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FORMULATION DEVELOPMENT AND *IN-VITRO* EVALUATION OF BUCOADHESIVE TABLET OF CHLORPHENIRAMINE MALEATE AND PHENYLEPHRINE HYDROCHLORIDE IN COMBINED DOSAGE FORM

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Keywords:

Chlorpheniramine Maleate, Phenylephrine Hydrochloride, Buccoadhesive, Carbopol 934P, HPMC

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ABSTRACT: Delivery of the desired drug as bioadhesive drug delivery systems has been subject of interest since 1980s. The various advantages associated with these systems made the buccal drug delivery as a novel route of drug administration. Buccal region offers an attractive route for the administration of systemic drug delivery. The objective of the study was to develop bucoadhesive buccal tablets of Chlorpheniramine Maleate and Phenylephrine Hydrochloride in combined dosage form. Buccal tablets were prepared by Wet granulation method using the Carbopol 934P, Hydroxy propyl methyl cellulose (HPMC), and sodium CMC as bioadhesive polymer. The tablets were evaluated for the precompression parameters and post compression parameter like bioadhesive strength, *In vitro* retention time, and *In vitro* drug release study and microbial analysis. The thickness and weight of the tablets, respectively, ranges from 3.82 ± 0.01 and 3.92 ± 0.02 and the weight of tablets ranges from 201-202mg.The Formulation containing sodium CMC and HPMC shows acceptable bioadhesive strength but erode respectively, with in 6 to 8 hours. The tablet formulation containing carbopol and Sodium CMC shows low bioadhesive strength, for release of drug and sufficient *In vitro* retention time. The optimized formulation obeys the zero order release kinetics.

INTRODUCTION: Buccal tablet is one which dissolves when it is held between the cheek and gum, permitting direct absorption of the active ingredient through the oral mucosa. Amongst the various routes of drug delivery, oral route is the most preferred to the patient. However, disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract limits its use for certain drugs.

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Different absorptive mucosa are considered as potential site for drug administration. E.g. nasal, rectal, vaginal, ocular and oral cavity. [1-3]

The use of the oral cavity membranes as sites of drug administration has been the topic of increasing interest for the past decade. These drug delivery systems utilize property of bio adhesion of certain water soluble polymers which become adhesive on hydration and hence can be used for targeting particular site. Buccal delivery is the administration of the drug via buccal mucosa (lining of the cheek) to the systemic circulation. [4-6]

Mucoadhesive polymer as drug delivery vehicles. The common principle underlying this drug administration route is the adhesion of the dosage

form to the mucous layer until the polymer dissolves or the mucin replaces itself. Benefits for this route of drug administration are: prolonged drug delivery, targeted therapy and often improved bioavailability. [7-9]

Chlorphenamine Maleate (CPM) is a Antihistamine used in the treatment of swelling, pain, increased heart rate, and blood pressure and PHE is a decongestant that shrinks blood vessels in the nasal passages. Phenylephrine (PHE) is used to treat nasal and sinus congestion, or congestion of the tubes that drain fluid from your inner ears, called the eustachian tubes. It is readily absorbed from the gastrointestinal tract is usually effective within an hour. The half-life may be as long as 24 hours. Therefore, it was selected for the design of a buccal drug delivery system (BDDS) with a view to improve its oral bioavailability.

In the present study, an attempt was made to design and optimize BDDS of CPM and PHE Carbopol and HPMC as the polymers and NaCMC.[10-20]

MATERIALS AND METHODS:

Chlorphenamine Maleate and Phenylephrine Hydrochloride (Centaur, Karaswada-Goa), Carbopol and HPMC (Laboratory Rosayan Selfine-Chem Limited), Sodium CMC (Research Lab fine Chem Industry), talc and lactose (Research Lab fine Chem Industry), Magnesium stearate and Sodium hydroxide (Laboratory Rosayan Selfine-Chem Limited), Acetone (Fischer Scientific).

Formulation of Buccal Tablets: Buccal tablets were prepared by wet granulation method. All the materials were taken according to **Table1.** in clean vessels. Weight of the drug taken as per adjusted calculation for LOD and assay value. Drug, lactose, polymer are sifted through 80mesh size. The talc and magnesium stearate are pass through mesh no.80.Sifted materials are transferred to a poly bag and mixed for 10 minutes by hand shaking. The drug, lactose and polymer are taken in an aluminium foil dish and few ml of acetone is added drop wise for preparing dough. Acetone is added as a granulating fluid and hand granulation is performed. Wet mass is dried for completed removal of acetone i.e. less than 2% W/W in tray drier. Dried granules are passed through 44mesh for sizing. Granules are lubricated by addition of talc and magnesium stearate. Lubricated blend compressed by using 8mm flat faced beveled edged with break line on one side using cadmach compression machine.

TABLE 1: COMPOSITION OF VARIOUS FORMULATIONS

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	S1 (mg)	S2 (mg)	S3 (mg)	S4 (mg)
Chlorphenamine Maleate	2	2	2	2	2	2	2	2
Phenylephrine Hydrochloride	10	10	10	10	10	10	10	10
Carbopol 934	25	50	60	30	-	-	-	-
Hydroxypropyl Methyl cellulose	-	-	-	-	50	25	30	60
Sodium Carboxy Methyl cellulose	73	68	38	88	68	73	88	38
Lactose	80	60	80	60	60	80	60	80
Acetone	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
Magnesium Stearate	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5
Total	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg

Evaluation parameters:

Pre-compression parameters:

Bulk Density (Db): It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume. From this the bulk density was calculated according to the formula mentioned below. It is expressed in gm/ml and is given by

$$Db = M/ Vb$$

Where, M and Vb are mass of powder and bulk volume of the powder respectively.

Tapped Density (Dt): It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 300 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 500 times and tapped volume was noted. Tapping

was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in gm/ml and is given by

$$Dt = M/ Vt$$

Where, M and Vt are mass of powder and tapped volume of the powder respectively.

Hausner's Ratio: Hausner's Ratio is an ease of index of powder flow. It is calculated by using the following formula:

Hausner's Ratio = Tapped Density / Bulk Density

Compressibility Index: The compressibility index of the power was determined by Carr's compressibility index

$$\text{Carr's index (\%)} = \{(Dt - Db)/ Dt \text{ X } 100\}$$

Angle of Repose: Funnel method was used to measure the angle of repose of powder. The accurately weighed powders were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder (2.0 cm above hard surface). The powders were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation: The frictional forces in a loose powder can be measured by the angle of repose.

$$\text{Angle of Repose } \theta = \tan^{-1}[H/R]$$

Where H = Height of the powder cone.
R = Radius of the powder cone

Evaluation of physical properties: The thickness, hardness, weight uniformity, diameter, friability were determined by in similar way as stated for conventional oral tablets in the pharmacopoeia.

Drug content uniformity: 20 tablets were powdered in a glass mortar and the powder equivalent to 10 mg of drug was placed in a stoppered 100 ml conical flask. The drug was extracted with phosphate buffer pH 6.8 with vigorous shaking for 15min and filtered. Further appropriate10ml of solution were pipette out and dilution were made by using phosphate buffer pH 6.8 to make 10 mcg/ml concentration and absorbance was measured at 262nm for CPM and 275nm for PEH against blank (phosphate buffer pH 6.8).

Swelling studies: The extent of swelling was measured in terms of percent of weight gained by the tablet. One tablet from each formulation was weighed and kept in petridish containing 10ml of phosphate buffer of pH 6.8. At the end of specified time intervals (1, 2, 3, 4, 5, 6 and 7 h) tablets were withdrawn from petridish and excess buffer blotted with tissue paper and weighed. The % of weight gained by the tablet was calculated by using following formula:

$$\text{\% Swelling index} = \{(W2 - W1)/W1\} \text{ X}100$$

Where,
W1= initial weight of the tablet
W2= Weight of the tablet after swelling.

Matrix erosion study: Each tablet weighed (W1) were immersed in a phosphate buffer pH 6.8 for pre determined time (1, 2, 4, 6 and 8hrs). After immersion of the tablets were wiped off by the excess of surface water by the use of filter paper. The swollen tablets were dried at 60oC for 24hr in an oven and kept in a dessicator for 48 hr prior to be reweighed (W2). The matrix erosion of the tablet was calculated by using the formula given in the equation i.e.

$$\text{Matrix Erosion (\%)} = (W1\text{-}W2)/W1 \times 100$$

Surface pH study: A combined glass electrode is used for this purpose. The tablet is allowed to swell by keeping it in contact with 1 ml of phosphate buffer pH 6.8 for 2 h at room temperature. The pH is identified by bringing the electrode into contact with the tablet surface and allowing equilibrating for 1 min.

Detachment Stress: This method is used to measure In vitro bioadhesive capacity of different polymers. It is a modified method developed by Mertti Marvole. Procaine buccal mucosa was obtained from local slaughter house & stored in kreb's buffer solution. The experiment was performed within the 3 h of procurement of mucosa. The procaine mucosa was washed with the distilled water & carefully tied to the glass slide with the help of thread.

This portion was put in the petridish with a 6.8 buffer solution. During the experiment the solution was kept at 37°C. The tablet was stuck on to the glass stopper by using cyano acrylate adhesive and that stopper tied with a thread. The other portion of that thread was tied to the plastic beaker. That tablet was put on mucosa by applying finger pressure for 30 s. After making contact between the tablet & mucosa for a fixed time of 3 s; the water was added through a pipe connected to a separating funnel containing water in a drop wise to that plastic beaker. The force needed to detach the tablet from the mucosa was measured.

Force of adhesion (N) = (Mucoadhesive strength (g) X 9.81)/100

***In- vitro* retention time:** The *In- vitro* retention time is one of the most important physical parameters for an adhesive formulation. The formulation was pressed over the excised porcine buccal mucosa for 30 s after previously being secured on a glass slab and was immersed in a beaker containing 500 ml of phosphate buffer, pH 6.8, at 37±2°C.One stirrer was fitted at a distance of 5cm from the tablet and rotated at 25 rpm. The time for complete erosion or detachment of the tablet from the mucosa was noted.

Disintegration test: The test was performed for buccal tablets which are not having backing; six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets. Apparatus was run for 4 hr and the basket was lift from the fluid, observe whether all of the tablets have disintegrated.

***In-vitro* drug release study:** *In-vitro* dissolution studies were carried out in USP type-II tablet dissolution apparatus using 900ml phosphate buffer pH 6.8 as dissolution media. The paddle was rotated at 50 rpm and the temperature was maintained at 37±0.5°C throughout the study. At predetermined time intervals 10 ml of the samples were withdrawn by. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium maintained at 37±0.5°C. The samples were analyzed for drug releases by measuring the absorbance at 262nm CPM and 273nm PEH using UV-Visible spectrophotometer. All the studies were conducted in triplicate. And analysis of *in-vitro* drug released by kinetic model and anti- microbial analysis.

Anti-microbial Analysis: 16.8g of nutrient agar was dissolved in 600ml of distilled water the nutrient agar was sterilized. After sterilization it was allowed to cool down for some time and then poured on the sterilized petridish dish. The nutrient agar was allowed to cool further and solidify. After solidification the plates were inverted to remove vapours. Then again the plates were inverted and divided into 4 quadrants. After this the bacterial cultures were spread over the plate evenly on each plate. The disk were dipped into each formulations dried and placed on the plates. The plates were kept in the incubator for 24 hrs at 37ºC. After 24hrs the zone of inhibition was measured and noted.

Fourier Transform Infra-red Spectroscopy Study: The tablet was crushed to form fine powder and compressed with KBr on Minipress (Jasco, Japan) to form a disk. The compressed disks were scanned over 400 to 4,000 cm−1, and characteristic peaks were recorded. The FTIR spectra of pure drug, polymers, excipients, physical mixture and formulations were recorded on Fourier transform infrared (FT-IR) instrument (Shimadzu, Japan) and characteristic peaks were recorded and matched with the standard peaks of pure Chlorphenamine Maleate and Phenylephrine Hydrochloride with the physical mixture of drug-excipients and formulations.

RESULTS AND DISCUSSION:

TABLE 2: MICROMERITIC STUDY OF POWDER MIXTURE OF VARIOUS FORMULATIONS

Formulation Code	F1	F2	F3	F4	S1	S2	S3	S4
Angle of Repose(°)	29.10	29.08	29.01	29.05	29.09	29.06	29.07	29.08
Bulk Density (gm/ml)	0.3848	0.3706	0.3847	0.3847	0.3845	0.3846	0.3845	0.3847
Tapped density (gm/ml)	0.5885	0.5885	0.5884	0.5884	0.5884	0.5885	0.5885	0.5884
Hausner's Ratio	1.529	1.428	1.529	1.529	1.529	1.529	1.428	1.429
Carr's Index	34.61	37.02	34.62	34.61	34.61	34.62	34.64	34.69

The powder mixtures of all the formulations were tested by various studies including angle of repose (ranging from 29.01° to 29.10°), bulk density (ranging from 0.37 to 0.38 gm/ml), tapped density (ranging from 0.5884 to 0.5885 gm/ml), Hausner's ratio (ranging from 1.428 to 1.529) and Carr's index (ranging from 34.61 to 37.02 %). All the results showed moderate flow property.

TABLE 3(a): PHYSICOCHEMICAL PROPERTIES OF VARIOUS TABLET FORMULATIONS

Formulations code	Weight variation(mg)	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)
F1	202.2	3.92	8.30	7.9
F2	202.1	3.86	8.32	8.1
F3	201.0	3.83	8.36	8.0
F4	201.2	3.82	8.37	7.9
S1	202.2	3.83	8.35	8.1
S2	201.2	3.85	8.32	8.0
S3	201.1	3.90	8.33	8.1
S4	202.2	3.87	8.36	7.9

TABLE 3(b): PHYSICOCHEMICAL PROPERTIES OF VARIOUS TABLET FORMULATIONS

Formulation code	Friability (%)	Drug content uniformity	
		CPM(λ_{max} 263nm)	PEH (λ_{max} 273nm)
F1	0.71	98.16	98.35
F2	0.70	99.07	99.17
F3	0.69	100.88	100.81
F4	0.70	97.24	98.76
S1	0.70	98.25	98.85
S2	0.69	99.05	98.65
S3	0.71	99.21	99.56
S4	0.69	98.89	99.23

The weight variation for different formulations (F1 to F4 and S1 to S4) was found to be ranging in between 201 to 202.2mg. The thickness of formulations from (F1 to F4 and S1 to S4) was 3.82 to 3.92 mm. The diameter of formulations from (F1 to F4 and S1 to S4) was 8.3to 8.37 mm. The hardness of formulations from (F1 to F4 and S1 to S4) was 7.9 and 8.1 Kg/cm2. The friability of all the formulations was measured by Roche friabilator and was found to be in the range of 0.69 to 0.71%. The content uniformity of all the formulations was within the limit of CPM and PEH showing satisfactory results as per Indian pharmacopoeia (IP) limit. It was observed that all the tablets of all batches had acceptable physical characteristics.

Swelling studies:

TABLE 4: POST COMPRESSION PARAMETER FOR SWELLING STUDIES TEST

Sr. No.	Time (hrs)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	S1(%)	S2(%)	S3(%)	S4(%)
1	1	49.05	48.61	50.12	36.78	48.89	49.23	45.21	46.25
2	2	54.13	56.72	53.43	38.82	56.25	55.42	55.23	52.45
3	3	55.05	59.50	57.08	47.43	57.54	57.21	57.21	57.32
4	4	62.94	59.91	59.07	53.76	61.20	60.12	59.22	58.87
5	5	64.62	62.27	59.89	59.20	65.41	62.36	62.36	64.74
6	6	67.93	65.25	62.58	64.87	68.23	65.85	65.21	67.11
7	7	69.29	66.98	65.45	66.58	69.20	68.65	68.89	69.05
8	8	70.96	70.14	70.73	70.13	70.89	70.91	70.85	70.53

The formulation containing Carbopol 934 along with Hydroxypropyl Methyl cellulose and Sodium Carboxy Methyl cellulose in all formulation showed a maximum swelling behaviour at all intervals.

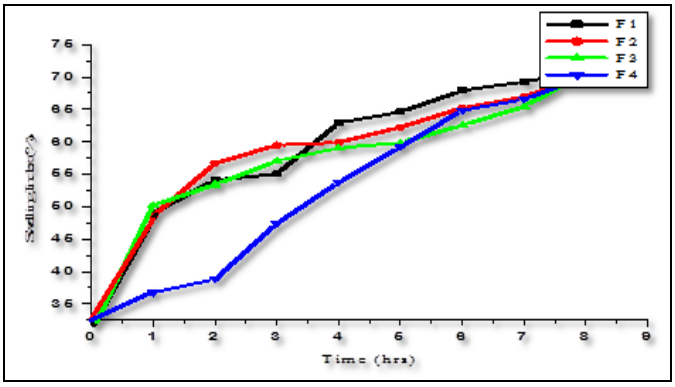

FIG. 1(a): SWELLING STUDY OF F1 TO F4

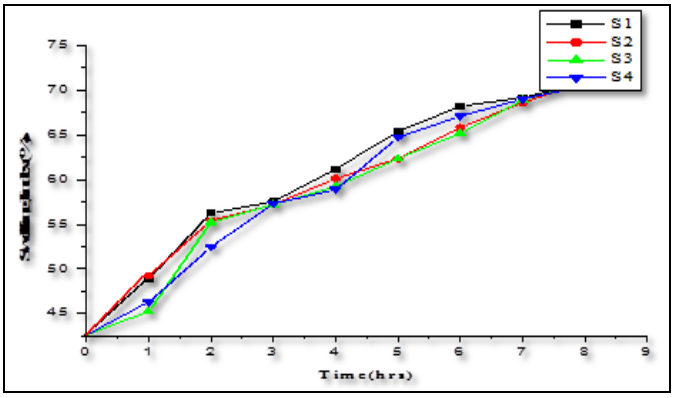

FIG. 1(b): SWELLING STUDY OF S1 TO S4

Matrix erosion study:

TABLE 5: POST COMPRESSION PARAMETER FOR MATRIX EROSION STUDY TEST

Formulation Code	F1	F2	F3	F4	S1	S2	S3	S4
Matrix erosion (%)	9.78	9.92	10.01	9.49	9.84	9.74	9.61	9.96

The mucoadhesive polymers used are hygroscopic and retain large amount of water. Tablets containing Na CMC as secondary polymer F1 to F4 and S1 to S4 showed the matrix erosion 9.78, 9.92, 10.01, 9.49, 9.84, 9.74, 9.61 and 9.96 respectively.

Surface pH study:

TABLE 6: POST COMPRESSION PARAMETER FOR SURFACE pH STUDY TEST

Formulation Code	F1	F2	F3	F4	S1	S2	S3	S4
Surface pH	6.75	6.79	6.81	6.76	6.77	6.78	6.76	6.79

Surface pH of the formulations F1 to F4 and S1 to S4 was found to be 6.75, 6.79, 6.81, 6.76, 6.77, 6.78, 6.76 and 6.79 respectively. This pH is near to the neutral.

Detachment Stress:

TABLE 7: FOR DETACHMENT STRESS TEST

Formulation Code	Mucoadhesive strength (gm)	Force of adhesion (N)
F1	16.511	1.619
F2	15.658	1.536
F3	15.760	1.546
F4	16.788	1.646
S1	16.526	1.621
S2	16.625	1.630
S3	16.745	1.643
S4	16.766	1.645

In all the formulations, as the polymer concentration increased, work of adhesion increased. The order of bioadhesion was HPMC < sodium CMC < Carbopol 934. Buccal tablets formulated with Carbopol 934 and HPMC showed low mucoadhesion.

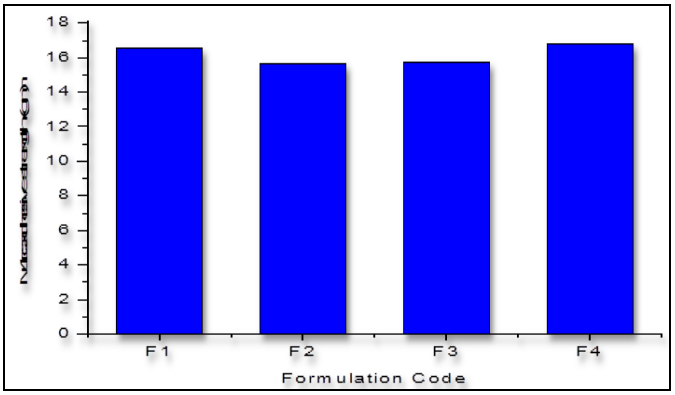

FIG. 2(a): DETACHMENT STUDY OF F1 TO F4

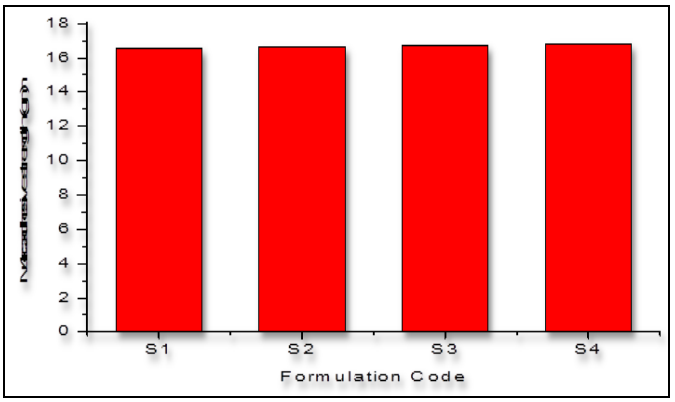

FIG. 2(b): DETACHMENT STUDY OF S1 TO S4

In- vitro retention time:

TABLE 8: FOR *IN-VITRO* RETENTION TIME TEST

Formulation Code	Time (hrs)
F1	5.90
F2	6.16
F3	6.07
F4	5.89
S1	5.98
S2	6.12
S3	6.02
S4	5.94

In this study, formulation no. 1, 2, 3, 4 contain greater amount of polymers showing greater retention time i.e with in a range.

Disintegration test:

TABLE 9: FOR DISINTEGRATION TEST

Formulation code	Time
F1	3hr,58min
F2	3hr,45min
F3	3hr,30min
F4	3hr,54min
S1	3hr,40min
S2	3hr,55min
S3	3hr,43min
S4	3hr,41min

The tablets disintegrate for at least 4hrs and it is within limit.

In-vitro drug release study:

In-vitro drug release for CPM at λ_{max} 263:

TABLE 10: PERCENTAGE OF AMOUNT OF DRUG RELEASED

Time in hrs	F1(%)	F2(%)	F3(%)	F4(%)	S1(%)	S2(%)	S3(%)	S4(%)
0	0	0	0	0	0	0	0	0
1	22.5	24.75	27	22.5	25.2	24.56	24.22	26.53
2	40.5	36.05	45	31.5	35.20	36.54	38.23	32.25
3	55.3	50.4	61.2	41.25	45.28	48.91	46.40	45.85
4	66.6	59.8	71	61.6	63.21	61.27	59.26	54.44
5	78.8	72.0	77.4	74.2	72.02	71.87	69.34	68.58
6	85.05	83.25	83.7	79.6	80.85	79.27	74.27	76.89
7	88.2	87.95	90.0	82.3	87.65	89.54	81.48	88.14
8	94.5	95.4	96.0	90.0	94.21	95.97	91.23	94.25

In-vitro drug released for PEH at λ_{max} 273:

TABLE 11: PERCENTAGE OF AMOUNT OF DRUG RELEASED

Time in hrs	F1(%)	F2(%)	F3(%)	F4(%)	S1(%)	S2(%)	S3(%)	S4(%)
0	0	0	0	0	0	0	0	0
1	23.4	25.2	28.8	22.5	24.54	24.87	23.56	25.89
2	35.1	36.9	44.1	30.6	31.20	40.69	39.21	39.85
3	45.9	60.3	59.4	44.1	48.25	59.27	48.58	51.23
4	61.2	71.1	67.5	52.2	56.24	67.30	59.63	64.08
5	68.4	75.6	78.3	59.2	63.45	76.74	67.22	75.36
6	80.1	85.5	88.2	67.5	72.11	82.64	76.65	83.02
7	87.3	90.0	93.6	81.9	86.33	89.23	87.53	90.12
8	92.7	96.3	98.1	90.9	91.02	96.24	94.23	95.87

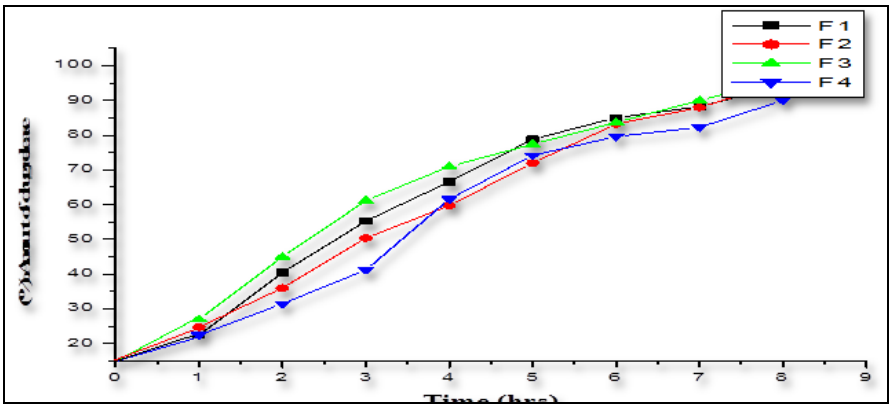

FIG. (a): PERCENTAGE OF AMOUNT OF DRUG RELEASED FOR CPM (F1 TO F4)

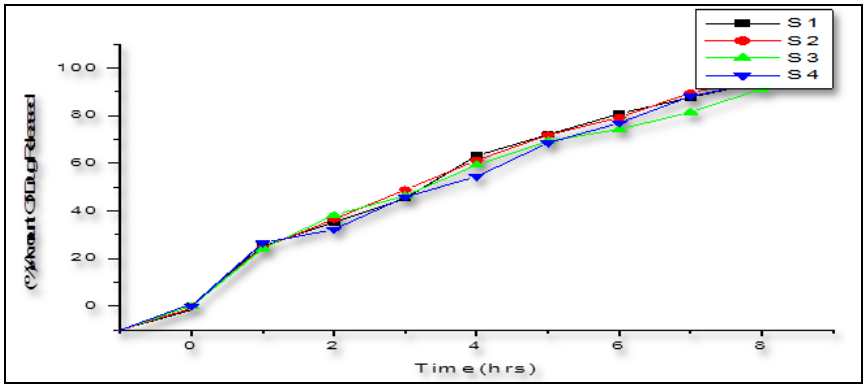

FIG. 3(b): PERCENTAGE OF AMOUNT OF DRUG RELEASED FOR CPM (S1 TO S4)

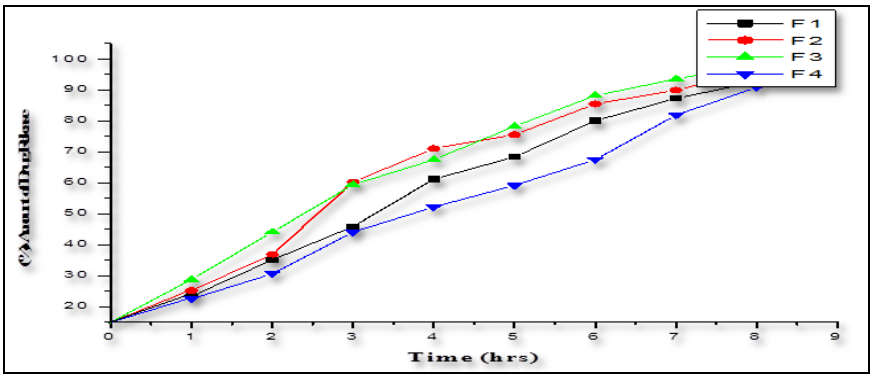

FIG. 4(a): PERCENTAGE OF AMOUNT OF DRUG RELEASED FOR PHE (F1 TO F4)

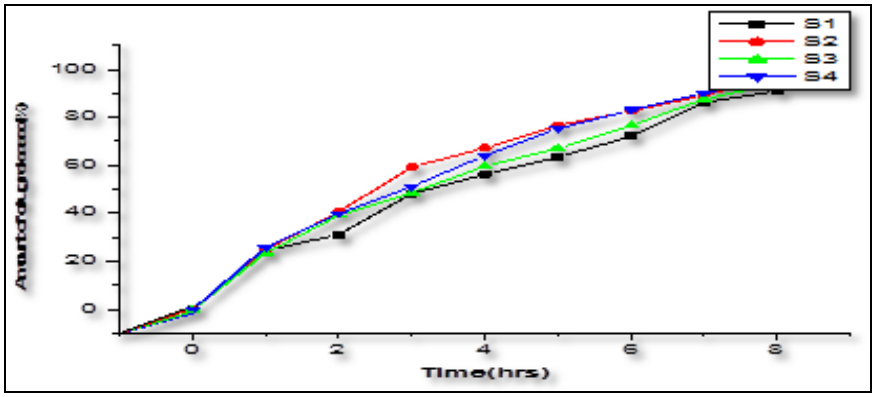

FIG. 4(b): PERCENTAGE OF AMOUNT OF DRUG RELEASED FOR PHE (S1 TO S4)

TABLE 12: DRUG RELEASE KINETICS OF DEVELOPED FORMULATIONS FOR CPM AT λ 263NM

R^2 Values		Formulation Code							
		F1	F2	F3	F4	S1	S2	S3	S4
Zero Order		0.987	0.988	0.984	0.983	0.985	0.987	0.982	0.984
First Order		0.825	0.856	0.893	0.836	0.835	0.865	0.874	0.836
Higuchi model		0.986	0.983	0.986	0.988	0.984	0.982	0.986	0.987
Korsmeyerpeppas	R^2	0.985	0.986	0.985	0.982	0.982	0.986	0.981	0.986
	N	0.772	0.775	0.789	0.761	0.774	0.786	0.773	0.779

TABLE 13: DRUG RELEASE KINETICS OF DEVELOPED FORMULATIONS FOR PEH AT λ 273NM

R^2 Values		Formulation Code							
		F1	F2	F3	F4	S1	S2	S3	S4
Zero Order		0.985	0.986	0.988	0.972	0.974	0.984	0.981	0.982
First Order		0.824	0.877	0.891	0.864	0.852	0.863	0.841	0.858
Higuchi model		0.985	0.986	0.993	0.981	0.976	0.984	0.974	0.981
Korsmeyerpeppas	R^2	0.983	0.985	0.989	0.974	0.972	0.984	0.973	0.979
	N	0.745	0.752	0.771	0.784	0.732	0.780	0.745	0.756

The results obtained for drug content uniformity test showed that the drug content in all formulation was in the range of 95-96%for CPM and for 96-98% for PEH. And for kinetic study it was conclude that both drug satisfied for zero order.

Microbial Analysis: The antimicrobial activity of CPM and PHE from different tablet formulations was studied using *S.para B* and *E.coli* bacteria.

TABLE 14: ZONE OF INHIBITION FOR *S.PARA B*

Zone of inhibition	After 1 hr	After 4 hr	After 8hr
F1	Slight	16mm	18mm
F2	Slight	20mm	27mm
F3	Slight	22mm	32mm
F4	Slight	17mm	18mm
S1	Slight	18mm	19mm
S2	Slight	26mm	29mm
S3	Slight	20mm	21mm
S4	slight	23mm	26mm

TABLE 15: ZONE OF INHIBITION FOR *E. COLI*

Zone of inhibition	After1 hr	After 4 hr	After 8hr
F1	Slight	16mm	27mm
F2	Slight	20mm	29mm
F3	Slight	22mm	32mm
F4	Slight	17mm	21mm
S1	Slight	18mm	23mm
S2	Slight	22mm	28mm
S3	Slight	19mm	21mm
S4	Slight	20mm	27mm

Drug shows good zone of inhibition for 4hr and 8hrs time in both bacteria but after one hrs it shows slight zone of inhibition.

FTIR:

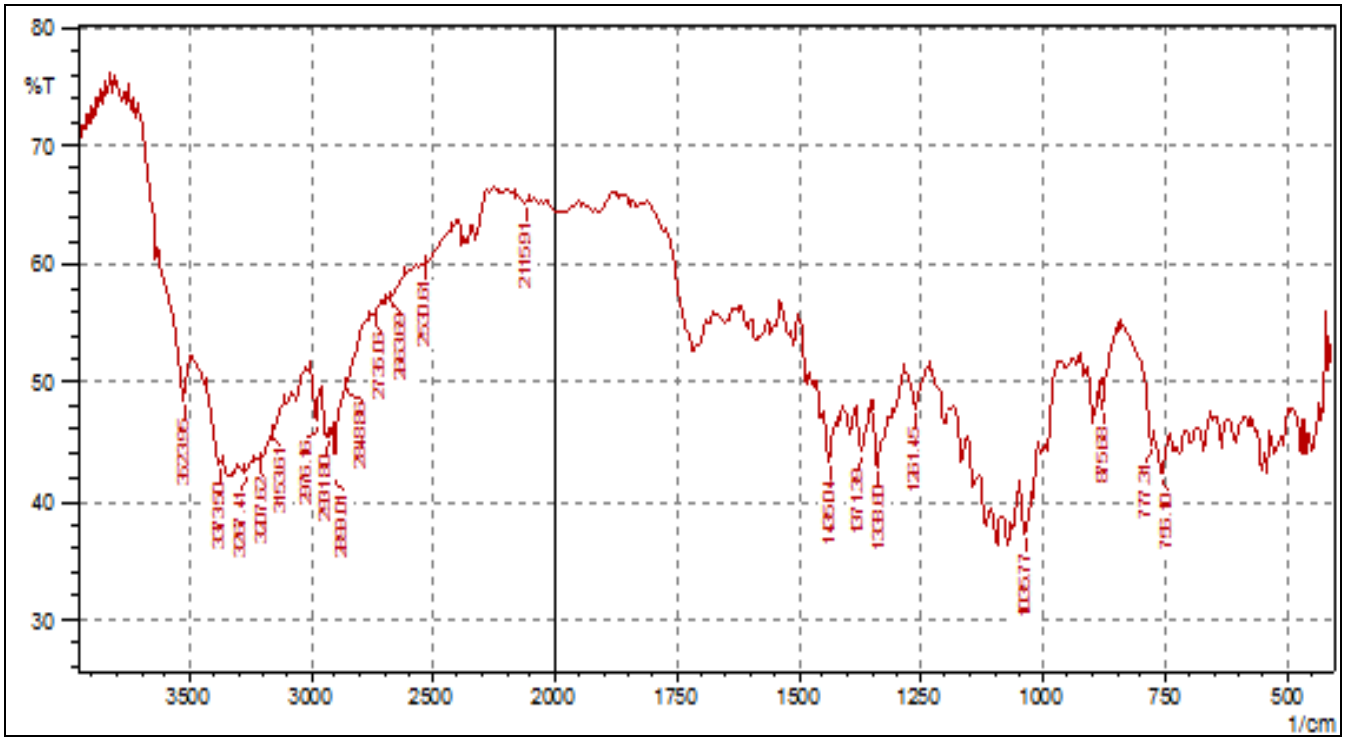

FIG. 5 (a): IR SPECTRA OF F3

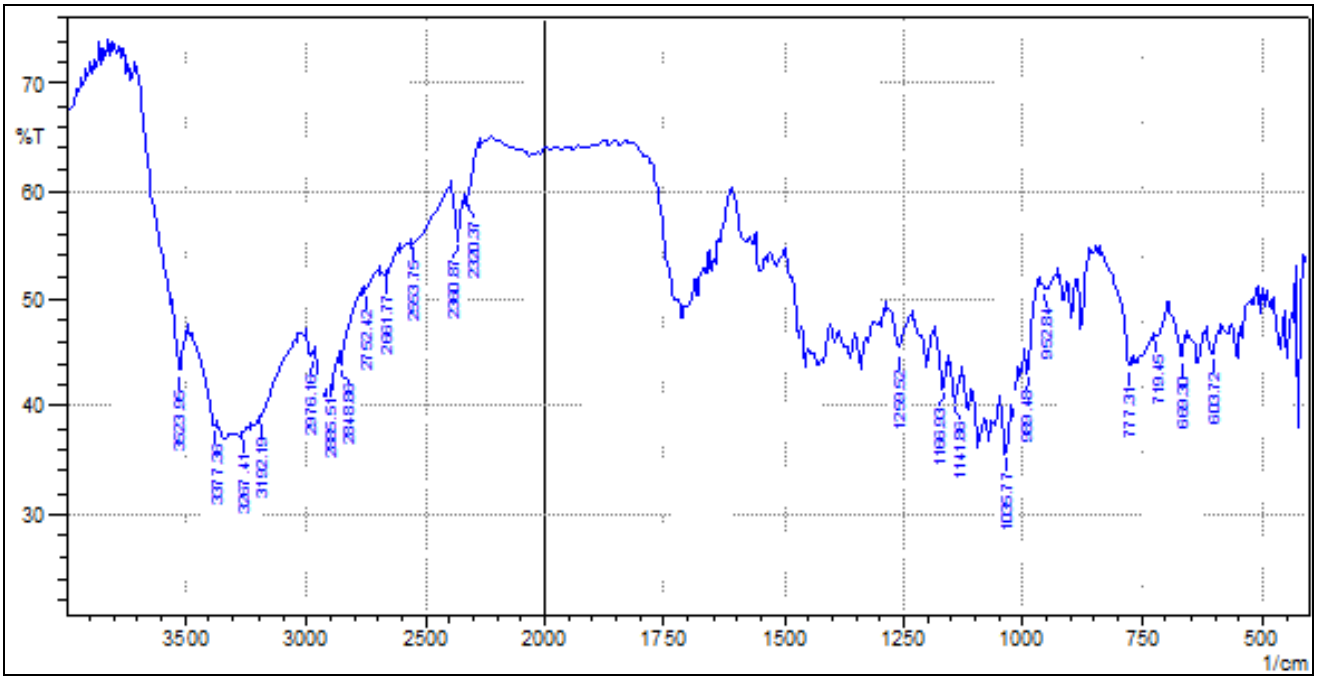

FIG. 5(b): IR SPECTRA OF S2

The compatibility evaluations were performed by Fourier transforms infra red spectroscopy, Studies implied that polymers and drug were compatible with each other. There was no interaction found between polymer and drug.

CONCLUSION: In the present study, an attempt was made to design and optimize BDDS of CPM and PHE using Carbopol and HPMC as the polymers. The compatibility evaluations were performed by Fourier transforms infra red spectroscopy, Studies implied that polymers and drug were compatible with each other. There was no interaction found between polymer and drug. Estimation of CPM and PHE in the prepared formulations was carried out by extracting the drug with phosphate buffer pH 6.8 solutions and the absorbance was measured at for CPM 263nm and for PHE 273nm.

The powder mixtures of all the formulations were tested by various studies including angle of repose (ranging from 29.01° to 29.10°), bulk density (ranging from 0.37 to 0.38 gm/ml), tapped density (ranging from 0.5884 to 0.5885 gm/ml), Hausner's ratio (ranging from 1.428 to 1.529) and Carr's index (ranging from 34.61 to 37.02 %). The tablets were prepared by direct compression method, four batches of different formulations were designed and from the results of evaluation data and all the formulations were evaluated for hardness, friability, drug uniformity, weight variation, surface pH study, Swelling index Study and matrix erosion study. It was observed that F3 and S2 tablet formulations had acceptable physical characteristics of all batches.

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