International Journal of Pharmacy
Journal Homepage: http://www.pharmascholars.com

Research Article **CODEN: IJPNL6**

SOLID DISPERSION–AN APPROACH TO ENHANCE THE DISSOLUTION RATE OF AMLODIPINE

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ABSTRACT

Solid dispersion refers to the dispersion of one or more active ingredients in an inert carrier in a solid state, frequently prepared by the melting method, solvent method, or fusion solvent method. The oral bioavailability of poorly water soluble drug remains as the most challenging aspects of drug development. Solid dispersion approach is to reduce particle size, therefore increases the dissolution rate and absorption of drugs. Amlodipine is poorly soluble drug. The solubility of this drug is enhanced by preparing the solid dispersions of amlodipine, with hydrophilic polymers like PEG4000, in different ratios (1:1, 1:2, 1:3, 1:4, 1:5 and 1:6). The amount of drug released is measured by UV spectroscopy at the wavelength of 238nm using methanol as blank.

Keywords: Amlodipine, dissolution, disintegration, friability

INTRODUCTION

Almost more than 90% drugs are orally administered. Drug absorption, sufficient and reproducible bioavailability, pharmacokinetic profile of orally administered drug substances is highly dependent on solubility of that compound in aqueous media. Hence, the enhancement of oral bioavailability of such poorly water soluble drugs remains one of the most challenging aspects of drug development. [1]

Solubilization is the process by which the apparent solubility of a poorly water soluble substance is increased. Solubilization of drugs in organic solvents or in aqueous media by the use of surfactants and cosolvents leads to liquid formulations that are usually undesirable. [2] Particle size reduction is commonly used to increase dissolution rate, there is practical limit for size reduction. [3] Commonly used methods for this are crystallization, grinding etc. Methods of preparation of solid dispersions include

1. Hot plate method
2. Solvent evaporation method
3. Hot-melt extrusion
4. Melting solvent method
5. Kneading method

Carriers commonly used in solid dispersion preparation are Sugars(dextrose, sucrose)polymeric materials(polyvinyl pyrolidone, polyethylene glycol), enteric or insoluble materials (hydroxypropyl methyl cellulose), polymers(eudragitL-100, eudragitRL). [4].

KNEADING METHOD: Solid dispersion is applicable for thermolabile substances, particles produced are with reduced particle size and improved wettability. [5]

Materials and preparations: Amlodipine from Reddy's laboratories, PEG600, methanol, potassium chloride, hydrochloric acid from Qualikems Fine Chems Pvt Ltd.

Preparation of 1.2 pH HCl buffer*:* 50ml of 0.2M potassium chloride was taken in 200ml of volumetric flask, add 85ml of 0.2M hydrochloric acid and then add water to make up to the volume.

Methodolgy:

Solid Dispersions Preparation -- Kneading method: In this method the drug and polymer were weighed according to their ratios (Table 1). They were triturated using a small volume of solvent (methanol-water) to obtain a thick paste, which was kneading for 30mins and then dried in an oven. The dried mass was then pulverized, passed through #30, stored in vacuum desiccators (48hrs) and passed through #60before packing in an air tight container.

Evaluation of solid dispersions:

1. All the batches of amlodipine solid dispersions were evaluated for color and appearance. [6]

2. Calibration curve of Amlodipine: A standard solution containing 1mg/ml of amlodipine was prepared in methanol by dissolving 50mg of pure amlodipine in 50ml of methanol. From this solution, working standard solutions of concentrations 5 to 20µg/ml of amlodipine was prepared by dilution with methanol. The absorbance was measured at 238nm against methanol. Calibration curve was plotted between concentration and absorbance as shown below in fig 1.

IN-VITRO DISSOLUTION STUDIES

Dissolution studies were carried out using USP-II paddle apparatus at 75RPM. The dissolution medium was 500ml of 0.01N HCL kept at $37\pm^{0}$ c. The drug or physical mixture or solid dispersion was dispersed in a medium. Aliquots of 5ml were withdrawn at different time interval and replenished by equal volume of dissolution medium. Samples were filtered and analysed spectrophotometrically at 238nm. Each preparation tested in triplicate and mean values were calculated by standard calibration curve of amlodipine in methanol.The same procedure is carried out for assay of prepared amlodipine solid dispersions and the values are tabulated in table 3. [7]

DISCUSSION

Solid dispersions of amlodipine were prepared by kneading method in various ratios (1:1 to 1:6). The in-vitro dissolution studies (table 3) revealed that the solubility of solid dispersions of amlodipine was found better than pure drug. The enhanced solubility of drug may be due increase in wetting property or change in crystallinity of drug. [8-11]

CONCLUSION

Solid dispersions of amlodipine with hydrophilic inert carriers prepared by kneading method in various ratios (1:1, 1:2, 1:3, 1:4, 1:5,1:6)showed significantly higher drug dissolution in comparison with pure drug. The solubility studies of amlodipine are increased linearly with increase in concentration of polymer showing a typical solubility curve. Hence amlodipine PEG4000 system can be considered for formulation of immediate release conventional tablets. The enhanced solubility of drug is due to increase in wetting property or change in crystallinity of drug. F-6 is optimized batch for formulation of immediate release conventional tablets.

Table 1: Formulation details

Carrier	Product name	Drug(mg)	Carrier(mg)	Ratio of drug carrier	Preparation and method
PEG4000	D	250	0	1;0	Kneading
PEG4000	A1	250	250	1;1	Kneading
PEG4000	A2	250	500	1;2	Kneading
PEG4000	A3	250	750	1;3	Kneading
PEG4000	A4	250	1000	1;4	Kneading
PEG4000	A5	250	1250	1;5	Kneading
PEG4000	A6	250	1500	1;6	Kneading

Table 2: Physical properties of solid dispersions

METHOD	COLOUR	APPEARANCE
Physical mixture	White	Fine powder
Solventevaporation method	White	Fine powder

Table 3: Dissolution profile of solid dispersion of amlodipine PEG 4000 system of 1:6 (F6) in pH 1.2 HCl buffer

Time	Absorbance	Amount of drug released	% amount of drug released	% drug unreleased	Log % drug Unreleased
5	0.739	8.86	88.60	11.4	1.056
10	0.750	9.00	90.00	10.00	1.000
15	0.765	9.18	91.80	8.20	0.913
30	0.785	9.42	94.2	5.80	0.760
45	0.825	9.90	99.00	1.00	0.000

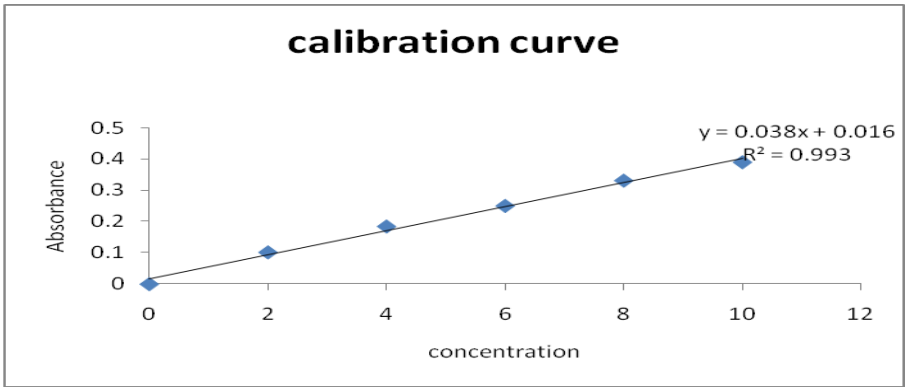

Figure 1: Calibration curve of Amlodipine

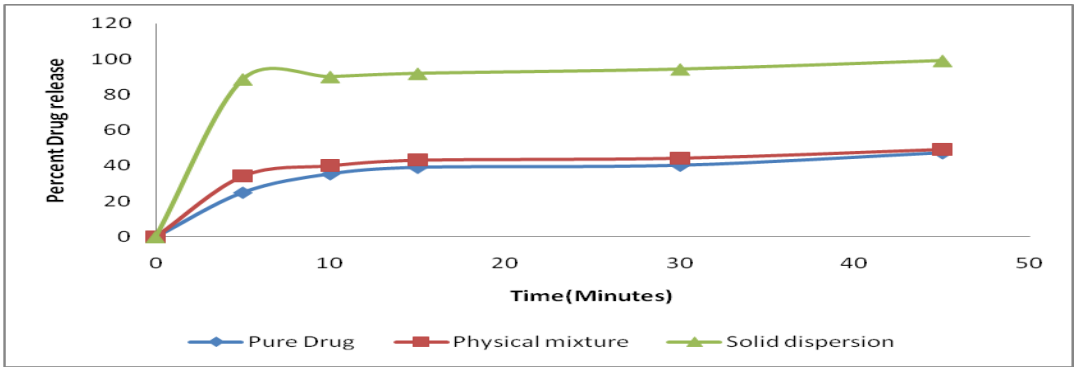

Figure 2: Dissolution profile of solid dispersion of amlodipine PEG 4000 system of 1:6 (F6) in pH 1.2 HCl buffer

REFERENCES

1. The complete drug profile by martindales, 34th ed: 862.
2. James K., Solubility and related properties, Marcel Dekker Inc, Newyork ,1986; 28:127-146, 355-395.
3. J. C. Chaumeil. Method Findings Experimental Clinical Pharmacology, 1998; 20: 211-215.
4. Pinnamaneni .S, Das. G, Das. SK. Pharmazie, 2002; 57: 291-300.
5. T. Kai, Y. Akiyama, S. Nomura, M. Sato. Chem Pharm Bull, 1996; 44: 568-571.
6. Ahmad M. Abdul-Fattah, Hridaya N. Bhargava. Int J Pharm, 2002; 17-23.
7. L. H. Emara, R. M. Badr, A. A. Elbary. Drug Dev Ind Pharm, 2002; 28: 795-807.
8. G. V. Betageri, K. R. Makarla. Int J Pharm, 1995; 126, 155-60.
9. Jac-Young Jung, Sun Dong Yoo, Sang-Heon Lee, Kye-Hyun Kim, Doo-Sun Yoon, Kyu-Hyun Lee. Int J Pharm, 1999; 187, 209-218.