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MUCOADHESIVE FORMULATIONS OF CETIRIZINE FOR BUCCAL DELEIVERY

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ABSTRACT

Buccal delivery administers drug through buccal mucosal membrane that is the lining of oral cavity. The drug reaches systemic circulation by internal jugular vein and drugs bypass through hepatic first pass metabolism which shows higher bioavailability. Cetirizine hydrochloride is Histamine antagonist that is commonly used to treat throat inflammations and irritation. The patient usually feels discomfort while administering the drug and so the buccal delivery is the best suited route of administration and the oral absorption is usually preferred in this respect. In this study a mucoadhesive formulation was prepared using mucoadhesive polymers and were investigated for the formulation parameters.

Keywords: Cetirizine HCl, Mucoadhesion, *in vitro* drug release.

INTRODUCTION

Buccal delivery administers drug through buccal mucosal membrane that is the lining of oral cavity. The drug reaches systemic circulation by internal jugular vein and drugs bypass through hepatic first pass metabolism which shows higher bioavailability. The buccal DDS (drug delivery system) was flexible and has bio adhesive properties, which can be retains in oral cavity for desired duration [1,2,3]. The drug bioavailability enhanced by developing bio adhesive formulation that undergoes substantial first pass of hepatic effect and controls drug release upto constant rate. It releases the drug in predicted and controlled manner in order to elicit required therapeutic response. Oral delivery shows different types of buccal mucosal dosage forms such S buccal tablets, buccal gels and buccal patches.

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CHEMICALS

Cetirizine was obtained as a gift sample from Aarovin Pharmaceuticals Pvt Ltd., all the polymers and the chemicals were of analytical grade and bought from SD Fine chem Ltd.

METHODOLOGY

Preformulation studies

As a part of preformulation studies, melting point determination and polymer and drug compatibility were determined using FTIR studies.

Preparation of standard graph

100 mg of Pure Drug was dissolved in small amount of Methanol (5-10 ml) ,allowed to shake for few minutes and then the volume was made up to 100ml with phosphate buffer pH 6.8, from this primary stock (1mg/ml), 10 ml solution was transferred to another volumetric flask made upto 100 ml with phosphate buffer pH 6.8. From this secondary stock 1.0, 2.0, 3.0, 4.0, 5.0, ml was taken separately and made up to 10 ml with phosphate buffer pH 6.8 to produce 10, 20, 30, 40, 50 µg/ml respectively. The absorbance was measured at 268nm using a UV spectrophotometer [6,7].

FORMULATION OF BUCCAL TABLET

Then the powder blend was compressed into tablets by the direct compression method using 6mm flat faced punches. The tablets were compressed using a sixteen station Cadmach rotary tablet-punching machine. Composition of the prepared bioadhesive buccal tablet formulations of Cetirizine HCl were given in Table 1.

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EVALUATION OF BUCCAL TABLETS

Weight variation

The percent deviation was calculated using the following formula:

% Deviation = (Individual weight – Average weight / Average weight) X 100

Tablet Thickness

The thickness and diameter of the tablets was determined using a Digital Vernier caliper. Ten tablets from each formulation were used and average values were calculated. The average thickness for tablets is calculated and presented with standard deviation [8].

Tablet Hardness

Hardness was determined using Monsanto hardness tester and the average was calculated. It is expressed in Kg/cm^2.

Friability

Tablet strength is measured by using Roche friabilator. Test subjects to number of tablets to the combined effect of shock, abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm for 4 minutes, dropping the tablets to a distance of 6 inches in each revolution [9].

Percent friability (% F) was calculated as

$F (\%) = [Wo\text{-}W/W_O] X100$

Where, W_0 is the initial weight of the tablets before the test and

W is the final weight of the tablets after test.

Assay

Six tablets of each formulation were taken and amount of drug present in each tablet was determined. Powder equivalent to one tablet was taken and added in 100ml of pH 6.8 phosphate buffer followed by stirring for 10 minutes. The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured by using UV-Visible spectrophotometer at 268nm using pH6.8 phosphate buffer.

In vitro release studies

The drug release rate from buccal tablets was studied using the USP type II dissolution test apparatus. The dissolution medium was 500 ml of pH 6.8 phosphate buffer at 50 rpm at a temperature of 37 ± 0.5 °C. Samples of 5 ml were collected at different time intervals up to 8 hrs and analyzed after appropriate dilution by using UV Spectrophotometer at 268 nm.

RESULT & CONCLUSION

Preformulation study

Preformulation studies are primarily done to investigate the physicochemical properties of drug and to establish its compatibility with other excipients used. FTIR spectra of pure drug and formulation with other ingredients were recorded**.** The FTIR Spectra of pure Cetirizine HCl drug and polymer was compared with the FTIR spectrum of drug. There was no appearance or disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Physico-chemical Properties

Acceptable physicochemical properties were observed for the prepared buccal tablets all the formulated tablets passed the weight variation test. The weight variations of all compressed tablets were within the limits as per USP. The thickness of the tablets varied from 3.38 to 4.64 all the batches showed uniform thickness. Hardness of the tablets was found to be good depending upon compression force applied (6.3-7.13kg/cm²). Friability was obtained between the ranges 0.56 to 0.78, which was below 1% indicating sufficient mechanical integrity of the tablets. The drug content estimation showed values in the range of 98.96±0.63 to 101.38±0.96 which reflects good uniformity in the drug content among different formulations. Assay of all compressed tablets were within the limits as per USP.

Table 1. Composition of buccal formulations

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Cetirizine HCl Pure Drug	50	50	50	50	50	50	50	50	50
Gum karaya	25	37.5	50	-	-	-	-	-	-
Sodium Alginate	-	-	-	25	37.5	50	-	-	-
Carbopol 974	-	-	-	-	-	-	25	37.5	50
Carbopol 941	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
PVP	5	5	5	5	5	5	5	5	5
MCC	107.25	95.25	82.75	107.25	95.25	82.75	107.25	95.25	82.75
Total Weight (mg)	200	200	200	200	200	200	200	200	200

Table 2. Standard graph of Cetirizine HCl in phosphate buffer pH 7.4

S.No	Concentration (µg/mL)	Absorbance
1	0	0
2	5	0.342
3	10	0.516
4	15	0.790
5	20	0.947
6	25	2.3

Table 3: Physico-chemical Properties of Formulations

Formulation Code	Weight Variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Assay (%)
F1	201.83 ± 0.72	3.41 ± 0.04	6.3±0.26	0.62	100.72 ± 0.53
F2	202.5 ± 0.95	4.64 ± 0.03	5.9±0.34	0.71	100.23± 0.82
F3	200.46± 0.84	3.53± 0.05	6.4±0.52	0.84	101.38 ± 0.96
F4	199.52 ± 0.73	3.48 ± 0.03	6.5±0.21	0.67	99.84± 1.37
F5	198.80 ± 2.03	3.24± 0.06	5.8±0.36	0.75	98.96 ± 0.63
F6	201.12± 0.91	4.56± 0.02	6.19±0.41	0.56	99.87± 0.99
F7	202.49± 0.87	3.72± 0.03	7.13±0.19	0.78	100.23 ± 0.86
F8	200.6 ± 0.76	4.47± 0.05	7.5±0.75	0.71	101.05 ± 0.52
F9	201.02± 0.92	3.38± 0.09	7.0±0.23	0.59	100.19± 0.80

Each value represents the mean ±SD (*n* =3).

Table 4. *In vitro* cumulative percentage drug release profile of Cetirizine Formulations

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	39.12	35.83	34.45	39.01	35.83	34.45	27.53	25.01	32.94
1	47.37	42.41	45.84	47.34	42.42	45.80	45.04	40.93	38.37
2	53.90	56.78	51.92	53.52	56.79	51.94	54.67	45.54	44.23
3	64.74	60.52	59.40	64.68	60.59	59.40	63.41	56.72	53.39
4	69	67.93	63.56	69	67.91	63.36	70.18	62.96	57.01
5	73.82	73.99	71.04	73.41	73.94	71.9	75.50	67.45	61.7
6	79.19	79.46	77.86	79.26	79.37	77.68	81.19	74.47	65.58
7	84.70	83.62	82.34	84.72	83.4	82.39	87.73	90.68	70.49
8	94.06	90.34	86.69	94.93	90.34	86.75	91.42	97.14	77.63

Fig 1: FTIR studies of drug and polymer

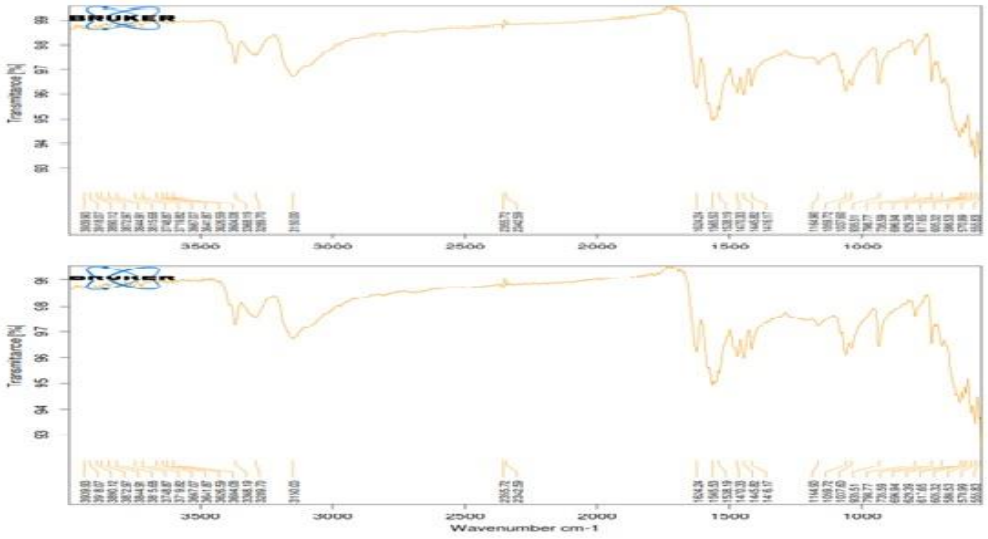
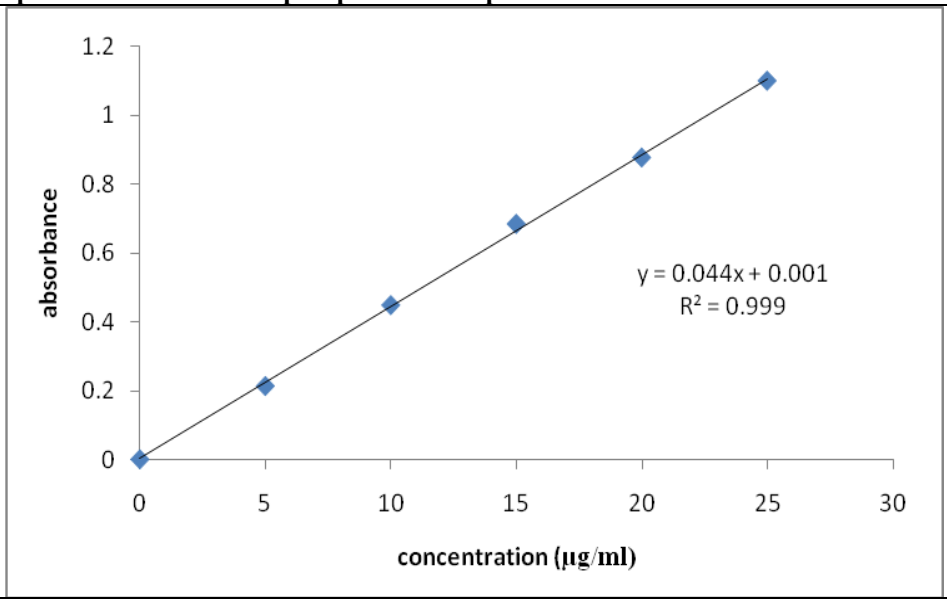


Fig 2: Standard graph of Cetirizine HCl in phosphate buffer pH 7.4



***In vitro* drug release**

In vitro drug release studies were conducted in phosphate buffer pH 6.8 and the studies revealed that the release of Cetirizine HCl from different formulations varies with characteristics and composition of matrix forming polymers as shown in graphs. Tablets formulated using Gum karaya, Sodium Alginate and Carbopol 974 P alone were eroded faster & dissolved completely within 1-2 hrs. While tablets containing Carbopol 941NF combination with polymers remain intactness and provide slow drug release up to 8 hrs. This might be due to swelling forming nature of Carbopol. As increase in the polymer concentration, causes an increase in the viscosity of the gel as well as formation of a gel layer with a longer diffusion path and decrease in diffusion coefficient of drug. Therefore, increased in polymers concentration leads to decrease in drug release. This was observed that there was a reduction in the amount of polymer ensures faster release. This may be attributed due to reduction in strength of gel layer which enhances drug diffusion and water uptake through matrix. From the Dissolution Data, it was evident that the F8 Formulation showed highest drug release 97.14% in 8 hours which consists of Carbopol 974 P, Carbopol 941NF.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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