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FORMULATION AND EVALUATION OF SOLID DISPERSION OF OLANZEPINE

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ABSTRACT

The poor dissolution rate of water-insoluble drugs is still a major problem conforming the pharmaceutical industry. Therefore, the enhancement of the dissolution rate of poorly water-soluble drugs after oral administration is one of the most challenging aspects of modern pharmaceutics. Olanzepine exhibits very slight solubility in water and as a consequence it exhibit low bioavailability after oral administration. Therefore, the improvement of olanzepine dissolution from its oral solid dosage forms is an important issue for enhancing its bioavailability and therapeutic efficacy. The purpose of present work is to improve the solubility of Olanzepine by preparing its dispersion with polymer PEG(Poly Ethylene Glycol) using solvent evaporation technique.

Keywords: Olanzepine, Solvent Evaporation, Solid Dispersion, Solubility.

INTRODUCTION

The enhancement of oral bioavailability of poorly water soluble drugs remains one of the most challenging aspect of drug development. The rate and extent of dissolution of the active ingredient from any solid dosage form determines rate and extent of absorption of the drug. In the case of poorly water soluble drugs dissolution is the rate limiting step in the process of drug absorption. Potential bioavailability problems are arising with extremely hydrophobic drugs due to incomplete absorption from the GIT. The solid dispersion approach has been widely and successfully applied to improve the solubility, dissolution rate and consequently the bioavailability of poorly water soluble drugs.[1] The concept of solid dispersion was introduced by Sekiguchi& Obi. In solid dispersion method drug is dispersed in inert water soluble carrier at solid state.[19]

MATERIALS AND METHODS

MATERIALS:

Olanzepine

PEG(Poly Ethylene Glycol)

Methanol

Phosphate Buffer pH 6.8

Distilled Water

METHODS:

Methods of estimation of Olanzepine

Preparation of Phosphate buffer pH 6.8:

Sodium hydroxide in quantity of 0.9 gm and 6.8 gm of potassium dihydrogen phosphate were dissolved in one liter of distilled water to produce phosphate buffer pH 6.8.

Preparation of Stock solution:

20mg of Oleanzepine was dissolved in sufficient quantity of methanol and dilute with phosphate buffer pH 6.8 to mark in 100ml volumetric flask to obtain a stock solution.

Determination of UV absorption maxima:

2µg/ml solution of olanzepine was prepared by addition of 2ml of stock solution in 100ml volumetric flask in phosphate buffer pH 6.8 and was scanned for for absorbance between 200-400nm using Shimadzu UV/Visible spectrophotometer.

Olanzepine exhibit UV absorption of maxima 254nm.

Preparation of Calibration curve:

Aliquots of 2,4,6,8and10ml were transferred to 100 ml volumetric flasks and were serially diluted with phosphate buffer pH 6.8, to the mark to obtain olanzepine conc. 2,4,6,8,10µg/ml respectively. Absorbance of each solution was measured at 254 nm using Shimadzu UV/visible spectrophotometer against phosphate buffer pH 6.8 as a blank. The results are shown in Table.

TABLE- 1 : PREPARATION OF CALIBRATION CURVE

Conc (µg/ml)	Abs
2	0.345
4	0.451
6	0.568
8	0.679
10	0.834

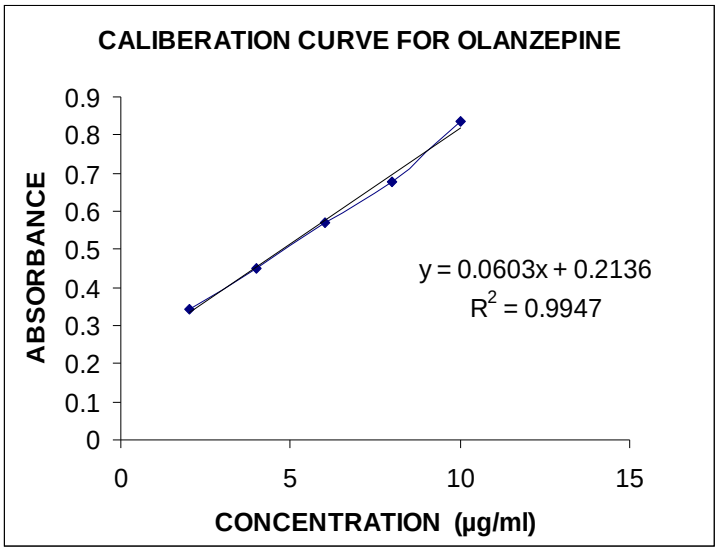


TABLE 2: FORMULATION TABLE FOR PHYSICAL MIXTURE AND SOLIDDISPERSION

MATERIALS	PHYSICAL MIXTURE				SOLID DISPERSION			
	P-1 1:2	P-2 1:3	P-3 1:4	P-4 1:5	S-1 1:2	S-2 1:3	S-3 1:4	S-4 1:5
OLANZEPINE(mg)	100	100	100	100	100	100	100	100
PEG (mg)	200	300	400	500	200	300	400	500
METHANOL	-	-	-	-	Sufficient Quantity			

PREPARATION OF PHYSICAL MIXTURE:

Olanzepine and PEG were weighed according to requirements for the preparation of capsules of different ratio [Olanzepine:PEG, P-1(100mg:200mg), P-2(100mg:300mg), P-3(100mg:400mg), P-4(100mg:500mg)]. And then capsules were filled with physical mixture and dissolution study was performed using Dissolution Apparatus for three hours and then 5 ml sample of each ratio was withdrawn at the interval of 30 min and its absorbance was measured and then finally percentage cumulative release was calculated.[7]

PREPARATION OF SOLID DISPERSION:

Time	% Cumulative Release

	P-1	P-2	P-3	P-4
10	0.19	1.50	3.14	8.05
30	2.95	5.94	9.55	25.46
60	6.13	8.04	15.16	40.11
90	7.89	10.64	21.16	43.10
120	11.8	13.40	29.14	58.01
150	19.79	29.29	44.20	66.11
180	27.8	45.92	65.32	69.08

Olanzepine and PEG were weighed according to requirements for the preparation of capsules of different ratio [Olanzepine:PEG, S-1(100mg:200mg), S-2(100mg:300mg), S-3(100mg:400mg), S-4(100mg:500mg)]. Then sufficient amount of Methanol was added to dissolve the olanzepine and PEG. Lastly the solvent was evaporated using solvent evaporation method on water bath. Crystals were collected and filled in capsules and dissolution study was performed using Dissolution apparatus for three hours and then 5 ml sample of each ratio was withdrawn at the interval of 30 min and its absorbance was measured and then finally percentage cumulative release was calculated.[7]

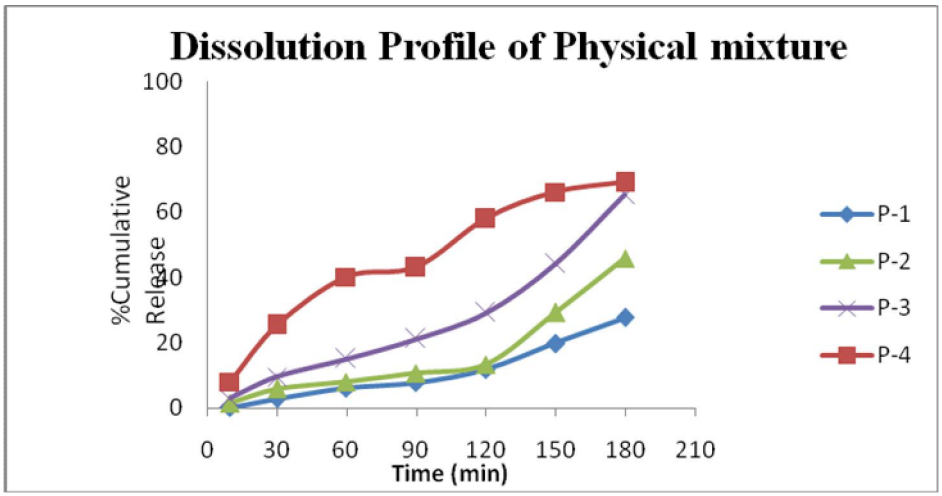
IN VITRO DISSOLUTION STUDY:

In vitro dissolution study of Olanzepine capsules were carried out in 900ml 6.8N buffer using USP basket apparatus. The temperature was maintained 37±0.5°C and agitation rate of basket was set to 100rpm. Sample (5ml) was withdrawn at predetermined time intervals, and dilute, if necessary with 6.8 pH buffer. The same volume of fresh dissolution medium was replenished immediately after the sample was withdrawn. The absorbance was measured at 254 nm using UV/visible spectrophotometer to determine cumulative % drug released. The amount of drug released was calculated using equation generated from standard calibration curve data.[8]

RESULT AND DISCUSSION

FOR PHYSICAL MIXTURE:

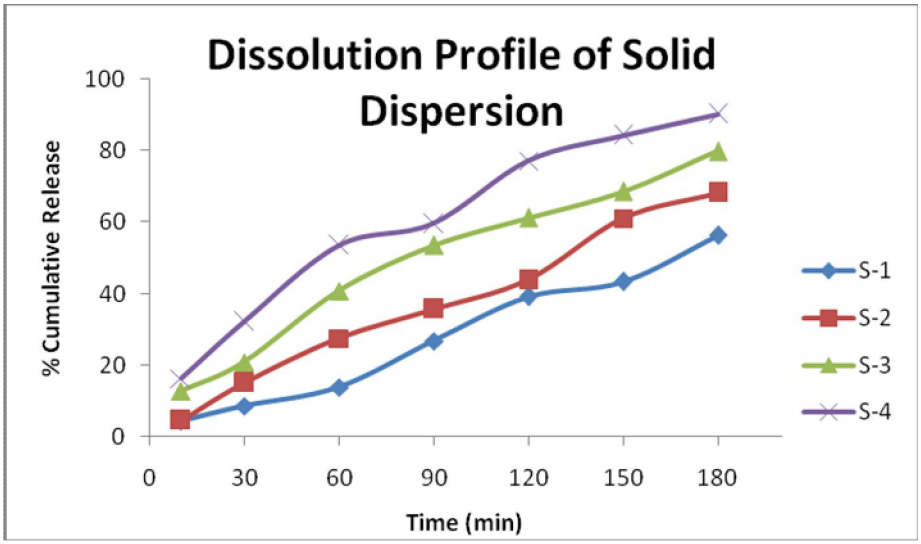
Dissolution Profile Of Physical mixture:



FOR SOLID DISPERSION:

Dissolution Profile Of Solid Dispersion:

Time (min)	% Cumulative Release			
	S-1	S-2	S-3	S-4
10	4.46	4.49	12.76	16.32
30	8.58	15.08	20.91	32.23
60	13.79	27.47	40.85	53.62
90	26.83	35.64	53.58	59.59
120	39.19	43.86	61.2	77.22
150	43.37	61.11	68.67	84.25
180	56.34	68.31	79.89	90.32



CONCLUSION

Olanzepine is practically insoluble in water. However, its very low aqueous solubility and poor dissolution can cause formulation problems and limit its therapeutic application by delaying the rate of absorption and the onset of action.By comparing the formulation and evaluation of solid dispersion of olanzepine with physical mixture of olanzepine. The obtained data showed that there was linearly increased in dissolution profile of solid dispersion and physical mixture compared to plain drug. So, it can be concluded that solid dispersion of olanzepine with PEG increased the solubility of drug.

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