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FORMULATION AND *IN-VITRO* EVALUATION OF CEFIXIME TRIHYDRATE SUSTAINED RELEASE MATRIX TABLETS

Dr. G. Pratap Kumar*, L. Rajya Lakshmi and T. Murali Krishna

Principal and Professor, MRR College of Pharmacy, Near DSP Office, Madhira Road, Nandigama-521185, Krishna District, Andhra Pradesh.

***Corresponding Author: Dr. G. Pratap Kumar**
Principal and Professor, MRR College of Pharmacy, Near DSP Office, Madhira Road, Nandigama-521185, Krishna District, Andhra Pradesh.
Email ID: pharmacy14443@gmail.com, pratapbt@gmail.com,

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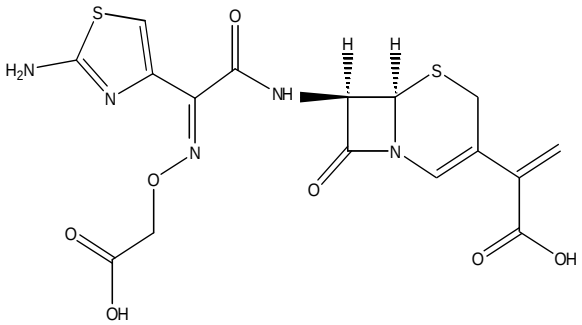
DRUG PROFILE

Cefixime Trihydrate
Systemic (IUPAC) name
(6R,7R)-7-{[2-(2-amino-1,3-thiazol-4-yl)-2-(carboxymethoxyimino)acetyl]amino}-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

Chemical Structure



Molecular Formula: $C_{16}H_{15}N_5O_7S_2$
Molecular Weight: 453
Description: A white to light yellow crystalline powder.

Solubility: Practically insoluble in water, in ether, in ethyl acetate and in hexane. Slightly soluble in alcohol, in acetone and in glycerol and freely soluble in methyl alcohol, soluble in propylene glycol, very slightly soluble in 70% sorbitol and in octanol.

Anti-bacterial Spectrum: Highly active against S. *pneumoniae* and S. *pyorgens*, H. *influenzae* and many Enterobacteriaceae; uncomplicated cervical/urethral gonorrhea due to N. *gonorrhoeae*.

Mode of action: Cefixime trihydrate inhibit mucopeptide synthesis in the bacterial cell wall, rendering it defective and osmotically unstable. These drugs are usually bactericidal, depending on the dose, tissue concentrations, organism susceptibility, and the rate at which organisms are multiplying. They are more effective against rapidly growing organisms while forming cell walls.

OBJECTIVE OF WORK

The main aim of present investigation is to formulate and evaluate sustained release matrix tablets of Cefixime trihydrate using various polymers in different ratios in order to improve patient compliance.

The objectives of the research work undertaken as follows:

1. Calibration curve for the estimation of Cefixime trihydrate.
2. Pre-formulation studies.
3. Formulation of sustained release Cefixime trihydrate matrix tablets prepared by using various polymers in different ratios.
4. Physical evaluations of matrix tablets.
5. Dissolution rate studies of matrix tablets.

PLAN OF WORK

To achieve this objective the following plan of work was envisaged

1. Preformulation studies

(i). Solubility studies,
(ii). Drug excipients compatibility studies

2. Micromeritical studies

Angle of repose, Bulk density, Tapped density and Percentage compressibility.

3. Formulations of matrix tablets

i. Formulations of matrix tablets by HPMC K4M
ii. Formulations of matrix tablets by Xanthan gum
iii. Formulations of matrix tablets by HPMC K100
iv. Formulations of matrix tablets by Eudragit-RL

v. Formulations of matrix tablets by HPMC K4M and Xanthan gum
vi. Formulations of matrix tablets by HPMC K4M and Ethyl cellulose (18cps).

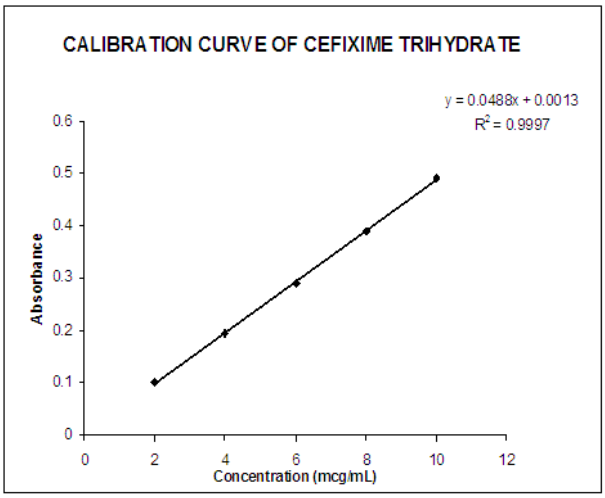
4. Physico-chemical evaluation of Cefixime trihydrate matrix tablets:
5. Weight variation, Friability, Hardness and invitro dissolution studies.

Standard Calibration Curve of Cefixime Trihydrate

Standard calibration curve of Cefixime trihydrate in 7.2 Phosphate buffer at 288 nm by plotting absorbance against concentration and it follows Beer's law. The results were tabulated below.

Calibration curve of Cefixime trihydrate

Concentration (mcg/mL)	Absorbance
2	**0.102**
4	**0.194**
6	**0.291**
8	**0.391**
10	**0.491**



Drug-excipients compatibility studies by observing physical appearance

The pure drug and along with formulation excipients were subjected to compatibility studies and studies were carried out by mixing definite proportions of drug and excipients and kept on glass vials which are stored in Desiccator for one month.

Table 1: Drug-Excipients compatibility studies.

Excipient	Ratio	Description	
		Initial	Final
API	1:0	White to light yellow powder	White to light yellow powder
API + Eudragit-RL	1:1	White to light yellow powder	White to light yellow powder
API + HPMC K100	1:1	White to light yellow powder	White to light yellow powder
API + HPMC K4 M	1:1	White to light yellow powder	White to light yellow powder
API + Xanthan gum	1:1	White to light yellow powder	White to light yellow powder
API + Talc	1:1	White to light yellow powder	White to light yellow powder
API+ Microcrystalline cellulose	1: 1	White to light yellow powder	White to light yellow powder
API + Magnesium Stearate	1:1	White to light yellow powder	White to light yellow powder

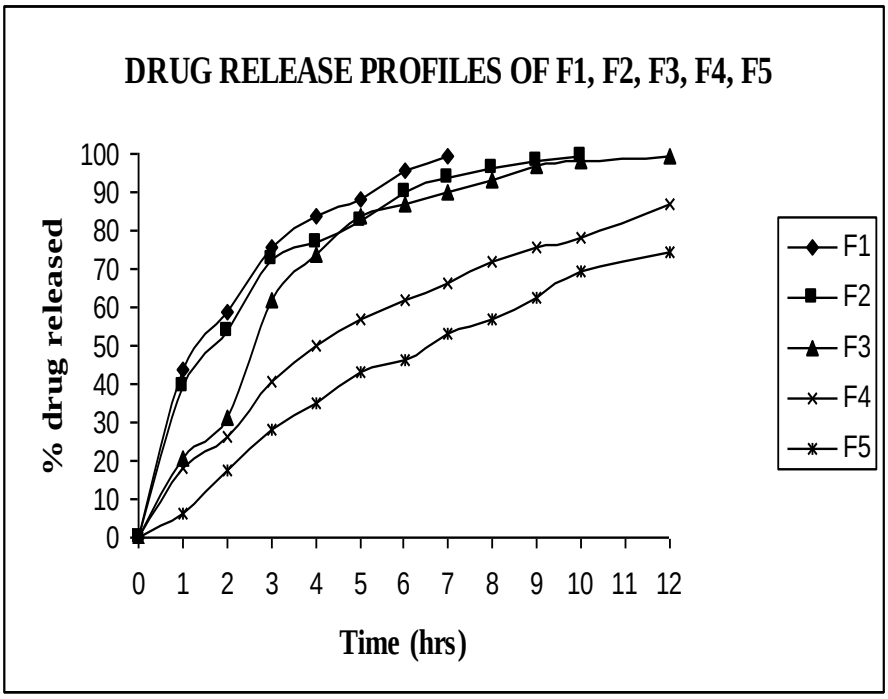
Table 2: Pre-compression parameters.

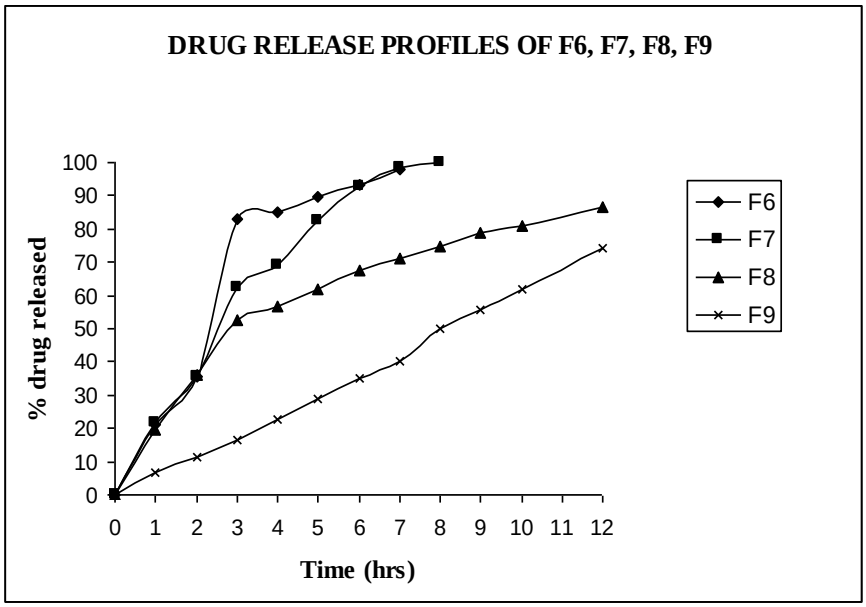
Powder blend	Angle of Repose (°)	Loose bulk density (g/cc)	Tapped density (g/cc)	Compressibility index (%)	Hausner ratio
F1	26	0.525	0.65	19.22	1.18
F2	27.5	0.528	0.645	18.1	1.22
F3	25	0.530	0.648	18.2	1.22
F4	29	0.571	0.660	15.58	1.16
F5	27.3	0.540	0.652	17.17	1.20
F6	31	0.482	0.582	17.18	1.21
F7	30	0.512	0.614	16.61	1.19
F8	31.5	0.554	0.685	19.12	1.23
F9	29	0.531	0.662	19.78	1.24
F10	28	0.516	0.651	20.73	1.26
F11	26.6	0.527	0.66	20.15	1.25
F12	26	0.533	0.651	18.12	1.22
F13	29	0.543	0.649	16.33	1.19
F14	27.9	0.541	0.652	17.02	1.20
F15	26	0.531	0.642	17.28	1.21
F16	28	0.523	0.637	17.81	1.21
F17	25.7	0.548	0.674	18.65	1.22

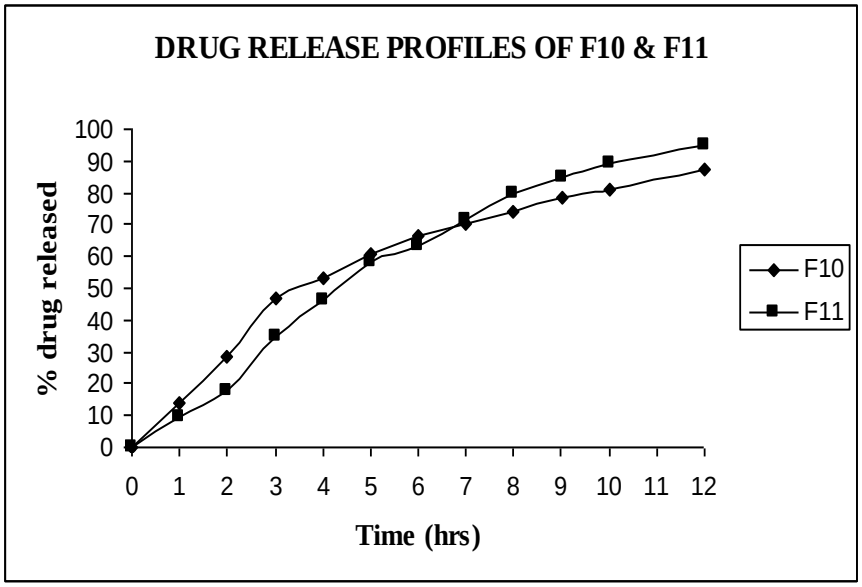
F18	29.1	0.532	0.645	17.51	1.21
F19	32.5	0.51	0.623	18.13	1.22
F20	28	0.498	0.601	17.13	1.20
F21	27	0.518	0.63	17.77	1.21
F22	30	0.525	0.628	16.40	1.19
F23	26.6	0.542	0.682	20.52	1.25

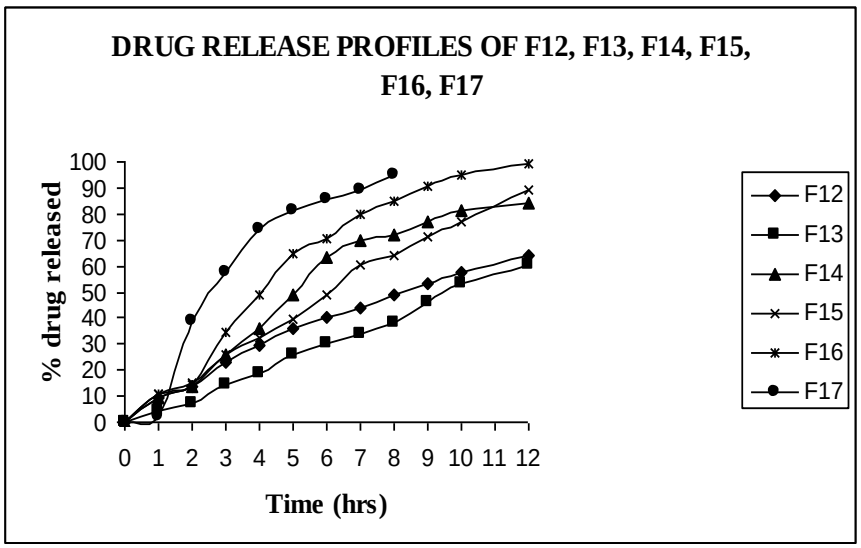
Table 3: Post-compression parameters.

Formulations	Average Weight (mg)	Friability (%)	Uniformity of dosage units (%)	Hardness (Kg/cm^2)	Thickness (mm)
F1	401	0.18	101.2	6	3.2
F2	403	0.39	101.5	5	3.2
F3	400	0.15	100.5	6	3.3
F4	399	0.76	99.5	4.5	3.1
F5	405	0.23	99.8	5.5	3.3
F6	402	0.11	100.1	5.5	3.0
F7	400	0.36	103.2	5.5	3.1
F8	398	0.39	102.2	5	3.2
F9	400	0.45	101.4	5.5	3.2
F10	404	0.18	100.3	6.5	3.2
F11	401	0.26	99.9	5	3.3
F12	403	0.19	99.7	6	3.3
F13	402	0.55	100.5	5	3.2
F14	399	0.34	100.1	5.5	3.1
F15	400	0.21	99.8	6	3.1
F16	402	0.15	101.5	6.5	3.2
F17	400	0.40	100	5.5	3.2
F18	399	0.17	99.5	6	3.2
F19	405	0.24	98.7	6	3.3
F20	802	0.21	100.9	5.5	6.4
F21	801	0.32	98.9	6	6.5
F22	800	0.15	100.9	6.5	6.5
F23	803	0.29	102.1	6	6.5




DRUG RELEASE PROFILES OF F6, F7, F8, F9
% drug released
Time (hrs)
F6
F7
F8
F9


DRUG RELEASE PROFILES OF F10 & F11
% drug released
Time (hrs)
F10
F11


DRUG RELEASE PROFILES OF F12, F13, F14, F15, F16, F17
% drug released
Time (hrs)
F12
F13
F14
F15
F16
F17

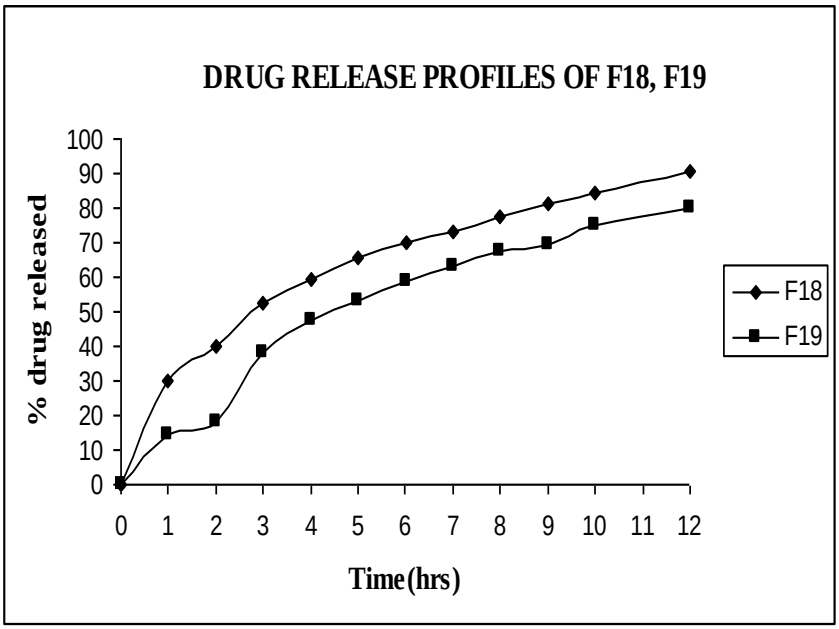


Table 4: Zero Order, first order, Higuchi & Peppas (n) values of all formulations.

Formula	Zero order		First order		Higuchi plot		Peppas plot	
	K_0	R_o^2	K_1	R_1^2	K_H	R^2	n	R^2
F1	9.015	0.9357	0.696	0.846	34.11	0.981	1.6	0.885
F2	6.207	0.871	0.464	0.959	5.6	0.253	1.47	0.968
F3	6.897	0.777	0.436	0.976	33.42	0.886	1.39	0.904
F4	6.134	0.944	0.159	0.99	28.52	0.99	1.02	0.984
F5	6.06	0.968	0.116	0.994	27.94	0.997	1.08	0.963
F6	12.59	0.785	0.572	0.946	48.71	0.86	1.6	0.895
F7	11.48	0.934	0.591	0.902	45.76	0.976	1.16	0.9734
F8	5.473	0.885	0.152	0.988	25.91	0.962	0.8	0.9494
F9	6.306	0.997	0.113	0.953	28.08	0.959	1.17	0.9946
F10	6.213	0.896	0.164	0.992	29.34	0.97	0.97	0.946
F11	8.086	0.945	0.254	0.978	37.52	0.987	1.48	0.972
F12	5.053	0.979	0.084	0.997	23.12	0.978	1.04	0.990
F13	5.259	0.995	0.080	0.978	23.55	0.968	1.12	0.990
F14	7.644	0.928	0.178	0.984	35.43	0.967	1.95	0.968
F15	7.471	0.993	0.181	0.938	33.69	0.979	1.45	0.989
F16	9.194	0.943	0.316	0.964	40.77	0.9704	1.12	0.946
F17	12.67	0.892	0.397	0.984	48.50	0.93	1.48	0.784
F18	5.23	0.934	0.170	0.992	24.43	0.989	0.83	0.9921
F19	5.99	0.911	0.133	0.987	28.09	0.969	1.004	0.9471
F20	7.90	0.973	0.102	0.963	36.26	0.993	1.407	0.992
F21	6.30	0.917	0.068	0.993	29.52	0.976	0.974	0.958
F22	6.87	0.945	0.081	0.9885	31.89	0.987	0.997	0.968
F23	7.09	0.938	0.087	0.990	33.02	0.985	0.998	0.967

RESULTS AND DISCUSSION

The present investigation was undertaken to formulate Cefixime trihydrate sustained release matrix Tablets for the treatment of respiratory tract infections, urinary tract infections and otitis media. All the experimental batches have been exposed to various evaluations like Angle of Repose, Bulk density, compressibility index, and Average weight, Thickness, Hardness, Friability, Assay, and In-vitro Dissolution.

The primary applications for rate controlling polymers are for decreasing dissolution rate and extend the release of water-soluble drug. Successful drug design with polymers depends largely on understanding the physical, chemical and physiological factors to promote bioavailability.

The linearity of Cefixime trihydrate standard curve was checked in the 7.2 phosphate buffer. It was found to be linear in the range of 2 mcg/mL to 10 mcg/mL.

1. Formulations F1, F2, F3, F4, F5, were made by using increasing concentrations of HPMC K4M with 200mg of Cefixime trihydrate. The details of the formulae were given in Table no: 7.The formula mixtures were evaluated for tests such as bulk density, tapped density, compressibility index and Hausner ratio. The results were shown in the Table no: 17. The compressed Tablets were tested for weight variation, thickness, hardness, friability, and uniformity of dosage units. Drug release profiles of formulations F1, F2, F3, F4 and F5 were conducted for about 12hrs.
2. Formulations F6, F7, F8, F9, were made by using increasing concentrations of Xanthan Gum with 200mg of Cefixime trihydrate. The details of the formulae were given in Table no: 8, the formula mixtures were evaluated for tests such as bulk density, tapped density, compressibility index and Hausner ratio.
3. The compressed Tablets were tested for weight variation, thickness, hardness, friability, and uniformity of dosage units The results were shown in the Table no:18.The Drug release profiles of formulations F6, F7, F8, F9 were conducted for about 12hrs.
4. Formulations F10, F11 was made by using different concentrations of HPMC K100 with 200mg of Cefixime trihydrate. The details of the formulae were given in Table no: 9.The formula mixtures were evaluated for tests such as bulk density, tapped density, compressibility index and Hausner ratio. The compressed Tablets were tested for weight variation, thickness, hardness, friability, and uniformity of dosage units. The Drug release profiles of formulations F1, F2, F3, F4, and F5 were conducted for about 12hrs.
5. Formulations F12, F13 F14, F15, F16, F17 was made by using different concentrations of Eudragit-RL and sodium starch glycolate with 200mg of Cefixime trihydrate. The details of the formulae were given in Table no: 10. The formula mixtures were evaluated for tests such as bulk density, tapped density, compressibility index and Hausner ratio. The compressed Tablets were tested for weight variation, thickness, hardness, friability, and uniformity of dosage units. The Drug release profiles of formulations F1, F2, F3, F4, and F5 were conducted for about 12hrs.

BIBLIOGRAPHY

1. Lachman L. and Lieberman H.A., *Pharmaceutical Dosage Forms*, In; Tablets, Vol. 2, Marcel Dekker, Inc., New York.
2. Leon Lachman et.al; *The Theory and Practice of Industrial Pharmacy*, 3rd edition, Page. No: 293- 345.
3. Remington: *The science and practice of pharmacy*, 20th edition volume1, Page. No: 858-863.
4. D.M. Brahmankar, *Biopharmaceutics and pharmacokinetics*, 1995; Page. No: 17-19.
5. M.E.Aulton, *Pharmaceutics - The science of dosage form design*, 2nd edition, Page No: 360-461.
6. Leon Shargel and Andrew, B.C.Y.U., *Applied Biopharmaceutics and Pharmacokinetics*, 1999; 4.
7. Bharmankar, D.M. and Sunil B. Jaiswal., *Biopharmaceutics and Pharmacokinetics*, 2004; 1,296.
8. *The Merck Index*, 13th edition, 2001; 6909.
9. James Swarbrick and James C. Boylan, *Encyclopedia of pharmaceutical technology*, 2nd edition, volume-1, Page. No: 642- 647.
10. Batra, Shirolkar V.S. and Deshpande A.D., *Indian J. Pharma. Educ. Res*, Oct-Dec., 2008; 42(4): 373-378.
11. Raymond C Rowe, Paul J Sheskey and Siaane Owen, *Handbook of Pharmaceutical Excipients*, 132, 188, 213, 214, 449, 701 and 764.
12. Stupak. E.I. and Bates, *J. pharm. Sci.*, 1972; 4: 61.
13. B.K. Sharma, *Instrumental methods of chemical analysis*, 26th edition-2007; S-283-314.
14. Leonards, *J. R., Clin. Pharmacol. Ther, 1963, Page. No: 4.*
15. Md.Mizanur rahman mogal., Md.Safiqul islam., Monzural Amin Roni., Ishtiaq Ahmed., Muhummad Rashedulislam and Habibur rahman, *IJPER*, 2008.
16. Hiremath.S.N, Patil.S.D, Swamy.P.V, and MD. Younus Ali, *IJPER*, 2009.
17. M.A.Roni, G.Kibria, R.Jalil, *Indian Journal of Pharmaceutical Sciences, 2009, Page.No:252.*
18. R.V.Keny, S.A.Mankame, C.F.Lourenco, *Indian Journal of Pharmaceutical Sciences, 2009; 295.*
19. K.P.R.Chowdary, M.N.Murali Krishna, and B.Madhava rao, *Indian Journal of Pharmaceutical Excipients, 2007; 84.*
20. Kothawade Kishore.B, Amrutkar jitendra.R, Gattani surendra.G, Patil ulhas.K, *Indian Journal of Pharmaceutical Excipients, 2007; 106.*