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Formulation and Evaluation of Omeprazole Buccoadhesive Tablets: Effect of Polymers

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Abstract
For the development of omeprazole buccoadhesive tablets, we studied the release and bioavailability of omeprazole delivered by buccal adhesive tablets. These tablets composed of carbopol, xanthum gum, sodium cmc, Hpmc, sodium alginate, croscarmellose sodium. Croscarmellose sodium enhanced the release of omeprazole from the tablets. It may be attached to the human cheek without collapse and it enhanced the stability of omeprazole in human saliva for at least 4 h, giving a fast release of omeprazole. Tablets were prepared by direct compression method and evaluated for buccoadhesive strength and *in vitro* dissolution parameters. Total twelve formulations were developed with varying concentration of polymers. Formulation F3 showed good buccoadhesive strength. Formulations F1 & F7 showed maximum release 98.75% and 99.96% in 7hrs. The selected best formulations followed zero order drug release pattern. FTIR studies showed no evidence of interaction between drug and polymers. The results indicate the suitable buccoadhesive tablet of Omeprazole with desired property can be prepared.
Keywords: Omeprazole, Buccal adhesive tablet, Sodium cmc, xanthum gum, Dissolution

Introduction
Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient. Transmucosal routes of drug delivery (i.e., the mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavity) offer distinct advantages over peroral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of presystemic elimination with in the gi tract.[1-7] Buccal formulations have been developed to allow prolonged localised therapy and enhanced systemic delivery. Ideal buccoadhesive system must have the following properties (i) Should adhere to the site of attachment for few hours (ii) Should release the drug in controlled fashion (iii) Should not cause any irritation or inconvenience to the patient (iv) Should provide the drug release in an unidirectional way towards the mucosa.

Omeprazole is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H^+/K^+-ATPase in the gastric parietal cell. By acting specifically on the proton pump. omeprazole blocks the final step in acid production, thus reducing gastric acidity.it is used as anti ulcer agent and enzyme inhibitor[8]. Freely soluble in ethanol and methanol, and slightly soluble in acetone, isopropyl alcohol, and very slightly soluble in water.The objective of the present investigation was the design and in vitro evaluation of more promising Omeprazole buccoadhesive tablets:effect of polymers based on (i) adhesive polymers like carbopol(940), (ii) rate controlling polymers like xanthum gum,sodium alginate, Hpmc, sodium cmc

Materials and Methods
Materials
Omeprazole were kindly provided by Banglore fine chem. Xanthum gum, Sodium alginate, Hydroxypropylmethyl cellulose(K14M), Sodium cmc, Mannitol, Magnesium stearate, Talc, Croscarmellose sodium.
Preparation of Omeprazole Buccoadhesive Tablets

Buccal tablets were prepared by a direct compression method, before going to direct compression all the ingredients were screened through sieve no.100, except lubricant all the ingredients were thoroughly blended in a glass motor with pestle for 15min. After sufficient mixing lubricant was added and again mixed for additional 2-3min the mixture is compressed using tablet compress machine.

Table 1: Formulation of Omeprazole buccoadhesive tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Drug	20	20	20	20	20	20	20	20	20	20	20	20
Carbopol	20	30	40	20	30	40	20	30	40	20	30	40
Xanthun gum	20	40	60	-	-	-	-	-	-	-	-	-
Sodium alginate	-	-	-	20	40	60	-	-	-	-	-	-
Sodium cmc	-	-	-	-	-	-	20	40	60	-	-	-
Hpmc	-	-	-	-	-	-	-	--	--	20	40	60
Mannitol	126	96	66	126	96	66	126	96	66	126	96	66
Mag.stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Croscarmellose sodium	10	10	10	10	10	10	10	10	10	10	10	10

Total tablet wt 250mg

Evaluation of Buccoadhesive Tablets

Thickness[9]:

Thickness was measured by using vernier callipers in mm

Hardness[10]:

The Monsanto hardness tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet, and zero reading is taken. The upper plunger is then forced against a spring by turning threaded bolt until the tablets break. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of break is recorded and zero force reading is deducted from it. It is expressed in kg/cm^2.

Weight Variation Test[11]:

Weight variation was determined to know whether different batches of tablets have uniformity. 20 tablets weighed individually, calculated the average weight and compared the individual tablet weights to the average. The tablets meet the test if not more than two tablets are outside the percentage limit and none of the tablet differs by more than two times the percentage limit. The weight variation tolerance for uncoated tablets differs depending on average weight of the tablets. It is expressed in %

Friability[12] :

The tablets were tested for friability using Roche friabilator. 20 tablets were weighted initially and transferred to the friabilator. The instrument was set to 25rpm for 4 min the resulting tablets were reweighed and percentage loss was calculated using the formula.

% Friability = Initial weight – final weight/initial weight×100

Drug Content[13]:

Ten tablets from each formulation were powdered individually and a quantity equivalent to 100mg drug was accurately weighed and is dissolved in 50ml of 6.8phosphate buffer from this further dilutions was done by taking 1ml of sample and diluting with 6.8 phosphate buffer. The absorbance was measured at 299.64nm by uv spectrophotometer to calculate percentage of drug content.

Surface PH[14]:

Surface pH was evaluated by initial dissolution in the stimulated salivary (pH 6.8). The surface pH varies range between 6.2±0.152 to 6.8±0.305. The results given in the table and its graphical representation showed that the surface pH of all the tablets was within the range of 6 to 6.8, which indicated that there is no risk of mucosal damage or irritation.

Buccoadhesive Strength[15,16,17]:

Buccoadhesive strength was measured by modifying physical balance in which left pan has been replaced by two vials. In which one is attached to the base and other vial is hanged with the thread. Goat buccal mucosa is attached to the two vials in between two vials tablet is placed. Weights are added to the right pan till the tablet detaches and that weight is considered as buccoadhesive strength.

Figure 1: Modified physical balance for buccoadhesive strength measurement

Swelling Studies [18]:

The tablets of each formulation were weighed individually (W1) and placed separately in petridishes containing 15ml of phosphate buffer(PH 6.8).At regular intervals(0.5,1 ,2 ,3, 4, 5, 6, 7, 8hrs) the tablets were removed from petridishes and excess water removed carefully using filter paper. The swollen tablets were re-weighed (W2) the swelling index of each formulation calculated by using the formula

Swelling index (S.I) = W1-W2/W1

W1= Initial weight

W2= final weight

***In vitro* Drug Release Study [19,20]:**

The drug release rate from buccal tablets was studied using the USP (II) dissolution test apparatus. The assembly is kept in a jacketed vessel of water maintained at 37±0.5^{0}c. Buccal tablets were made to stick on bottom of the falsk. The beaker is filled with 900ml of phosphate buffer pH 6.8. The vessel maintained at 50rpm at various intervals of time samples were withdrawn and analysed by U.V spectrophotometer at 299.64nm.

Kinetic Modelling of Drug Release Profiles

The dissolution profiles of all formulae in 6.8 phosphate buffer were fitted to zero-order, first-order, Higuchi and Hixon, Korsmeyer–Peppas kineticmodels[21-24]. The model with the highest correlation coefficient was considered to be the best fitting one.

Results and Discussions

Flow property characteriazation of Omeprazole Buccoadhesive tablets

Table 2: Bulk density, tapped density, carrs index, hausner's ratio,angle of repose of F1-F12 formulations

Formulations	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (degrees)
F1	0.46±0.015	0.51±0.02	12.62±1.168	1.10±0.01	27.65±1.154
F2	0.42±0.02	0.47±0.02	10.51±0.850	1.09±0.02	27.30±1.090
F3	0.5±0.015	0.56±0.025	9.40±0.264	1.13±0.015	26.31±0.985
F4	0.37±0.02	0.43±0.02	15.80±0.015	1.23±0.015	25.92±0.565
F5	0.49±0.015	0.53±0.025	13.61±0.025	1.20±0.017	25.63±0.564
F6	0.47±0.025	0.53±0.030	12.51±0.02	1.17±0.014	25.02±0.353
F7	0.62±0.02	0.52±0.04	7.34±0.015	1.11±0.015	28.95±1.035
F8	0.53±0.015	0.49±0.02	9.06±0.023	1.13±0.02	27.84±1.304
F9	0.71±0.022	0.47±0.03	10.01±0.049	1.16±0.01	26.79±1.25
F10	0.47±0.02	0.59±0.046	15.59±0.026	1.20±0.02	25.92±0.45
F11	0.32±0.025	0.61±0.039	14.39±0.020	1.19±0.015	25.63±0.44
F12	0.48±0.035	0.42±0.056	12.68±0.1	1.24±0.011	25.34±0.22

Table 3: weight variation, Thickness, Hardness, Friability of F1-F12 formulations

Formulations	Weight Variation (%)**	Thickness (mm) *	Hardness (Kg/cm^3) *	Friability (%)**
F1	120.3±0.21	1.75±0.02	3.2±0.152	0.49±0.015
F2	119.9±0.32	1.79±0.015	2.7±0.2	0.43±0.03
F3	121.0±0.5	1.98±0.025	3.0±0.25	0.41±0.02
F4	120.3±0.32	1.85±0.015	3.9±0.15	0.50±0.03
F5	119.6±0.25	1.96±0.01	2.8±0.15	0.51±0.04
F6	120.1±0.37	1.94±0.020	2.3±0.3	0.46±0.01
F7	124.3±0.2	1.93±0.025	3.3±0.25	0.52±0.04
F8	125.1±0.26	1.91±0.030	2.9±0.30	0.48±0.06
F9	130.1±0.35	1.89±0.01	3.6±0.20	0.44±0.03
F10	129.3±0.25	1.76±0.01	3.7±0.05	0.55±0.05
F11	132.1±0.26	1.80±0.025	4.0±0.152	0.50±0.02
F12	141.9±0.41	1.78±0.02	4.2±0.2	0.56±0.03

Table 4: Drug content, surface pH, buccoadhesive strength of F1-F12 formulations

Formulations	Drug content (%)*	Surface pH*	Buccoadhesive strength(gm)
F1	98.70±0.005	6.6±0.264	20±0.5
F2	95.64±0.040	6.5±0.152	22±1.15
F3	93.59±0.041	6.8±0.152	25±1.15
F4	87.81±0.025	6.7±0.251	21±2.03
F5	86.11±0.045	6.3±0.208	23±2.30
F6	85.49±0.036	6.0±0.251	24±1.52
F7	99.64±0.035	6.4±0.100	19±1
F8	97.65±0.035	6.3±0.152	20±1.52
F9	96.95±0.025	6.1±0.305	22±2
F10	84.63±0.01	6.6±0.300	10±2.30
F11	83.32±0.020	6.5±0.200	10±6.24
F12	79.34±0.04	6.8±0.173	18±4.93

Table 5: Swelling studies of Omeprazole buccoadhesive tablets

Time(hrs)	F1	F2	F3	F4	F5	F6
0.5	6.51±2.60	6.90±0.693	9.13±2.36	4.37±2.02	6.97±2.28	9.06±1.48
1	7.27±1.41	7.36±0.75	10.11±2.0	6.13±2.40	7.01±1.43	9.98±1.09
2	10.31±1.27	10.42±1.27	16.21±1.56	9.12±1.38	10.29±1.32	15.31±2.99
3	14.7±2.21	15.85±1.46	27.9±2.11	10.23±1.31	15.34±2.00	24.6±2.20
4	32.5±2.43	35.5±3.4	37.3±3.33	21.3±1.91	28.4±2.20	35.3±2.49
5	46.5±1.22	48.1±2.75	49.5±1.77	36.2±3.40	39.5±1.23	42.3±1.92
6	53.3±1.86	55.6±3.31	57.3±2.77	49.3±2.48	53.2±2.12	57.7±1.95
7	65.5±1.5	69.3±3.35	71.2±3.77	54.5±1.65	56.3±2.49	59.9±1.62
8	70.2±1.4	72.6±2.21	74.2±1.70	69.3±3.35	70.9±1.70	71.3±1.40

Time(hrs)	F7	F8	F9	F10	F11	F12
0.5	7.07±0.63	8.36±1.20	9.81±1.25	1.57±0.52	1.96±0.95	2.32±0.90
1	9.87±0.80	10.42±1.88	13.2±1.70	3.21±1.66	4.11±1.88	6.03±1.61
2	14.7±1.23	15.1±1.95	19.9±1.34	6.23±1.41	6.84±2.02	7.12±1.94
3	29.6±1.66	30.21±1.19	32.62±1.47	10.9±1.73	11.3±1.60	12.21±1.16
4	35.7±2.55	36.81±1.97	40.32±1.36	13.2±1.71	14.15±1.63	15.2±2.40
5	48.9±1.35	49.12±1.77	50.31±1.30	25.6±2.15	26.2±1.9	27.12±2.03
6	55.6±1.06	56.3±3.00	60.81±2.12	38.7±1.64	39.5±2.66	40.6±1.51
7	69.5±1.81	70.3±2.00	74.12±1.50	43.3±2.20	45.8±1.55	50.84±1.25
8	71.6±0.7	73.4±2.15	75.2±1.47	58.6±1.20	60.5±1.33	63.7±1.15

Table 6: *In vitro*Drug Release Profile

Time(hrs)	F1	F2	F3	F4	F5	F6
0.5	10.06±3.9	7.96±2.5	9.53±3.9	4.58±2.1	2.28±2.3	1.77±3.4
1	20.36±2.5	10.23±2.3	11.19±2.1	10.1±3.6	8.85±3	6.78±2.9
2	40.26±2	28.36±0.9	20.36±0.6	23.2±4.1	21.72±4.8	8.68±4.4
3	69.97±3.2	39.31±3	36.23±2.85	28±3.3	25.93±3.4	12.26±2.2
4	73.33±0.9	72.61±0.8	59.47±4.5	49.74±2.5	43.21±2.5	30.87±3.5
5	86.46±4.8	85.90±2.65	68.86±3.2	68.55±2.6	59.20±3.6	51.41±3.8
6	92.58±2.5	89.97±2	72.79±3.4	75.06±2.9	69.77±4.3	63.17±2.6
7	98.75±3.9	93.05±4.65	85.90±2.5	84.62±2.2	80.38±3.9	73.36±2.4
8		97.12±2	94.10±3.2	88.31±2.6	85.87±3.6	81.19±3.7

Time(hrs)	F7	F8	F9	F10	F11	F12
0.5	18.3±2.4	16.49±3.5	13.33±4.9	3.97±3.64	1.99±2.4	0.99±2.1
1	24.64±3.4	21.93±4.8	20.34±2.2	9.75±2.5	7.70±3.1	5.08±3.2
2	59.24±3.6	42.57±2.5	32.26±3.5	22.65±4.25	20.38±3.8	7.12±4.1
3	62.42±3.8	58.93±3.5	49.41±4.5	26.09±2.8	23.84±3.1	11.02±2.8
4	72.35±4	64.5±4.6	58.90±2.9	32.43±4.3	29.69±4.6	29.72±3.9
5	83.66±4.2	76.82±3.9	69.13±3.1	53.34±3.5	49.24±3.12	48.33±4.2
6	99.96±3	82.85±3.4	72.11±2.4	62.63±3.8	59.51±2.8	56.83±3.5
7		97.526±2.9	84.41±2.5	71.67±2.5	70.28±2.5	69.23±2.1
8			96.44±2.33	78.01±3.8	72.69±2.7	75.94±3.3

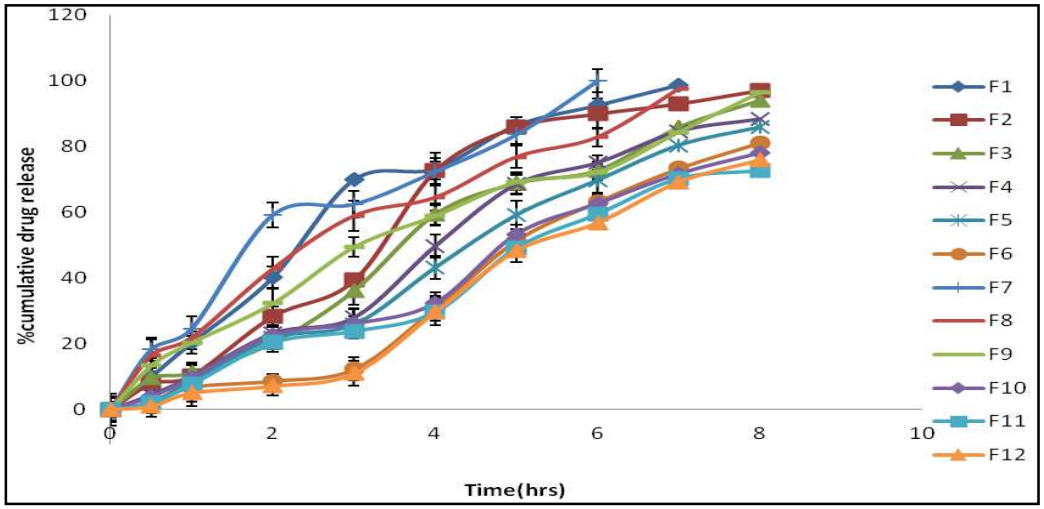

Figure 2: Drug release profile

Table 7: *In vitro*Drug Release kinetics

S.no	Formulations	Zero order	First order	Higuchi	Hixon-crowell	Korsemeyer peppas
1	F1	0.9424	0.1437	0.959	0.1073	1.6804
2	F2	0.9422	0.1383	0.92	0.129	1.7482
3	F3	0.9814	0.0249	0.9266	0.0409	1.6662
4	F4	0.9799	0.0063	0.9137	0.0232	1.723
5	F5	0.9903	0.0002	0.9075	0.0092	1.7707
6	F6	0.9584	0.0037	0.8202	0.001	1.8643
7	F7	0.9421	0.0223	0.9679	0.0737	1.6982
8	F8	0.9665	0.0458	0.979	0.0444	1.5645
9	F9	0.9777	0.0563	0.9137	0.0398	1.471
10	F10	0.986	0.1437	0.9055	0.0002	1.6276
11	F11	0.9825	0.0192	0.8944	0.0023	1.7114
12	F12	0.9593	0.0134	0.8202	0.0004	1.3639

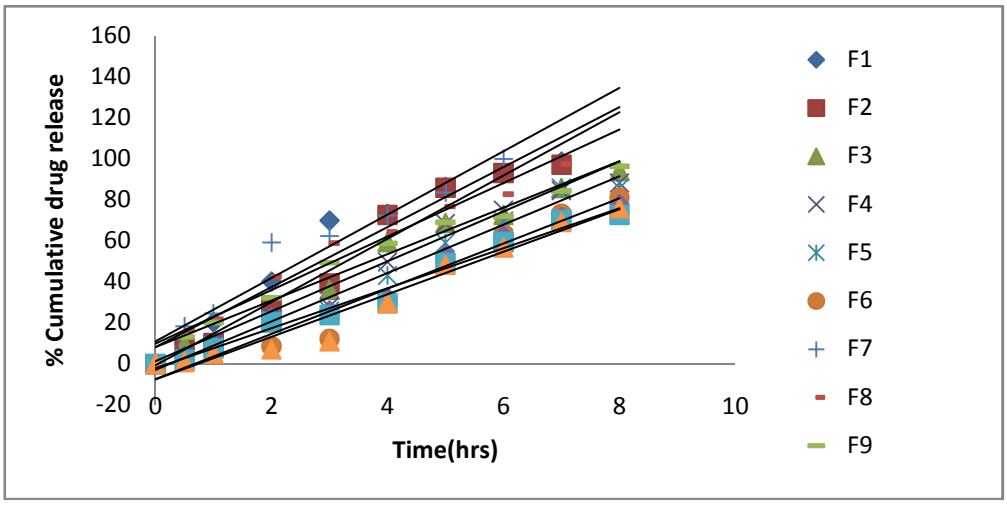

Figure 3: Zero order plots of F1-F12 Formulation

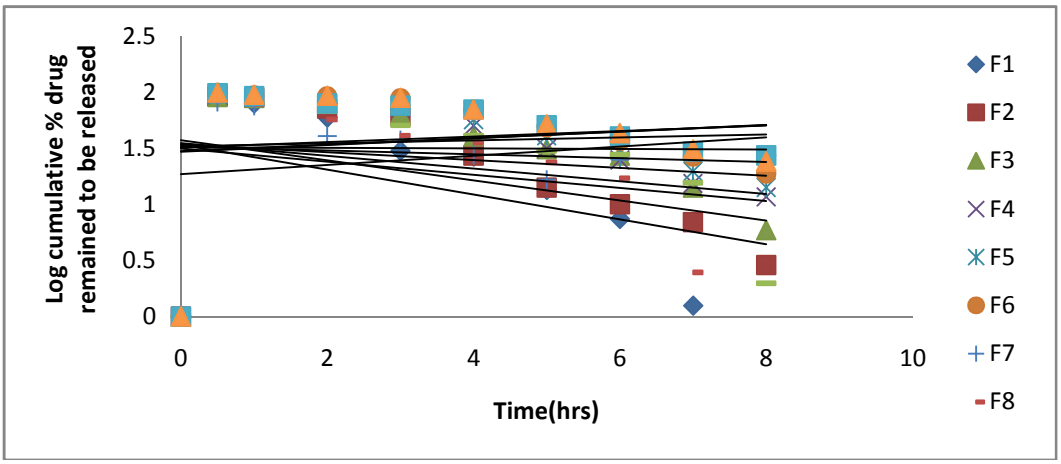

Figure 4: First order plots of F1-F12 Formulations

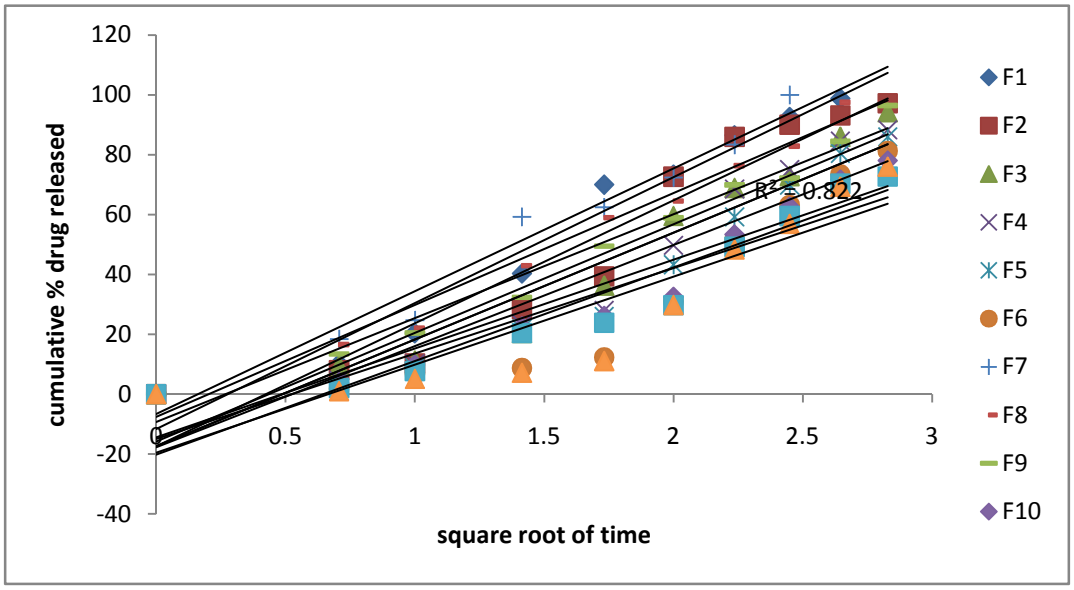

Figure 5:Higuchi plots of F1-F12 Formulations

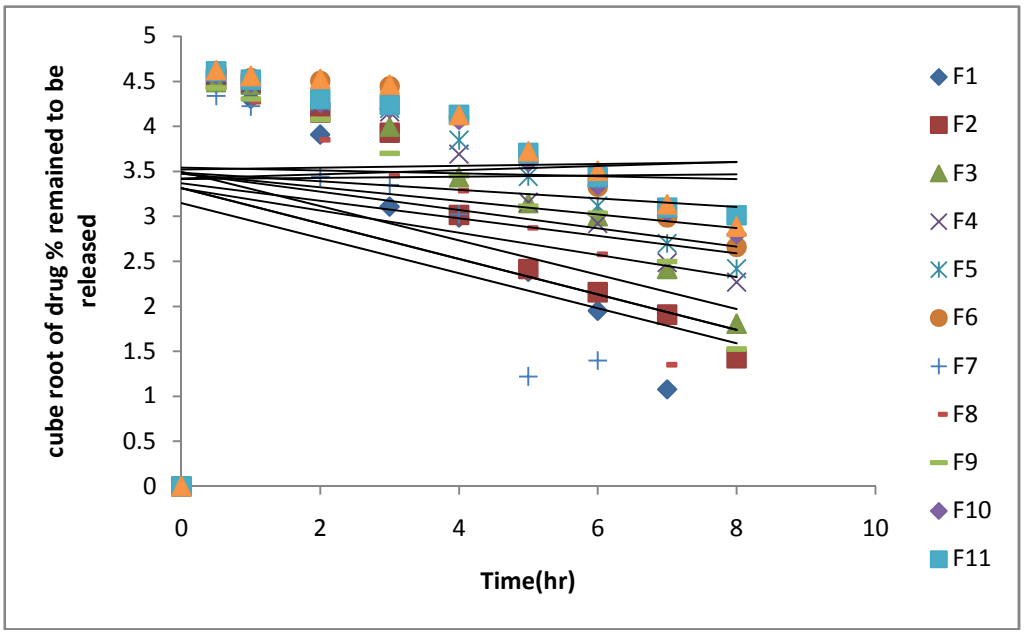

Figure 5: Hixon- crowell plots of F1-F12 Formulations

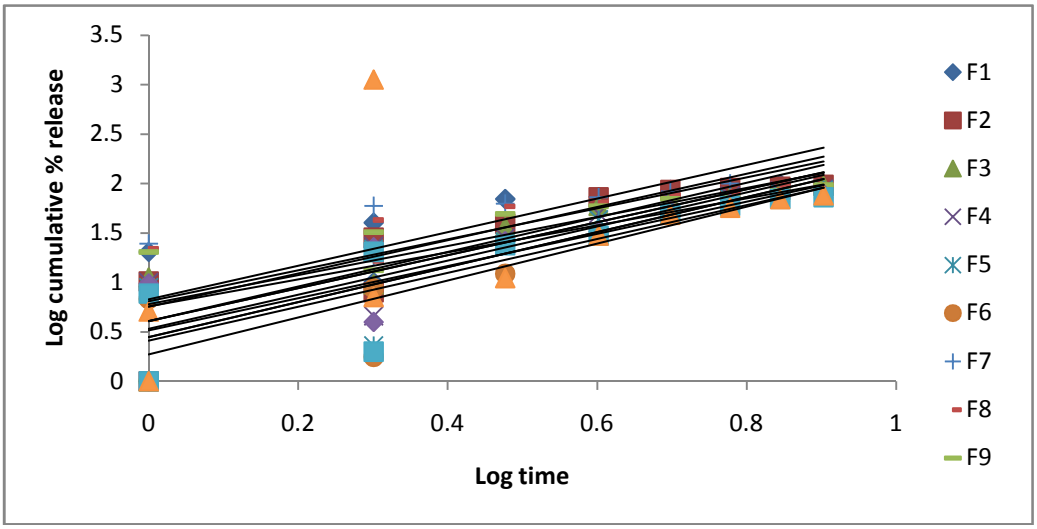

Figure.6: Korsemeyer peppas plots of F1-F12 Formulations

Conclusion

Omeprazole Buccoadhesive tablets are formulated using xanthum gum, sodium alginate, sodium cmc and hpmc. buccoadhesive tablets were prepared by direct compression method. Swelling studies indicate that formulation with polymer sodium cmc have good swelling property that of other formulations. The in vitro release studies revealed that the drug release was 98.72% & 99.96% from F1 and F7 formulation after 7hrs. The results of kinetic data treatment suggested that all formulations follows zero order kinetics and Higuchi.

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