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Effectiveness of Compression Coated Tablet Formulation for Colon Specific Diseases and Disorders

Mohammed Jameel patel*[1], Sadath Ali [2], Roshan S[1]

[1] Department of Pharmaceutics, K.C.T. College of Pharmacy Gulbarga, Karnataka, India.
[2] Hemalaya Institute of Pharmacy and Research Dahradoon, India.

ABSTRACT

The effective colon specific dosage form is to release the drug in definite concentration and at specific time on arrival of dosage form in colonic environment, which was achieved by using compression coated tablet formulation of different concentration of coating polymer ethyl cellulose and cellulose acetate phthalate. Drug release was controlled on arrival in colonic region and release was found to be 90.46%, 87.38% and 86.07% from different formulation of compression coated polymer in colonic pH 6.8. Pectin a natural polysaccharide drug carrier was involved in the formulation to disintegrate the tablet and release entire contents in presence of microbial flora of colon.

Keywords: colon, compression coating, cellulose acetate phthalate, pectin.

Corresponding author
Email: jameel_patel@yahoo.co.in

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INTRODUCTION

The site specific delivery of drug to target receptor sites has the potential to reduce the side effects and improve the pharmacological response [1]. Oral control release formulation for small intestine and colon have, however, receive considerable attention in the past 20-25 years for the variety of reasons including pharmaceutical superiority and clinical benefits derived from the drug release pattern that are not achieved with traditional, immediate or sustained release formulation [2].

Oral delivery is still the preferred route of drug administration, especially for chronic therapies where repeated administration is required.

The colon is vulnerable to a number of disorders including ulcerative colitis, crohn's disease, irritable bowel syndrome and carcinomas [3]. Targeted drug delivery to the colon, by means of combination of one or more controlled release mechanisms, hardly releases drug in the upper part of the GIT but rapidly releases in the colon following oral administration. Specifically delivering drug to the colon, a lot of benefits would be acquired in terms of improving safety and reducing toxicity when treating local or systemic chronic diseases [4].

In drug delivery devices, such as tablets, maintaining a constant systemic drug concentration within the circulatory system is the key performance metric. Pharmaceutical coatings are an essential tool to achieve the desired formulation of pharmaceutical dosage forms. Coatings are applied to achieve superior esthetic property of a dosage form (e.g., color, texture, mouth feel and taste masking), physical and chemical protection for the drugs in cores, and modified drug release characteristics. Coating techniques mostly used in pharmaceutical industry are aqueous or organic coatings, which present some disadvantages like time consuming, stability for heat labile and hydrolysis of degradable drug and polluted environment problems. Thereby, non-solvent coating is introduced as an alternative coating technique to overcome these disadvantages. Non solvent coatings have been categorized as press coating, hot melt coating, supercritical fluid spray coating, electrostatic coating, dry powder coating and photo curable coating [5]. Among these techniques, compression coating is the absolute dry coating without solvent and heat use. The compression coated tablet dosage form (i.e., the tablet-in-tablet design) is a time and rate controlled drug delivery device, which consists of a core tablet and an outer layer that is considerably thicker than typical tablet coats and which completely surrounds the core (inner) tablet.

The present piece of work was to design the compression coated tablet formulation which released drug in controlled fashion in presence of exact ratio and concentration of coating polymer, and drug release by disintegration of tablet by involvement of biodegradable drug carrier pectin.

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Material

A model drug Tinidazole Gift sample from SUN Pharmaceutical Industries Ltd., Ahmednagar, Pectin, Ethyl cellulose Sd Fine Chemicals, Mumbai, Cellulose acetate phthalate Qualigens Fine Chemicals, Mumbai, all the other chemicals used were of analytical grade. Tablet Press used was korch CKO, korch Germany).

Method

A. Pre-compression characteristics of different powders used in formulation.

Different ingredients used in the formulation were subjected to pre-formulation studies to get optimum data (Table No.2) for power flow, compressibility and bulk density.

Table No.2: Precompression Parameters/ Evaluation of Powders

Ingredients	Angle of Repose Tan θ=h/r	Bulk Density gm/ml		Compressibility Index (%)
		LBD	TBD	
Tinidazole	25^0-27^0	0.83	0.93	11.82
Pectin	33^0-35^0	0.65	0.75	13.33
Ethyl Cellulose	27^0-29^0	0.60	0.74	14.00
Cellulose Acetate Phthalate	28^0-30^0	0.50	0.60	28.57
Lactose	28^0-30^0	0.75	0.81	7.40

Angle of repose: The frictional forces in a loose powder or granules can be measured by the angle of repose. It is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. Angle of repose was determined as per the reported method[6]. A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on a graph sheet was taken to measure the area of pile, thereby evaluating the flow ability of the granules. Height of the pile is then measured. Angle of repose is calculated by

$$\text{Formula: } \theta = \tan^{-1} (h/r)$$

Bulk density: Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another.

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of 2g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10mL measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2-second intervals. The tapping was continued until

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no further change in volume was noted. LBD and TBD

Were calculated using the following formulas:

$$LBD = \frac{\text{Weight of the Powder}}{\text{Volume of the packing}}$$

$$TBD = \frac{\text{Weight of the powder}}{\text{Tapped volume of the packing}}$$

Compressibility Index (I) :

The compressibility index of the granules was determined by Carr's Compressibility index.

Carr's Index (%) = (TBD –LBD)/TBD x 100

B. Preparation of core tablet:

Each core tablet was prepared for further compression coating ingredients as per Table No.1. The materials were weighed, mixed and passed through #60 mesh to ensure complete mixing. The thoroughly mixed materials were then directly compressed into tablets using 7 mm round, flat and plain punches on tablet press (korch CKO,korch Germany). Tablets were evaluated for physiochemical parameters as per the reported standards for weight variation, hardness, friability, thickness, drug content uniformity[7].

Table No 1: Formulae used to prepare Pectin based Tinidazole tablets

Formmulation Code	Drug	Pectin	Ethyl Cellulose	Cellulose Acetate Phthalate	Lactose	Total
Core Tablet **(mg)**	100	25	--	--	--	125
F1**(mg)**	100	50	5%	5%	120	300
F2**(mg)**	100	50	7.5%	7.5%	105	300
F3**(mg)**	100	50	10%	10%	90	300

C. Preparation of pectin based tinidazole compression coated layered tablet using different ratios of ethyl cellulose and cellulose acetate phthalate:

The core tablets were compression coated with different quantities (Table No.1) of coating material containing of half of the Pectin, Firstly inner coat was prepared by placing half the quantity of the coating material Ethyl Cellulose the die cavity and the core tablet was carefully placed in the centre of the die cavity and was filled with the other

half of the ethyl cellulose. Secondly outer layered for tablet was prepared by placing the half of the quantity of cellulose acetate phthalate, in the 7mm die cavity and placing the above prepared tablet (ethyl cellulose compression coated tablet) carefully in centre of the die cavity and was filled with other half of cellulose acetate phthalate and using 7 mm round, flat and plain punches 25kN using (korch CKO,korch Germany).[8]

Further all the tablets formulations were evaluated for their physiochemical parameters as per the reported standards for weight variation, hardness, friability, thickness (Table No.3) and dissolution rates was determined for Different Ratios of Ethyl cellulose coated: cellulose acetate phthalate compression coated tablet taken in the separate basket of the dissolution test apparatus Electrolab, TDT-06 P;USP XXXIII standards containing 900ml of dissolution medium. The basket was adjusted to rotate at 40±2rpm. A temperature of 37±1ºC was maintained throughout the experiment.

Table No.3: Physicochemical Parameters of the tablets

Sl. No.	Parameters	Limit	F1	F2	F3
1.	Hardness (kg/cm^2)	--	6.20-6.90	6.00-6.60	6.00-6.70
2.	Friability	NMT 1%	0.00	0.00	0.00
3.	Disintegration time (min)	Uncoated = 15 min Compression coated = 30 min Compression coated = 60 min	---	---	---
4.	Weight variation (mg)	< 250 mg – 10% 250 mg – 7.5% > 250 mg – 5%	298±1.09	298±1.02	306±1.02
5.	Thickness (mm)		6.15±0.4	6.40±0.6	6.55±0.3
6.	Drug content	95-105%	99.80	98.60	100.04

The dissolution process was carried out in different dissolution medium of pH 1.2 for 2 hours and pH 7.4 for subsequent 4 hours and at pH 6.8 for further 24 hours. 10ml of aliquots of samples were withdrawn at predetermined time intervals and were replacing with fresh dissolution medium to maintain sink conditions. The samples withdrawn were suitably diluted if necessary and absorbance was measured at wavelengths 318nm to know the amount of tinidazole released on Systronics 119 UV visible spectrophotometer [9].

D. Evaluation of Physico-chemical Properties of Tablets:

All the following physico-chemical parameters are as per British pharmacopoial methods for Color and shape of tablet, Thickness and diameter test, Uniformity of weight, Hardness, Friability, Disintegration time and Drug content uniformity [7].

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RESULT AND DISCUSSION

Preformulation studies given in Table No.2, such as Precompression Parameters and Evaluation of Powders like angle of repose found to be fairly good to excellent flow property of all powder mix, bulk density of the powder was within the limit that different ingredients can be used for direct compression, all the powders in the formulation showed excellent compressible characters which can be used for compression coating.

Evaluation parameters shown in Table No.3 like hardness and friability indicated that the tablets so prepared were mechanically stable and complied with necessary pharmacopoeial specifications. *In-vitro* disintegration test for tablets also complies with the pharmacopoeial standards. Percentage weight variation and drug content uniformity were found to be uniform.

In vitro drug release for Tinidazole compression coated tablets of different coating polymer in varied concentration was carried out for 24 hours dissolution to study its sustained release characteristics for F1, F2 and F3 formulation no evidence of drug release in pH 1.2 was, on further studies in simulated intestinal fluid (SIM) pH 7.4 evidence of drug release after 5 hours was 4.16%, 2.105% and 0.57% respectively release continued further in pH 6.8 i.e. pH of colon for 24 hours and was 90.46%, 87.38% and86.07% after 24 hour, showed in Table No.4, 5, 6 and Figure No.1. This indicated that enteric coating protected drug from gastric degradation and further drug release was prolonged up to 24 hours due to varied concentration of Ethyl cellulose and Cellulose acetate phthalate. This revealed that intactness of formulation upon reaching on colon is fairly good.

Table No.4*: In vitro* drug release profile for 5% Ethyl cellulose: 5% Cellulose Acetate Phthalate compression coated Tinidazole Tablet (F1)

Sl.no.	Time (hr)	Absorbance at 318 nm	Conc. in g/ml	Conc. in 900ml (mg)	CLA (mg)	Cum. Drug Released (mg)	Cum. % Drug Released
1	1	0	0	0		0	0
2	2	0	0	0	0	0	0
3	3	0	0	0	0	0	0
4	4	0	0	0	0	0	0
5	5	0.13	1.422535	6.401408	0	6.401408	4.1676056
6	6	0.164	3.031657	27.28492	12.80282	40.08773	28.725155
7	8	0.246	4.558659	41.02793	12.9544	53.98233	35.388222
8	10	0.368	6.83054	61.47486	13.18233	74.65719	49.761462
9	12	0.498	9.251397	83.26257	13.52386	96.78643	64.524286
0	16	0.578	10.74115	96.67039	13.98643	110.6568	73.771214
1	20	0.687	12.77095	114.9385	14.52349	129.462	86.308023
2	24	0.72	13.38547	120.4693	15.16203	135.6313	90.462872

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Table No.5*: In Vitro* Drug Release Profile For 7.5% Ethyl Cellulose: 7.5% Cellulose Acetate Phthalate Compression Coated Tinidazole Tablet (F2)

Sl.no.	Time (hr)	Absorbance at 318 nm	Conc. in g/ml	Conc. in 900ml (mg)	CLA (mg)	Cum. Drug Released (mg)	Cum. % Drug Released
1	1	0		0		0	0
2	2	0	0	0	0	0	0
3	3	0	0	0	0	0	0
4	4	0	0	0	0	0	0
5	5	0.09	0.71831	3.232394	0	3.232394	2.1049296
6	6	0.03	0.536313	4.826816	6.464789	11.2916	7.6477362
7	8	0.161	2.975791	26.78212	6.491604	33.27373	22.182485
8	10	0.299	5.545624	49.91061	6.640394	56.55101	37.700672
9	12	0.451	8.376164	75.38547	6.917675	82.30315	54.868767
10	16	0.546	10.14525	91.30726	7.336483	98.64375	65.762497
11	20	0.672	12.49162	112.4246	7.843746	120.2683	80.178885
12	24	0.731	13.59032	122.3128	8.468327	130.7812	87.387451

Table No.6*: In Vitro* Drug Release Profile For 10% Ethyl Cellulose: 10% Cellulose Acetate Phthalate Compression Coated Tinidazole Tablet (F3)

s.no	Time (hr)	Absorbance at 318 nm	Conc. in g/ml	Conc. in 900ml (mg)	CLA (mg)	Cum. Drug Released (mg)	Cum. % Drug Released
1	1	0	0	0		0	0
2	2	0	0	0	0	0	0
3	3	0	0	0	0	0	0
4	4	0	0	0	0	0	0
5	5	0.06	0.190141	0.855634	0	0.855634	0.5710525
6	6	0.06	1.094972	9.854749	1.711268	11.56602	7.7122775
7	8	0.251	4.651769	41.86592	1.766016	43.63194	29.087959
8	1	0.333	6.178771	55.60894	1.998605	57.60754	38.405029
9	1	0.439	8.1527	73.3743	2.307543	75.68184	50.454563
10	16	0.536	9.959032	89.63128	2.715178	92.34646	61.564309
11	20	0.645	11.98883	107.8994	3.21313	111.1126	74.429982
12	24	0.752	13.98138	125.8324	3.812571	129.645	86.075047

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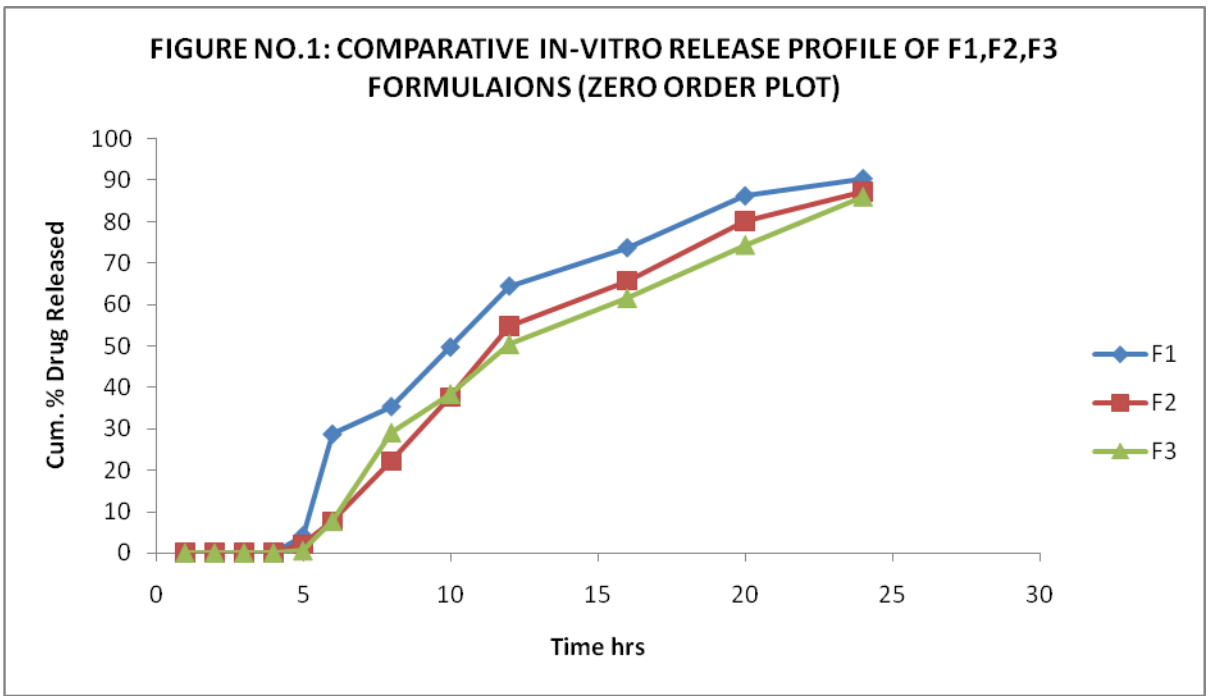

CONCLUSION

Most of the conventional drug delivery systems for treating the colon disorders and diseases are failing as the drugs do not reach the site of action in appropriate concentrations. Thus an effective and safe therapy of these colonic disorders and diseases, using site specific drug delivery systems is a challenging task to the pharmaceutical technologists. To get an effective concentration of drug at the site of action present formulation was designed by set of ingredients used Table No.1 by direct compression, the method used direct compression was advantageous for avoidance of toxic solvent systems for polymer and binders, and also exposure of granulations to dry at higher temperature cause degradation of ingredients was prevented.

Controlled release effect was achieved for F1, F2 and F3 formulation no evidence of drug release in pH 1.2, but drug released was in simulated intestinal fluid (SIM) pH 7.4 after 5 hours, further drug release continued in pH 6.8 i.e. pH of colon for 24 hours and was 90.46%, 87.38% and 86.07% after 24 hour, This indicated that enteric coating protected drug from gastric degradation and further drug release was prolonged up to 24 hours due to increased concentration of Ethyl cellulose and Cellulose acetate phthalate and onset of drug release depends on the polymer coating. From the results we can conclude that the set of ingredients used in the formulation in specific concentration is the best fit model for targeting the colon specific drug delivery and further this formulation can be used as a scope for *in vivo* animal studies, and clinical studies in human.

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Table No.7: Kinetic Values Obtained From *In-Vitro* Release Profile for Tablets

FORMULATION	ZERO ORDER KINETIC DATA			FIRST ORDER KINETIC DATA		
	Slope	Regression coefficient (r)	k value	Slope	Regression coefficient (r)	k value
F1	6.386	0.7811	9.0739	-0.0785	0.9821	-0.1901
F2	6.754	0.9126	8.5804	-0.0775	0.9821	-0.1743
F3	6.286	0.9307	7.7607	-0.060	0.9852	-0.1385

Table No.8: Kinetic Values Obtained From *In-Vitro* Release Profile for Tablets

Formulation	HIGUCHI MATRIX KINETIC			HIXON-CROWELL MODEL			PEPPAS KINETIC DATA			
	Slope	Regression coefficient	k value	Slope	Regression coefficient	k value	Slope	Regression coefficient	K value	n-value
F1	24.76	0.9820	26.9643	0.1921	0.9681	-0.0477	0.3786	0.9787	33.6656	0.3703
F2	25.24	0.9912	24.7567	0.1902	0.9814	-0.0443	0.4896	0.9878	24.9719	0.4860
F3	23.35	0.989	22.5337	-0.1440	0.985	-0.0732	0.5206	0.9913	21.3019	0.5140

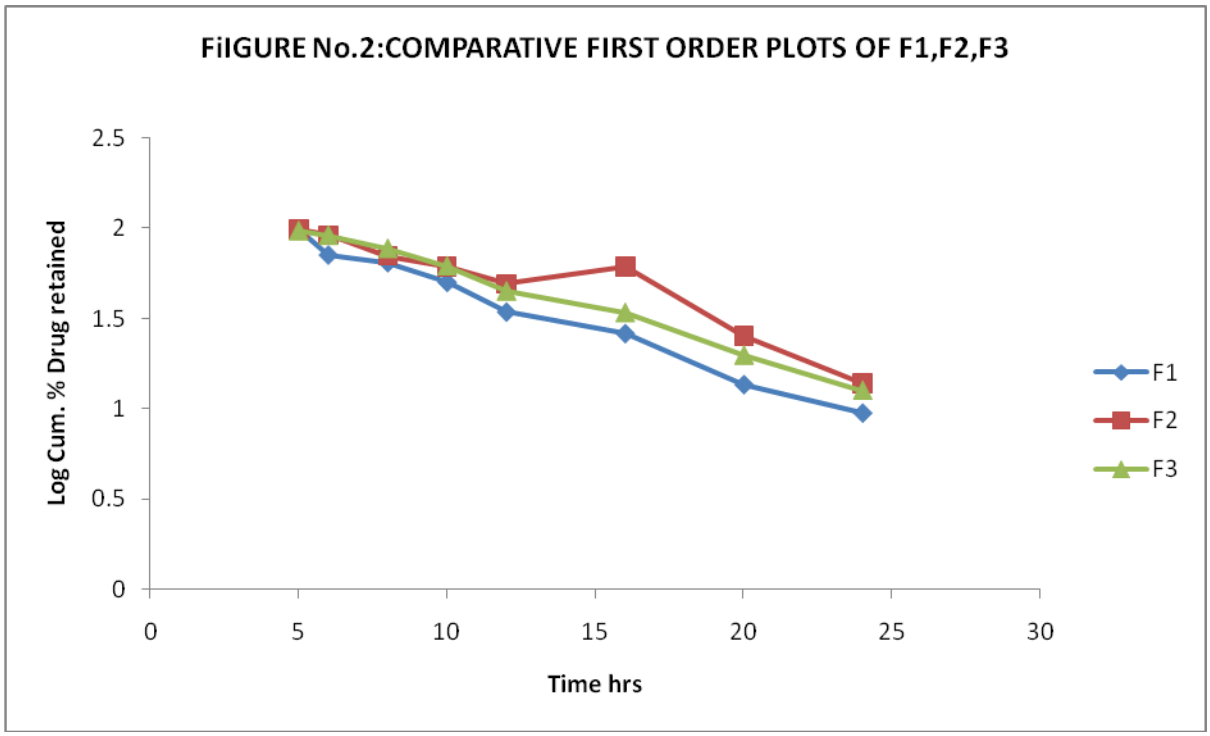

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FIGURE No.3: COMPARATIVE HIGUCHI MATRIX PLOTS FOR F1,F2,F3 FORMULATION

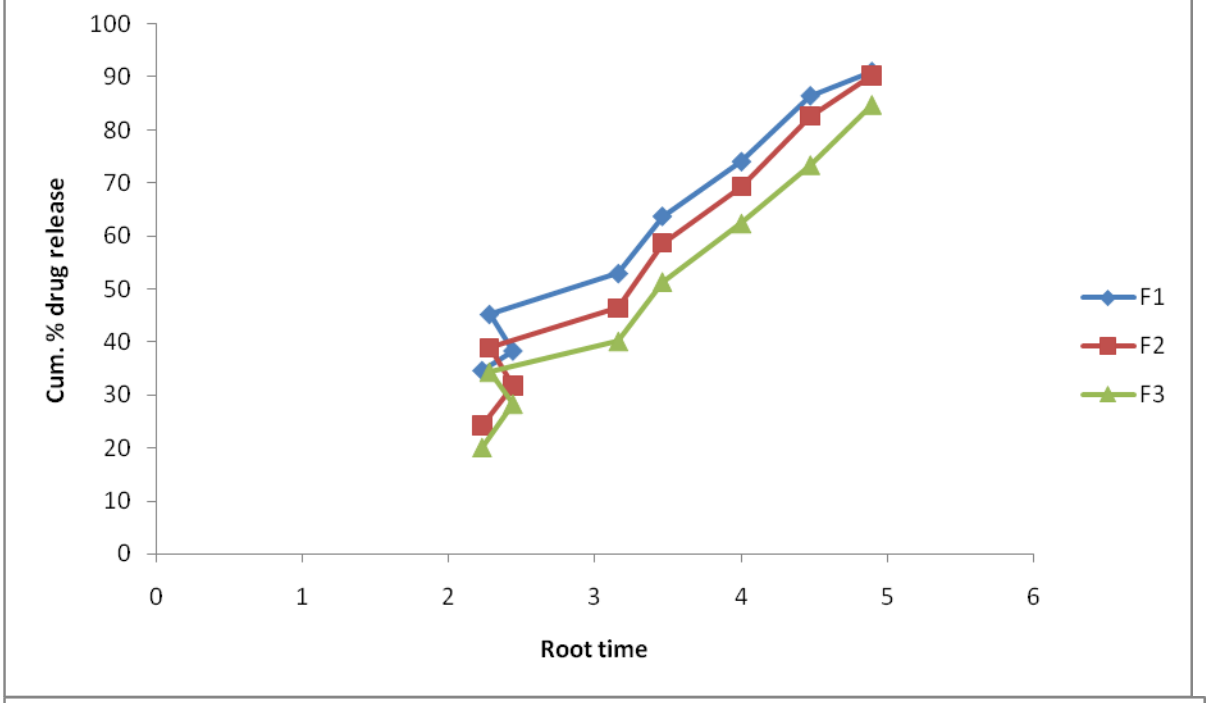
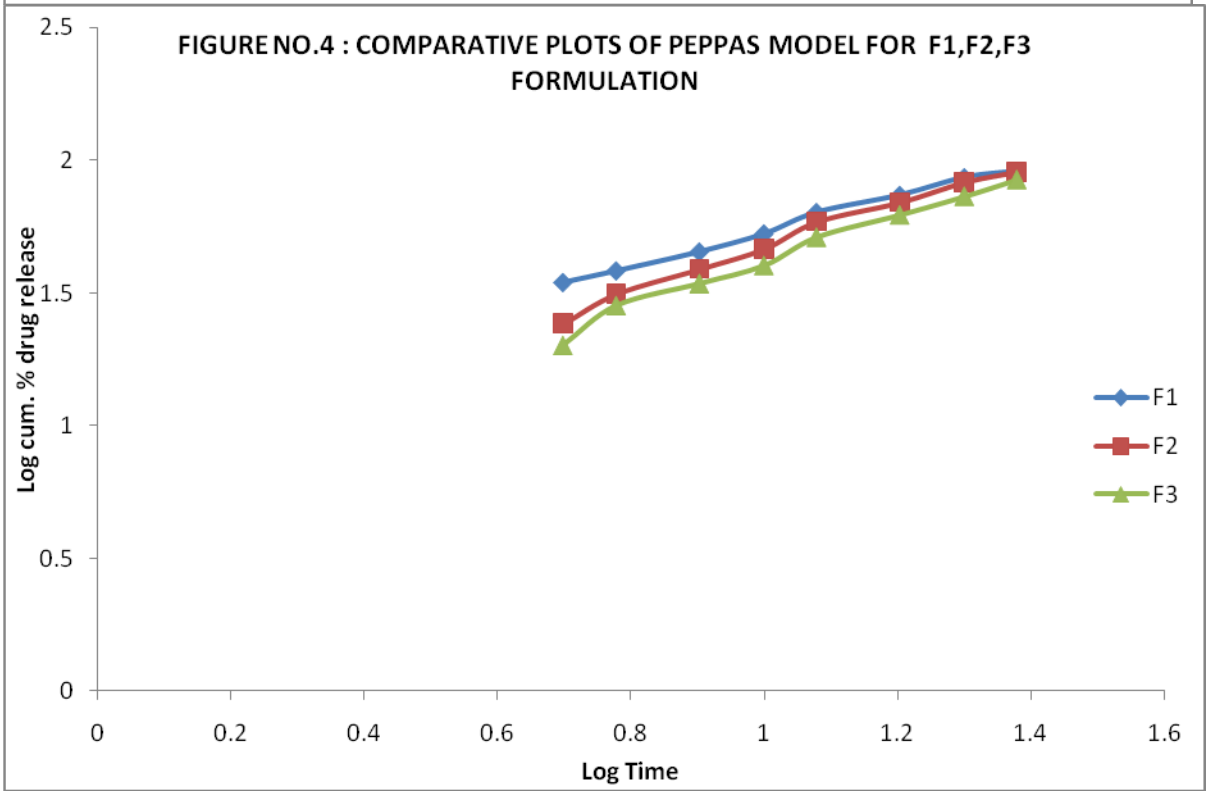


FIGURE NO.4 : COMPARATIVE PLOTS OF PEPPAS MODEL FOR F1,F2,F3 FORMULATION



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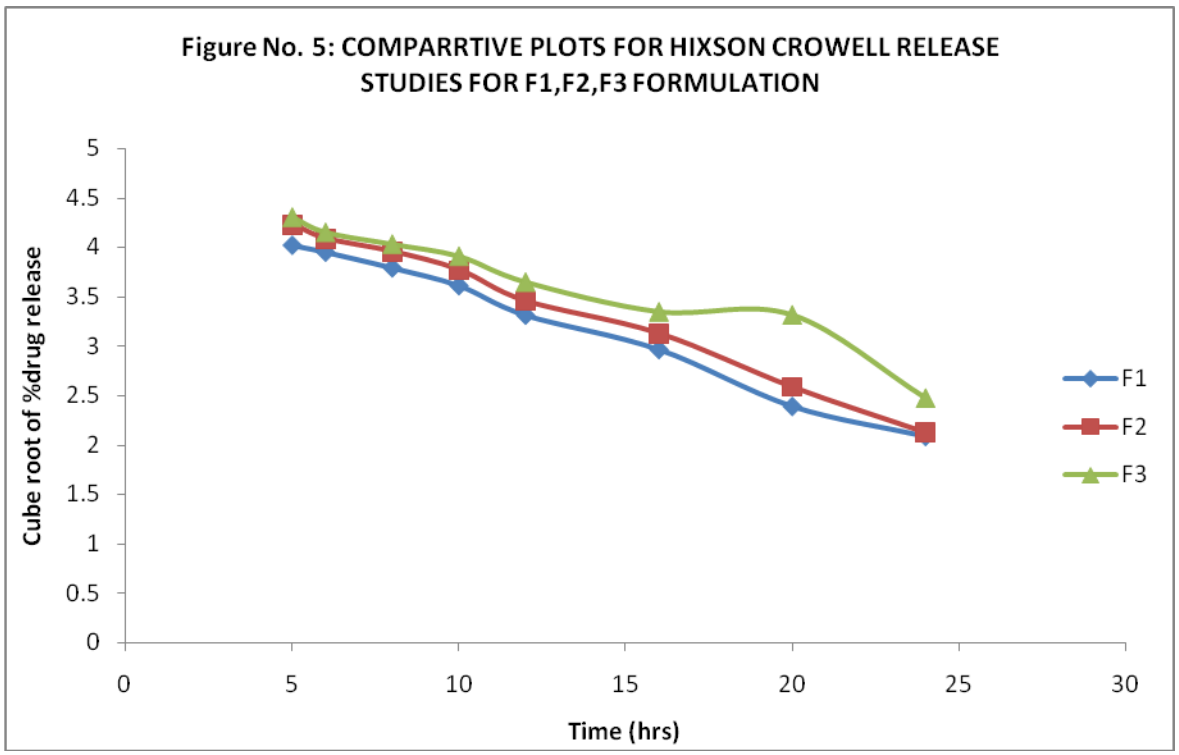

REFERENCES

[1] Vyas SP and Khar. Controlled Drug Delivery, Vol. II, 1999; Ch-6: 218-253.

[2] Joseph Fix. Oral drug delivery, small intestine and colon, Yamanauchi Shaklee. P Ceutical Res Center, California, 1998; 698-742.

[3] Abdul B, Bloor J. Perspectives on colonic drug delivery, business briefing. Pharmtech 2003:185-90.

[4] Cheng G, Jou MJ, Sun J, Hao XU, He YX. World J Gastroenterol 2004; 10(12):1769-74.

[5] Bose S, Bogner RH. Pharm Dev Technol 2007; 12(2): 115–131.

[6] Staiforth J. Powder flow. In: Aulton ME, editor, Pharmaceutics: The Science of Dosage Form Design. 2nd edn. Rdinburgh: Churehill livingstone. 2001:200-8.

[7] British Pharmacopoeia, 1995; 5th Edn. A-70.

[8] Kiran B, Girija B Bhavar, Hemant P Josh, Sanjay R. J suadi p society 2001; 32(2): 17-24.

[9] Maheshwari RK, Chaturvedi SC, Jain NK. Ind J Pharm Sci 2006; 68(2):195-8.