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OPTIMIZATION OF COATING MATERIAL FOR SUSTAINED RELEASE VENLAFAXINE HYDROCHLORIDE TABLET

ANSHUL JAIN[2]*, RAJENDRA CHAUHAN[1], SATYAVEER SINGH[2], SUNISHA KULKARNI[1] AND SUMAN JAIN[1]

[1]SOS in Pharmaceutical Sciences, Jiwaji University, Gwalior (M. P.), India.
[2]Gurukul College of Pharmacy, Gwalior (M. P.), India.

ABSTRACT

Venlafaxine is widely prescribed for the treatment of depression, depression with associated symptoms of anxiety, generalized anxiety disorder and social anxiety disorder. Because of its short half life, multiple dosing is required to maintain blood concentration. A properly designed, sustained release dosage form of venlafaxine will show uniform pharmacological response and reduce the frequency of administration. The present research endeavor was directed towards the optimization and development of proper coating dispersion to produce a sustained release dosage form of venlafaxine. Hydrophobic and hydrophilic polymers were tried in combination to obtain a desired release profile. The aqueous coating surpasses the environmental and hazardous problem of organic coating while in other perspective organic coating reduces the process time of aqueous coating. Reservoir type aqueous and organic coated once daily sustained release tablets of venlafaxine were successfully formulated using Eudragit® RS30D, Eudragit® RL30D, Aquacoat ECD 30(ethyl cellulose), Eudragit® RSPO and Eudragit® RLPO as coating materials.

KEYWORDS: ***anxiety disorder, sustained release, coating dispersion, aqueous and organic coating.***

INTRODUCTION

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration to obtain rapid and complete systemic drug absorption. Immediate-release products result in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects. In many instance, potential problems associated with conventional drug therapy can be overcome. When this is the case, the drug given in conventional dosage forms by multiple dosing can produce the desired drug blood level for an extended period of time. Frequently these problems are significant enough to make drug therapy with conventional dosage forms less desirable than sustained release drug therapy. (Brahmankar DM and Jaiswal SB, 1995) There are different reasons for tablet coating. The major ones are change in appearance, to eliminate dust generation, taste masking, odor masking, isolation of incompatible materials, protection from environmental conditions, improvement in product stability, change in release characteristics – drug release profile from the dosage form can be tailored by coating techniques for example – delayed release (by enteric coating), extended release (by semi-permeable membrane coating or mixing of pellets which are coated to various degree or with different coating materials). **(**Khan GM, 2001)

Film Coating (Lehman K, and McGinity, JW, 1997)

Three main types of tablet coatings are in use: Film coating, Sugar coating and Press coating. Of these, film coating is the major technique; virtually all new products introduced on to the market are film coated. Sugar coating is the more traditional technology and has seen no real development in recent years. A film coating is thin polymer based coat applied to a solid dosage form such as a tablet, granule or other particle. The thickness of such a coating is usually between 20 and 100 µm. Film layers may be formed from either polymeric

solution (organic-solvent or aqueous-based) or aqueous polymeric dispersion (commonly called latex). In the majority of film-coating formulations, polymer is the main ingredient. They may be from different origins, including cellulosics, acrylics, vinyls and combination polymers. Thus, viscosity, chemical structure, molecular weight, film modifiers and molecular weight distribution of the polymers play a critical role. Polymeric film coatings have been utilized widely for controlled release of an active substance from pharmaceutical dosage forms because the coated dosage forms enable the sustained and precise release of drug with good reproducibility. Most film coatings are applied as aqueous or organic-based polymer solutions. Organic solvent-based coating provides a variety of useful polymer alternatives, but there are several disadvantages associated with its use. Organic solvents are generally flammable and toxic. Their vapor causes safety hazards to coating-equipment operators. Moreover, the toxicity of the residual solvent in the coatings and the high cost of organic solvents and their recovery, in addition to strict environmental regulations placed on the use of organic solvents have further restricted the application of organic-solvent-based film coatings. Aqueous-based coatings have been increasingly used compared with organic-based coatings. However, the heat and water involved in the process can degrade certain drugs. Another difficulty encountered with aqueous coating systems is the validation of coating dispersions for controlling microbial presence. Thus, the limitations of solvent-based coating techniques are associated primarily with the use of solvents and their removal during the coating process. (Aulton ME, 2002) Polymers for extended release are in general insoluble in water over the entire pH-range. The drug release is thus controlled by diffusion through the hydrated polymer or through cracks or water-filled pores. Polymers employed for these tasks are cellulose acetate, ethylcellulose or the methacrylic acid copolymers Eudragit® RS, Eudragit® RL and Eudragit® NE.

MATERIALS AND METHODS

Preparation of Venlafaxine Hydrochloride Uncoated Tablet

All ingredients were weighed accurately and passed through 40 mesh sieve. Drug was mixed with Avicel 102 and Ludipress LCE for 10 min. Weighed quantities of talc and magnesium stearate were passed through 40 mesh sieve and then blended with the above mass for 5 min. Tablets were compressed by weighing 400 mg of blended mass by using 10.5 mm standard concave shaped punches on tablet compression machine.

Preparation of Different Coating Dispersions

Various formulations were prepared using different percentage of coating load of Eudragit® RS30D - Eudragit® RL30D, Eudragit® RSPO - Eudragit® RLPO and Aquacoat ECD 30D.

Acrylic-Based Aqueous Polymeric Dispersions

Micronized talc and triethyl citrate as a plasticizer were homogenized in water using a homogenizer for 10 min, making sure that the powder was quickly wetted and no lumps were formed. The desired amount of the Eudragit® RS30D and Eudragit® RL30D were mixed separately. Both the materials prepared were mixed stirred for 20 min and adjusted to the final volume with purified water to produce a coating dispersion with polymer solid content of 20-25%.

Aquacoat ECD Based Aqueous Polymeric Dispersion

Micronized talc and triethyl citrate as a plasticizer were homogenized in water using a homogenizer for 10 min, making sure that the powder was quickly wetted and no lumps were formed. The desired amount of the Aquacoat ECD and distilled water were mixed separately. Both the materials prepared above were mixed stirred for 20 min and adjusted to the final volume with purified water to produce a coating dispersion with polymer solid content of 20-25%.

Acrylic-Based Organic Polymeric Dispersion

Triethyl citrate as a plasticizer was homogenized in acetone and isopropyl alcohol 1:1 mixture using a homogenizer for 10 min. The desired amount of the Eudragit® RSPO and Eudragit® RLPO were added in above mixture separately. Stirred the entire mixture for 20 min and adjusted to the final volume with organic solvent to produce a coating dispersion with polymer solid content of 20-25%.

Table 1
Composition of coating dispersion/solution containing Eudragits and Aquacoat ECD

Formulation code	Total Eudragit polymer (gm)	Total ethyl cellulose polymer (gm)	Eudaragit RS (gm)*	Eudragit RL (gm)*	Aqua coat ECD (gm)*	Talc gm	Triethyl Citrate (gm)	Channel forming agent PVP (gm)	Amount of Solvent (ml)	Solvent
F1	1.2	-	3.33	0.67	-	0.6	0.24	-	10	Water
F2	2	-	5.56	1.1	-	1.0	0.4	-	17	Water
F3	2.8	-	7.8	1.53	-	1.4	0.56	-	18.80	Water
F4	-	1.2	-	-	4	0.6	0.24	0.2	10	Water
F5	-	1.6	-	-	5.33	0.8	0.32	0.172	8.60	Water
F6	-	2.0	-	-	6.67	1.0	0.40	0.340	17	Water
F7	0.8	-	0.72	0.08	-	-	0.16	-	4.8	IPA: Acetone
F8	1.6	-	1.44	0.16	-	-	0.32	-	9.60	IPA: Acetone
F9	2.4	-	2.16	0.24	-	-	0.48	-	14.40	IPA : Acetone

**** Eudragit® RS30D and Eudragit® RL30D is the 30 percent dispersion of Eudragit® RS and Eudragit® RL***
**** Aquacoat ECD 30D is a 30 percent dispersion of ethyl cellulose***

Coating of Venlafaxine Hydrochloride Tablets
Forty grams of tablets were used for each batch of coating. Tablets are preheated for 15 min at 70°C at slow rpm prior to coating. Coating dispersion was continuously sprayed onto the tablet surface until desired weight gain was obtained. Coated tablets were further dried for 20 min at 70°C at slow rpm in a coating pan. The resultant coated tablets were dried in an oven at 45°C for 12 hr. Total nine formulations were prepared using Eudragit® RS30D and Eudragit® RL30D and Aquacoat ECD 30D for aqueous coating and Eudragit® RSPO and Eudragit® RLPO for organic coating. Coating of venlafaxine hydrochloride tablets were performed in Pharma R & D coater. Coating condition used for tablet coating is as follows

Table 2
Coating Parameters

Coating parameters	Specifications for aqueous coating	Specifications for organic coating
Coating pan speed	28 to 30 rpm	35 to 38 rpm
Atomization pressure	1.3 kg/cm^2	1.3 kg/cm^2
Inlet air temperature	70-75°C	50-55°C
Outlet air temperature	65-70°C	45-50°C
Prewarming	25 to 30 min at slow rpm	15 to 20 min at slow rpm
Post drying	25 to 30 min at slow rpm	15 to 20 min at slow rpm

Table 3
Coated Venlafaxine Hydrochloride Formulations

Coating techniques	Formulation code	Polymer ratio	% of Coating load
Aqueous	F1	5:1(RS:RL)	3%
	F2	5:1(RS:RL)	5%
	F3	5:1(RS:RL)	7%
Aqueous	F4	---	3%
	F5	---	4%
	F6	---	5%
Organic IPA : Acetone (1:1)	F7	9:1(RSPO:RLPO)	2%
	F8	9:1(RSPO:RLPO)	4%
	F9	9:1(RSPO:RLPO)	6%

Evaluation of Coated Venlafaxine Hydrochloride Tablets

Physical appearance/ visual inspection

The relative coated tablet qualities viz. roughness, hardness and color uniformity were checked. Resistance of coated tablets to abrasion: It is determined by rubbing the coated tablet on a white sheet of paper.

Film thickness

Film thickness of coated tablets was determined by micrometer screw gauge.

Scanning electron microscopy

Scanning electron microscopy was used to study the morphology of the polymeric films and coated tablets. The dried samples were coated with platinum by using auto fine coater (JFC 1600; Jeol, Tokyo, Japan). Which was observed under different magnifications with an analytical scanning electron microscope at 25kV (JEOL-JSM 6360A-Japan).

In-vitro dissolution studies

The *in vitro* drug release studies were carried out using USP type II dissolution apparatus, at 37± 0.5°C with paddle speed of 50 rpm in distilled water. The aliquots were withdrawn at first half an hour and then every single hour. The amount of drug release was determined spectrophotometrically at 225 nm. The graphs of % cumulative release vs. time were plotted. The in vitro drug release study for the marketed tablet was also conducted.

Stability Studies (Grimm W, 1993)

In any rational design and evaluation of dosage forms for drugs, the stability of the active component must be a major criterion in determining their acceptance or rejection. During the stability studies the product is exposed to normal conditions of temperature and humidity. However the studies will take a longer time and hence it would be convenient to carry out the accelerated stability studies where the product is stored under extreme conditions of temperature. Formulations F3, F6, F9 were subjected to stability studies.

Stability protocol

The tablets were strip packed (Al–Al strip)**.** The tablets were subjected to stability as per ICH guidelines at the following condition **(**40°C / 75 % RH). The tablets were subjected to the stability for the period of three months. Sampling was done at predetermined time intervals of 0, 15, 30, 60, 90 and 180 days.

Test parameters and testing methods

The samples were observed periodically for any change in the following physico-chemical parameters.

a) Appearance: The tablets were inspected for any change in size, shape, colour and surface texture.

Drug Content using UV spectroscopy

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.1 g of venlafaxine hydrochloride, shake with 50 ml of water for 10 minutes, dilute to 100 ml with distilled water and filter. Dilute 5 ml of the filtrate to 100 ml with water. Further dilute 4 ml to 10 ml (20 µg/ml) with water and measure the absorbance of the resulting solution at the maximum at about 225 nm. The drug content was determined by referring to the calibration curve.

Drug Content using RP – HPLC

About 75 mg equivalent of venlafaxine was weighed accurately and transferred to 10 ml volumetric flask to which 10 ml of HPLC grade water was added and sonicated for 15 min. The

formed solution (7500 µg/ml) was filtered through Whatmann filter paper. 1 ml of this solution was withdrawn and further diluted up to 10 ml using water to get solution of conc. 750 µg/ml. From above 1 ml solution was pipetted out and diluted to 10 ml with water to get 75 µg/ml from which 4 ml was diluted to 10 ml (30 µg/ml) and from this 2 ml to 10 ml to obtained 6 µg/ml. Measure the AUC of the resulting solution at the maximum at about 224 nm. The drug content was determined by referring to the calibration curve.

In-vitro dissolution studies

The *in vitro* drug release studies were carried out using USP type II dissolution apparatus, at 37± 0.5°C with paddle speed of 50 rpm in distilled water. The aliquots were withdrawn at first half an hour and then every single hour. The amount of drug release was determined spectrophotometrically at 225 nm. The graphs of % cumulative release vs. time were plotted.

RESULTS AND DISCUSSION

Drug excipients compatibility was checked by Fourier transform infrared spectroscopy (FTIR) and DSC thermogram. Interpretation indicates that there was no significant change in the position of peak of venlafaxine hydrochloride with polymers. So, it can be concluded that the excipients and drug do not interact with each other. Also venlafaxine hydrochloride doesn't form a complex with the excipients as the endothermic peaks do not change position or broaden.

Evaluation of Uncoated Venlafaxine Hydrochloride Tablets

Venlafaxine hydrochloride tablets showed thickness values in the range of 4.21 ± 0.03 to 4.32 ± 0.02 mm. Tablets from each batch showed uniformity of weight as per I. P. limits. Average weight of the tablet was found to be 400.45 ± 3.5 mg and hardness values ranging from 5-6 kg/cm^2 for all formulations. Conventional compressed tablets that lose less than 1% of their weight are generally considered acceptable and good for coating. In present study, the friability values for all the tablet formulations were found to be <1%, indicating that the friability is within the prescribed limits. Dissolution data of venlafaxine hydrochloride tablet showed 97% drug release at the end of 70 min.

Evaluation of coated Venlafaxine hydrochloride tablets

Physical appearance/ Visual inspection

Coated tablets were found to be of acceptable appearance and without any coating defects.

Film thickness

The film thickness values of various formulations are shown in the table no 4.

Table 4
Film thickness

Formulation code	Polymer ratio	Coating level	Thickness (mm)
F1	5:1(RS:RL)	3%	0.05
F2	5:1(RS:RL)	5%	0.07
F3	5:1(RS:RL)	7%	0.09
F4	---	3%	0.07
F5	---	4%	0.08
F6	---	5%	0.10
F7	9:1(RSPO:RLPO)	2%	0.05
F8	9:1(RSPO:RLPO)	4%	0.06
F9	9:1(RSPO:RLPO)	6%	0.08

Scanning electron microscopy

The surface morphology of coated venlafaxine hydrochloride tablet was examined by scanning electron microscope before and after dissolution. The surface characteristic of aqueous coated formulations F3 and F6 was similar before and after dissolution. The films were found to be intact after dissolution. The coating thickness increased as the coating level increased. Also, no holes and cracks appeared on the tablet surface. The organic coated formulation F9 shows comparatively rough surface than that of aqueous coated formulations. The film remains intact during dissolution and shows roughness on surface after dissolution.

In-vitro dissolution studies

Comparison of release characteristic of formulations with aqueous coating

When comparisons were made among the six aqueous coated formulations coated with Eudragit RS30D and Eudragit RL30D in 5: 1 ratio and Aquacoat ECD 30 (ethyl cellulose) at different coating levels, it was found that there was difference in the release of venlafaxine hydrochloride. The release rate of venlafaxine hydrochloride from F1, F2, F4 and F5 was remarkably faster than those from F3 and F6 (Figure 1). All the aqueous coated formulations followed zero order release kinetics except formulations F2 and F4 which follows Korsmeyer peppas kinetic model (Table 5a). The $t_{25\%}$ for F3 and F6 was found to be 3.3 h and 3.2 h. The $t_{50\%}$ of formulations F3, F6 was found to be 7.6 h and 7.9 h respectively. The $t_{90\%}$ of formulations F3 and F6 was found to be 14.5 h and 14.6 h (Table 5b). (Wesseling M and Bodmeier R, 1999; Pearnchob N and Bodmeier R, 2003)

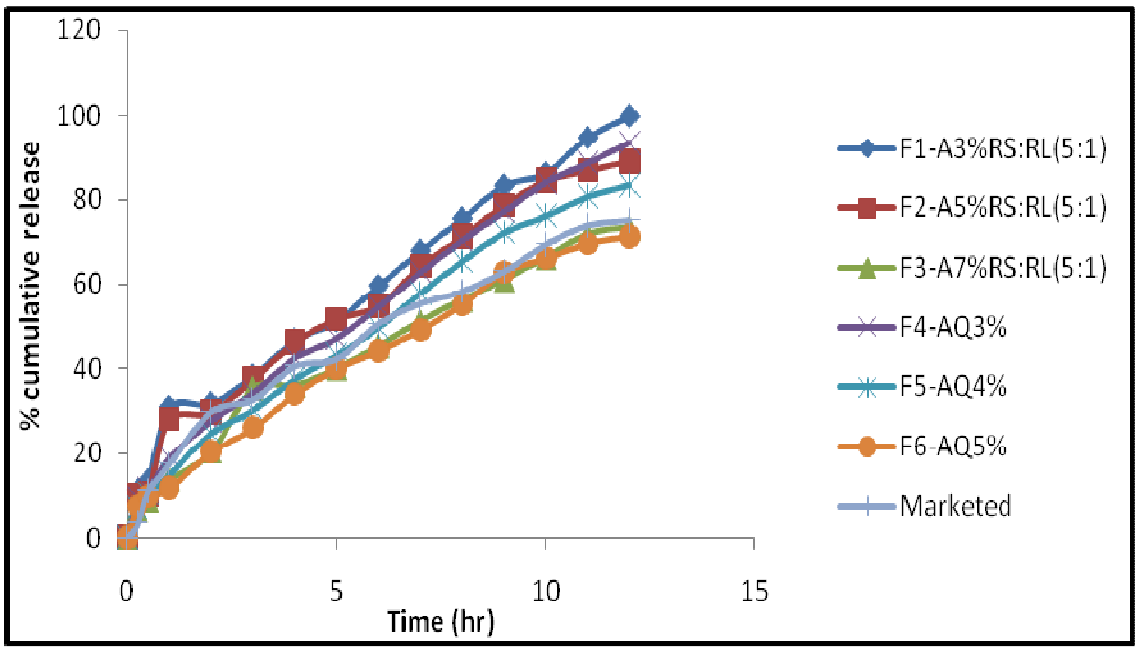

Figure 1

Comparative dissolution profile of formulations with aqueous coating

Table 5
Dissolution kinetics with model fitting

Formulation	Best fit model	r^2	n Value	Drug release till 12 hrs
F1	Zero order	0.9874	0.5619	99.84%
F2	Korsmeyer peppas	0.9855	0.6546	89.00%
F3	Zero order	0.9845	0.6612	73.45%
F4	Korsmeyer peppas	0.9933	0.6311	93.57%
F5	Zero order	0.9667	0.6676	83.38%
F6	Zero order	0.9936	0.6547	71.55%
Marketed	Zero order	0.9838	0.7066	75.22%

Table 5
Dissolution kinetics

Formulation	$t_{25\%}$	$t_{50\%}$	$T_{90\%}$
F1	1.9	4.8	10.8
F2	2.5	5.1	11.7
F3	3.3	7.6	14.5
F4	1.7	5.0	10.3
F5	2.0	5.3	12.3
F6	3.2	7.9	14.6
Marketed	3.5	7.8	14.6

The formulation F3 & F6 were considered to be as the optimized formulations as they showed the desired sustained release effect of venlafaxine hydrochloride over a period of 12 hrs. The metabolite of venlafaxine is active and having a half life of 11 hours. So, the formulation which shows 70 to 75% drug release over the period of 12 hr or 95 to 100% drug release over the period of 16 hrs maintains the plasma therapeutic concentration over a period of 24 hrs. The formulation F3 & F6 also showed a comparable release profile with that of marketed formulation (Figure 1).

Comparison of release characteristic of formulations with organic coating

The organic film coated formulation F9 with Eudragit 6% RSPO: RLPO (9:1) gave 75.38% release in 12 hrs. When comparisons were made among the organic coated formulations coated with Eudragit RSPO and Eudragit RLPO in 9: 1 ratio, it was found that the formulation F7 with 102.90% and F8 with 88.55%, shows faster drug release than that of formulation F9 (Figure 2). All the organic coated formulations followed zero order release kinetics (Table 6 a). The $t_{25\%}$, $t_{50\%}$ and $t_{90\%}$ for F9 was found to be 3.2 h, 7.8 h and 14.2 h respectively (Table 6 b).

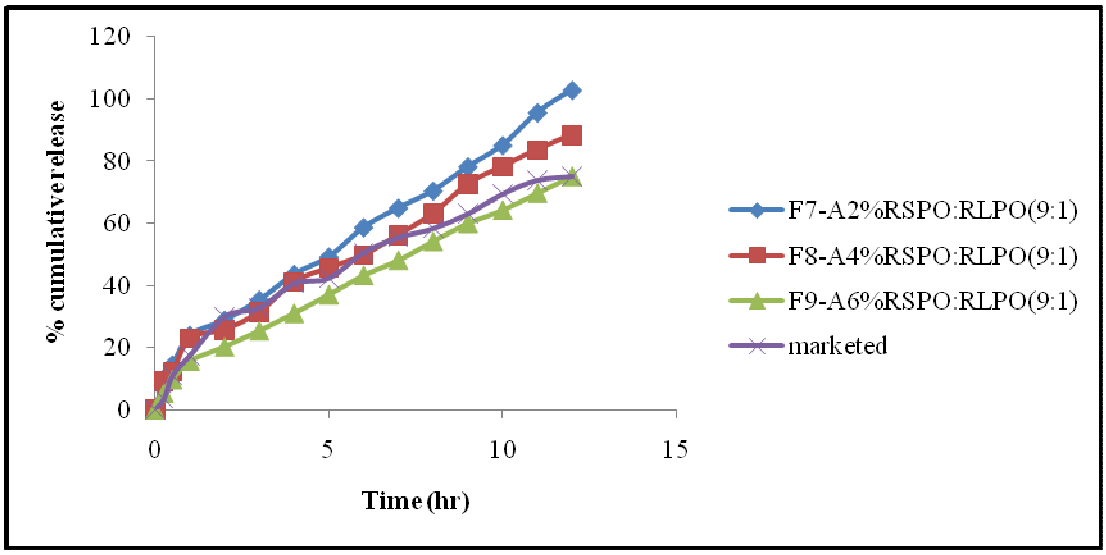

Figure 2
Comparative dissolution profile of formulations with organic coating

Table 6
Dissolution kinetics with model fitting

Formulation	Best fit model	r^2	n Value	Drug release till 12 hrs
F7	Zero order	0.9578	0.5690	102.90%
F8	Zero order	0.9884	0.6121	88.55%
F9	Zero order	0.9876	0.6121	75.38%
Marketed	Zero order	0.9838	0.7066	75.22%

Table 6
Dissolution Kinetics

Formulation	t 25%	t 50%	t 90%
F7	1.7	4.9	10.7
F8	2.1	5.4	12.7
F9	3.2	7.8	14.2
Marketed	3.5	7.8	14.6

The percentage of coating load for desired release of Eudragit in organic film coating was found to be less [F9 with Eudragit 6%RSPO: RLPO (9:1)] than that of aqueous film coating [F3 with Eudragit 7% RS: RL (9:1)] because in organic film coating the ratio of Eudragit RS was on higher side than that of aqueous coating. The percentage of coating load is reduced as Eudragit RS is more hydrophobic than that of Eudragit RL which plays a prominent role in desired sustained release. (Karanjit K and Kwonho K, 2009; Bando H and McGinity JW, 2006; Crotts G et al. 2001; Thomaa K and Bechtoldb K, 1999)

Comparison of release characteristics of optimized formulations with marketed and uncoated (U1) tablets

The release characteristics of uncoated and coated

tablet with marketed formulation are compared in Figure 3. The conventional venlafaxine hydrochloride tablet showed 97 % drug release over 70 min. The release rate decreased as the percentage of coating load increased. The aqueous coated formulations F3 with 7% Eudragit® [RS (5): RL (1)] and F6 with 5% Aquacoat ECD showed 73.45% and 71.55% release over the period of 12 h. The organic coated formulation F9 with 6% Eudragit® [RSPO (9): RLPO (1)] showed 75.38% release over the period of 12 h. The marketed formulation showed 75.22% drug release over the period of 12 h. The $t_{25\%}$, $t_{50\%}$ and $t_{90\%}$ for marketed formulation was found to be 3.5 h, 7.8 h, 14.6 h respectively and followed zero order release kinetics (Table 5a). The *f2* value for formulations F3, F6, F9 was found to be 72.15, 78.23 and 73.89. The *f2* value exhibited that formulations F3, F6 and F9 had a dissolution profile similar to the marketed product.

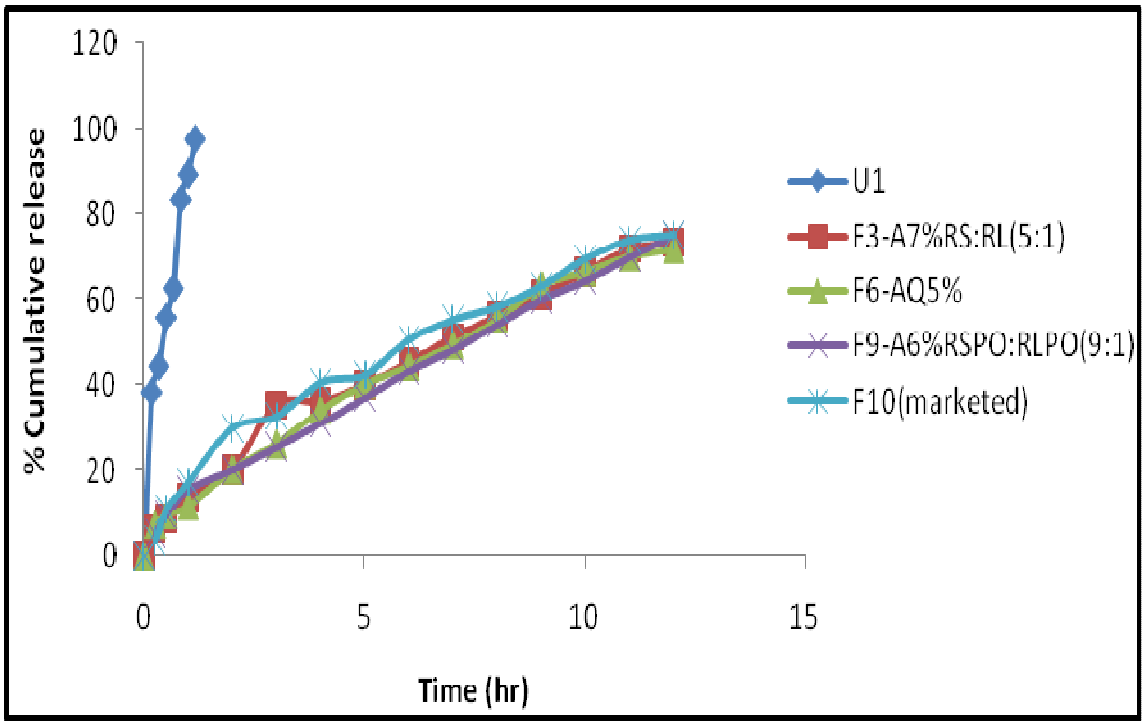

Figure 3
Comparison of release characteristics of optimized formulations with marketed and uncoated (U1) venlafaxine hydrochloride tablet

Comparison of release characteristics of all optimized formulations in different media

The release of aqueous coated formulation F3 with 7% Eudragit® [RS (5): RL (1)], F6 with 5% Aquacoat ECD and F9 with 6% Eudragit® [RSPO (9): RLPO (1)] in different media was determined. The release was found to be 73.45%, 76.45% and 71.45% in water, pH 1.2 and pH 6.8 phosphate buffers respectively for F3, 71.55%, 74.29% and 70.89% in water, pH 1.2 and pH 6.8 phosphate buffers respectively for F6 and be 75.22%, 73.59% and 74.08% in water, pH 1.2 and pH 6.8 phosphate buffer respectively for F9. (Lorck CA et al.1997; Ceballos A et al. 2005; Knop K, 1996; Heun G et al. 1998; Omari DM et al. 2004)

Stability Studies

Appearance: Tablets kept for stability studies were removed and examined. The color of aqueous coated formulations F3, F6 and organic coated formulation F9 was similar before and after stability studies without any coating defects.

Drug content

Table 7
Drug Content During Stability Studies

Time (days)	F3 at 40°C & 75% RH	F6 at 40°C & 75% RH	F9 at 40°C & 75% RH
0**0jj0**	100.22 ± 0.50	99.32 ± 0.34	100.39 ± 0.11
15	99.06 ± 0.91	100.06 ± 0.41	99.37 ± 0.31
30	99.79 ± 0.58	99.51 ± 0.98	99.61 ± 0.48
60	99.78 ± 0.24	100.65 ± 0.28	100.65 ± 0.28
90	100.09 ± 0.23	99.04 ± 0.42	99.42 ± 0.78

Dissolution profile of aqueous coated formulation F3, F6 and organic coated formulation F9 at 40°C & 75% RH

Accelerated stability studies over a 3 month period were performed with Eudragit coated tablet F3, Aquacoat ECD coated tablet F6 and Eudragit coated tablet F9 formulation. No changes in drug release were seen after 3 months of storage under 40°C, 75% relative humidity. For all the formulations F3, F6, and F9, tablets released desired amount of drug over a period of 12 h at the end of 90 days when kept at 40°C and 75 %RH. The total drug release was 71.47%, 74.81% and 74.17% for F3, F6 and F9 formulations respectively, which was almost similar to the initial total drug release at RT.

Stability study using RP – HPLC: Drug content

The chromatogram of formulation F3 at the end of 90 days showed same retention time and AUC as that of on 0 days. There were no degraded peaks found with the principle peak of drug in the chromatogram of formulation F3. The drug content was found to be 99.12 ± 0.68 at the end of 90 days. Thus, we conclude that the formulation F3 is not degraded during the stability study. The chromatogram of formulation F6 at the end of 90 days showed same retention time and AUC as that of on 0 days. There was no degraded peak found with the principle peak of drug in the chromatogram of formulation F6. The drug content was found to be 99.34 ± 0.54 at the end of 90 days.

Table 8
Drug Content During Stability Studies By HPLC

Time (days)	F3 at 40°C & 75% RH	F6 at 40°C & 75% RH	F9 at 40°C & 75% RH
0**0jj0**	100.02 ± 0.70	100.79 ± 0.44	100.41 ± 0.34
90	99.12 ± 0.69	99.34 ± 0.54	99.52 ± 0.42

Thus we conclude that the formulation F6 is not degraded during the stability study. The chromatogram of formulation F9 at the end of 90 days showed same retention time and AUC as that of on 0 days. There was no degraded peak found with the principle peak of drug in the chromatogram of formulation F9. The drug content was found to be 99.52 ± 0.42 at the end of 90 days. Thus we conclude that the formulation F9 is not degraded during the stability study. (Chaudhary A.et al. 2011; Mylavarapu P. et al. 2011)

CONCLUSION

The aim of the present investigation was to develop once a day sustained release reservoir type coated tablets of venlafaxine hydrochloride with aqueous and organic coating. The uncoated venlafaxine hydrochloride tablets were prepared by direct compression technique, have good hardness so that they can withstand mechanical shocks. When comparisons were made among the six aqueous coated formulations coated with Eudragit RS30D and Eudragit RL30D in 5: 1 ratio and Aquacoat ECD 30 (ethyl cellulose) at different coating levels, it was found that the release rate of venlafaxine hydrochloride from F1, F2, F4 and F5 was remarkably faster than those from F3 and F6. When comparisons were made among the organic coated formulations coated with Eudragit RSPO and Eudragit RLPO in 9: 1 ratio, it was found that the formulation F7 and F8 shows faster drug release than that of formulation F9. Release profiles of venlafaxine hydrochloride were independent of pH in dissolution media because the drug released continuously as the pH increases. Increasing the coating level led to a decrease in the rate of drug

release, indicating that the film was controlling the release process. In formulations F3, F6 and F9 slow release of drug was observed. This was due to the higher concentration of the polymer which is slightly permeable to the dissolution medium and prevents the drug release. The formulations F3, F6 and F9 are considered as optimized formulations as they shows 70-75% drug release in 12 hrs which is desired. The marketed formulation was compared with uncoated venlafaxine hydrochloride tablet (U1) and optimized formulations F3, F6 and F9 shows 75.22% drug release till the period of 12 hrs. The *f2* value exhibited that formulations F3, F6 and F9 had a dissolution profile similar to the marketed product. The optimized formulations were also studied for drug release in pH 1.2 acidic buffers and phosphate buffer pH 6.8. There is no significant difference found in the drug release profile indicating that both drug and polymers shows pH independent release. All the optimized formulations F3, F6 and F9 follow zero order release kinetic. Formulations F3, F6 and F9 were kept for the stability studies for a three months period. No changes in drug release were seen after 3 months of storage under 40°C, 75% relative humidity. In conclusion, reservoir type aqueous and organic coated once daily sustained release tablets of venlafaxine were successfully formulated using Eudragit® RS30D, Eudragit® RL30D, Aquacoat ECD 30(ethyl cellulose), Eudragit® RSPO and Eudragit® RLPO as coating materials.

CONFLICT OF INTEREST

Conflict of interest declared none.

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