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RESEARCH ARTICLE

SPRAY DRYING APPROACH IN PREPARATION AND CHARACTERIZATION OF SOLID DISPERSION OF EPROSARTAN MESYLATE

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ABSTRACT
Spray drying methods were used to make solid dispersions of the medication Eprosartan Mesylate, which is poorly water-soluble. X-ray Powder diffraction, Fourier transform infrared spectroscopy, and differential scanning calorimetry were used to characterize the products' physicochemical features as well as drug-polymer interactions. Eprosartan Mesylate was shown to be dispersed amorphously in both solid dispersion systems, with a drug to polymer weight ratio of 1:4.The drug and polymer created hydrogen bonds, according to the spectrum data. Both techniques utilized in this investigation enhanced Eprosartan Mesylate solubility. Solid dispersions, on the other hand, performed significantly better, dissolving completely in 5 minutes and at a rate that was about 20 times faster than API within the first 15 minutes. Spray drying is a good way to boost the bioavailability of drugs that are poor water solubility.

KEYWORDS: Eprosartan mesylate, Solid dispersion, Spray drying, Poorly water-soluble drug, Bioavailability.

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INTRODUCTION
Eprosartan mesylate is a non-biphenyl, non-tetrazole, nonpeptide angiotensin II antagonist with antihypertensive properties. Eprosartan methane sulfonate is a sodium salt of methane sulfonate, has eprosartan in it and crystalline powder with less water solubility. Eprosartan mesylate is given in a dose of 400 to 800 mg once or twice in a day for 13 weeks to mild to severe hypertensive patient. By reducing angiotensin II-induced vasoconstriction and angiotensin II-mediated stimulation of aldosterone secretion by the adrenal cortex, this lowers salt and water excretion while increasing potassium excretion.(1)

Eprosartan mesylate is classed as a class 2 drug by the Bio-pharmaceutics Classification System because of its low water solubility (1 mg/mL at 25°C) (BCS). A BCS class 2 medicine's oral bioavailability can be improved by using a method like solid dispersion to increase its water solubility. Eprosartan mesylate is administered in large dosage, because of limited efficacy. Eprosartan Mesylate Drug Dissolution Enhancement could increase its oral efficacy and reduce the requirement for high doses.

Eprosartan Mesylate water solubility and lipophilicity is pH dependant, which could lead to varied absorption as the molecule moves through the gastrointestinal tract. The consequent bioavailability is around 13% due to substantial hepatic first pass metabolism in the liver and relatively low solubility. As a result, a high dose of 800 mg is frequently prescribed for the treatment of hypertension and other heart issues, which frequently results in negative undesirable side effects.(2)

Eprosartan Mesylate binds significantly to plasma proteins (98%) and has a mean terminal elimination half-life of 20 hours at 600 mg oral dosing. Eprosartan Mesylate has a low oxidative and hydrolytic metabolism, with approximately 90% of the unaltered drug eliminated in the stool.(3)

Procedures that have been shown to increase the solubility and solubilisation of poorly water-soluble API's usually involve micronization, nanoparticle formation, surfactant Solubilization, micro emulsions, cyclodextrin Complexation, hydrophilic polymeric wall materials encapsulating, self-emulsifying drug delivery systems, and hydrophobic medicines dispersed in hydrophilic polymer matrix. This technique, that includes dispersing a hydrophobic drug in a hydrophilic polymer, such as a polymer such as polyvinyl Pyrrolidone (PVP), along with the inclusion of a surfactant, has been shown to be rather effective in improving the Water-insoluble medication dispersion and dissolution.(4)

A ternary solid dispersion is better at improving the dispersion and dissolution of BCS class 2 drugs than a binary solid dispersion (a binary solid dispersion). The kneading method, the solvent evaporation method, and the lyophilization technique are useful for solid dispersions. Solid dispersions generated by the solvent evaporation technique may be useful for increasing the dispersion and dissolution rates of water-insoluble compounds. Wetting rises because the drug is adjacent to the hydrophilic carriers, and amorphization is helped by the crystalline components becoming amorphous.(5)

In this investigation, we employed the solvent evaporation methodology to synthesise a range of eprosartan mesylate-

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containing solid dispersions using PVP K25. Solid dispersions were used to assess the medication's water solubility and dissolution. The structural, thermal, morphological, and spectroscopic properties that exhibit the extremely excellent dispersion and dissolution were evaluated using X-ray diffraction (XRD), differential scanning calorimetry (DSC), scanning electron microscopy (SEM), and Fourier transform infrared spectroscopy (FTIR). [6,7,8]

MATERIALS AND METHODS

Materials

Eprosartan Mesylateis kind gift sample procured from Dr. Reddy's Laboratories Ltd., Hyderabad, India. All of the substances utilized in this research were of pharmaceutical quality.

Method

Eprosartan Mesylate Solid Dispersions Prepared with PVP K25:

Spray Drying Method

A co-axial nozzle and a co-current flow mini-spray-dryer were used to feed Eprosartan Mesylate solutions and combinations with Polyvinyl Pyrrolidone K25(ratio=1:1,1:2,1:3 and 1:4). The solutions were concentrated to a final concentration of 5% by weight. The entrance temperature of the drying chamber was regulated between 110 and 20 degrees Celsius, while the output temperature was regulated between 60 and 50 degrees Celsius. The aspirator's flow rate was set to 35 m3/h. 5.5 mL/min-1 was the spray feed rate.All the spray-dried powders were manufactured in duplicate. A yield of above 60% has been recorded. Physical mixes (PMs) of Eprosartan Mesylate and PVP K25 were also generated by combining the two components at weight ratios of 1:1, 1:2, 1:3, and 1:4 until the formulation had homogenized.[9]

Evaluation of Formulated solid dispersion

Scanning Electron Microscopy (SEM)

At a 20-kV accelerating voltage, a scanning electron microscope was utilised to investigate particle size and form.The samples were adhered on aluminium stubs with mutual conductive adhesive tape before being sputter coated with a 250 A° gold–palladium coating.[10]

Particle Size Analysis

Particle size distribution was performed by using a laser diffraction size analyser. Tests were performed in silicone oil, in which the samples were suspended. and ultrasonically treated for 1 minute. The analyser was then fed the dispersed samples.[11]

Fourier Transform Infrared Spectroscopy (FTIR)

KBr pellets were generated and scanned in the 400–4000 cm^{-1} range. Averaging 32 photos with a resolution of 2 cm^{-1} was used to construct the spectra.[12]

In-vitro Dissolution Studies

The dissolving rate of Eprosartan Mesylate samples was analyzed using Simulated gastric fluid (SGF) was produced without pepsin, which has a pH of 1.2, and had been brought to the proper temperature in USP apparatus II (paddle). The equivalent of 10 ± 0.2 mg piroxicam was added to 500 mL of dissolving media in each dissolving vessel. The paddle rotation speed was set at 50 revolutions per minute, and the bath temperature was set at 37 ± 0.2 degrees Celsius. The dissolved quantity of API was determined using a UV Spectrophotometer at 246 nm.[13, 14]

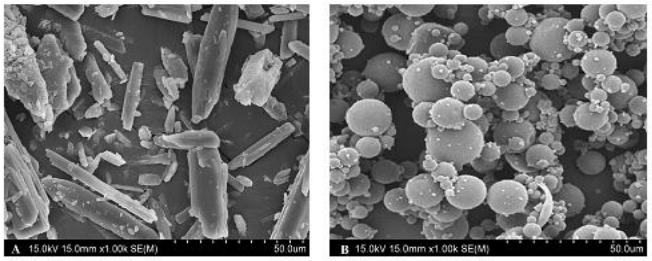
Drug content determination using UV-VIS Spectrophotometer

A UV-Vis spectrophotometer was used to determine the amount of Eprosartan Mesylate in the solid dispersion samples. After dissolving a 10 mg sample in 100 mL methanol, 1 mL of the stock solution was diluted with pepsin-free simulated gastric liquid (SGF) to 50 mL. The absorbance at 246 nm was used to determine the drug content.[15,16]

RESULTS AND DISCUSSION

Scanning Electron Microscopy (SEM)

The morphological features of solid Eprosartan Mesylate dispersions (ratio 1:4) were investigated using scanning electron microscopy, as illustrated in Figure 1.



(a) (b)

Figure 1: SEM of F-4 ratio (1:4) a) Pure Drug b) Spray dried formulation

Particle Size Analysis

A laser diffraction analyzer was used to measure the component size. The solid dispersion's size distribution has a significant impact on its releasing qualities. The faster the drug is released from the solid dispersion, the smaller it is, and the larger it is, the more protracted or regulated the drug release will be. The particle size ranges for four formulations are shown in below Table 1. Solid dispersion batches generated had particle sizes ranging from 45.30 to 47.24 µm.

Table 1: Particle size analysis of prepared solid dispersion

Formulations	Core:CoatRatio	Particle size (µm)
F-1	1:1	45.30
F-2	1:2	46.33
F-3	1:3	46.98
F-4	1:4	47.24

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR, a sophisticated method, can be used to detect the interaction presence in solid distributions of drug-carrier. The presence or absence of peaks, as well as their appearance and location, are typically suggestive of interactions such as hydrogen bonding. Eprosartan Mesylate has a single hydrogen donor (–OH), with absorption bands for CO at 3106 cm^{-1} and 1714 cm^{-1}. In addition, a large, well-defined band in the 1600–1700 cm^{-1} range of the PVP K25 spectra was linked to the carbonyl stretching vibration. The carbonyl group inside each PVP polymer pyrrole ring is greater conducive for hydrogen bonding. The physical combination's spectrum, as shown in

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Figure 2, was a simple sum of pure medicine and PVP K25, showing that the two elements seemed to have no substantial interaction.

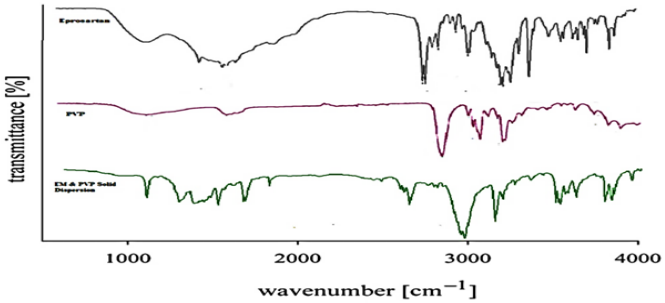

Figure 2: FTIR Spectrum of Eprosartan Mesylate, PVP and Solid dispersion

Drug content determination

The solid dispersion's API content was assessed using the approach described before. In the table below, the drug composition of the various batches is listed. The solid dispersion of formulations F-4 contains the most mg of drug, as shown in below Table 2, followed by formulations F-1, F-2, and F-3.

Table 2: Drug content of formulations F-1 to F-4

Formulations	Core:CoatRatio	Drug content (mg)
F-1	1:1	52
F-2	1:2	61
F-3	1:3	76
F-4	1:4	88

***In-Vitro* Dissolution Study**

Spray drying solid dispersions of Eprosartan Mesylate and Polyvinyl Pyrrolidone K25 were used to dissolve the goods to improve Eprosartan Mesylate dissolving. Solid dispersions can be dissolved in two ways: drug-controlled dissolution and carrier-controlled dissolution.

Table 3: Comparative dissolution study of F-1 to F-4 with varied polymer ratios

Time (hrs)	Percentage drug release			
	F-1	F-2	F-3	F-4
0	0.000	0.000	0.000	0.000
1	6.046	7.234	9.651	9.476
2	14.584	15.674	16.380	16.752
3	24.596	25.505	26.432	27.431
4	34.211	35.035	36.450	38.760
5	49.187	51.062	53.434	55.255
6	61.290	62.796	63.977	65.753
7	70.684	73.410	75.792	80.485
8	81.069	83.632	85.551	88.130

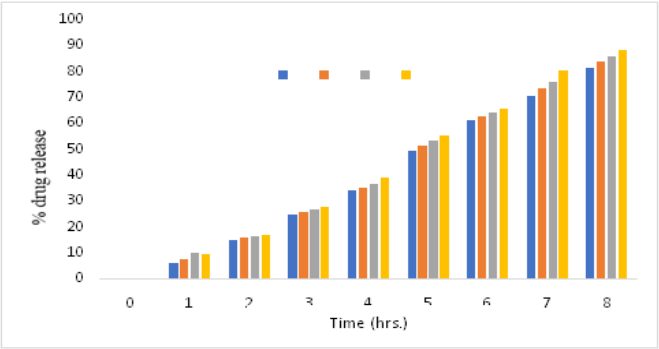

Figure 3: Comparative dissolution study of F-1 to F-4 with varied polymer ratios

CONCLUSION

Spray drying approaches for the process of producing fast dosage forms that dissolve Eprosartan Mesylate, a Bio-pharmaceutics Classification System Class II Active Pharmaceutical Ingredient, were investigated using Polyvinyl Pyrrolidone K25. Eprosartan Mesylate dispersion of solids with Polyvinyl Pyrrolidone K25 were created and characterised using FTIR, SEM and in-vitro dissolution tests. The solid dispersions generated by this approach lacked crystalline nature and disintegrated rapidly in simulated gastric fluids with a pH of 1.2 devoid of pepsin. The amorphous Eprosartan Mesylate was dispersed in Polyvinyl Pyrrolidone K25 in a dispersion of solids via hydrogen bonding. Due to the extreme tiny size of their products, spray drying technique may make solid dispersions that dissolve swiftly. Since this manufacturing is more effective at regulating size of the particles and the character of the physical transition technology does not interfere with drug-carrier interactions, it may be used to manage in vitro performance without aggravating the stability problem. The higher solubility of Eprosartan Mesylate is expected to boost its bioavailability, although additional research is needed to figure out how Eprosartan Mesylate/PVP K25 combinations dissolve.

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