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Development and Characterization of Venlafaxine Orodispersible Films Incorporating Natural-Synthetic Polymer Blends for Improved Patient Compliance

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Abstract: The present study aimed to develop and characterize Venlafaxine (VLF) HCl-loaded orodispersible films incorporating natural–synthetic polymer blends for improved patient compliance. Pullulan was selected as the natural film-forming polymer and HPMC E5 as the supporting semi-synthetic polymer. Glycerol, sucralose and peppermint flavour were used as plasticizer, sweetener and taste-masking aid, respectively. Seven formulations, VF1 to VF7, were prepared by solvent casting method and evaluated for appearance, thickness, weight variation, folding endurance, surface pH, moisture content, disintegration time, drug content, content uniformity, in vitro drug release, release kinetics and stability. VLF HCl showed good aqueous solubility and linear UV response at 225 nm. All films were smooth, flexible and rapidly disintegrating. Drug content ranged from $96.84 \pm 1.18\%$ to $99.18 \pm 0.98\%$. VF5 was selected as optimized formulation due to balanced mechanical strength, rapid disintegration and $95.42 \pm 3.92\%$ drug release within 30 min. Stability study confirmed acceptable formulation stability. Thus, the developed ODF may support convenient oral administration of VLF.

Keywords: Venlafaxine HCl; Orodispersible films; Pullulan; HPMC E5; Natural-synthetic polymer blend; Solvent casting; Patient compliance.

INTRODUCTION

Depressive and anxiety disorders often require prolonged pharmacotherapy. During long-term treatment, dosage-form acceptability can influence whether patients take medication consistently. Swallowing difficulty, tablet aversion, need for water, and dislike of conventional solid dosage forms are therefore relevant formulation considerations [1–4].

Venlafaxine hydrochloride is a serotonin–norepinephrine reuptake inhibitor used in depressive and anxiety-related disorders. It is highly water soluble and is conventionally administered as tablets or

extended-release capsules. A rapidly disintegrating film is an alternative dosage-form concept intended primarily to simplify administration rather than to establish superior clinical efficacy [5–8].

Orodispersible films are thin hydrophilic polymeric strips placed in the mouth, where they hydrate and disintegrate before the drug-containing dispersion is swallowed. An acceptable film must combine adequate tensile and folding strength with rapid oral disintegration, uniform drug distribution, non-irritant surface pH, and reproducible release [9–12].

Pullulan is a natural film-forming polysaccharide that hydrates rapidly and produces smooth films. HPMC E5 can reinforce the film matrix and improve handling. Combining these polymers provides a means of balancing mechanical strength against disintegration time, while glycerol improves flexibility and sucralose and peppermint flavour support palatability [13–16].

Previous oral-film studies have shown that polymer type and concentration strongly affect thickness, folding endurance, disintegration, and drug release [17–20]. The present study therefore developed seven venlafaxine HCl orodispersible films using pullulan–HPMC E5 blends and evaluated their physicochemical properties, rapid disintegration, drug content, in vitro release, and stability.

MATERIALS AND METHODS

Chemicals

VLF HCl was obtained from Gift sample from Unichem Laboratories Ltd., Mumbai. Pullulan and Sucralose was obtained from Otto Chemie Pvt. Ltd., Mumbai. HPMC E5 was obtained from Loba Chemie Pvt. Ltd., Mumbai. Glycerol was obtained from Merck Life Science Private Ltd. Peppermint flavour was obtained from Jindal Drugs Pvt. Ltd., Mumbai.

Preformulation and analytical studies

Venlafaxine hydrochloride was evaluated for appearance, melting behaviour, solubility, and UV absorbance at 225 nm.

FTIR study

The drug excipient compatibility study was performed by using FTIR spectroscopy

Formulation design

Seven formulations, VF1–VF7, were prepared with 250 mg venlafaxine in a 15 mL casting solution while pullulan and HPMC E5 concentrations were varied. Glycerol, sucralose, and peppermint flavour were maintained according to the formulation design.

Table 1: Formulation composition of venlafaxine-loaded orodispersible films

Formulation	VLF (mg)	Pullulan (% w/v)	HPMC E5 (% w/v)	Glycerol (% v/v)	Sucralose (% w/v)	Peppermint flavour (% v/v)	Purified water q.s.
VF1	250	3.00	0.50	1.00	0.20	0.10	15 mL
VF2	250	3.50	0.50	1.00	0.20	0.10	15 mL
VF3	250	4.00	0.50	1.00	0.20	0.10	15 mL
VF4	250	3.50	0.75	1.00	0.20	0.10	15 mL
VF5	250	4.00	0.75	1.00	0.20	0.10	15 mL
VF6	250	4.50	0.75	1.00	0.20	0.10	15 mL
VF7	250	4.00	1.00	1.00	0.20	0.10	15 mL

Preparation method

Pullulan was dissolved in purified water and HPMC E5 was separately hydrated. The polymer phases were combined, venlafaxine solution was added, and glycerol, sucralose, and peppermint flavour were incorporated. After deaeration, the casting solution was poured onto a level surface, dried at $40 \pm 2^\circ\text{C}$, peeled, and cut into 3×3 cm films.

Evaluation

Films were evaluated for appearance, thickness, weight variation, folding endurance, surface pH, moisture content, disintegration time, drug content, and content uniformity.

In vitro drug release

In vitro release was assessed over 30 min under the phosphate-buffer conditions specified in the thesis and quantified at 225 nm.

Stability study

Optimized VF5 was stored at $40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH for three months and reassessed for the principal film-quality and release attributes.

RESULTS AND DISCUSSION

FTIR compatibility study

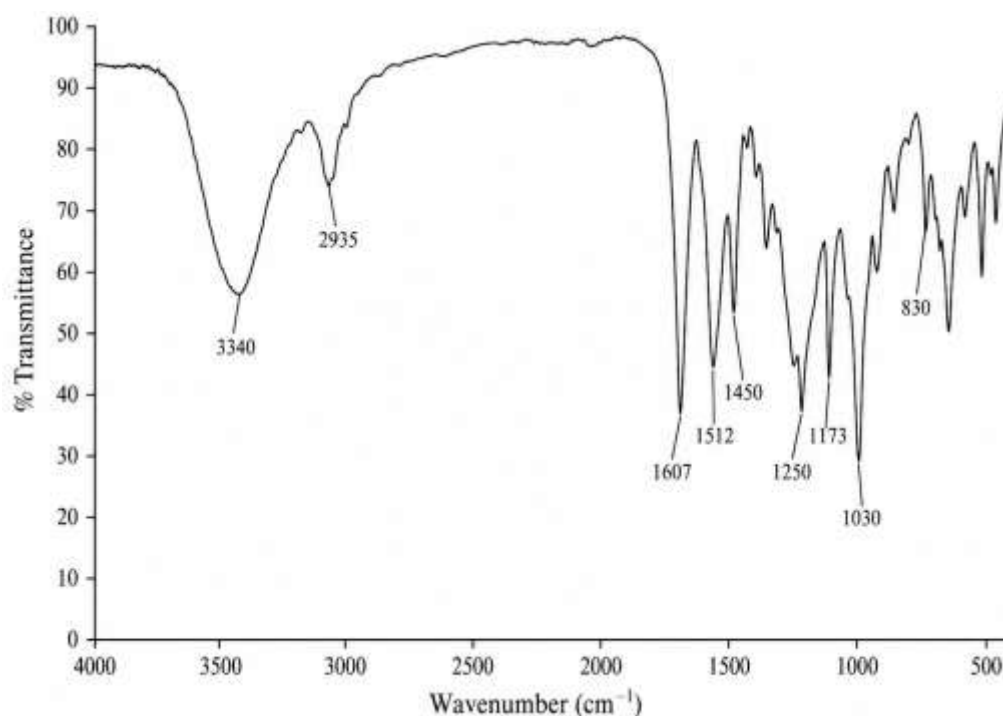


Fig 1: FTIR spectrum of pure venlafaxine.

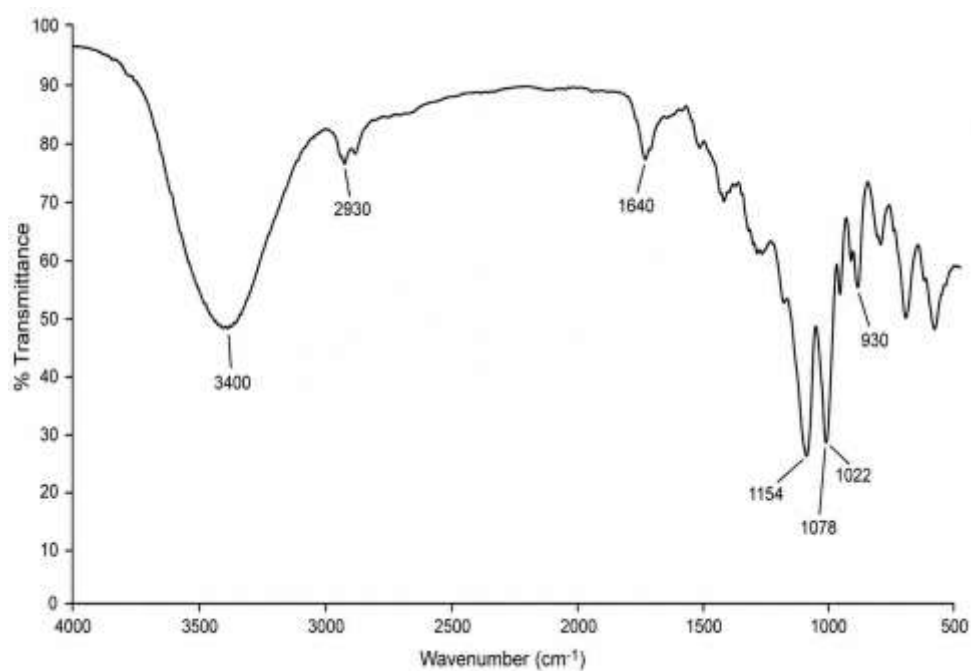


Fig 2: FTIR spectrum of the pullulan.

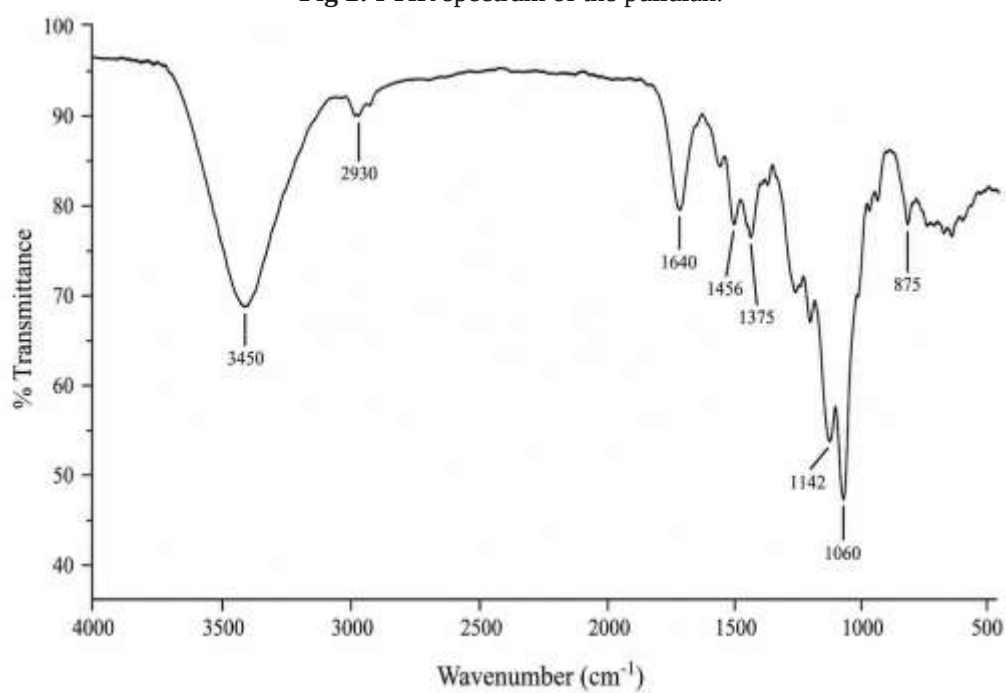


Fig 3: FTIR spectrum of the HPMC E5.

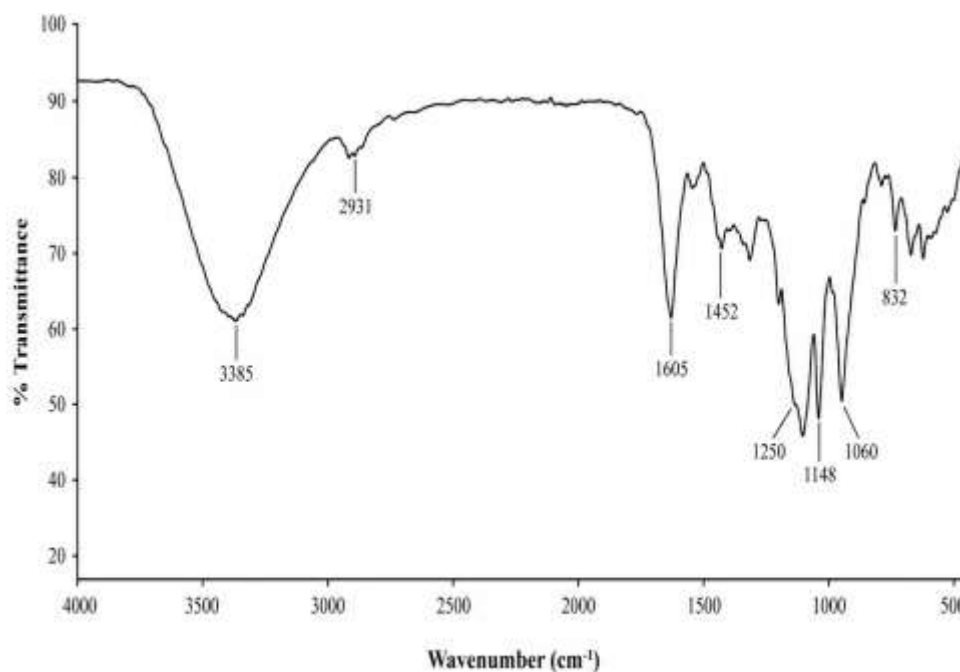


Fig 4: FTIR spectrum of the optimized formulation.

Table 2: Comparative FTIR peaks

Functional group	Pure Venlafaxine (cm ⁻¹)	Pullulan (cm ⁻¹)	HPMC E5 (cm ⁻¹)	Optimised formulation (cm ⁻¹)
O–H stretching	3340	3400	3450	3385
Aliphatic C–H stretching	2935	2930	2930	2931
Aromatic C=C stretching and H–O–H bending	1607	1640	1640	1605
CH ₂ bending	1450	—	1456	1452
C–N stretching	1250	—	—	1250
C–O–C stretching	1173	1154	1142	1148
C–O stretching	1030	1078, 1022	1060	1060
Aromatic C–H out-of-plane bending	830	930	875	832

The FTIR spectrum of pure venlafaxine showed major peaks at 3340, 2935, 1607, 1450, 1250, 1173, 1030, and 830 cm⁻¹. Pullulan and HPMC E5 showed characteristic polymeric bands mainly in the hydroxyl, aliphatic C–H, absorbed moisture, ether, and C–O regions. In the optimised formulation, the principal peaks appeared at 3385, 2931, 1605, 1452, 1250, 1148, 1060, and 832 cm⁻¹. The slight shift and broadening of the hydroxyl band indicate hydrogen bonding between venlafaxine and the hydrophilic polymers. The characteristic venlafaxine peaks, particularly at 1605, 1250, and 832 cm⁻¹, were retained without appearance of new unexpected bands. Therefore, the FTIR results indicate compatibility of venlafaxine with pullulan and HPMC E5 in the optimised formulation.

Preformulation and physical characteristics

Venlafaxine was freely soluble in the tested aqueous media, supporting rapid dissolution from hydrophilic films. All formulations produced smooth, transparent to slightly translucent films. Increasing polymer

concentration increased film thickness, weight, folding endurance, and moisture content while generally prolonging disintegration.

Table 2: Solubility profile of venlafaxine hydrochloride

Solvent	Observation	Solubility inference
Purified water	Clear solution	Freely soluble
Phosphate buffer pH 6.8	Clear solution	Freely soluble
0.1 N HCl	Clear solution	Freely soluble
Methanol	Clear solution	Soluble
Ethanol	Clear to slightly opalescent solution	Soluble
Simulated salivary pH medium	Clear solution	Freely soluble

Table 3: Physical appearance of venlafaxine-loaded orodispersible films

Formulation	Appearance
VF1	Thin, transparent, smooth, slightly delicate film
VF2	Transparent, smooth and flexible film
VF3	Smooth, uniform and flexible film
VF4	Transparent, smooth and peelable film
VF5	Smooth, flexible, uniform and easily peelable film
VF6	Slightly thick, smooth and flexible film
VF7	Smooth, slightly thick and firm film

Table 4: Physicochemical properties of venlafaxine-loaded films

Formulation	Thickness (mm)	Average weight (mg)	Folding endurance	Surface pH	Moisture content (%)
VF1	0.118 ± 0.006	92.4 ± 3.1	126 ± 7	6.72 ± 0.04	3.18 ± 0.20
VF2	0.132 ± 0.007	101.8 ± 3.4	154 ± 8	6.69 ± 0.04	3.46 ± 0.22
VF3	0.148 ± 0.008	112.6 ± 3.8	182 ± 9	6.66 ± 0.05	3.82 ± 0.24
VF4	0.154 ± 0.007	116.4 ± 3.6	196 ± 10	6.64 ± 0.04	4.08 ± 0.26
VF5	0.171 ± 0.008	128.2 ± 4.1	226 ± 11	6.61 ± 0.04	4.46 ± 0.28
VF6	0.192 ± 0.010	140.6 ± 4.6	214 ± 10	6.58 ± 0.05	5.04 ± 0.32
VF7	0.204 ± 0.011	146.8 ± 4.8	238 ± 12	6.55 ± 0.05	5.36 ± 0.34

Disintegration and drug content

All films disintegrated rapidly, with the lower-polymer formulations disintegrating fastest but showing lower mechanical robustness. Drug content ranged from $96.84 \pm 1.18\%$ to $99.18 \pm 0.98\%$. VF5 provided a suitable balance between film strength, disintegration, and content uniformity.

Table 5: Disintegration time, drug content, and content uniformity

Formulation	Disintegration time (sec)	Drug content (%)	Content uniformity (%)
VF1	24 ± 2	96.84 ± 1.18	96.72 ± 0.76
VF2	29 ± 3	97.46 ± 1.12	97.38 ± 0.70
VF3	36 ± 3	98.12 ± 1.06	98.04 ± 0.66
VF4	39 ± 3	98.36 ± 1.04	98.28 ± 0.62
VF5	46 ± 4	99.18 ± 0.98	99.04 ± 0.54
VF6	58 ± 5	98.62 ± 1.10	98.48 ± 0.68
VF7	64 ± 5	98.54 ± 1.14	98.36 ± 0.72

In vitro drug release and optimized formulation

All formulations showed rapid venlafaxine release. Increasing the pullulan–HPMC E5 matrix level slightly slowed release because of greater film thickness and a stronger hydrated network. VF5 released $95.42 \pm 4.06\%$ within 30 min and was selected as the optimized formulation because it combined acceptable flexibility, rapid disintegration, uniform drug content, and high release.

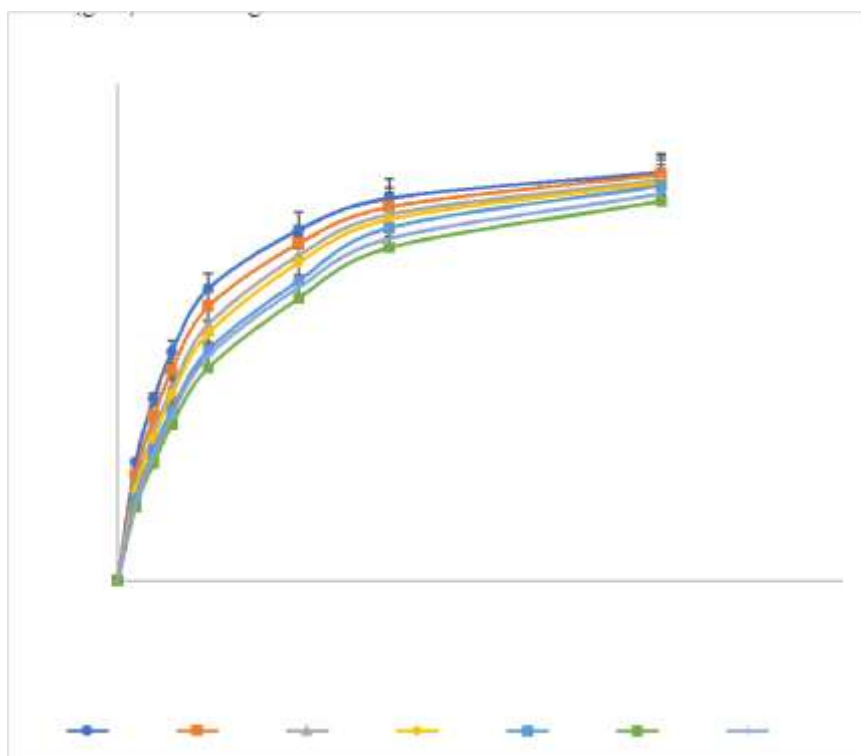


Fig 1: In vitro drug-release profiles of VF1–VF7.

Stability

VF5 showed no significant change in appearance, folding endurance, surface pH, disintegration time, drug content, or release during three months of accelerated storage.

CONCLUSION

Venlafaxine hydrochloride orodispersible films were successfully prepared using a pullulan–HPMC E5 polymer blend. Polymer concentration controlled film strength, moisture uptake, disintegration, and release. VF5 showed the best overall balance of mechanical integrity, rapid disintegration, drug uniformity, and release, with $95.42 \pm 4.06\%$ drug released within 30 min. The optimized formulation remained acceptable during three months of accelerated storage.

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