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EVALUATION OF RELEASE RETARDING EFFICIENCY OF OLIBANUM GUM – A NATURAL POLYMER IN COMPARISON TO KNOWN POLYMERS

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Abstract

The objective of the present study is to make a comparative evaluation of the drug release retarding efficiency of olibanum gum, a natural polymer in comparison to known polymers namely hydroxyl propyl methyl cellulose (HPMCK15M), sodium alginate, and guar gum. Matrix tablets of Venlafaxine Hcl (37.5 mg) were prepared employing olibanum gum and the other polymers at a drug: polymer concentration of 1:4 and the tablets were evaluated. Venlafaxine Hcl release from all the matrix tablets formulated with olibanum gum and various other polymers and release was slow and spread over 12 - 24 hours. Non – fickian diffusion was the release mechanism from all the matrix tablets prepared. The order of increasing release retarding effect with various polymers was guar gum< sodium alginate < HPMCK15M < olibanum gum. Olibanum gum is a better release retarding polymer than sodium alginate, guar gum, and HPMC for obtaining sustained release over 24 hours.

Keywords: Olibanum gum, Sustained release, Venlafaxine Hcl, Matrix tablets.

Introduction

Oral sustained release systems continue to dominate the market despite the advancements made in other drug delivery systems in order, to increase the clinical efficacy and patient compliance. Drug release from the systems should be at a desired rate, predictable and reproducible. Oral sustained release systems are mainly grouped into three types, e.g. reservoir, monolithic and matrix types[1, 2]. Polymers which are used as release retarding materials in the design of controlled – release dosage forms play a vital role in controlling the delivery of drug from these dosage forms. Though a wide range of polymers and other release retarding materials are available, there is a continuous need to develop new, safe and effective release retarding polymers for controlled release. Olibanum gum is a natural polymer, was currently employed to control the drug release from the pharmaceutical dosage form. Venlafaxine is a unique antidepressant that differs structurally from other currently available antidepressants[3]. Venlafaxine and its active metabolite, o- desmethyl venlafaxine, inhibit the neuronal uptake of norepinephrine, serotonin and to a lesser extent dopamine [4,5], but have no monoamine oxidase inhibitory activity and a low affinity for brain muscarinic, cholinergic, histaminergic or alpha adrenergic receptors[6,7]. Hence, it lacks the adverse anticholinergic, sedative and cardiovascular effects of tricyclic antidepressants. The successful treatment of depression depends on the maintenance of effective drug concentration level

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in the body for which a constant and uniform supply of drug is desired. It is a highly water soluble drug (Class I) with the biological half life of 5 hrs thus requires two to three time daily dosing to maintain plasma drug concentration [8]. So providing its slow release to maintain therapeutic level is the major need of this formulation. A few sustained release formulations of Venlafaxine HCl are available commercially. In the present study release retarding and rate controlling efficiency of Olibanum gum was compared with that of known polymers. Matrix tablets of Venlafaxine were prepared employing Olibanum gum and other known polymers and comparative evaluation of their release characteristics were made.

Materials and methods

Materials

Venlafaxine is a gift sample obtained from EMCO industries, Olibanum gum is a gift sample obtained from Nutritroma located at Moosapet, Hyd. Hydroxy propyl methyl cellulose (K15M, Colorcon), sodium alginate and guargum were procured from commercial sources. All other materials used were of Pharmacopoeial grade.

Methods

Preparation of olibanum gum powder: It is available in crystal form. Crystal form of Olibanum gum is dried for 4hrs in hot air oven. Then the dried form is crushed in a mortar to get powder. The obtained powder is passed through 200# size to get fine powder.

Preparation of tablets

Tablets were prepared as per the formulae given in Table1 using wet granulation techniques. Required quantities of medicament and matrix materials were mixed thoroughly in a mortar by following geometric dilution technique. Binder solution (mixture of alcohol and purified water at 1:1 ratio) was added to obtain wet mass. Then pass the obtained wet mass through 14# size and allow it to dry for 30min in hot air oven. After drying, dry sieve it through 20# size to obtain uniform granules. Then dried granules were blended with magnesium stearate and talc for 2-3 min to improve flow property. Then granules were compressed into tablet weighing 300mg each using 8mm flat punches in a Rotary tablet press.

Table No. 01: Formulae of Venlafaxine Hcl Matrix Tablets employing various polymers

Ingredients(mg)	Formulations			
	F1	F2	F3	F4
Venlafaxine Hcl	37.5	37.5	37.5	37.5
Olibanum gum	150	-	-	-
HPMC K15M	-	150	-	-
Sodium alginate	-	-	150	-
Guar gum	-	-	-	150
Lactose	102.5	102.5	102.5	102.5
Magnesium Stearate	5	5	5	5
Talc	5	5	5	5
Total(mg/tablet)	300	300	300	300

*Granulating agent: Hydro alcoholic solution (1:1)

Evaluation of Powder Blends

Angle of repose

Angle of Repose of powder was determined by the funnel method. Accurately weighed powder blend were taken in the funnel. Height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. Powder blend was allowed to flow through the funnel freely on to the surface. Diameter of the powder cone was measured and angle of repose was calculated using the following equation [9, 10]

Tan θ= h/r

Where,

h= height of powder cone;

r= radius of powder cone

Bulk density and Tapped density

An accurately weighed quantity of the blend **(W)**, was carefully poured into the graduated cylinder and the volume ($\mathbf{V_O}$) was measured. Then the graduated cylinder with lid, set into the density determination apparatus (Tapped Density Apparatus, (ElectrolabLTD1020). The density apparatus was set for 1250 taps and after that the

volume **(V_f)** was measured which was tapped volume. The bulk density and tapped density were calculated by using the following formula's, [9, 10]

Bulk density = W/ V_0

Tapped density = W/ V_f

Compressibility index (CI)/ Carr's index

It was obtained from bulk and tapped densities. It was calculated by using the following formula [9, 10]

CI= Tapped density-Bulk density x 100
Tapped density

Hausner's ratio

Hausner's ratio is a number that is correlated to the flowability of a powder[9, 10]. It is measured by ratio of tapped density to bulk density.

Hausner's index = Tapped density
Bulk density

Table No. 02: Preformulation studies for the powder blend F1-F4

Formulation code	Bulk density (g/cm^3)*	Tapped density (g/cm^3)*	Carr's index (%)*	Hausner's ratio	Angle of repose (θ)*
F1	0.47	0.59	20	1.25	32.7
F2	0.49	0.59	16.9	1.2	32
F3	0.48	0.60	20	1.25	32.3
F4	0.47	0.59	20	1.25	32.7

Evaluation of Tablets

Thickness

Thickness of the tablets was determined using a digital vernier caliper MITUOTYO.

Weight variation Test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance and the test was performed according to the official method [11].

Estimation of Venlafaxine HC

Venlafaxine HCl content of the tablets was estimated by UV spectrophotometric method based on the measurement of absorbance at 224 nm in water of pH 7. The method was validated for linearity, precision and accuracy. The method obeyed Beer's Law in the concentration range 0-10 µg/ml. When a standard drug solution was assayed repeatedly (n=6), the mean error(accuracy) and relative standard deviation (precision) were found to be 0.6 and 0.8 %, respectively. No interference from the excipients used was observed.

Hardness

Hardness of the tablets was determined using Monsanto tablet hardness tester

Friability

Friability of the tablets was measured in a Rosche friabilator. 20 tablets were accurately weighed (W_0) and placed in friability test apparatus. They were observed for 100 rotations. After 100 rotations they were weighed again (W). The weight loss should not be more than 1% w/w[12].

%Friability = (W_0-W) / W_0 x 100

Table No. 03: Uniformity of weight, Hardness, Friability, Thickness, Drug content and Disintegration time of Matrix Tablets Prepared

Formulation	Uniformity of weight(mg)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Drug content (%)	Disintegration time
F1	302	12	0.66	4	98	Non-disintegrating
F2	303	11.5	0.59	4.5	97	Non-disintegrating
F3	298	10	0.62	4	96	Non-disintegrating
F4	299	11	0.54	4	98	Non-disintegrating

Drug release study

Drug release from the matrix tablets prepared was studied using 8 station dissolution rate test apparatus (Lab India, Disso 2000) employing a paddle stirrer at 50 rpm and at 37±1°C. water of pH 7 (900 ml) was used as dissolution fluid. Samples of 5 ml of each were withdrawn at different time intervals over a period of 24 h. Each sample withdrawn was replaced with an equal amount of fresh dissolution medium. Samples were suitably diluted and assayed at 224 nm for Venlafaxine Hcl using double beam UV-spectrophotometer.

Table No. 04: Drug Release profiles of Venlafaxine Hcl (37.5mg) Matrix Tablets prepared employing various polymers.

Time	% Drug Release ± s.d (n=3)			
	F1	F2	F3	F4
0	0	0	0	0
1	8.8±0.13	6±0.25	13±0.32	15.2±0.16
2	25±0.15	11±0.16	19.5±0.65	23.4±0.13
3	36±0.26	27±0.53	28.9±0.14	34.6±0.62
6	58.8±0.62	60.1±0.21	69.7±0.32	71.4±0.24
12	73.8±0.46	77.2±0.36	98±0.21	98.6±0.11
16	87.5±0.28	94.5±0.52	-	-
24	89.7±0.63	-	-	-

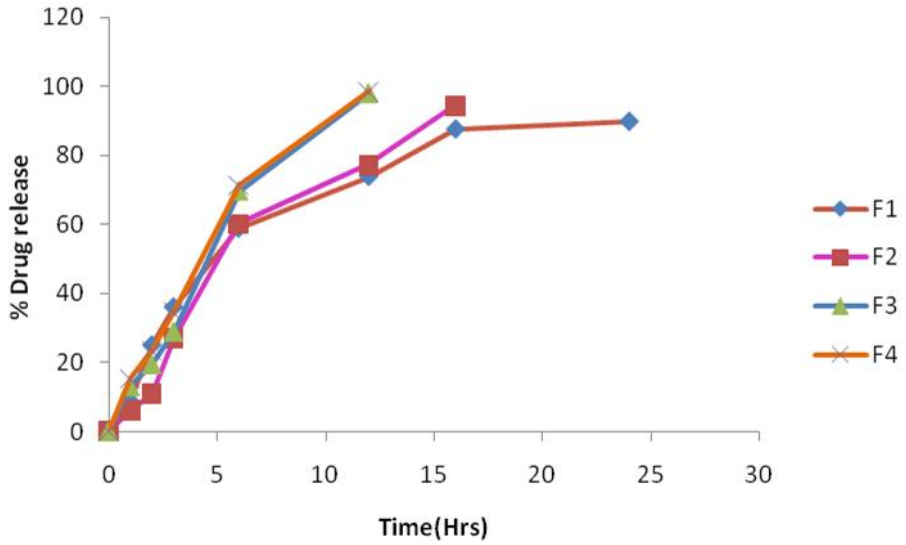

Fig: No. 01: Drug Release profiles of Venlafaxine Hcl (37.5mg) Matrix Tablets prepared employing various polymers

Data analysis

Release data were analyzed as per zero order, first order, Higuchi [13] and Peppas [14] models to assess the drug release kinetics and mechanism from tablets given in Table5.

Table No. 05: Correlation Coefficient(R) Values, Slope Values in the Analysis of Release Data as Per Zero Order, First Order, Higuchi, Peppas Equation Models

Formulation	Zero order		First order		Higuchi		Korsmeyer Peppas
	R	K	R	K	R	K	K
F1	0.9093	5.187	0.9839	-0.010	0.9736	23.292	0.835
F2	0.9403	6.015	0.9539	-0.011	0.9405	26.106	0.9500
F3	0.9583	8.332	0.953	-0.016	0.9276	30.383	0.9276
F4	0.9521	8.210	0.9513	-0.017	0.9507	30.409	0.796

Results and discussion

Matrix tablets each containing 37.5 mg of Venlafaxine Hcl were prepared employing olibanum gum, sodium alginate, HPMCK15M, and guar gum by conventional wet granulation method. A drug: polymer ratio of 1: 4 was used in all the cases. All the tablets prepared contained Venlafaxine Hcl within 100±3 % of the labeled claim. Hardness and friability of the tablets were within official (IP) and GMP limits. All the tablets were found to be non – disintegrating in water and aqueous fluids of acidic (1.2) and alkaline (7.4) pHs. As such the prepared tablets were of good quality with regard to drug content, hardness and friability. As the tablets formulated with various polymers were non – disintegrating with acidic and alkaline fluids, they are considered suitable for oral controlled release (Table 3).

Venlafaxine Hcl release from all the tablets was slow and spread over longer periods of time (Fig. 1). Analysis of the release data as per zero and first order kinetic models indicated that the drug release from the matrix tablets formulated employing various polymers followed both zero order and first order kinetics (Table 5). The correlation coefficient (r) values were nearly same in the zero order model and in first order model. When the release data were analyzed as per peppas equation, the release exponent 'n' was found in the range of 0.796 – 0.9550 indicating non – fickian (anomalous) diffusion as the release mechanism from all the tablets prepared. Plots of percent released versus square root of time were found to be linear (r > 0.9276) with all tablets prepared indicating that the drug release from the tablets was diffusion controlled. Venlafaxine Hcl release parameters of various tablets prepared are summarized in Table 4. All the release parameters indicated variations or differences in drug release from the tablets formulated with different polymers though all the polymers were used at the same drug: polymer ratios i.e., 1:4 in the formula. The drug release was relatively rapid in the case of sodium alginate, guar gum and HPMCK15M the release was completed within 12 – 16 hours with these tablets. Whereas in the case of olibanum gum the release was slow, gradual and spread over 24 hours. The order of increasing release retarding effect with various polymers was guar gum < Sodium alginate < HPMCK15M < Olibanum gum. Thus Olibanum gum was found to be a better release – retarding polymer than guar gum, sodium alginate and HPMCK15M could be used in the formulation of sustained release matrix tablets for 24 hours.

Conclusions

Venlafaxine Hcl release from all the matrix tablets formulated with olibanum gum and other polymers was slow and spread over 12 - 24 hours. Non – fickian diffusion was the release mechanism from all the matrix tablets prepared with various polymers. Venlafaxine Hcl release from the matrix tablets prepared employing sodium alginate, guar gum and HPMC K15M was relatively rapid and the release was complete in 16 hours. Whereas Venlafaxine Hcl release was slow and spread over 24 hours with Olibanum gum. The order of increasing release retarding effect with various polymers was guar gum < sodium alginate < HPMC K15M < Olibanum gum. Olibanum gum is a better release retarding polymer than HPMC, guar gum& sodium alginate for obtaining controlled release over 24 hours.

References

1. Lordi NG. Sustained release dosage forms. In Lachman L, Lieberman HA, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy, 3rd edition, Lea & Febiger, Philadelphia, PA, 1987; 430-456.
2. Thomas WYL, Joseph RR. Controlled release drug delivery systems. In Gennaro AR. Remington: The Science and Practice of Pharmacy, Lippincott Williams and Wilkins, Philadelphia, 2000; 903 – 906.
3. Holliday SM, Benfield P. Venlafaxine: A review of its pharmacology and therapeutic potential in depression drugs. Drugs. 1995;49: 280–94.
4. Haskins JT, Moyer JA, Muth EA, Sigg EB. Inhibition of noradrenergic neuronal activity by the novel bicyclic compounds, Wy-45, 030 and Wy-45, 881. Soc Neurosci Abstr. 1984;10: 262.
5. Muth EA, Moyer JA, Haskins JT, Andree TH, Husbands GEM. Biochemical, neuro physiological and behavioural effects of Wy-45,233, its enantiomers and other identified metabolites of the antidepressant venlafaxine. Drug Dev Res. 1991; 23: 191–9.
6. Cusack B, Nelson A, Richelson E. Binding of antidepressants to human brain receptors: focus on newer generation Compounds. Psychopharmacology. 1994; 114:559–65.
7. Muth EA, Haskins JT, Moyer JA, Husbands GE. Antidepressant biochemical profile of the novel bicyclic compound Wy-45,030, an ether cyclohexanol derivative. Biochem Pharmacol. 1986;35:4493–7.
8. Madgulkar AR, Bhalekar MR, Kolhe VJ, Kenjale YD. Formulation and optimization of sustained release tablets of Venlafaxine resonates using response surface methodology. Indian J Pharm Sci 2009; 71 (4): 387-394.
9. Wells J; Pharmaceutical Preformulation: The physiochemical properties of drug substances. In: Aulton ME. ed. Pharmaceutics the science of dosage form design. London: Churchill Livingstone, 2002; 247.
10. Banker G, Rhodes C.T. Modern Pharmaceutics, Marcel Dekker, inc., 2000.

11. Indian Pharmacopoeia, Published by The Indian Pharmacopoeia Commission, Ministry of Health and Family welfare, Govt. of India, 2007; vol. 2: 1319-1320.
12. Lachman L., Liberman A., Kinig J.L. The theory and practice of industrial Pharmacy; 4th edition, Varghese publishing house, Bombay; 1991; 67-68.
13. T. Higuchi, J. Pharm. Sci., 52, 1145 (1963).
14. P.L. Ritger and N.A. Peppas, J. Control. Release, 5, 37 (1987).