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Formulation And Evaluation Of buccal Tablet Of Clozapine

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ABSTRACT:
The objective of this study was to develop mucoadhesive dosage form of Clozapine. The unidirectional buccal tablets of Clozapine were prepared by direct compression method. Mucoadhesive Buccal tablet were prepared by using different concentration of HPMC K 4 M, HPMC K 15 M as a mucoadhesive polymer. Ethyl cellulose was used as a backing membrane. The prepared tablets were evaluated for weight variation, hardness, friability, % swelling index, surface pH, content uniformity, mucoadhesion strength and in vitro drug release study. The formulation containing HPMC K15 M show better mucoadhesive strength and in vitro drug release. The formulation remained stable during stability study. The prepared unidirectional buccal tablets provided optimum drug release in 8 h, optimum swelling and good bioadhesive strength which indicates a potential alternative drug delivery system of Clozapine.

KEY WORDS: Buccal tablet, Clozapine, Mucoadhesion

I. INTRODUCTION:

Amongst the numerous routes of drug delivery system, oral drug delivery system is possibly the maximum preferred to the patient. However, it has following demerits together with hepatic first pass metabolism and enzymatic degradation within the gastrointestinal tract, that restrict oral administration of certain classes of drugs mainly peptides and proteins. Consequently, different absorptive mucosa is taken into consideration as potential sites for drug administration.

Transmucosal routes of drug delivery system like the mucosal linings of the rectal, vaginal, ocular, nasal, and oral cavity offer distinct merits over peroral administration for systemic drug delivery system. These merits consist of possible bypass of first pass effect, avoidance of pre systemic elimination in the gastrointestinal tract, and, contingent upon the specific medication, a superior enzymatic flora for drug absorption.[1]

Buccal adhesive drug delivery structures as promising alternative for persisted research. The buccal mucosa lines the inner cheek and buccal dosage form are put in the mouth between the upper gums and cheek to treat systemic and local conditions. The buccal route gives one of the potential routes for generally large, unstable proteins and hydrophilic, oligonucleotides and polysaccharides, as properly as conventional small drug molecules. The oral cavity has been utilized as a site for systemic and local drug delivery[2,3].

Clozapine is a psychiatric medication and is the first atypical antipsychotic. It is primarily used to treat people with schizophrenia and schizoaffective disorders who have had an inadequate response to other antipsychotics or who have been unable to tolerate other drugs due to extrapyramidal side effects. It belongs to BCS class II.[4]

II. MATERIAL AND METHOD [5-8]

Clozapine was obtained as a gift sample from, Aripolis Biotech, Ludhiana, Punjab. HPMC K 4 M, HPMC K15 M, HPMC K 100 M was purchased from SD fine chemicals. All other ingredients were used of analytical grade .

METHOD OF PREPARATION[9]

First all the excipients were weighed accurately.Then all the excipients except talc and magnesium stearate were mixed well in mortar pestle.After that talc and magnesium stearate were added. then drug –excipient mixture was weighed and directly compress in the tablet punching machine.After that 80 mg of ethyl cellulose were weighed and fill in die cavity.Above that core tablet was placed and the tablet was punched.

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Ingredients(mg)	B1	B2	B3	B4	B5	B6	B7	B8	B9
Clozapine	25	25	25	25	25	25	25	25	25
HPMC K4M	10	20	30	10	20	30	10	20	30
HPMC K15M	10	10	10	20	20	20	30	30	30
EthylCellulose	80	80	80	80	80	80	80	80	80
MCC	102.5	92.5	82.5	92.5	82.5	72.5	82.5	72.5	62.5
PVPK 30	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
Mg. Stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Totalwt. (mg)	250	250	250	250	250	250	250	250	250

Table1:CompositionofClozapineBuccalTablet

EVALUATION STUDY [10-13]

- The prepared buccal tablets were evaluated for their physical parameters such as weight variation, Hardness, friability and drug content.
- Surface pH Study: The buccal tablet was kept in contact with 1 ml of water and keepaside to swell for 2 h at room temperature. The pH was measured by bringing the pH meter electrode in contact with the surface of the tablet.
- In-vitro swelling study: The test was performed to determine the amount of water absorption and swelling of the polymer which affect drug release. Buccal tablets were weight individually (W1) and place separately in phosphate buffer (50 mL, pH 6.8, 37 ± 1 °C). At predetermined time intervals (1, 2, 3, 4, 5, 6, 7, 8 h), the tablets were removed from the buffer, reweighed (W2), and the swelling index (SI) was calculated using the Equation:

S=W2 – W1/ W1 *100

- In vitro drug release study: The buccal tablets were subjected to in vitro dissolution. Dissolution test was carried out using USP type 2 paddle method. The stirring rate was 50 rpm, pH 6.8 phosphate buffer was used as dissolution medium and dissolution medium is maintain at 37±0.5°C. Samples of 5 ml were withdrawn at regular intervals of time, filter and replace with 5 ml of fresh dissolution medium, dilutions were made wherever necessary and were analysed for clozapine at 290 nmby using UV-visible spectrophotometer.
- Ex-vivo mucoadhesive strength: Ex-vivo mucoadhesive strength of tablet was performed with goat Oral mucosa which wascollected from slaughter house, using a modified physical balance. On one side of the balance, a rubber closure was tied withthread which was attached and on other side empty polythene bag is attach.

III. RESULT AND DISCUSSION:

Batch	Bulk density(gm/ cm^3)	Tappeddensity (gm/ cm^3)	Carr'sindex (%)	Hausner'sratio	Angle ofrepose(∅)
B1	0.542±0.012	0.639±0.032	15.17±0.51	1.17±0.014	27.45±2.04
B2	0.534±0.024	0.621±0.016	12.50±0.38	1.16 ± 0.021	28.12±1.45

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B3	0.526±0.021	0.609±0.023	13.62±0.46	1.15 ± 0.013	28.98±1.12
B4	0.551±0.068	0.652±0.043	15.49±0.22	1.18 ± 0.031	27.82±1.52
B5	0.548±0.018	0.637±0.028	13.97±0.41	1.16 ± 0.013	29.01±0.98
B6	0.539±0.035	0.619±0.032	12.92±0.68	1.14± 0.027	30.36±1.05
B7	0.549±0.049	0.657±0.039	16.43±0.52	1.19 ± 0.019	28.65±0.72
B8	0.532±0.032	0.625±0.021	14.88±0.48	1.17 ± 0.036	29.81±1.29
B9	0.528±0.05	0.612±0.027	13.72±0.31	1.15± 0.024	31.17±1.18

Table2:Pre-compressionalparametersofB1-B9(n=3,± SD)

Batch	**Weightvariation (mg) (n=20)**	**Hardness(kg/ cm^2)(n=3)**	**Friability(%)**	**pH(n=3)**	**DrugContent(n =10)**	**Ex vivomucoadhesive (gm) (n=3)**
B1	247.67±4.26	6.88±0.46	0.62	6.75±0.24	99.15±2.38	18.03±0.81
B2	254.12±2.41	7.14±0.68	0.35	6.74±0.37	98.12±3.86	20.84 ± 2.03
B3	248.51±3.89	7.35±0.76	0.59	6.67±0.18	98.89±2.05	22.65 ± 1.87
B4	251.85±3.01	7.48±0.51	0.25	6.82±0.33	99.46±1.89	26.76 ± 0.65
B5	249.73±3.76	7.43±0.32	0.31	6.58±0.27	97.65±2.67	23.20 ± 1.52
B6	253.38±3.64	7.26±0.87	0.64	6.63±0.36	98.23±3.02	25.60 ± 0.76
B7	246.18±4.52	6.74±0.36	0.53	6.72±0.32	97.38±2.53	22.14 ± 1.37
B8	255.46±4.82	7.45±0.64	0.27	6.81±0.38	98.42±2.75	24.16± 1.54
B9	247.16±3.49	7.38±0.43	0.74	6.78±0.25	98.57±3.16	25.80 ± 1.12

Table 3:PostcompressioncharacterizationofB1-B9(n=3,± SD)

%SWELLINGINDEX:

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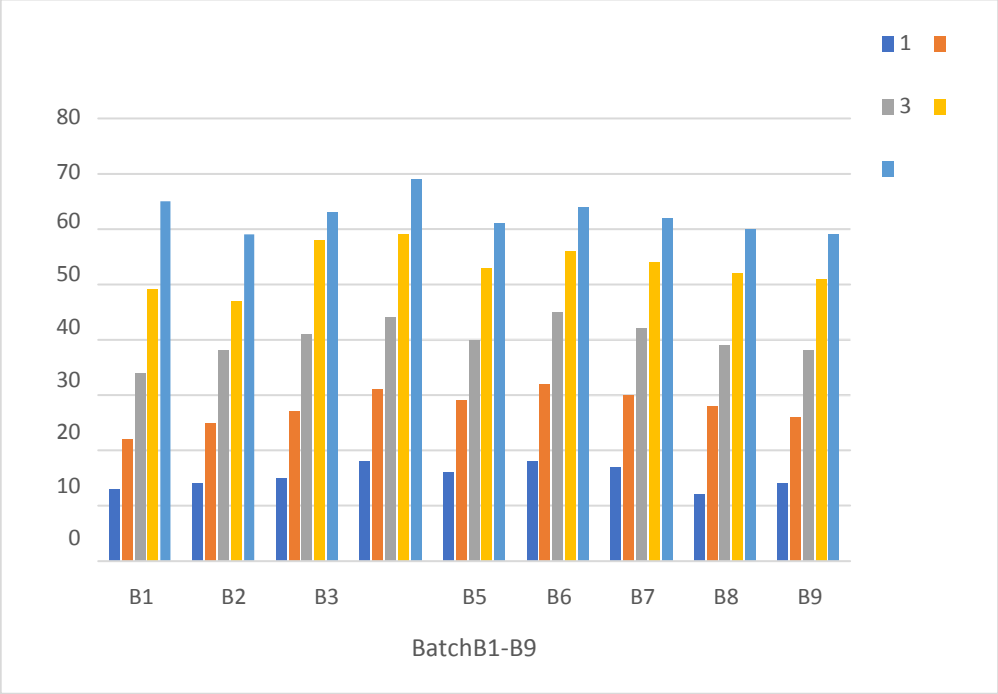

INVITRODRUG RELEASESTUDY:

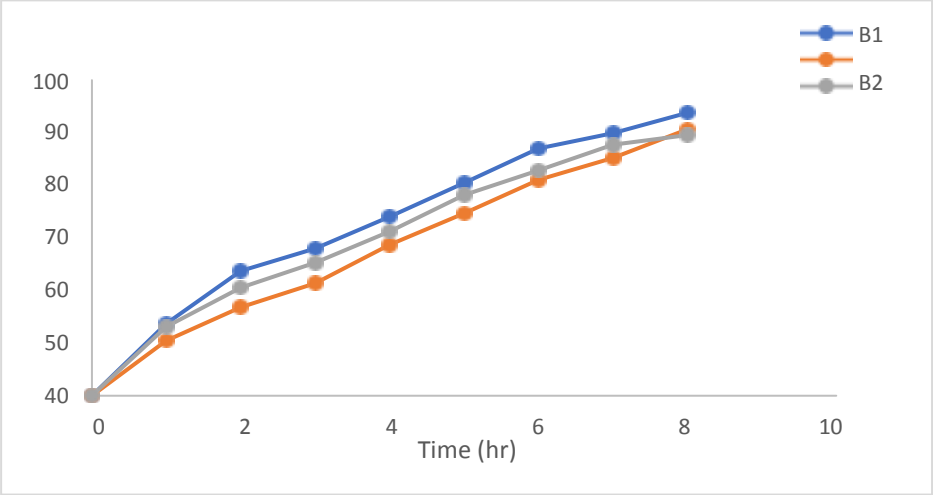

Figure2:In-vitrodrugreleasefrom B1-B3

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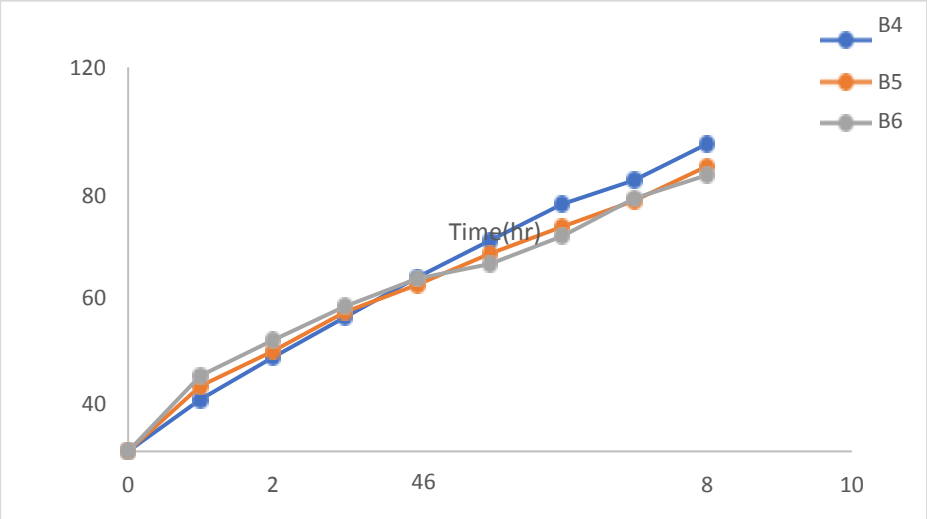

Figure3:In-vitrodrugreleasefromB4-B6

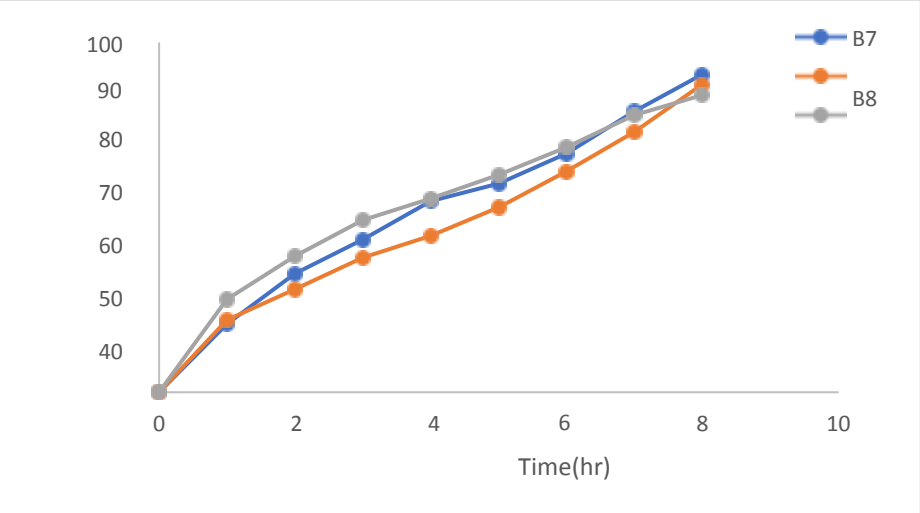

Figure4:In-vitrodrugreleasefromB7-B9

IV. DISCUSSION:

From the above evaluation study, it was concluded that B4 shows the highest drugrelease inwhichHPMCK4MandHPMCK15 Mcontained10mgand20mgrespectivelyshows 96.13%drugreleaseat 8 hrs.

V. CONCLUSION:

From the present work it can be concluded that clozapine can be administered via buccal drug delivery system, which provides controlled release and reduces the frequency of drug administration and also reduce the first pass metabolism of drug it can enhance the patient compliance due to ease of application and removal of formulation also it is a non-invasive method.

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