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Formulation and *In-Vitro* Evaluation of Sustained Release Matrix Tablet of Desvenlafaxine Succinate by Interpolyelectrolyte Complex (IPEC) Formation Technique.

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ABSTRACT

The objective of this investigation was to prepare extended release tablet containing interpolyelectrolyte complex (IPEC) formation technique using Eudragit E100 and Eudragit L100 polymers andEE was selected as the cationic polymer. The other cationic types of Eudragit cannot be used because they are insoluble in aqueous solutions. And, EL, which is usually used as an enteric coating, was used as the anionic polymer The main goal of controlled drug delivery systems is to improve the effectiveness of drug therapies. Controlled drug delivery is delivery of drug at a rate or at a location determined by needs of body or disease state over a specified period of time. In which the drug is delivered over an extended time period. to study its *in vitro* release and *in vivo* absorption. The design of dosage form was per-formed by choosing *Eudragit E100*, *EudragitL100*, *Mg Steret* and *Talk* and *PVP-K30* as granulating polymers. Granules were prepared by composing drug with interpolyelectrolyte complex. Optimized formulation of Desvenlafaxine succi-nate was formed by using interpolyelectrolyte complex (IPEC) formation technique using Eudragit E100 and Eudragit L100 polymers This extended the release period up to 10 h *in vitro* study. Similarity factor and mean dissolution time were also reported to compare various dissolution profiles. The network formed Eudragit E100, L100 polymers had been coupled satisfactorily with the controlled resistance. Biopharmaceutical study of this optimized dos-age form in rabbit model showed 10 h prolonged drug release *in vivo*. A close correlation (R2 = 0.9833) was established between the *in vitro* release and the *in vivo* absorption of drug. The results suggested that wet by interpolyelectrolyte complex (IPEC) formation technique, is a suitable method to formulate sustained release Desvenlafaxine succinate and it can Perform therapeutically better than conventional immediate release dosage form.

Keywords: Desvenlafaxine; Pharmacokinetics; ER Matrix Tablet; *In Vitro* Kinetics; Depression, Interpolyelectrolyte complex.

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INTRODUCTION

Developing oral-sustained release formulations for highly water-soluble drugs with constant rate of release has be-come a challenge to the pharmaceutical technologists. Fast release drug generally causes toxicity if not formu-lated as extended release dosage form. Among various formulation approaches, in controlling the release of wa-ter-soluble drugs, the development of interpolyelectrolyte complex (IPEC) formation has a unique advantage of lessening the chance of dose dumping which is a major problem when highly water-soluble drug is formulated as matrix tablets. Most of the researchers have worked on matrix tablets and multilayered matrix tablets. In the present study, a sustained release dosage form of Desvenlafaxine (DV) has been developed that enables less frequent adminis-tering of drug. Interpolyelectrolyte complex (IPEC) were formed by appropriate combination Eudragit E100 and Eudragit L100 polymers, Isopropyl alcohol Magnesium Stearate, and PVP – K 30 was chosen to form the granules of extend duration of drug release.

Desvenlafaxine (o-desmethyl venlafaxine) is an active metabolite of Venlafaxine. Inhibits the neuronal uptake of nor epinephrine, serotonin and to a lesser extent do-pamine but have no monoamine oxidase inhibitory activ-ity and low affinity for brain muscaranic, cholinergic, histaminergic or alpha adrenergic receptors. The solubility of Desvenlafaxine is highly dependent on pH; the significant pH dependency of solubility percents challenges the development of controlled release formu-lations of Desvenlafaxine for obtaining consistent disso-lution profiles [1-5].

The objectives of this work were: 1) to evaluate the physical characters of prepared Tablets 2) to elucidate the effect of polymer composition and the release kinet-ics, 3) *in vivo* study.

MATERIALS AND METHODS

Desvenlafaxine Succinate was obtained from Dr Reddy Ltd, , Eudragit E100, Eudragit L100 were ob-tained as a gift sample from ColorconAsiaPvt Ltd. Kol-lidon K30 and Microcrystalline cellulose (Avicell) was obtained from Evonic Pvt Ltd. Hyderabad. All other solvents, Reagents and Excipient were purchased from local vendors, India, and were of analytical grade.

Synthesis of solid Inter-polyelectrolyte complex: [4]

Eudragit E (EE) solution was prepared by gradually dissolving 3.75 g of EE into a mixture of 5 ml of 0.1 N of CH3COOH and 5 ml distilled water and mixed well using a magnetic stirrer for 24 h until it completely dissolved. Then the solution was titrated by 0.1 N NaOH to the final pH value of 6.0. Eudragit L (EL) solution was prepared by gradually dissolving 3.375 g of EL into a mixture of 5 ml of 0.1 N of NaOH and 5 ml distilled water and mixed well using a magnetic stirrer for until it completely dissolved. Then the solution was titrated by 0.1 N CH3COOH to the final pH value of 6.0. EE solution was subsequently mixed with EL solution at room temperature for at pH 6.0 and subsequently centrifuged at 5000 rpm at 5^0C in a centrifuge (or the mixture can be filtered using a Buchner funnel and precipitate was washed well using distilled water. The final precipitate was then dried for 48 h at 40°C for 48 hrs.

Degree of swelling of polymeric matrix: [6-7]

The degree of swelling was investigated in a pH 6.8 buffer solution. The polymeric matrix was placed in a tarred basket (from dissolution test equipment) which was immersed into the thermostated bath (37± 0.5^0C). The volume of the swelling medium was 40 ml. After every 15 min the basket was removed from the medium, accurately dried by filter paper and weighted. For determination of equilibrium degree of swelling a final weighting was performed after 24 h. The degree of swelling (H, %) was calculated as:

$$H\% = (m2 – m1 / ml) \times 100$$

In which m 1 is the weight of the dry sample and m2 the weight of the swollen sample.

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Preparation of Desvenlafaxine Succinate Tablets

Preparation of Desvenlafaxine Succinate Wet Granulation Method. Drug is mixed with required amount of polymers or IPEC. All the excipients are passed through sieve no.40, mixed and granulated with 10% solution of PVP K-30 in isopropyl alcohol. The wet mass is passed through sieve no.16 and dried at 45°C for 2 hrs. Dried granules then passed through sieve no.21 and mixed with magnesium stearate and talc. Tablets were compressed using 6 mm punches.

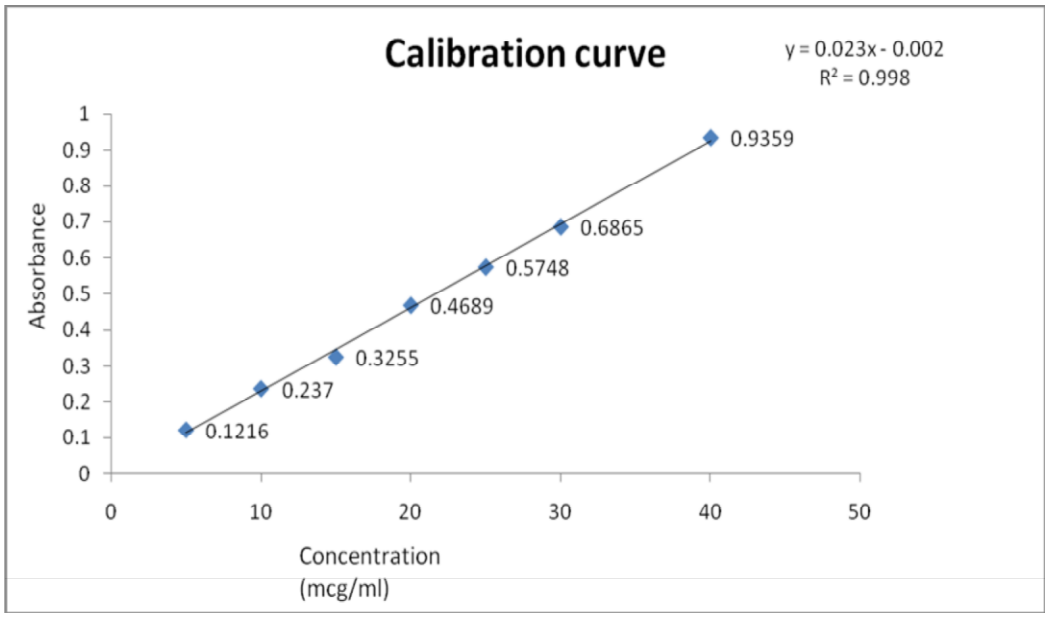
Formulations Table

Sr.No	F1	F2	F3	F4	F5	F6	F7	F8
DVS	75	75	75	75	75	75	75	75
Eudragit E100	50	30	40	50	----	----	-----	-----
EudragitL100	70	50	40	30	----	----	-----	----
IPEC	----	---	---	----	70	90	100	120
Mg Steret	4	5	6	7	8	8	8	7
PVP-K30	QS	QS	QS	QS	QS	QS	QS	QS
Talk IP	3	3	3	8	6	4	5	3
Totle weight	**204**	**204**	**204**	**204**	**204**	**204**	**204**	**204**

RESULTS AND DISCUSSION

Calibration curve for Desvenlafaxine Succinate in pH 6.8 buffer solution:

Sr. No.	Concentration (µg/ml)	Absorbance
0.	0	0
1.	1.00	0.122
2.	2.00	0.237
3.	3.00	0.325
4.	4.00	0.469
5.	5.00	0.575
6.	6.00	0.686
7.	7.00	0.935



The λ max of Desvenlafaxine Succinate Succinate was sfound to be 224nm.

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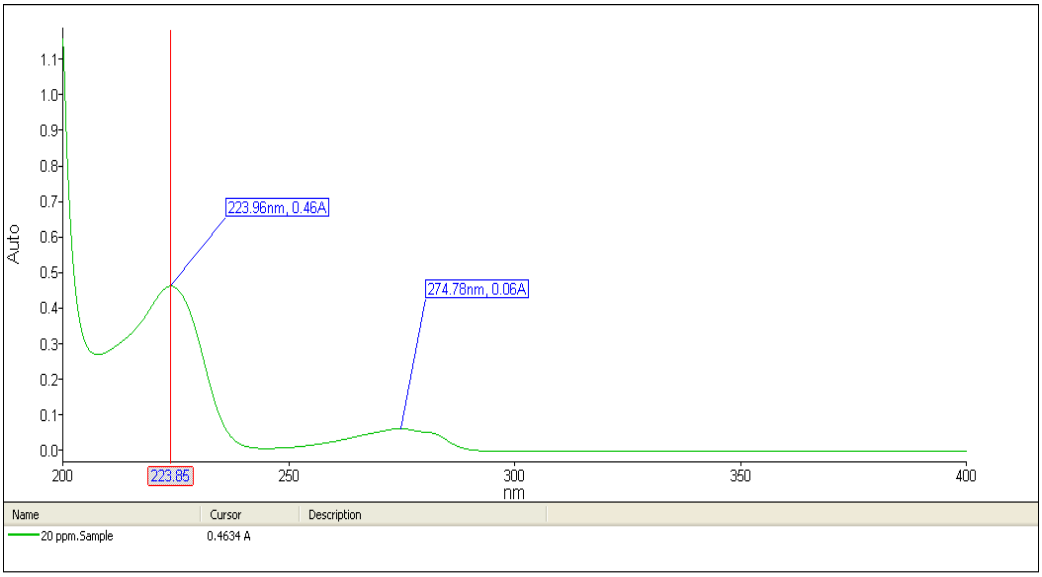
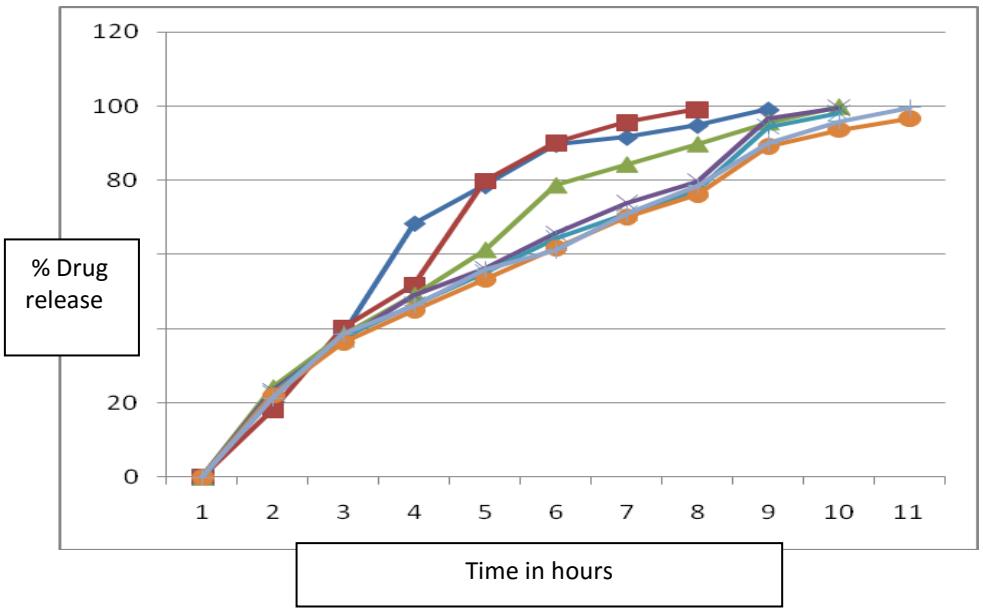


Time in Hrs.	Percentage drug release %						Marketed tablet
	F1	F2	F3	F4	F5	F6	
0	0	0	0	0	0	0	0
1	21.34	18.29	24.23	23.31	22.54	22.13	21.24
2	38.61	40.21	38.36	37.26	37.71	36.43	38.65
3	68.42	51.82	49.14	48.97	46.58	45.14	46.28
4	78.54	79.91	61.25	56.18	55.07	53.32	55.89
5	89.68	90.08	78.64	65.73	64.38	61.74	61.19
6	91.59	95.61	84.26	73.91	71.13	70.16	70.94
7	94.81	99.14	89.72	79.69	77.42	76.29	78.56
8	99.12		95.62	96.71	94.53	89.25	89.92
9			99.81	99.64	98.14	93.71	95.85
10						96.79	99.51

***In-vitro* dissolution test results**

Observation: F_6 shows prolonged release comparable to other formulations.

Comparative plots for dissolution of all formulations



The prepared all formulation studied for *in-vitro* drug release profile. Among the all formulation F_6 shows prolonged release comparable to other formulations and equivalent drug release profile to marketed formulation. The formulation F2 has very fast release profile compare to other formulation. The formulation F3, F4 and F5 has

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