INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Research Article

Design, Development And In-Vitro Evaluation Of Paroxetine Hydrochloride Controlled Release Tablets

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ARTICLE INFO

Received: 07 June 2024
Accepted: 11 June 2024
Published: 19 June 2024
Keywords:
Paroxetine, antidepressants, Sustained – release, Dissolution, Povidone K30, Eudragit
DOI:
10.5281/zenodo.12602803

ABSTRACT

The main aim of the present study is to develop a pharmaceutically equivalent, low-cost quality improved formulation and stable controlled release tablets of Paroxetine HCl comparable to innovator product. Paroxetine is a selective serotonin reuptake inhibitor, chemically unrelated to tricyclic, tetracyclic, or other antidepressants; presumably, the inhibition of serotonin reuptake from brain synapse stimulated serotonin activity in the brain. The conventional form of Paroxetine tablets have many side effects therefore a controlled release Paroxetine Hydrochloride is designed in order to improve its therapeutic profile and safety, and for reducing the dosing frequency.

INTRODUCTION

For many decades treatment of an acute disease or a chronic illness has been mostly accomplished by delivery of drugs to patients using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, creams, ointments, liquids, aerosols and injectables as drug carriers. The design of oral sustained drug delivery system is subject to several inter-callated variables of considerable importance. Among these are the type of delivery system, the disease being treated, the patient, the length of therapy, a Pharmaceutical products designed for oral delivery and currently available in market are mostly the immediate-release type, which are designed for immediate release of drug for rapid absorption. 1,,2 All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of mode of delivery (immediate, sustained or controlled release) and the design of dosage form (solid, dispersion or liquid) must be

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

developed within intrinsic characteristic of gastrointestinal (GI) physiology.3,4

ADVANTAGES OF CONTROLLED RELEASE DOSAGE FORMS

1. Patient compliance due to reduction in the frequency of dosing.
2. Employ minimum drug.
3. Minimize or eliminates local and systemic side effects.
4. Obtain less protentiation or deduction in drug activity with chronic use.
5. Minimize drug accumulation with chronic dosing.
6. Improves efficacy in treatment.

DISADVANTAGES OF CONTROLLED RELEASE DOSAGE FORMS

1. They are costly.
2. Unpredictable and often poor in-vitro in-vivo correlations, dose dumping, reduced potential for dosage adjustment and increased potential first pass clearance.
3. Poor systemic availability in general.
4. Effective drug release period is influenced and limited by GI residence time.

RATIONALE OF CONTROLLED DRUG DELIVERY

The basic rationale for extended drug delivery is to alter the pharmacokinetic and pharmacodynamics of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and/or physiological parameters inherent in a selected route of administration.5,6 It is desirable that the duration of drug action become more to design properly.7 Rate controlled dosage form, and less, or not at all, a property of the drug molecules inherent kinetic properties.8 As mentioned earlier, primary objectives of extended drug delivery are to ensure safety and to improve efficiency of drugs as well as patient compliance. This can be achieved by better control of plasma drug levels and frequent dosing. For conventional dosage forms, only the dose (D) and dosing interval (C) can vary and, for each drug, there exists a therapeutic window of plasma concentration, below which therapeutic effect is insufficient, and above which toxic side effects are elicited. This is often defined as the ratio of median lethal dose (LD 50) to median effective dose (ED50) 9, 10

MATERIALS AND EQUIPMENTS

CHEMICALS

Paroxetine Hcl	(Milton Drugs Pvt Limited,Puducherry)
Povidone K30	(M/s Signet Chemical, Mumbai)
Ethyl Cellulose	(Rankem Limited, Mumbai)
HPMC	(M/s Dow Chemical Company, USA,)
Eudragit	(Rohm GmbH, Thane)
Aerosil	(Rankem Limited, Mumbai)
Magnesium stearate	(Rankem Limited, Mumbai)

EQUIPMENTS

Electronic balance	Mettler Toledo, Switzerland.
Tablet compression machine	Rimek, Mumbai.
Friabilator	Electrolab, Mumbai.
Bulk density apparatus	Electrolab, Mumbai.
Hardness tester	Monsanto hardness tester
Electronic Balance	Mettler Toledo, Switzerland.
USP Dissolution Apparatus	Electrolab, Mumbai.
Stability chambers	Thermolab, Mumbai
Coating pan	Gans coater
U.V spectrophotometer	Shimadzu u.v-2201, Japan
Sieves	Jayanth test sieves, Mumbai.
Sieve shaker	Electrolab, Mumbai.
pH meter	Electrolab, Mumbai.

Sonicator	Electrolab, Mumbai.

EXPERIMENTAL WORK

PREFORMULATION STUDIES-

Organoleptic character

All the organoleptic character of paroxetine Hydrochloride was studied and it was found that all the character complies with IP standards.

Bulk density and Tapped density

The density of Paroxetine Hydrochloride was found 0.206 g/ml .Tapped density was found 0.466g/ml. The results are shown in table 15.

Carr's index

The measurement of free flowing powder can also be done by Carr's index. The Carr's index for all the formulations was found to be 55.682%, which reveals that the powder has poor flow character. The results are shown in table 15.

Angle of repose

The angle of repose for Paroxetine Hydrochloride was done as per the procedure. There was no proper flow through the funnel, indicates that powder has poor flow property. The results are shown in table 1.

Sr. No.	Drug	Bulk density ($g/cm^{3)}$	Tapped density(g/cm^3)	Carr's index (%)	Hausner's ratio	Angle of repose
1	Paroxetine Hydrochloride	0.206±0.02	0.466±0.009	55.682%	2.256	No flow through funnel.

PARTICLE SIZE

The Particle size was determined using mechanical sieve shaker as per the procedure. since 95% of the drug is retained on sieve # 50, the particle size of the drug lies between #50 and #18 i.e. 300 um an 1.00 mm. The results are shown in the table 2

Table 2:Particle size analysis

Sieve No	Microns (µ)	Wt ofdrug + sieve (g)	Wt of the drug retained (g)	% ofdrug retained
#18	1000	381.4	0.4	1.9
# 50	297	374	20	95.24
#70	210	335.6	0.6	2.86
#120	125	329	0	0
#140	105	323	0	0
#170	88	321	0	0
#200	74	322	0	0
#200 pass		502	0	0
			21	100

Solubility:

The solubility of Paroxetine Hcl was carried out in different buffers as per the procedure and the results are show in the table 3 and figure 1.

Table 3: Solubility of Paroxitine Hcl in different pH conditions

Buffers	Solubility(mg/ml)
1.2	1.93
4.5	6.31
6.8	1.39
7.4	1.23

DM water	3.13

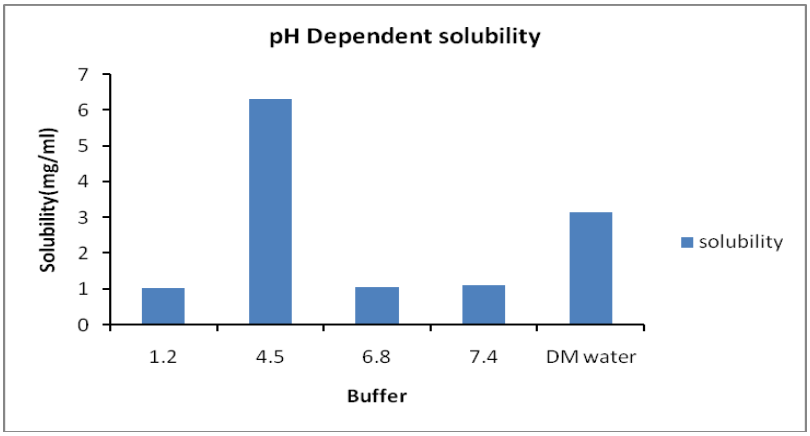


Figure 1 : Solubility of Paroxitine Hcl in different pH condition

PHYSICAL STABILITY OF THE ADMIXTURE

The drugs along with the excipients were kept under conditions specified and the results are given in table 4.

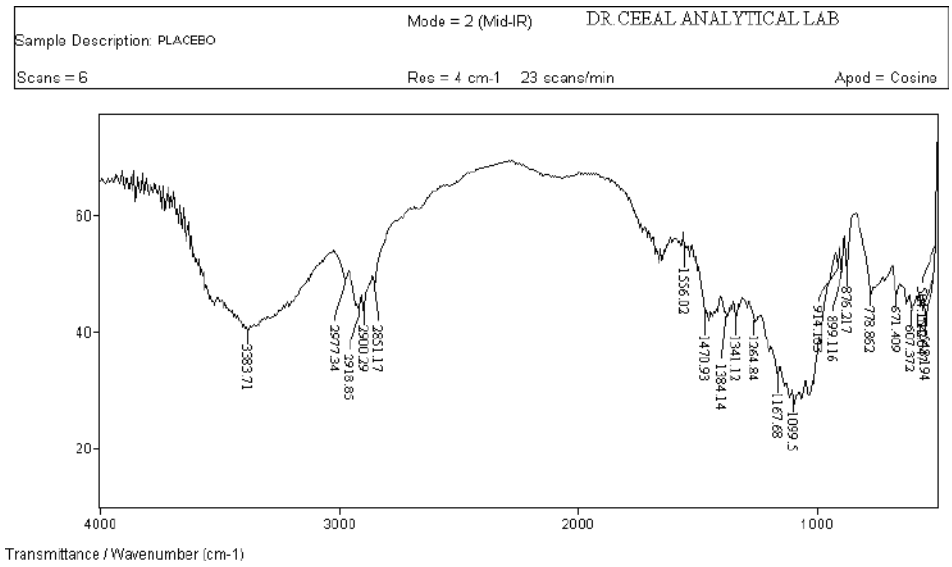
Table 4 : Drug – Excipient stability profile

Sr. No	ITEM	1 month / control	1 month / 60ºC
1.	API	No Change	No Change
2.	API + HPMCK4M	No Change	No Change
3.	API + HPMC K100M	No Change	No Change
4.	API + HPMC E5	No Change	No Change
5.	API + Povidone	No Change	No Change
6.	API + spray dried lactose	No Change	No Change
7.	API + Ethyl cellulose	No Change	No Change
8.	API + Aerosol	No Change	No Change
9.	API + Talc	No Change	No Change
10.	API + Magnesium Stearate	No Change	No Change

There was no physical change observed in the admixture after one month at 60 ºC

Drug Excipient Compatibility Studies

FTIR analysis was conducted for the structure characterization and drug excipient Compatibility to which Paroxetine Hydrochloride showed the following character. All the FTIR characterization of drug excipient was analyzed and results showed that there was no shift of peak that correspond to pure drug as shown in fig 12.



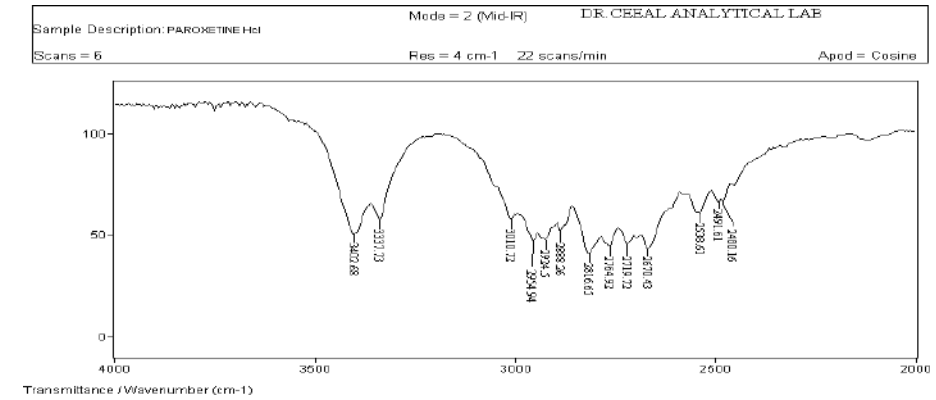
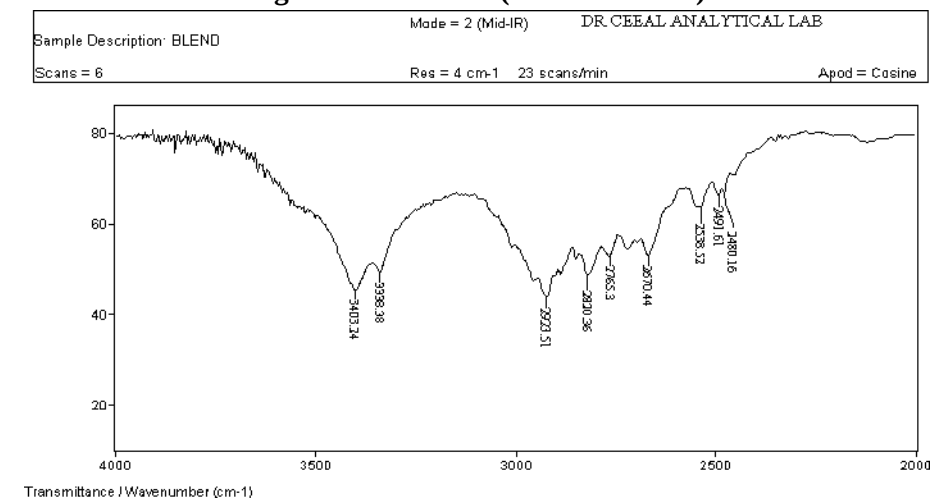


Figure 2 : IR of API(Paroxetine Hcl)



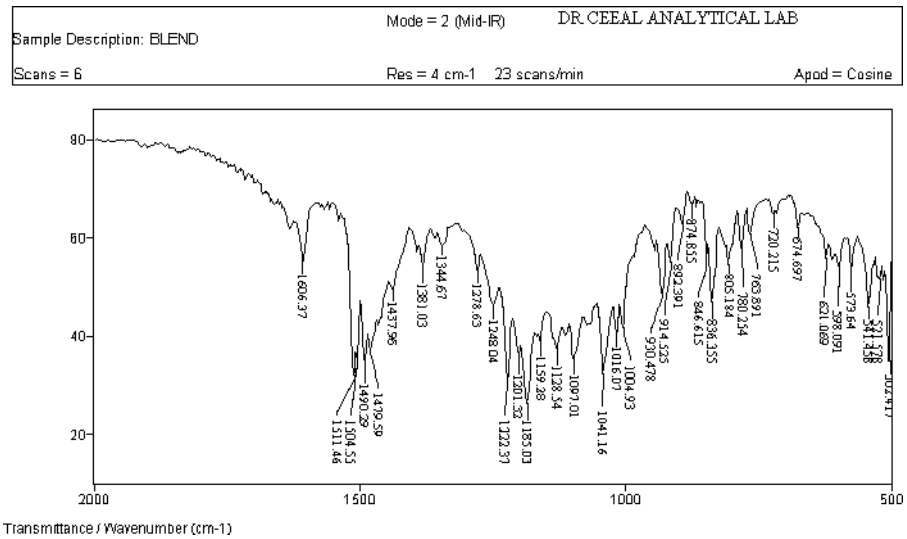


Figure 3: IR of API +Excipients

The FTIR of Paroxetine Hcl (drug) showed intense band at 3402.68 cm-1, 1606.26 cm-1 , 2954.94 cm-1 corresponding to the functional groups , NH, C=C and C-H bending as shown in Figure 11. The FTIR of drug and excipients shown intense bands at 3403.24 cm-1,1606.37 cm-1 , 2923.51 cm-1 indicates no change in the functional groups NH, C=C and C-H as shown in Fig 12. The FTIR of Placebo shown that there are no intense bands at groups NH, C=C and C-H this shows that drug peaks are missing in it as shown in Fig 10. From the above interpretation it is understood that there is no major shifting in the frequencies of above said functional groups. Hence these drug and polymers are compatible with each other.

Calibration curves

Table 5: Standard plot of Paroxetine Hydrochloride in 0.1 N HCl

Concentration (ppm)	Area at 295 nm
0.1	864
0.5	3538
1	6920
5	33996
10	66856
20	125710
40	255356
60	390315

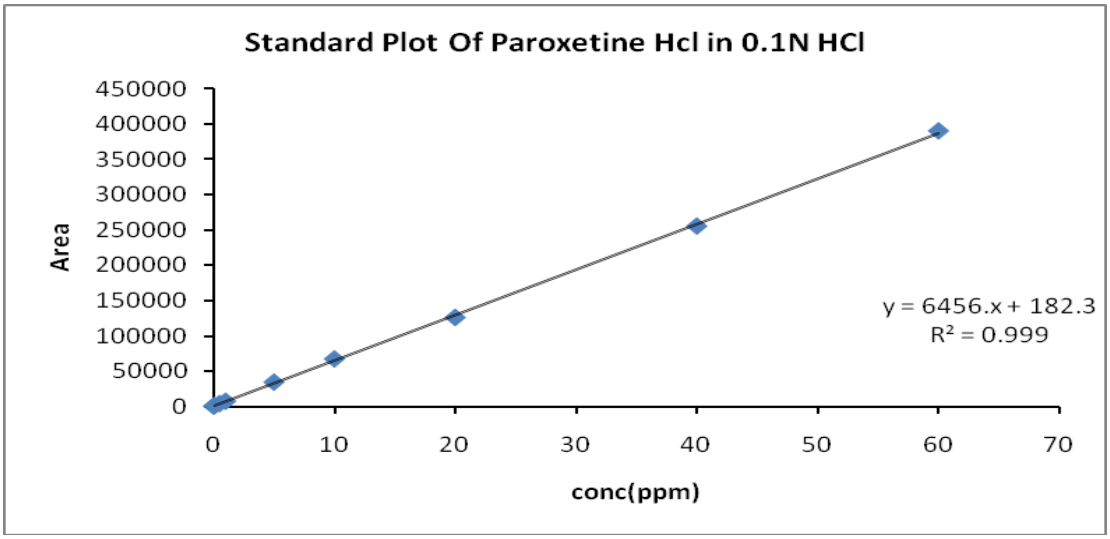


Figure 4: Standard plot of Paroxetine Hydrochloride in 0.1 N HCl

Table 6: Standard plot of Paroxetine Hydrochloride in phosphate buffer

Concentration (ppm)	Area at 295 nm
0.1	1045
0.5	3482
1	6821
5	33180
10	67054
20	126562
40	253532
60	389759

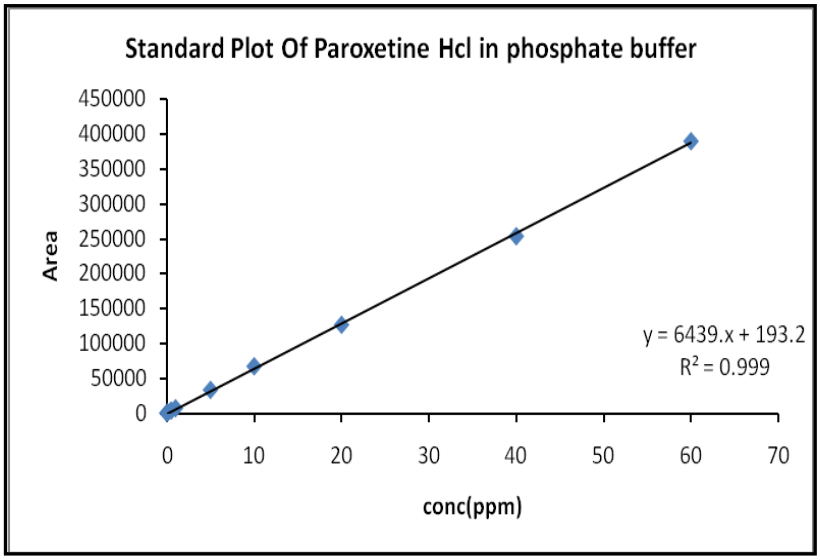


Figure 5: Standard plot of Paroxetine Hydrochloride in phosphate buffer

The present analytical method obeyed Beer's law in the concentration range of 0.1 to 60ppm and is suitable for paroxetine hydrochloride. The correlation coefficient (r) value for the linear regression equation was found to be 0.999, 0.999 in pH1.2, pH6.8 respectively, indicatingpositive

correlation between the concentration of paroxetine hydrochloride and the corresponding area values. The summary of the calibrated curve is shown in the table 21,22.

Table 7 : Formulation of Paroxetine Hydrochloride matrix tablets using different ratios of polymers (F1-F6)

Sr. No	INGREDIENT (in mg)	FORMULATION					
		F1	F2	F3	F4	F5	F6
1	Paroxetine Hydrochloride	42.66	42.66	42.66	42.66	42.66	42.66
2	HPMC K4M	30.00	40.00	50.00	40.00	40.00	30.00
3	HPMC K100M	-	-	-	10.00	-	10.00
4	Ethyl Cellulose	-	-	-	-	10.00	10.00
5	Povidone	10.00	10.00	10.00	10.00	10.00	10.00
6	Spray Dried Lactose	141.34	131.34	121.34	121.78	121.78	121.78
7	Aerosil	2.00	2.00	2.00	2.00	2.00	2.00
8	Magnesiumstearate	4.00	4.00	4.00	4.00	4.00	4.00
9	Total Weight	230	230	230	230	230	230

ENTERIC COATING:

Coating solution preparation:

20% w/w of ACRYL-EZE.in water was prepared with continuous stirring for 1hr. It contains Methacrylic acid copolymer type C, Sodium carbonate, talc, silica, SLS and triethyl citrate. The final solution was passed through 100#. pH of the solution = 5.3

Table 8 : Enteric coating of formulation F7

Sr. No.	INGREDIENT (in mg)	FORMULATION(F7)		
	Enteric Coating	4.378%	5.19%	6.76%
1	Paroxetine Hydrochloride	42.66	42.66	42.66
2	HPMC K4M	40.00	40.00	40.00
3	HPMC K100M	-	-	-
4	Ethyl Cellulose	10.00	10.00	10.00
5	Povidone	10.00	10.00	10.00
6	Spray Dried Lactose	121.78	121.78	121.78
7	Aerosil	2.00	2.00	2.00
8	Magnesium steareate	4.00	4.00	4.00
9	Total Weight	239.16	240.62	243.86

Table 9: Formulation of paroxetine hydrochloride matrix with varied concentrations of HPMC K4M and Ethyl cellulose

Sr. No.	INGREDIENT (in mg)	FORMULATION						
		F8	F9		F10		F11	
		6.8%	6.9%	7.2%	6.4%	7.36%	6.8%	7.66%
1	Paroxetine hydrochloride	42.66	42.66	42.66	42.66	42.66	42.66	42.66
2	HPMC K4M	45.00	35.00	35.00	30.00	30.00	30.00	30.00
3	HPMC K100M	-	-	-				

4	Ethyl Cellulose	5.00	15.00	15.00	20	20	30.00	30.00
5	Povidone	10.00	10.00	10.00	10.00	10.00	10.00	10.00
6	Spray Dried Lactose	141.34	131.34	131.34	121.34	121.34	121.78	121.78
7	Aerosil	2.00	2.00	2.00	2.00	2.00	2.00	2.00
8	Magnesiumsteareate	4.00	4.00	4.00	4.00	4.00	4.00	4.00
9	Total Weight	243.04	245.47	247.22	249.99	245.84	245	246.77

Enteric Coating for formulations F8, F9, F10, F11:

Coating solution was prepared using 400gm of Acryl white 20% w/w in water . Coating parameters:

Pan rpm = 35rpm
Pump rpm = 01
Pan size = 6”
Inlet temperature = 60 oC

Table 10: Development of different % of enteric coating

Parameters	F8	F9	F10	F11
Uncoated tablets				
100 tablets wt. (gm)	22.92, 22.95	23.1, 23.1	--	23.01, 23.05
50 tablets (gm)	11.487	11.559	11.869	--
Wt. of tablets taken (gm)	57.365	57.841	11.869	64.597
Average wt. (mg)	229.46	231.36	237.38	230.7
Tablets wt. after warming (gm)	56.867	57.373	11.7414	64.174
Average wt. (mg)	227.46	229.49	234.83	229.19
Tablets wt. after coating (gm)	60.76	61.369	12.4997	68.60

Table 11: Development of different % of enteric coating

Parameters	F10	F11
Uncoated tablets		
Wt. of tablets (gm)	91.857	68.998
No. of tablets	400	300
Average wt. (gm)	229.65	229.99
After warming		
Wt. of tablets (gm)	91.5956	68.764
Average wt. (gm)	228.99	229.21
After coating		
Wt. of tablets (gm)	98.339	74.031
Average wt. (gm)	245.847	246.77
% Coated	**7.36**	**7.66**

EVALUATION OF TABLETS

CHARACTERIZATION OF PAROXETINE HYDROCHLORIDE MATRIX TABLETS (POST COMPRESSION PARAMETERS)

The tablets of different formulations of Paroxetine Hydrochloride were subjected to various evaluation tests, such as hardness, thickness weight variation, friability and drug content. All the result is shown in Table 20.

Thickness

The thickness of the tablets was found out using Vernier Caliper and the thickness found to be in the range of 4.02-4.12mm for the uncoated tablets (F1-F6). For the enteric coated tablets the

thickness ranged from 4.21-4.30.Thus all formulations showed uniform thickness.

Hardness test

The hardness of tablet was measured by Monsanto hardness tester. Ten tablets from the batch were used for hardness studies and results showed they were in between 6.1-8.0 Kg/cm2. This is appropriate for matrix tablet.

Weight variation test

In a weight variation, the pharmacopoeial limit for the percentage deviation for tablets of more than 250 mg is ±5%. The average percentage deviation of all tablet formulations was found to be within the above limit, and hence all formulations passed the test for uniformity of weight as per official requirements.

Friability test

The Friability of all the formulation was below 1% as per IP specification. Drug content analysis/ Paroxetine Hydrochloride matrix tablet was tested for their drug content and all the formulation showed drug content more than 95%. All the tablet formulations showed acceptable pharmacotechnical properties and complied with the in-house specifications for weight variation, drug content, hardness, and friability.

Table 12: Characterization of Paroxetine Hydrochloride matrix tablets

Batch	Thickness (mm)	Hardness (Kg/cm^2)	Friability(%)	Weight Variation(mg)	Content Uniformity (%)
UNCOATED TABLETS					
F1	4.02 ± .012	6.2 ± 0.5	0.4 5± 0.005	225 ± 2	100.2 ±2.4
F 2	4.01 ± 0.09	6.6 ± 0.3	0.32 ±0.0041	227 ± 2	98.2 ± 1.6
F 3	4.05 ± 0.16	6.4 ± 0.5	0.19 ± 0.003	226 ± 4	98.7 ±2.2
F 4	4.09 ± 0.07	6.6 ± 0.2	0.21 ± 0.002	220 ± 2	101.2 ±2.4
F 5	4.11 ± 0.05	7.1 ± 0.3	0.54 ± 0.004	228 ± 4	102.3 ±1.3
F 6	4.02 ± 0.19	6.8 ± 0.2	0.49 ± 0.011	232 ± 2	101.5 ±1.6
ENTERIC COATED TABLETS					
F7	4.378%	4.28± 0.12	7.4±0.05	0.502±0.01	240± 2
	5%	4.21± 0.08	7.2±0.04	0.408±0.027	239± 2
	6.76%	429.± 0.09	6.8±0.11	0.418±0.012	243± 2
F8	6.8%	4.24± 0.01	6.4 ± 0.5	0.501±0.010	242± 2
F9	6.9%	4.26± 0.13	7.1±0.04	0.41 ± 0.011	244± 2
	7.2%	4.28± 0.09	6.6 ± 0.2	0.538±0.013	247± 2
F10	6.4%	4.28± 0.12	7.4 ± 0.5	0.11 ± 0.003	248± 2
	7.36%	4.27± 0.08	7.0 ± 0.2	0.034±0.012	244± 2
F11	6.8%	4.29± 0.13	6.8 ± 0.5	0.0 5± 0.005	246± 2
	7.66%	4.30± 0.09	6.6 ± 0.2	0.32 ± 0.004	245± 2

In vitro dissolution studies

COMPARISION OF FORMULATIONS WITH MARKETED FORMULATION PAXIL CR USING SIMILARITY FACTOR (F2):

The similarity factor (f2) was calculated for all the formulations as per the procedure and the values are shown in the table 30.

Table 13:Similarity factor(f2)

Formulations	Similarity Factor(F2)

F1		30
F2		37.4
F3		44
F4		34
F5		50
F6		33.5
F7	4.378%	64.7
	5%	64.2
	6.76%	49.6
F8	6.8%	47.6
F9	6.9%	60.4
	7.2%	58.1
F10	6.4%	66.7
	7.36%	**68.7**
F11	6.8%	49.6
	7.66%	67.2

The similarity factor of all the formulation ranged from 30-70. The f2 value of formulation F10 was higher when compared to other formulations therefore F10 formulation was found to be similar to that of the marketed formulation (PAXIL CR).

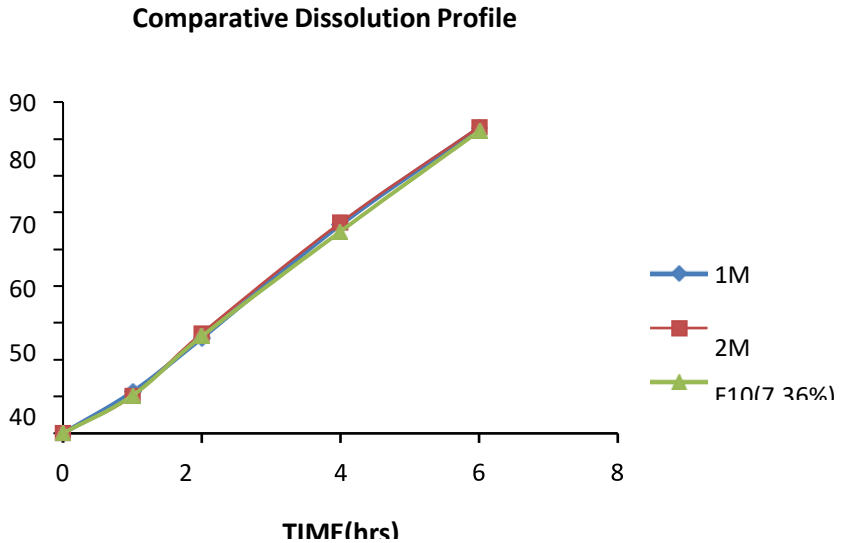


Figure 7: Stability dissolution profile of formulation (F6) at 25°c/ 60% RH

Table 14:cumulative drug release profile of stabilized formulation (F10)

Time (hrs.)	**Stability Data of 7.36% coating formulation (F10)**			
	40°c/ 75% RH		**25°c/ 60% RH**	
	Mean(1M)	**Mean(2M)**	**Mean(1M)**	**Mean(2M)**
% Drug release in acid stage	0.0	0.0	0.0	0.0
1hr	10.3	9.8	11.2	10.1
2hr	25.8	26.2	25.9	27.1
4hr	54.7	55.7	56.7	57.2
6hr	84.8	83.2	82.9	82.1

Optimized formulation (F10) was kept for stability studies, and observed that assay after 1st, 2nd month was complies with optimized formulation. Dissolution profile of stability samples after 1st, 2nd months were compared with formulation (F10)(7.36%).There is no significant change in In vitro release profile in both conditions when compared with F10ssssss. It shows that it is stable formulation.

CONCLUSION

In formulations (F7-F11) concentrations of HPMCK4M and ethyl cellulose in the formulations (F7-F11) were varied. The tablets were prepared by direct compression method after subjecting the blend to preformulation studies like Angle of repose, Bulk density, Tapped density, Carr's Index. Post compression parameters like Hardness, Weight variation, Friability, Drug content analysis were carried out .The results obtained were satisfactory. Similarity factor (f2) was calculated for all formulations and found that f2 value was higher for F10 formulation. Among all formulations F10 was selected as optimized formulation as the in-vitro profile complied with the innovator Paxil CR.

Different kinetic models were applied to the formulation optimized and observed that formulation (F10) followed zero order kinetic model and it was complied with Paxil CR (Innovator sample). Stability studies were conducted for the optimized formulation and it was found that the product was stable. It may be concluded from the present study that slow, controlled release of Paroxetine over a period of 6 h was obtained from matrix tablets . It is evident from the results that Hydrophilic matrix of HPMC could not control the Paroxetine release effectively where as a combination of hydrophilic and hydrophobic matrix prepared by HPMCK4M and ethyl cellulose is a better system for controlled delivery of water-soluble drug like Paroxetine hydrochloride.

REFERENCES

1. Martins Emeje olobayo o. Kunle1 sabinus Ofoefule Effect of the molecular size of carboxymethylcellulose and some polymers on the sustained release of theophylline from a hydrophilic matrix. Acta Pharm 2006;56:325-35.
2. Chein YW, James Swarbrick, editors. Novel Drug Delivery System. 2nd ed. New York: Marcel Dekker; 1992.p.139-96.
3. Robert S Langer, Donald L Wise, editors. Medical Application of Controlled release:classes of system. CRC Press; 1984.p.159.
4. Brahmankar DM, Sunil B Jaiswal, editors. Biopharmaceutics and pharmacokinetics a treatise.1sted. Delhi: Vallabh Prakashan Publications;2001.p. 348-35.
5. Steward PA. Review of Pharmaceutical Controlled Release Methods and Devices[online].[2000Nov11];Availablefrom :URL:www.initium.demon.co.uk.
6. www.inintium.demon.co.uk Singh (1968) Nakagami(1991) Donbrow & Friedman (1975) [online].
7. Xiaoling I, Bhaskar R.J. Design of Controlled Release Drug Delivery Systems, 2006.p. 155
8. Peter G Welling, Michael R Dobrinska, Robinson JR, Lee VHL, editors. Controlled Drug Delivery: Fundamentals and Applications. 2nd ed. New York: Marcel Dekker; 1987.p. 255-259.
9. Lippincott Williams, Wilkins, Thomas Wai-Yip Lee, Joseph R Robinson, editors. Remington's The Science and Practice of Pharmacy. 20th ed. Maryland; 2000.p.903-914.

10. Robinson JR, Lee VH. Controlled drug delivery: fundamentals & application. 2nd ed. New York(NY): Marcel Dekker; 1987.p. 36.
11. Welling PG, Dobrinska MR, Robinson JR, Lee VH. Controlled Drug Delivery: Fundamentals and Applications, 2nd ed. New York: Marcel Dekker; 1987.p. 255-259.
12. Howard C. Ansel, Loyd V. Allen, Nicholas G. Popovich. Ansel's Pharmaceutical Dosage forms and Drug Delivery Systems: 268
13. Sandip BT, Krishna Murthy T, Raveendra Pai M, Pavak RM, Chowdary P. Controlled Release Formulation of Tramadol Hydrochloride Using Hydrophilic and Hydrophobic Matrix System. AAPS PharmSciTech. 2003;4(3):31.
14. Gruenhagen HH. Polymer/drug-melt extrusion: therapeutic and technological appeal. Pharmaceutical Technology Europe1996;11:22-27.
15. Aulton ME editor. Pharmaceutics- The Sciences of Dosages form design. International student Edition: Churchill Livingston; p.129-191.
16. 16. Leon Lachmann, editor. Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia: Lea & Febiger; 1986.p .430-456.
17. Remingtons, Pharmaceutical Sciences. 16th ed. Mack Publishing Company: 1980.p.1677-1683.
18. Sunil Kamboj, Gupta GD, Jagmohan Oberoy. Matrix Tablets:An Important Tool for Oral Controlled-Release Dosage Forms. 2009;7(6).

HOW TO CITE: Reetesh Yadav, Shagun Upadhyay, Tammanna Donadkar, Design, Development And In-Vitro Evaluation Of Paroxetine Hydrochloride Controlled Release Tablets, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 7, 43-55. https://doi.org/10.5281/zenodo.12602803