Research Article CODEN: IJPRNK ISSN: 2277-8713
Mukendra Panjiyar, IJPRBS, 2014; Volume 3(1): 359-369 IJPRBS

INTERNATIONAL JOURNAL OF
PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

FORMULATION AND *IN-VITRO* EVALUATION OF EFFERVESCENT FLOATING TABLET OF CIPROFLOXACIN HYDROCHLORIDE

MUKENDRA PANJIYAR, SUKHEE BAJRACHARYA, PRATICHHYA GUNI, ANISH SHRESTHA, EROJ YEMI (NAKARMI), DIPESH KHANAL
Department of Pharmacy, Kathmandu University, Dhulikhel, Kavre, GPO Box. 6250, Nepal.

Accepted Date: 10/02/2014; Published Date: 27/02/2014

Abstract: The study is performed to formulate effervescent floating tablet of Ciprofloxacin Hydrochloride. Ciprofloxacin has short elimination half -life of 4 hours. It has narrow absorption window and is absorbed in proximal areas of gastro intestinal tract. So gastro retentive drug delivery system is required. This drug delivery system helps to increase the patient compliance and solve the problems regarding conventional dosage form. The aim of the study was to develop an optimised gastric floating drug delivery system containing ciprofloxacin hydrochloride. 11 different formulations with three polymers hydroxy propyl methyl cellulose K4M, hydroxyl propyl methyl cellulose K100M and carbopol with different concentrations were used. The combination of sodium bicarbonate and citric acid was used as gas generating agent. All the formulations were evaluated for different in- vitro characteristics. The tablets showed physiochemical properties as required. The data were analysed using mathematical model. The result indicates that the formulation with lowest concentration of polymer showed the highest release profile. The formulations F2, F3, F5, F6 and F10 followed first order kinetics and formulation F1, F4, F7, F8, F9 and F11 followed higuchi model of kinetics and all the formulations showed excellent floating behavior. According to two way ANNOVA test, significant difference was found in relation to variation in polymers and variation in concentration of polymer. ANOVA was done at 0.05 level of significance.

Keywords: Effervescent Floating Tablet, Ciprofloxacin Hydrochloride, Hydroxypropyl Methyl Cellulose, Sodium Bicarbonate and Citric Acid.

PAPER-QR CODE

Corresponding Author: Mr. MUKENDRA PANJIYAR

Access Online On:

www.ijprbs.com

How to Cite This Article:

Mukendra Panjiyar, IJPRBS, 2014; Volume 3(1): 359-369

INTRODUCTION

Oral drug delivery is the most used and preferred route of administration with the obvious advantage of ease of administration and patient acceptance. To develop a drug delivery system for oral administration, it is necessary to optimize not only the release rate of an active ingredient from the system but also the residence time of the system in the gastrointestinal tract.

Floating dosage form is also known as hydro dynamically balanced system (HBS). It is an oral dosage form that is designed to prolong the residence time of the dosage form within the GI tract. It is formulation of a drug and gel forming hydrocolloids meant to remain buoyant on stomach contents. The retentive characteristics of the dosage form in gastric content are most significant for drugs which are insoluble in intestinal fluid, that acts locally and that exhibits site-specific absorption. Floating drug delivery system have bulk density less than that of gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolong period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. However, beside a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of meal. To measure the floating force equivalent to F (as a function of time) that is required to maintain the submerged object.

Ciprofloxacin is the most potent first generation fluoroquinolone active against a broad range of bacteria, the most susceptible ones are the aerobic gram negative bacilli, especially the Enterobacteraceae and Neisseria. The MIC of ciprofloxacin against these bacteria is usually <0.1 mcg/ml, while gram positive bacteria are inhibited at relatively higher concentrations.

Ciprofloxacin is rapidly absorbed orally, but food delays absorption, and first pass metabolism occurs. The drug is freely soluble in water, generally 1gm in 25ml and has a short elimination half-life of about 4 hours, various sustained-release preparations were prepared aiming to enhance its antibacterial activity. Moreover, it has a narrow absorption window and is mainly absorbed in the proximal areas of GIT. Therefore, certain Ciprofloxacin HCl floating systems were developed. To overcome the frequent dosing of ciprofloxacin and to provide patient compliance an effort was made to develop sustained release formulations of ciprofloxacin hydrochloride. Floating tablet of quinolone antibacterial agent like ciprofloxacin was prepared with an aim to reduce bacterial colony by delivery of drug in upper gastrointestinal tract. Current therapy involves administration of proton pump inhibitor or surgery, in either case any bacterial colony might not reduce, therefore, there is strong need to deliver broad spectrum

antibiotics like ciprofloxacin, which can deliver the drug to stomach and has long resident time in gastric pouch. So, floating delivery of ciprofloxacin is essential.

This apparatus helps in optimizing Floating Drug delivery system with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseable intragastric buoyancy capability variation.

RW or $F = F_{(buoyancy)} - F_{(gravity)}$

$= (D_f - D_s)\, gV$

Where RW = total vertical force, D_f = fluid density, D_s = object density, V = volume and g = acceleration due to gravity.

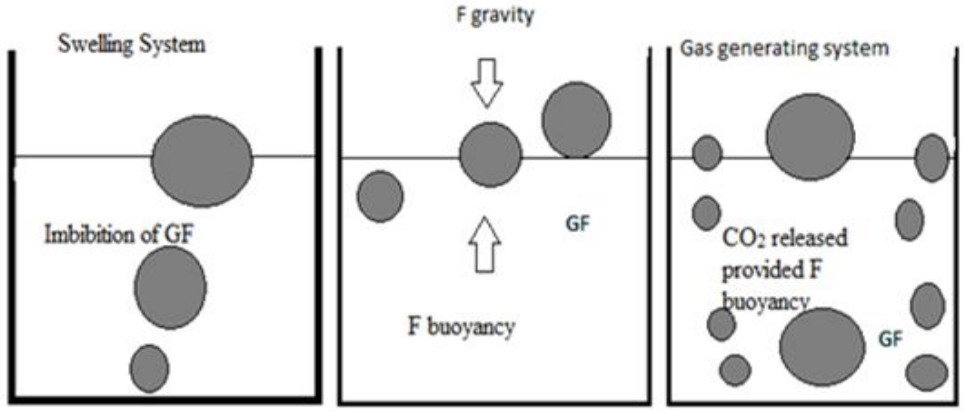

Figure 1: Mechanism of Floating

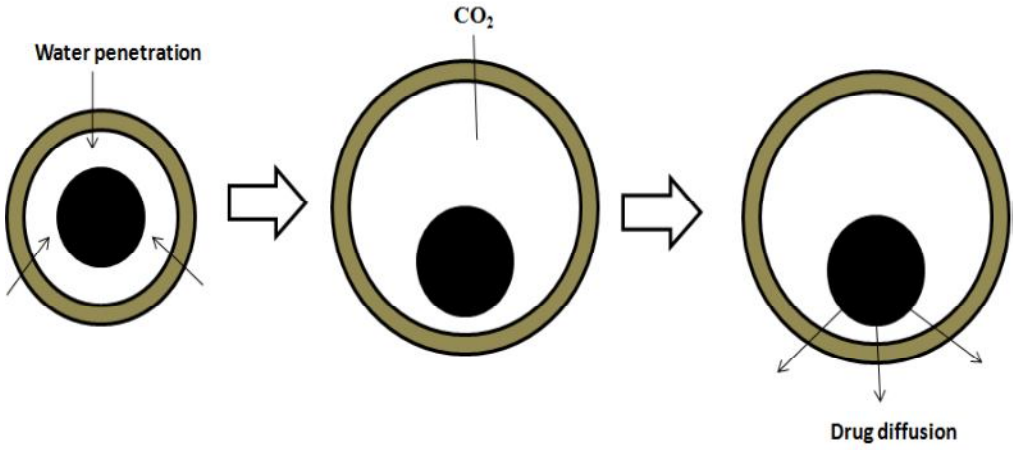

Figure 2: Drug release from effervescent (gas generating) systems

MATERIALS AND METHODS

Materials

Ciprofloxacin HCl and Carbopol were obtained as gift sample from Lomus Pharmaceuticals Pvt. Ltd; Gothatar, Kathmandu. HPMCK4M was obtained from Deurali-Janta Pharmaceuticals Pvt. Ltd; Dhapasi, Kathmandu. Poly vinyl pyrolidone K-30, Sodium Bicarbonate, Lactose, Citric acid and Magnesium Stearate were obtained from the laboratory of the Department of Pharmacy, Kathmandu University, Dhulikhel. All other materials used were of analytical grade.

Method

Floating matrix tablets of Ciprofloxacin were prepared by wet granulation technique varying concentration of different grades of polymer such as HPMC K4M, HPMC K100M and Carbopol. The composition of each tablet is shown in **Table 1.** The excipients were weighed and passed through sieve # 80. Mixing of active ingredient, lactose, polymers, sodium bicarbonate and citric acid were done in polybag. Granulation was done by using solution of PVP K-30 in isopropyl alcohol. After the formation of granules these were dried in hot air oven at 50°C for one hour. Then the granules formed were passed through mesh # 20. Magnesium Stearate was added into the polybag containing the granules for lubrication and the mixture was blended. The was was then compressed into tablets on a ten station rotary punch tableting machine using 8 mm punch.

Table 1: Composition of Effervescent Floating Tablet of Ciprofloxacin Hydrochloride

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Ciprofloxacin hydrochloride	291	291	291	291	291	291	291	291	291	291	291
HPMC K4M	100	150	200	_	_	_	_	_	_	50	50
HPMC K100M	_	_	_	100	150	200	_	_	_	50	_
Carbopol	_	_	_	_	_	_	100	150	200	_	50
Sodium bicarbonate	30	30	30	30	30	30	30	30	30	30	30
Citric acid	15	15	15	15	15	15	15	15	15	15	15
Magnesium stearate	15	15	15	15	15	15	15	15	15	15	15
PVP K-30	30	30	30	30	30	30	30	30	30	30	30
Lactose	219	169	119	219	169	119	219	169	119	219	219
Total Weight	700	700	700	700	700	700	700	700	700	700	700

Evaluation of tablets

The prepared tablets were evaluated for the following parameters.

Thickness

Thickness of tablets was measured using digital vernier callipers.

Hardness

Hardness of the tablet was determined using Monsanto hardness tester.

Friability test

The friability of tablets was determined using Roche Friabilitor. Tablets equivalent to 6.5gm were placed in the friabilitor, which was given 100 revolutions and the tablets were reweighed. The percent friability was calculated based upon the formula as follows:

% Friability =Wo- W/Wo*100

Where,

Wo = Initial weight of tablets

W= Final weight of tablets

Uniformity of weight

20 tablets were weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within permissible limits or not.

Floating Test

For each formulation, the tablets were kept in basket with 200ml of 0.1N HCl maintained at 37 ± 0.5°C. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and the time during which the dosage form remain buoyant called Total Floating Time (TFT) were measured.

Tablet swelling test

The swelling behaviour of tablets was determined. A tablet was weighed (W1) and placed in a glass beaker, containing 200 ml of 0.1 N HCl, maintained in a water bath at 37 ±0.5°C. At different time intervals of 0.5, 1,2,4,8 and12 hours, the tablet were removed and the excess

surface liquid was carefully removed by a filter paper. The swollen tablet was then reweighed (W2). The swelling index (SI) was calculated by:

SI=W2-W1/W1

Where,

SI= swelling index

W1 = initial weight

W2 = Final weight

Drug content

10 tablets were taken and crushed using mortar and pestle. A quantity of powder equivalent to the mass of one tablet (700 mg) was dissolved in 100 ml of 0.1N HCl. The solution was filtered through a cellulose acetate membrane (0.45 µm). The drug content was determined by UV spectroscopy at a wavelength of 278 nm after a suitable dilution with 0.1 N HCl.

In vitro dissolution studies

In-vitro release studies was conducted using USP dissolution test apparatus type 2 (paddle). 900 ml of 0.1 N HCl was filled in dissolution basket and the temperature of the medium were set at 37° C ± 0.5°C. The tablet was put inside the dissolution vessel. The speed was set at 100 rpm. 10 ml of sample was withdrawn at 30 minutes, 1 hour, 2 hour, 4 hour, 8 hour and 12 hour with replacement of the volume being withdrawn. The withdrawn samples were analyzed for drug content against 0.1N HCl as blank at λmax 278nm using UV spectrophotometer. The dissolution of the drug was expressed as percentage drug dissolved.

Kinetic modeling of drug release profiles

The dissolution profiles of all formulation in 0.1 N HCl were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas kinetic models. The model with the highest correlation coefficient was considered the best fitting one.

RESULT AND DISCUSSION

The data obtained from the various parameters such as thickness, hardness, friability, uniformity of weight, drug content, swelling index, kinetics model followed and drug release shown in table 2. The weight variation were within the limits. Hardness of tablets was found to be in the range of 5-6 kg/cm². Friability of tablets was less than 1%. The drug content obtained was found to be within the required limits (**Table 2**).

Formulation with Carbopol has least floating lag time. Other polymers showed floating lag time less than 35 seconds. No variation was found in total floating time with variation in polymer. All the formulations floated for more than 12 hours.

Table 2: Evaluation data of prepared tablets

Formulations	Polymers used	Thickness	Weight Variation (gm)	Hardness (Kg/cm^2)	Content uniformity (mg)	Percentage release (12 hr)	Swelling index (12 hr)	Kinetics model followed
F1	HPMC K4M 100mg	5.176±0.047	0.689±0.0056	5.344±0.141	252.649±0.032	82.035	1.09	Higuchi model
F2	HPMC K4M 150mg	5.169±0.046	0.691±0.009	5.384±0.106	260.218±0.043	72.439	1.21	First order
F3	HPMC K4M 200mg	5.142±0.260	0.688±0.088	5.411±0.09	243.818±0.075	68.073	1.54	First order
F4	HPMC K100M 100mg	4.779±0.068	0.696±0.005	5.441±0.048	261.059±0.0874	60.295	3.23	Higuchi model
F5	HPMC K100M 150mg	4.809±0.057	0.688±0.006	5.781±0.340	258.116±0.0747	43.989	3.60	First order
F6	HPMC K100M 200mg	4.720±0.051	0.666±0.016	5.991±0.332	251.64±0.0435	42.221	3.41	First order
F7	Carbopol 100mg	5.102±0.033	0.696±0.005	5.770±0.282	262.153±0.065	93.476	2.27	Higuchi model
F8	Carbopol 150mg	5.182±0.037	0.679±0.011	5.981±0.293	253.658±0.0756	75.465	2.84	Higuchi model
F9	Carbopol 200mg	5.176±0.034	0.686±0.007	5.819±0.371	252.985±0.0865	60.711	2.98	Higuchi model
F10	HPMC K4M+HPMC K100M (100mg, 1:1)	5.164±0.031	0.682±0.008	6.27±0.503	256.097±0.0987	67.466	1.98	First order
F11	HPMC K4M+Carbopol (100mg, 1:1)	5.174±0.037	0.682±0.006	6.07±0.513	252.481±0.657	70.565	1.01	Higuchi model

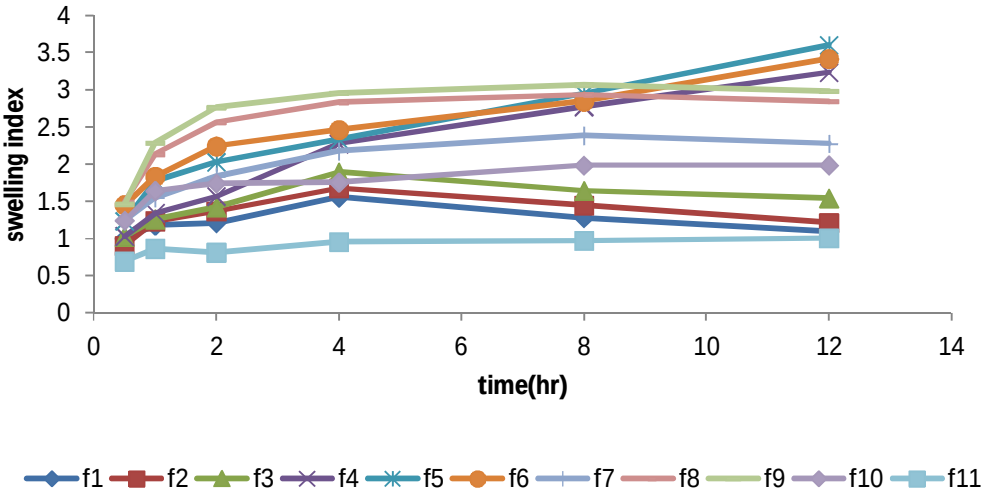

Figure 3: Graph showing swelling index vs. time

Formulation containing HPMC K100M showed maximum swelling behaviour while formulations with HPMC K4M showed least swelling behaviour. HPMC K4M showed least swelling index as it could not remain in matrix integrity up to12 hours. Carbopol does not have highest swelling index. This might be due to the erosion of formulations made from this polymer. The swelling index for each formulation is listed in **(Table 2).**

Table 3: Drug Release profiles

Time Hrs.	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
0.5	10.359	6.850	4.806	9.706	4.558	5.299	8.782	7.083	5.027	6.465	8.465
1	18.988	11.749	13.615	16.266	6.581	9.579	16.020	13.636	8.896	10.366	14.464
2	26.551	19.396	20.146	24.740	11.788	12.506	29.019	26.364	23.025	17.465	21.336
4	39.520	34.307	29.871	35.769	19.009	18.838	49.288	43.364	39.027	31.366	35.747
8	63.841	59.19	55.529	44.338	34.360	23.903	80.708	58.363	49.649	49.756	53.546
12	82.035	72.439	68.073	60.295	43.989	42.221	93.476	75.465	60.711	67.466	70.565

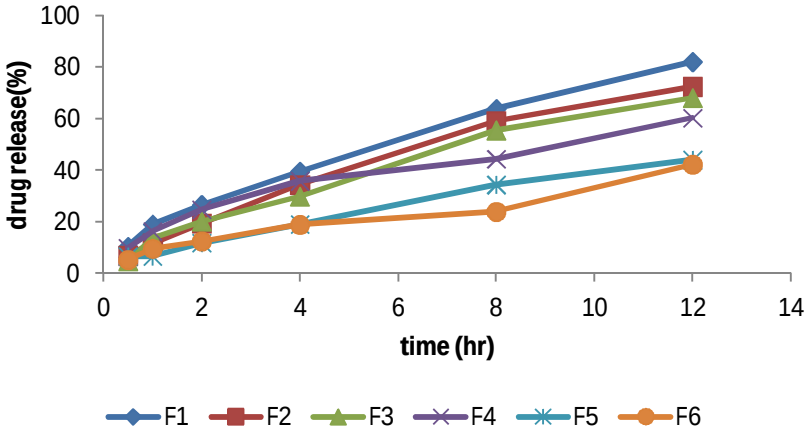

Figure 4: Graph showing percentage drug release Vs. Time

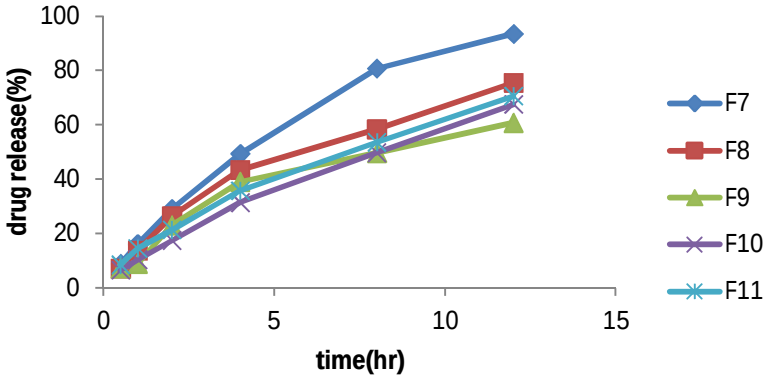

Figure 5: Graph showing percentage drug release vs. time

The dissolution profiles of various tablet formulations are shown in **Table 3.** Release of drug was found to be appreciable in case of F1 and F7. Low amount of release was found in case of HPMC K100M which may be due to its viscous nature which affects diffusion and water permeability. Thin layer of polymer matrix formed in F1 and F7 due to low concentration of polymer which show good release.

Combination of polymers HPMC K4M and Carbopol showed lower drug release when compared to the individual use of polymer.

CONCLUSION

The Effervescent Floating Tablets of Ciprofloxacin Hydrochloride using various polymers by wet granulation method were formulated. The Dissolution data revealed that all the formulation showed sustain release. Release of drug was appreciable in formulation F1 and F7 with low concentration of HPMC K4M and carbopol. Formulation containing cabopol have short floating lag time than others. HPMC K100M showed highest swelling index.

ACKNOWLEDGEMENT

The Authors are thankful to head of the Department Professor Dr.Panna Thapa, supervisor and other faculty members who directly or indirectly assist for our project. Authors are also thankful to Lomus Pharmaceuticals and Deurali Janta Pharmaceuticals Ltd. for providing needed ingredients as a gift sample.

REFERENCES

1. Yadav A and Dinesh J: Preparation and characterization of intragastric Gastroretentive drug delivery system of Diltiazem Hydrochloride. Journal of drug delievery research. 2012; 12-13.

2. Chug I et al: Oral sustained release drug delivery system: An overview. International research journal of pharmacy 2012; 3(4): 57.

3. Pandey A et al: A Review on current approaches in gastro retentive drug delivery system. Asian Journal of Pharmacy and Medical Science 2012; 2.

4. Tadros MI: Controlled-release effervescent floating matrix tablets of ciprofloxacin hydrochloride: Development, optimization and in vitro–in vivo evaluation in healthy human volunteers. European Journal of Pharmaceutics and Biopharmaceutics 2010; 332–339.

5. Arza AK, Gonnugunta RS, and Veerareddy PR: Formulation and Evaluation of Swellable and Floating Gastroretentive Ciprofloxacin Hydrochloride Tablets. AAPS PharmSciTech. 2009; 10(1): 220–226**.**

6. Rowe CR, Sheskey PJ and Owen SC: Handbook of Pharmaceutical Excipients. 5th edition; 379-389.

7. Dash S et al: Kinetic modelling on drug release from controlled drug delivery systems. Acta Poloniae Pharmaceutica-Drug Research 2010; 3: 217-223.

8. Sharma A. Floating drug delivery system as an approach to increase the gastric retention of drugs. Pharmaco tutor. School of Pharmaceutical Sciences, Shoolini University Solan, H.P.

9. Tripathi KD: Essentials of medical pharmacology. Antimicrobials.6th edition. 68-86.

10. Rynolds TD et al: Polymer erosion and drug release characterization of hydroxy propyl methylcellulose matrices 1988; 87.

11. Aulton ME: Aulton's Pharmaceutics the design and manufacture of medicine. Tablet and compaction; 3rd edition: 441.

12. Lachmam L and Lieberman HA: The theory of practice of industrial pharmacy. Sustained release dosage forms 2009; 430-457.

13. Patel D et al: Formulation and evaluation of bilayer floating tablet for gastric retention. International journal of pharmaceutical research and bio-science; 2: 191-214.

14. Modi AS, Gaikwad PD, Bankar VH, Pawar SP: Sustained release drug delivery system: A review. International journal of pharma. Research and development-online 2011.

15. Khan AD and Bajpai M: Floating Drug Delivery System: An Overview. International Journal of PharmTech Research; 2: 2497-2505.

16. Arora S, Ali J, Ahuja A, Khar R, Baboota S: AAPS PharmSciTech. Floating Drug Delivery Systems 2005; 6 (3): 372-387.

17. Kumar R et al: Formulation and Evaluation of Effervescent Floating Tablet of Famotidine. International Journal of PharmTech Research 2009;1:754-763.

18. Pare A, Yadav SK and Patil UK: Formulation and Evaluation of Effervescent Floating Tablet of Amlodipine besylate. Research journal of pharmacy and technology 2008; ISSN 0974-3618.

19. Shankar S. J, Bansal GS and Basavaraj B.V: Formulation and evaluation of controlled release matrix tablets of an antimicrobial drug. International Journal of Pharma. Research and Development. ISSN 0974 – 9446.

20. Habade BM, Kamble V and Wagh RM: Formulation and evaluation of floating drug delivery system of ciprofloxacin. International journal of pharmaceutical research and development. 2012; 3.

21. Johnson RA: Miller and Freund's Probability and statistics for engineers. Analysis of Variance 2008; Ed.7th: 397-425.