

## SPRAY DRIED SUSTAINED RELEASE SOLID DISPERSION OF VENLAFAXINE HYDROCHLORIDE

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### ABSTRACT

Sustained release solid dispersion of venlafaxine hydrochloride, an antidepressant agent, was prepared by the spray drying technique using various concentration of ethyl cellulose. Characterization was done using thermal analysis (DSC), X-ray diffraction (XRD) and infrared spectroscopy (FTIR). Drug content and dissolution rate studies and its kinetics were also performed. Dissolution studies revealed that the drug release from the solid dispersion matrix was significantly reduced.

**Keywords:** *Venlafaxine hydrochloride; Ethylcellulose; Sustained release; Solid dispersion.*

### INTRODUCTION

Ideally a dosage form should deliver the drug in an amount sufficient to maintain the therapeutic drug level over an extended period for optimum therapeutic action. Most drugs are inherently not long lasting in the body and require multiple daily dosing to achieve the desired blood concentration to produce therapeutic activity. To overcome such problems, controlled-release and sustained release delivery systems are receiving considerable attention from pharmaceutical industries worldwide<sup>1-3</sup>. Traditionally solid dispersion has been extensively used for enhancement of dissolution rate but in the recent years, the concept of solid dispersion has been explored using insoluble carrier materials<sup>4</sup>. These systems are suitable for formulating sustained-release dosage forms. The concept of sustained release by solid dispersion was introduced in 1984 by, El-Fattah *et al.* They developed a new approach for controlling the release rate of pheniramine aminosalicylate via solid dispersion in different type of Eudragit and reported a significant decrease in dissolution rate<sup>5</sup>. Since then there has been a significant amount of research going on in this field<sup>6-11</sup>. Venlafaxine hydrochloride is an antidepressant agent with small duration of action which requires repeated administration. Thus controlled release formulation of venlafaxine hydrochloride would be helpful so as to provide the necessary drug release over a longer period of time and reduce dosing frequency<sup>12</sup>. In the present studies, the technique of spray drying has been utilized to prepare sustained release solid dispersion of venlafaxine hydrochloride using ethyl cellulose as insoluble carrier.

### MATERIAL AND METHODS

#### Materials

Venlafaxine hydrochloride was obtained from Ind-Swift Laboratories Limited, Chandigarh. Ethylcellulose (Viscosity at 25°C-22 cps) and Ethanol (GR-99.7-100%)

was obtained from Loba Chemie Pvt. Ltd. All other chemicals were of analytical reagent grade and used as received.

#### Preparation and Characterization

Sustained release solid dispersions of venlafaxine were first prepared by the spray drying technique. Accurately weighed quantity of drug and ethylcellulose in the 1:10, 1:15 and 1:20 ratio were mixed to obtain a homogenous mixture. Ethyl alcohol was preheated to about 60°C and gradually added to the drug-ethylcellulose mixtures to dissolve the blend. The solvent was evaporated using Spray Dryer (Jay Instruments & Systems Pvt. Ltd., Mumbai, India). The solid dispersions prepared were characterized using Differential Scanning Calorimetry ((DSC Q10 V9.0, Build 275 model, Waters Ltd.), Fourier transform infrared spectroscopy(Nicolet FT-IR Impact 410 instrument), X-ray diffraction(Xpert Pro's Pan Analytical Instrument, Model Philips PW 3040/60) and In-Vitro Dissolution rate studies using USP XXIII Type II apparatus.

### RESULTS AND DISCUSSION

The solid dispersions prepared by spray drying were characterized by DSC as shown in Figure 1. The DSC curve for venlafaxine hydrochloride exhibited a sharp melting endotherm at 210.95°C. The DSC curve for ethyl cellulose showed no endotherm signifying the complete amorphous nature of ethyl cellulose. Each type of solid dispersion also exhibited no endothermic peak corresponding to the melting of venlafaxine hydrochloride indicating that the drug is dispersed amorphously in the ethylcellulose matrix. FT-IR spectra showed no chemical interaction between drug and polymer. The X-ray diffraction patterns as shown in Figure 2 for the pure drug showed numerous sharp peaks demonstrating the crystalline nature of the drug whereas, ethyl cellulose showed diffused peaks

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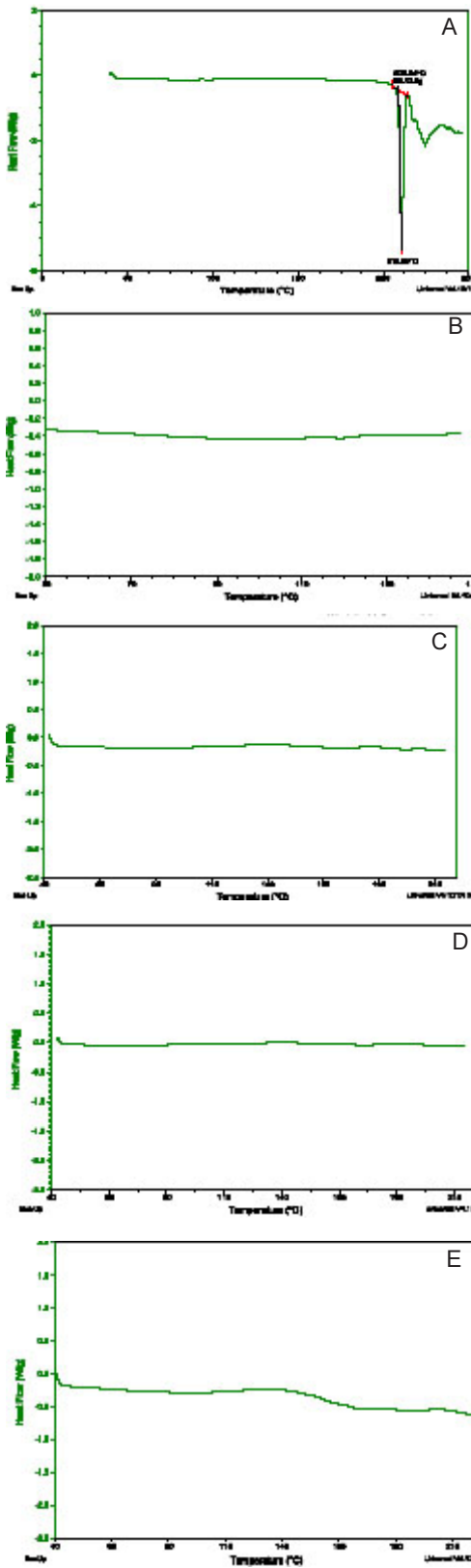


Fig.1 DSC thermograms of (A) Venlafaxine hydrochloride, (B) Ethyl cellulose, (C) solid dispersions of drug carrier ratios 1:10, (D) 1:15 and (E) 1:20

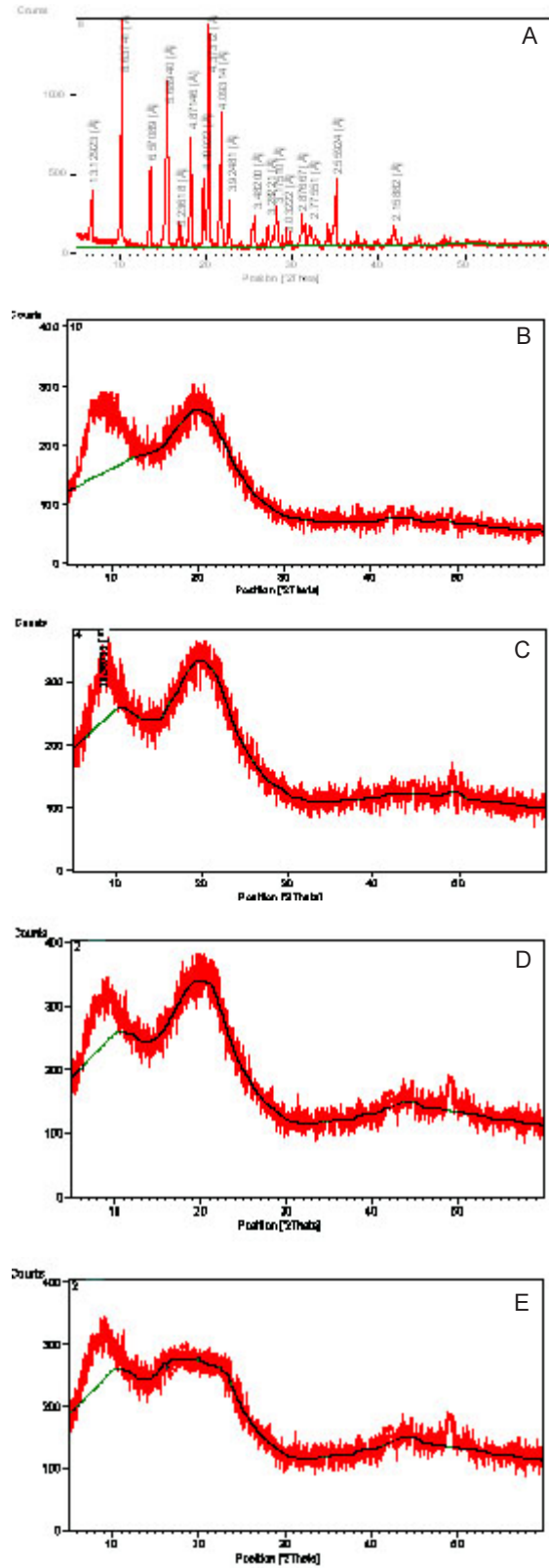


Fig.2 : The X-ray diffraction patterns for (A) Venlafaxine hydrochloride, (B) Ethyl cellulose, solid dispersions of drug carrier ratios (C) 1:10, (D) 1:15 and (E) 1:20.

## Solid Dispersion of Venlafaxine

indicating the amorphous nature of the polymer. All the solid dispersion showed diffused peaks indicating that the drug is dispersed at the molecular level in the polymer matrix.

Comparison of Dissolution Profile of Solid dispersions and Marketed Product is shown in Table 1. Results indicated that a pronounced reduction in the dissolution rate was obtained in each case. This was attributed to the coating of the drug particles with a water insoluble ethylcellulose coat through which the drug has to diffuse before reaching the dissolution medium, and as the dissolution rate is inversely related to the diffusion path length a reduction in the dissolution rate resulted.

**Table 1** : Comparative dissolution profile of solid dispersions of drug polymer ratio of 1:10, 1:15, 1:20 and marketed product

Sr. No.	Time (hours)	1:10	1:15	1:20	Marketed Product
1	0	0.000±0.00	0.000±0.00	0.000±0.00	0.000±0.00
2	1	16.477±0.48	11.796±0.37	10.026±0.21	18.812±0.16
3	2	28.424±2.09	23.147±1.06	12.027±0.25	30.323±0.46
4	3	35.469±2.95	35.507±0.58	20.780±0.17	45.364±2.72
5	4	41.319±1.10	45.934±0.84	27.031±0.63	54.885±2.59
6	5	48.558±2.37	51.159±0.42	35.887±0.20	61.888±0.21
7	6	58.087±0.93	54.666±0.95	40.263±0.01	66.964±0.58
8	7	60.926±0.10	58.800±0.66	43.206±0.20	70.062±0.52
9	8	63.199±0.52	61.190±0.18	47.359±0.42	73.564±0.68

## CONCLUSION

Application of ethyl cellulose to achieve the controlled release of venlafaxine Hydrochloride using the solid dispersion technique was investigated. Ethyl cellulose proved useful as a rate controlling polymer to produce a controlled release formulation of venlafaxine Hydrochloride using the solid dispersion technique.

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