail.com

ABSTRACT

Solid dispersion is a most simple and efficient technique for increasing the aqueous solubility of a drug. PEG 8000, PVP K 30 and SLS solid dispersion were used to prepare at weight ratios of 1:1, 1:2, 1:4 and 1:8, using three different preparation methods, physical trituration, kneading and solvent evaporation values of First order was maximum i.e. 0.917 hence indicating drug release from formulations was found to follow first order kinetics. The present investigations showed that solubility of Pravastatin sodium was markedly increased by its solid dispersion using PVP K30 as carrier. The formulation SDF_8 containing (1:8) shows highest dissolution rate. Hence the solid dispersion a way is useful technique in providing fastest onset of action of Pravastatin sodium as well as enhanced dissolution rate.

Keywords: Solid Dispersion, Pravastatin Sodium, Formulation, Dissolution Studies.

INTRODUCTION

Solid dispersion method allows the preparation of physically modified forms of the drug that are much more rapidly soluble in water than the pure compound. The most commonly used hydrophilic carriers for solid dispersions include polyvinyl pyrrolidone, polyethylene glycols, and plasdone-S630. Surfactants may also be used in the formation of solid dispersions. Surfactants like Tween-80, Myrj-52, and Pluronic-F68 and sodium lauryl sulfate are used. Chiou and Riegelman, (1969) [1] recommended polyethylene glycol, a water-soluble polymer, as an excellent universal carrier for improving the dissolution rate and oral absorption of water insoluble drugs. They reported that the dissolution of griseofulvin, as well as its absorption and total availability in both dog Chiou and Riegelman, (1971)[1] and man Chiou and Riegelman, (1971), was significantly higher when the solid was dispersed in polyethylene glycol 4000, 6000, or 20,000, as compared with the traditionally micronized form of the drug.

The oral route of drug administration is the most common and preferred method of delivery. However, several orally administered drugs have a reduced bioavailability due to poor water solubility. In biopharmaceutical classification system drugs with low aqueous solubility, slow dissolution rate, high dose, and high membrane permeability are categorized as Class II drug. To overcome low bioavailability, many of the modern oral drug delivery systems emphasize on formulation strategies such as alteration of solvent composition, carrier systems as well as chemical and physical modifications. Solid dispersion of drug in a water soluble polymer has been shown to be one of the most promising strategies to improve solubility. Increasing the bioavailability of a poorly soluble drug is a challenging aspect of drug development. Because of the poor aqueous solubility the drug possess dissolution problems due to which the in vivo absorption of the drug is reduced and thus the bioavailability is reduced, making the drug inappropriate for oral consumption and therefore solubility

enhancement become necessary for such drug candidate. Solid dispersion is a most simple and efficient technique for increasing the aqueous solubility of a drug.

Pravastatin is a cholesterol-lowering agent that belongs to a class of medications known as statins. It was derived from microbial transformation of mevastatin, the first statin discovered. It is a ring-opened dihydroxy acid with a 6' -hydroxyl group that does not require in vivo activation. Hence the objective of the present work was to obtained faster onset of action and successfully enhanced the bioavailability by developing solid dispersion.

Thus, it was decided for present study we develop solid dispersion of pravastatin for enhancement of solubility.

MATERIAL AND METHODS

Drug Profile

Pravastatin is a cholesterol-lowering agent that belongs to a class of medications known as statins. It was derived from microbial transformation of mevastatin, the first statin discovered. It is a ring opened dihydroxy acid with a 6'-hydroxyl group that does not require *in vivo* activation. Pravastatin is one of the lower potency statins; however, its increased hydrophobicity is thought to confer advantages such as minimal penetration through lipophilic membranes of peripheral cells, increased selectivity for hepatic tissues, and a reduction in side effects compared with lovastatin and simvastatin.

Preformulation Study

Physical Evaluation

It refers to the evaluation by sensory characters-taste, appearance, odor, feel of the drug, etc.

Solubility: Solubility of the drug was determined by taking some quantity of drug (about 1-2 mg) in the test tube separately and added the 5 ml of the solvent (water, ethanol, methanol, 0.1N HCl, 0.1 N NaOH and Chloroform) Shake vigorously and kept for some time. Note the solubility of the drug in various solvents (at room temperature).

Melting point: It is one of the parameters to judge the purity of drugs. In case of pure chemicals, melting points are very sharp and constant. Since the drugs contain the mixed chemicals, they are described with certain range of melting point [2].

Identification Test

FTIR Spectroscopy

Identification of Pravastatin sodium was done by FTIR Spectroscopy with respect to marker compound. Pravastatin sodium was obtained as White or off-white powder. It was identified from the result of IR spectrum as per specification [3].

Loss on drying: The moisture in a solid can be expressed on a wet weight or dry wet basis. On a wet weight basis, the water content of a material is calculated as a percentage of the weight of the weight solid. The term loss on drying is an expression of moisture content on a wet weight basis.

PREPARATION OF SOLID DISPERSIONS

Preparation of Solid Dispersions Using PEG 8000, PVP K 30 and SLS

PEG 8000, PVP K 30 and SLS solid dispersion were used to prepare at weight ratios of 1:1, 1:2, 1:4 and 1:8, using three different preparation methods, physical trituration, kneading and solvent evaporation.

Method of Preparation of Inclusion Complexes

Physical Trituration Method

In the physical trituration method, drug and PEG 8000, PVP K 30 and SLS were weighed, sieved and mixed evenly by slowly adding drug into EG 8000, PVP K 30 and SLS separately in a mortar with light trituration. The mixture was continuously mixed for an hour (magnetic stirrer, Fisher, UK) until a homogeneous mixture was obtained. The mixtures were passed through a #65 mesh sieve (0.211mm) and kept in a closed container.

Kneading Method

In the kneading method, PEG 8000, PVP K 30 and SLS in a mortar was wetted with sufficient amount of water (10% w/w) to obtain a paste and drug was slowly added into the paste. Kneading was performed manually for an hour and suitable amount of water was added from time to time to maintain the consistency of the paste. The mixture was dried overnight for 24 hr in an oven (Electronic India) at 50°C. The dried complex was ground using mortar and pestle. After sieving through a #65 mesh sieve, the complex was kept in a closed container.

Solvent Evaporation Method

In the solvent evaporation method, drug was dissolved in 25 mL of methanol, while PEG 8000, PVP K 30 and SLS were dissolved in 50 mL of distilled water. The two solutions were mixed together and stirred for 1 hr (Magnetic stirrer, Electronic India) methanol was evaporated off by heating at 40°C under constant stirring. Water was then removed under reduced pressure using rotary evaporator. The mixture was placed overnight for 24 hr in an oven at 40°C to remove the residual solvent. The inclusion complex was ground using mortar and pestle. After sieving through a #65 mesh sieve, the inclusion complex was kept in a closed container[5-8].

Solubility Studies

Solubility study was performed by adding an excess amount of solid dispersions in 50 mL of distilled water. The flasks were vortex-mixed for 3 min and agitated at 120 rounds per minute in a water bath maintained at 30°C for 72 hours. Samples of 3mL were withdrawn and filtered through a 0.45µm nylon membrane filter. Filtrate (0.1ml) was diluted appropriately and measured spectrophotometrically

(Labindia 3000+) at 243 nm [9-11]. Each measurement was repeated three times.

RESULTS AND DISCUSSION

Results of Solubility Study

EVALUATION OF DISPERSION GRANULES OF OPTIMIZED FORMULATION SDF8

Percentage Drug Content: For the determination of Pravastatin sodium content, dispersion granules equivalent to 10 mg of drug, were weighed and extracted with 10 ml of methanol by mechanical mixing for 5min followed by centrifugation at 10,000 rpm for 5 min on a centrifuge. The supernant was filtered through 0.45µ membrane filter, and the filtered solutions were suitably diluted and analyzed for Pravastatin sodium at 243 nm using a validated UV spectrophotometric method.

Drug Content

As the solid dispersion exhibited no endothermic peak corresponding to the melting point of drug that the drug is dispersed amorphously in solid matrix.

Table 1. List of Drug and Excipients Used

S. No.	Name of Chemical/Drug	Supplier
1.	Pravastatin sodium	Bioplus life science, Bangalore
2.	Methanol	Qualigens Fine Chemicals, Mumbai
3.	Ethanol	Qualigens Fine Chemicals, Mumbai
4.	Chloroform	Qualigens Fine Chemicals, Mumbai
5.	PVP	Loba Chemie PVT. LTD. Mumbai
6.	Sodium lauryl sulfate	S. D. Fine Chem. Ltd., Mumbai
7.	Propylene Glycol	S. D. Fine Chem. Ltd., Mumbai

Table 2. List of Sensory characters

S. No.	Sensory characters	Result
1.	Colour	White or off-white powder
2.	Odor	Odorless

Table 3. Preparation of Solid Dispersion Complexes

S. No.	Inclusion complexes		
	Drug: PEG 8000	Drug: PVP K30	Drug: SLS
1.	1:1	1:1	1:1
2.	1:2	1:2	1:2
3.	1:3	1:3	1:3
4.	1:4	1:4	1:4

Table 4: Solubility of Different Solid Dispersion Complexes

F. code	Complex	Solubility (mg/ml)		
		Physical method	Kneading Method	Solvent Evaporation Method
	Pure Drug	0.178 mg/ml		
SDF1	Drug: PEG 8000 (1:1)	0.895	0.458	1.112
SDF2	Drug: PEG 8000 (1:2)	1.125	0.658	1.125
SDF3	Drug: PEG 8000 (1:3)	1.126	0.965	1.125
SDF4	Drug: PEG 8000 1:4)	1.129	1.112	1.165
SDF5	Drug: PVP K 30 (1:1)	0.985	0.898	1.115
SDF6	Drug: PVP K 30 (1:2)	1.256	0.998	1.116
SDF7	Drug: PVP K 30 (1:3)	1.265	1.112	1.289
SDF8	Drug: PVP K 30 (1:4)	1.325	1.256	**1.569**

SDF9	**Drug: SLS (1:1)**	0.365	0.658	0.985
SDF10	**Drug: SLS (1:2)**	0.569	0.789	0.658
SDF11	**Drug: SLS (1:3)**	0.985	0.941	1.115
SDF12	**Drug: SLS (1:4)**	1.125	1.112	1.265

Table 5: Results of Drug Content

Formulation	Label claim (mg)	Amount found (mg)	Label claim (%) Mean ± S.D.	% RSD
SDF8 Drug: PVP K 30 (1:4)	10	9.99	99.90 ±0.08	0.012

Figure 1: DSC analysis of pure Pravastatin sodium

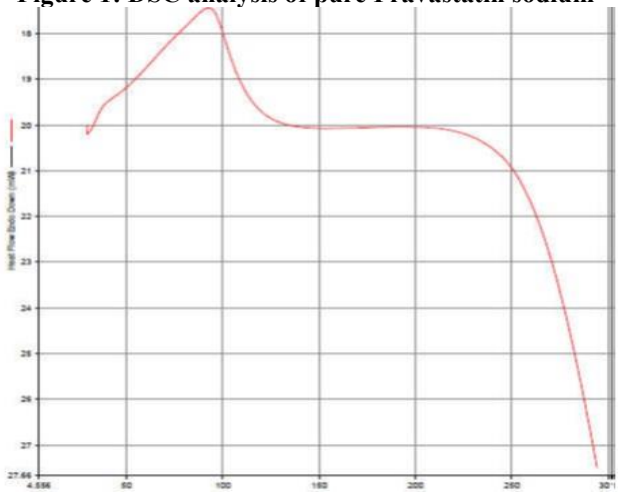


Figure 2: DSC analysis of Optimized Batch SDF8

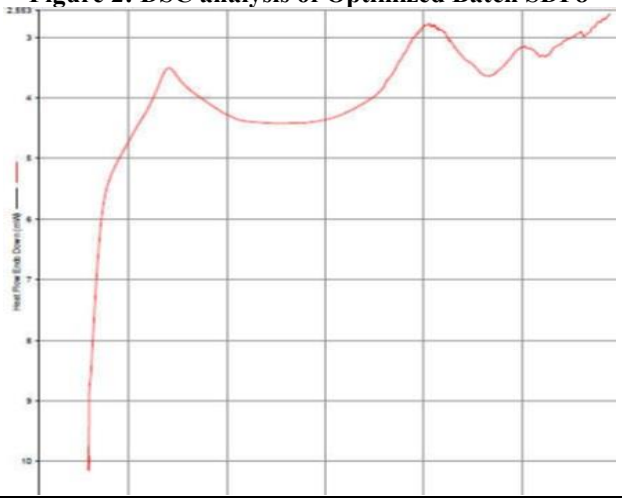


Figure 3: Graph of zero order release Kinetics of formulation SDF8

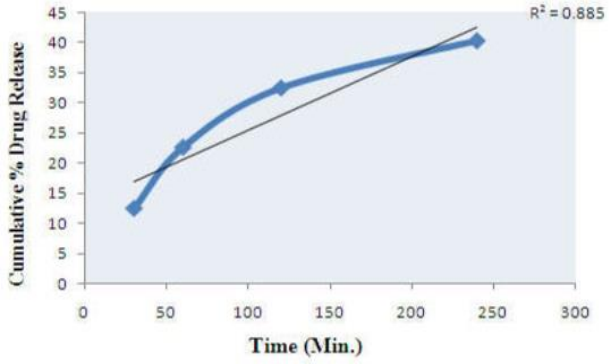
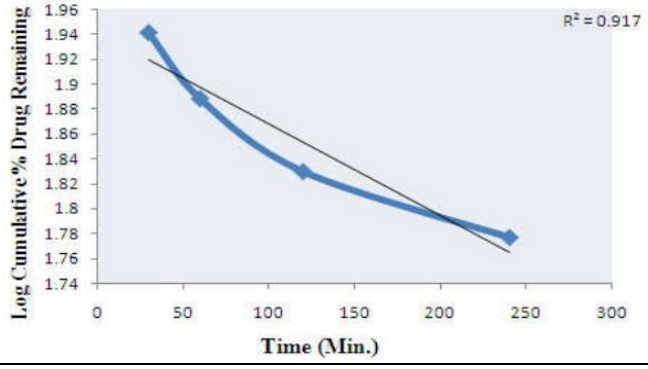


Figure 4: Graph of first order release kinetics of formulation SDF8



CONCLUSION

Increasing the Bioavailability of a poorly soluble drug is a challenging aspect of drug development. Because of the poor aqueous solubility the drug possess dissolution problems due to which the *in vivo* absorption of the drug is reduced and thus the bioavailability is reduced, making the drug inappropriate for oral consumption and therefore solubility enhancement become necessary for such drug candidate.

Preformulation of drug and excipient was performed in which physiochemical properties and other parameters of drug were studied. Physiochemical parameters such determination of solubility, melting point, partition coefficient, drug-excipient interaction λ_{max} scan using UV-spectrophotometry, FT-IR spectrophotometry were performed in this study. The obtained data from these studies were matched with the data given in standard monographs to confirm the authenticity of procured drug. Procured Pravastatin

sodium was odorless and White to off-white powder in nature. In solubility study it was found that drug was freely soluble in methanol and soluble in 0.1 N hydrochloric acid ethanol chloroform phosphate buffer pH 7.2. It was slightly soluble in distilled water. Melting point of drug was found 171 - 173°C while it was 170ºC reported in standard monograph.

The obtained FT-IR characteristic peaks of drug was matched with the peaks of drug given in standard monograph was revealed similar. Identification of Pravastatin sodium sample was done by infrared spectroscopy. Moisture content of Pravastatin sodium was found 0.0543 mg.

The drug solution was scan on UV-spectrophotometer at 200-400 nm in Wavelength range to determine the maximum absorbance (max) and it was found at 243nm. The calibration curve was prepared in 0.1 N HCl. The regression coefficient (R^2) was 0.998 which was shows the linearity of curve. The line of equation for the standard curve was y = 0.022x - 0.009.

REFERENCES

1. Chiou W, Riegelman S. Preparation and Dissolution Characteristics of Several Fast Release Solid Dispersion of Griseofulvin. *Journal of Pharmaceutical Science,* 58, 1969, 1505.
2. Ahuja Naveen, Katare Om Prakash, Singh Bhupinder. Studies on dissolution enhacement and mathematical modeling of drug release of a poorly water-soluble drug using water-soluble carriers. *International Journal of Pharmaceutics*, 2006, 44-54.
3. Charbit G, Badens E, Boutin O. Supercritical Fluid Technology for Drug Product Development, Drugs and Pharmaceutical Sciences, vol. 138, 2004, Marcel Dekker Inc., New York.
4. Chokshi R, Hossein Z. Hot Melt Extrusion Technique: A Review. *International Journal of Pharmaceutical Research*, 3, 2004, 3-16.
5. Constantinides PP. Lipid micro-emulsions for improving drug dissolution and oral absorption: physical and biopharmaceutical aspects. *Pharmaceutical Research.* 12, 1995, 1561-1572.
6. Jung J, Perrut M. Particle design using supercritical fluids: literature and patent survey. *Journal of Supercritical Fluids* 20, 2001, 179 219.
7. Kakumanu VK, Bansal AK. Supercritical Fluid Technology in Pharmaceutical Research. Business briefing: *Labtech*, 2004, 70-72.
8. Kaushal AM, Guptam P, Bansal AK. Amorphous drug delivery systems: molecular aspects, design, and performance. *Critical Review in Therapeutic Drug Carrier System*, 21(3), 2004, 133-193.
9. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. *European Journal of Pharmaceutics and Biopharmaceutics*. 50(1), 2000, 47-60.
   Majerik V, Horvath G, Charbit G, Badens E, Szokonya L, Bosc N, Teillaud E. Novel particle engineering techniques in drug delivery: review of formulations using supercritical fluids and liquefied gases, *Hungarian Journal of Industry and Chemistry*. 32, 2004, 41-56.
10. Mayersohn M, Gibaldi M. New method of solid state dispersion for increasing dissolution rates. *Journal of Pharmaceutical Science.* 55, 1966, 1323-1342.
11. Narang A, Shrivastava A. Melt extrusion solid dispersion technique. *Drug Development and Industrial Pharmacy*, 26(8), 2002, 111-115.