Research Article

Available Online at: www.ijpir.com

International Journal of Pharmacy and Industrial Research

ISSN Print 2231 – 3648
Online 2231 – 3656

PREPARATION OF VILOXAZINE SUSTAINED RELEASE DRUG DELIVERY SYSTEM BY USING HYDROPHILIC BIOPOLYMER HYDROXY PROPYL METHYL CELLULOSE

*HariHaran D, Senthilkumar M, Suresh babu N, Mohan M, Valarmathi S
Annai Veilankanni's College of Pharmacy, Saidapet, Chennai, Tamilnadu, India - 600015.

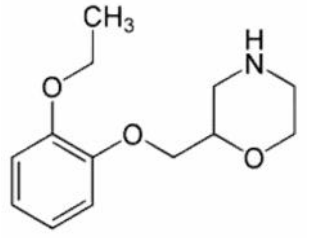
Abstract

The present study behind this work is to find to prepare sustained release tablets of Viloxazine by compression method. First of all to formulate Viloxazine sustained release tablets using the hydroxy propyl methyl cellulose under various ratio's like 1:0.25, 1:0.50, 1:0.75,1:1.00,1:1.25 .Five batches were made in various concentrations of hydroxy propyl methyl cellulose is used by keeping the drug as constant. Then evaluation of Viloxazine sustained release tablets was carried out for characteristics like drug content in tablet, UV analysis. In vitro release starts from 1hr and up to 24hrs. It shows the percentage of gradual drug release as 17.6%, 27.0%, 34.67%, 44.14%, 50.23%, 56.39%, 60.42%, 65.88%, 71.15%, 76.42%, 81.29%, 84.22% & 98.14% against the label claim as 40mg.

Keywords: Hydrophilic, Hydroxy propyl methyl cellulose, Viloxazine, Sustained release tablets, UV Analysis.

Introduction

Viloxazine HCl is chemically (*RS*)-2-[(2-ethoxy phenoxy) methyl] morpholine.



.HCl

Viloxazine Hydrochloride contains not less than 95.0 per cent and not more than 105.0 per cent of $C_{13}H_{19}NO_3$, calculated on the anhydrous basis. It is White to off-white crystalline powder. Soluble in Acetic acid, Methanol and Water. Viloxazine Hydrochloride is used in the treatment of depression. It is a Nor-adrenaline reuptake inhibitor (NRI). It also weakly inhibits the dopamine re-uptake. It is also reported to have little affinity for Muscarinic, Histaminirgic or α_1-adrenergic receptors. The drug is readily absorbed from the GIT. Following oral administration, it undergoes extensive first pass metabolism in the liver mainly to the active metabolite O-desmethyl Viloxazine. Peak plasma concentrations of Viloxazine and O-desmethyl Viloxazine appear about 2 and 4 hours after administration respectively. Protein bindings

Author for Correspondence:
HariHaran D,
Annai Veilankanni's College of Pharmacy,
Saidapet, Chennai,
Tamilnadu, India - 600015.
Email: haran_pharma@yahoo.com

of Viloxazine e and O-desmethyl Viloxazine are low. (Approximately 25%). Formation of O-desmethyl Viloxazine is mediated by the CytochromeP-450 isoenzyme CYP2D6. Other metabolites include N-desmethyl Viloxazine and N, O-didesmethyl Viloxazine. The mean plasma elimination half life of Viloxazine and O-desmethyl Viloxazine 6 and 8 hrs respectively. Viloxazine is excreted predominantly in the form of its metabolites, either free or in conjugated form, about 2% is excreted in the faecus. Side effects include Nausea, Dizziness, dry mouth, Sexual dis-function, may cause sustained rise in BP, needs BP monitoring. It should be used with caution in those with history of myocardial infraction or unstable heart disease. It should also be used with caution in patients with a history of epilepsy and should be discontinued any patient developing a seizure. Viloxazine is known to increase plasma levels of phenytoin by an average of 37%.It is also known to significantly increase plasma levels of theophylline and decrease its clearance from the body, sometimes resulting in accidental overdose of theophylline.

Viloxazine conventional formulations were been developed and evaluated but no sustained release formulation are been developed. Here in this study Viloxazine sustained formulations are been developed with the help of hydroxy propyl methyl cellulose (HPMC K 100) and it is been evaluated with the help of U.V.

Hydroxy Propyl Methyl Cellulose chemically Cellulose 2- hydroxyl propyl methyl ether, It is odorless, tasteless, white or creamy-white colored fibrous or granular powder Soluble in cold water forming viscous colloidal solution, in mixtures of ethanol and dichloromethane, mixtures of methanol and dichloromethane. Practically insoluble in chloroform, ethanol, ether. It is stable, although it is hygroscopic after drying. It is stable between pH 3 – 11. Increasing temperature reduces viscosity. Aqueous solutions are enzyme resistant but prone to microbial spoilage. It is non-toxic and non-irritant, but excessive oral consumption has laxative effect. HPMC used in tabletting technology, 2–5% w/w is used as binder and 2–10% w/w of polymer is used in film coating. Higher viscosity grades may be used in matrix tablet to retard the water soluble drug release, In ophthalmic preparations, it is used as thickening and suspending agent, In topical gels and ointments, used as emulsifier, suspending, stabilizing agent & film former in tablet dosage form.

Materials and methods

The instruments used for the study are eight stage dissolution apparatus model tdt-08l ELECTROLAB, UV-VIS double beam spectrophotometer (UV-1700 SHIMADZU). The drug used for the study is Viloxazine Hydrochloride and the polymers used for the study are hydroxy propyl methyl cellulose (HPMC K 100).

Formulation of Viloxazine SR tablets: Preparation of Viloxazine SR tablets by using HPMC K 100 which were prepared by wet granulation & compression method. During this procedure Viloxazine Hydrochloride SR tablets were prepared by wet granulation method where HPMC K 100 & Viloxazine Hydrochloride are combined together in which HPMC K 100 is a carrier molecule and Viloxazine Hydrochloride is an Hydrophobic drug is mixed with Di calcium phosphate. Now this dry mix is added with HPMC K 100 by using PVP K 90 as binder solution.

Steps involved in preparation of Viloxazine SR tablets:

Step I: Viloxazine Hydrochloride was passed through sieve no 40# then it was mixed with Di calcium phosphate.

Step II: The dry mix was added with HPMC K 100

Step III: Then binder solution PVP K 90 was added to the above dry mass & dried at 60^0c for 30 minutes

Step IV: The above granules were pre lubricated with talc & Aerosil then finally lubricated with magnesium stearate.

Drug Content Analysis: Twenty tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 40mg of Viloxazine was transferred into a 100ml volumetric flask and extracted with distilled water. Then it was filtered and suitable dilutions were made and absorbance was measured by using Shimadzu UV-Visible spectrophotometer (UV-1601) at 273nm.

Dissolution study of the Viloxazine SR tablets was done by the six stage dissolution apparatus model tdt-08l ELECTROLAB, with USP specifications. The medium content of the dissolution was 900ml

of phosphate buffer pH 6.8 was placed in a dissolution basket. The medium was allowed to equilibrate to the temperature 37± 0.5°C.The rpm maintained for this analysis was 100. The analysis was carried out for 24hours. The percentage of drug release was analyzed by the help of UV-spectrophotometer for each formulation. All release rate was based upon the amount of drug released was calculated from the calibration curve. Volume taken is 5ml from which suitable dilutions where made to get desired concentration of drug. The λmax of Viloxazine HCL was found to be 270nm. The % of drug release of different formulations carried out at 270nm.

Table No. 01: The tabular column showing the ratio of drug & polymer concentration.

S.No	Formulations	Ratio of Concentration	Concentration of Viloxaine HCL	Concentration of HPMC K 100
1.	F I	1:0.25	50mg	12.5mg
2.	F II	1:0.50	50mg	25.0mg
3.	F III	1:0.75	50mg	37.5mg
4.	F IV	1:1.00	50mg	50.0mg
5.	F V	1:1.25	50mg	62.5mg

Table No. 02: Drug content in tablets

		Amount of drug in matrix tablets(mg)			
S.No	Formulation	Sample1	Sample2	Sample3	Mean
1	I	40.6	40.8	40.57	40.65
2	II	40.2	40.3	39.40	39.96
3	III	40.3	39.8	40.91	40.33
4	IV	40.6	40.6	39.49	40.23
5	V	40.1	40.7	40.53	40.44

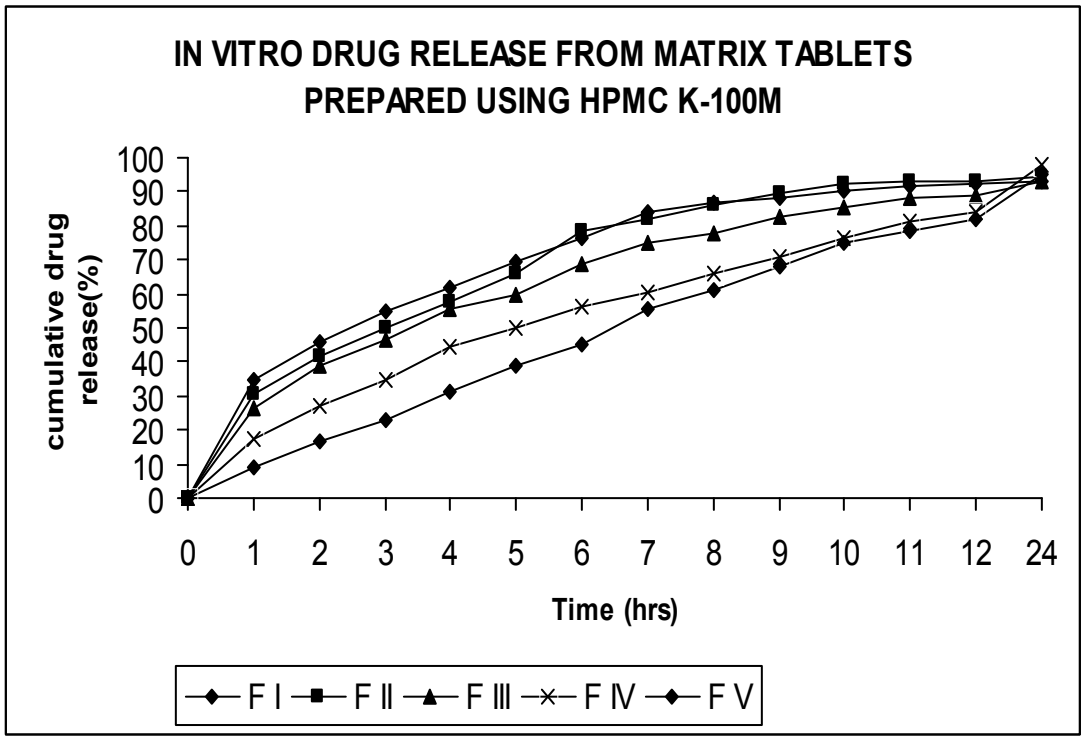


Fig. No. 01

Tabl No. 03: *In vitro* drug release for formulation F IV

S.No	Time(hrs)	Absorbance	Concentration (mcg/ml)	Cumulative release(mg)	Cumulative Percentage drug release±SD
1	1	0.058	1.58	7.09	17.62
2	2	0.078	2.16	10.86	27.00
3	3	0.035	0.60	13.95	34.67
4	4	0.073	1.35	17.76	44.14
5	5	0.097	1.83	20.21	50.23
6	6	0.121	2.31	22.69	56.39
7	7	0.139	2.66	24.31	60.42
8	8	0.158	3.04	26.50	65.88
9	9	0.177	3.42	28.62	71.15
10	10	0.197	3.82	30.74	76.42
11	11	0.215	4.17	32.70	81.29
12	12	0.225	4.37	33.88	84.22
13	24	0.278	5.43	39.48	98.14

Results and discussion

Formulations F-I to F-V were prepared as per table no 1. Granules were prepared by wet granulation method. The prepared granules were evaluated for bulk density, angle of repose and compressability.

Bulk density for all the formulations ranged between 0.43 to 0.54. The angle of repose for all formulations ranged between 25˚.64 to 29˚.25 the bulk density indicates good packing characters. The value of angle of repose (between 25˚-30˚) for all the formulation indicates good flow property. The value of Carr's index for all the formulations ranged between7.57-9.73. The value of Carr's index (between 5-15%) indicates free flowing material. The granules were then compressed to tablets. The tablets were evaluated for uniformity of weight, hardness, friability, drug content and dissolution. The tablets prepared were white in color, oval shape. They were smooth, uniform and free from crack and chipping.

Thicknesses of all fabricated formulations are in the range of 3.2-3.6 mm. Weight variation was found with in specifications of I.P limits The hardness of all fabricated formulations were in the range of 80 –95N.

Friability for all the formulations were in the range of 0.36-0.61. The value of hardness and percent friability indicates good handling property of prepared tablets. The results for the above parameters were found to be in the recommended range.

The results of drug content for all formulations were found to be between 39.40 mg - 40.57 mg per tablet with ±S.D.

Formulations containing different ratios of HPMC showing following drug release profiles FI and FII released more than 80% of drug at 7^{th} hour, where as FIII, FIV and FV released more than 80% of drug at 9^{th}, 11^{th} and 12^{th} hours respectively. Whereas our selected formulations FIV releases 98.14% of drug in 24 hours respectively.

Conclusion

From the results and discussions, amongst the 5 different formulations designated as FI, FII, FIII, FIV and FV. The formulation FIV was found to be the better formulation in terms of sustained release and maximum percentage drug release.

To conclude, hydroxyl propyl methyl cellulose at a concentration ratio of 1: 1 is suitable for preparing sustained release matrix tablets of Viloxazine hydrochloride.

Acknowledgement

We are thank full to our Principal Mr. M.Senthil kumar M.pharm, PhD., for his kind & cooperation to finish the work.We are thanking our beloved chairman Dr.S.Devaraj for his encouragement & for providing the facilities to complete the work. We thank all our staff & Friends for their support & help for successful completition.

References

1. Chein YW, Novel drug delivery system. 2nd ed.Marcel Dekker Inc. 1992; 1-10.
2. Joseph R Robinson.Sustained release drug delivery system.Remington pharmaceutical sciences. 18th ed.The edition Mac publishing company. 1990; 1682-1698.
3. Joseph R, Robinson, Vincent HL. Lee. Controlled drug delivery. 2nd edition, vol 29, 373-421, 1978.
4. Lee VH, Robinson JP. Sustained and controlled release drug delivery systems. Marcel Dekker: New York. 1978; 7-11.
5. Avaraham Yacob, Eva Halperin-Walgega. In: Oral sustained release formulations, design and evaluation; Pergamon press; 1988; 35-39.
6. Pabon CV, Frutos P, Lastres JL, Frutos G. In vitro study of mixed controlled release matrix tablets containing HPMC and polyamide 12. Drug Dev Ind Pharm; 1992; 18(21); 2163-2171.
7. Hiremath SN, Neelima K, Swamy PV, Singh P, Shirsand SB, Raju SA. Formulation and evaluation of sustained release matrix tablets of Metformin hydrochloride. Indian drugs; 2007; 44(1); p 51-53.
8. http://en.wikipedia.org/wiki/Viloxazine.
9. Reynolds JEF Martindale. The Complete Drug Reference. 36th ed. Royal Pharmaceutical Society, London. 2009.
10. http://www.seqchem.com
11. British Pharmacopoeia 2009. CD-ROM. Vol. I and II.
12. Tripathi KD. Drugs used in mental illness: antidepressants and antimanic drugs. In: Essentials of medical pharmacology. Tripathi: Editor. Jaypee publications p 405-418.
13. Raymond C Rowe, Paul J Sheshkey and Marian E Quinn Hand Book of Pharmaceutical Excipients sixth edition 2009.
14. Indian pharmacopoeia 2010.
15. Leon Lachman, Herbert A. Lieberman, Joseph L. Kanig. The theory and practice of industrial pharmacy, 3rd edition, Varghese Publishing house.1990; 311-317.