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RESEARCH ARTICLE

Formulation and In-vitro Evaluation of Cetylpyridinium Chloride Buccal Patch

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ABSTRACT
In present study buccal drug delivery of Cetylpyridinium was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Matrix type of buccal patches was developed by using polymers Eudragit-L100, HPMCk_4M and HPMCk15M.Buccal patches were prepared by employing solvent casting method. Propylene glycol and Tween80 were selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1-F12, and all the formulations were evaluated for various physical parameters Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake, Moisture content and Swelling study and all the results were found to be were found to be within the pharmacopeial limits, in-vitro drug release studies by using dialysis membrane. Among all the 12 formulations F6 formulation which contain HPMC K4M 300mg and Eudragit L-100 60mg had shown 94% cumulative drug release within 12 hours. And compared to HPMC K15M, HPMC K4M showed better drug release profile. For F6 formulation release kinetics were plotted and the Regression coefficient value was found to be high for Korsmeyer-peppas release model i.e., 0.9892. The n value was found to be 0.6203 which indicates the drug release pattern was found to be non-Fickian diffusion.
Keywords: cetylpyridinium, buccal, patches

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CONTENTS

1. Introduction

Buccal route of drug delivery provides the direct access to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability. Other advantages such as excellent

accessibility, low enzymatic activity, suitability for drugs or excipients that mildly and reversibly damage or irritate the mucosa, painless administration, easy withdrawal, facility to include permeation enhancer/ enzyme inhibitor or pH modifier in the formulation, versatility in designing as multidirectional or unidirectional release system for local or systemic action. Buccal penetration of Cetylpyridinium cannot be increased by niosomes or liposomes because of its size and rigid character of lipid layer. Hence there is a need for preparation of Cetylpyridinium patch for enhanced penetration through the buccal cavity, thereby reducing dose, minimizing frequency of administration and adverse affects, hence resulting in better patient compliance.

2. Materials and method

Cetylpyridinium, Ethanol, Eudragit L-100, HPMCk15M, HPMCk4M, Methanol chemicals were Laboratory grade made of SD Fine chemicals Pvt Ltd

Formulation:

Development of Buccalpatches:

Buccal drug delivery patches were prepared by solvent casting method.

Solvent casting method:

Eudragit L100, $HPMCK_4M$ and HPMCK15M were weighed in requisite ratios and they were then dissolved in dichloromethane and ethanol as solvent using magnetic stirrer. Cetylpyridinium (36mg), Propylene glycol and Tween 80 was added to the above dispersion under continuous stirring. The uniform dispersion was poured in the petri plate. The rate of evaporation of solvent was controlled by inverting cut funnel over the patches. After 24h, the dried films were taken out and stored in desiccator.

Evaluation of Buccal patch

Physical appearance, Thickness, Weight variation, Flatness, Folding endurance, Moisture uptake, Moisture content, Swelling study, Drug content determination, *In vitro* permeation studies using dialysis membrane

Table 1: Formulations of Cetylpyridinium Buccal Patch

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Drug (mg)	40	40	40	40	40	40	40	40	40	40	40	40
2	Eudragit-L100(mg)	200	250	300	-	-	-	-	-	-	150	150	-
3	$HPMCk_4M$(mg)	-	-	-	200	250	300	-	-	-	150	-	150
4	$HPMCk_{15}M$(mg)	-	-	-	-	-	-	200	250	300	-	150	150
5	Dichloromethane(ml)	8	8	8	8	8	8	8	8	8	8	8	8
6	Ethanol(ml)	8	8	8	8	8	8	8	8	8	8	8	8
7	Propylene glycol(ml)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
8	Tween-80(ml)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3

3. Results & Discussion

Standard Calibration curve of Cetylpyridinium:

Table 2: Concentration and absorbance obtained for calibration curve of Cetylpyridinium in (pH 6.8)

S. No.	Concentration (µg/ml)	Absorbance* (at 271 nm)
1	2	0.128
2	4	0.267
3	6	0.456
4	8	0.589
5	10	0.762
6	12	0.963

It was found that the estimation of Cetylpyridinium by UV spectrophotometric method at λ_{max}271 nm in 6.8 pH phosphate buffer had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2-10µg/ml. The regression equation generated was y = 0.0636x + 0.0751.

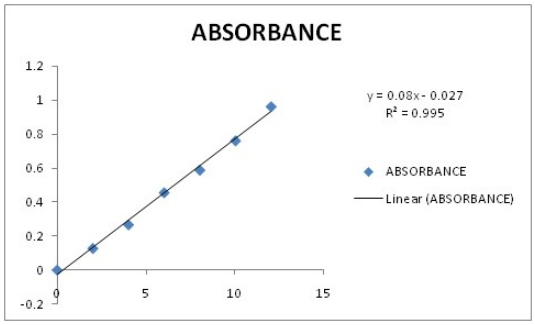

Figure 1: Standard graph of Cetylpyridinium in pH 6.8 Phosphate buffer

Evaluation of Cetylpyridinium Buccal patches:

Physical appearance: All the Buccal patches were visually inspected for colour, clarity, flexibility.

Flatness: All the Buccal patches were found to be flat without any foams.

Table 2: Evaluation of Buccal patch by physical methods

Formulation	Thickness (mm)	Folding endurance	Drug content (%)	Moisture uptake (%)	Moisture content (%)
F1	0.3569	20	45	7.98	3.77
F2	0.3520	25	65	25.05	9.2
F3	0.3470	27	57.5	13.09	5.16
F4	0.3496	24	60	15.63	5.66
F5	0.3460	30	67.5	11.73	4.87
F6	0.3517	32	92.5	19.65	12.67
F7	0.3478	40	101.7	9.42	3.43
F8	0.3437	37	85	10.87	4.72
F9	0.3503	34	55	16.44	6.62
F10	0.3532	29	62.5	13.08	6.17
F11	0.3546	26	85	20.63	7.94
F12	0.3503	31	82.5	15.73	6.55

The prepared Cetylpyridinium Buccal patches were evaluated by physical methods such as Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake and Moisture content and all the results were found to be within the pharmacopeial limits.

Table 3: Evaluation of Buccal patch by In-vitro permeation studies using dialysis membrane

Time (hrs)	% Drug release											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
1	9.05	15.1	10.1	9.49	10.9	20.2	17.5	12.0	11.1	12.7	10.0	20.4
2	13.3	19.8	12.8	11.3	19.6	27.8	21.9	17.5	13.0	17.9	12.5	25.4
4	14.6	28.3	21.5	22.6	24.9	42.8	33.5	23.4	23.3	27.4	23.6	33.0
6	21.9	34.1	25.9	32.3	31.2	53.5	40.0	30.9	33.4	32.7	30.9	41.7
8	32.7	41.1	33.4	43.9	38.0	66.3	46.5	48.1	52.7	50.6	36.7	47.9
10	40.4	50.1	44.5	56.3	50.3	82.0	64.2	60.0	66.4	63.0	45.9	63.0
12	54.2	65.8	56.7	69.4	65.9	94.7	91.9	78.7	79.1	74.8	56	80.9

Table No 4: kinetics of In-vitro permeation studies using dialysis membrane

Cumulative (%) release Q	Time (T)	Root (T)	Log (%) release	Log (T)	Log (%) remain	Release rate (cumulative % release/t)	1/cum% release	Peppas log Q/100	% drug remain	Q01/3	Qt1/3	Q01/3 - Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
20.2356	1	1.000	1.306	0.000	1.902	20.236	0.0494	-0.694	79.7644	4.642	4.305	0.337
27.80759	2	1.414	1.444	0.301	1.858	13.904	0.0360	-0.556	72.19241	4.642	4.164	0.478

42.87958	4	2.000	1.632	0.602	1.757	10.720	0.0233	-0.368	57.12042	4.642	3.851	0.790
53.59293	6	2.449	1.729	0.778	1.667	8.932	0.0187	-0.271	46.40707	4.462	3.594	1.048
66.38743	8	2.828	1.822	0.903	1.527	8.270	0.0151	-0.178	33.61257	4.642	3.227	1.414
82.0877	10	3.162	1.914	1.000	1.253	8.209	0.0122	-0.086	17.9123	4.642	2.616	2.025
94.7055	12	3.464	1.976	1.079	0.724	7.892	0.0106	-0.024	5.294503	4.642	1.743	2.899

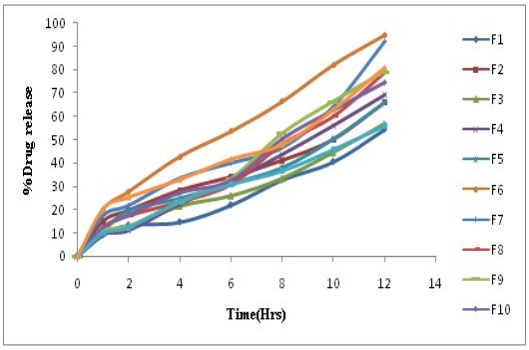

Figure 2: Release profile of In-vitro permeation studies using dialysis membrane

The prepared Cetylpyridinium Buccal patches were evaluated for In-vitro permeation studies using dialysis membrane, among all the 12 formulations F6 formulation which contain HPMC K4M 300mg and Eudragit L-100 60mg had shown 94% cumulative drug release within 12 hours. And compared to HPMC K15M, HPMC K4M showed better drug release profile.

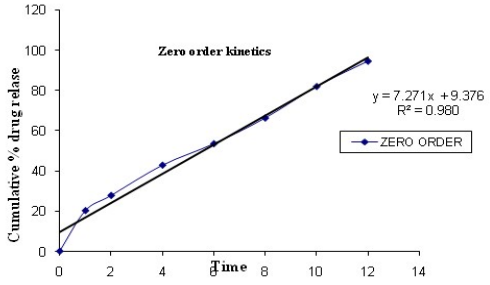

Figure 3: Zero order kinetics

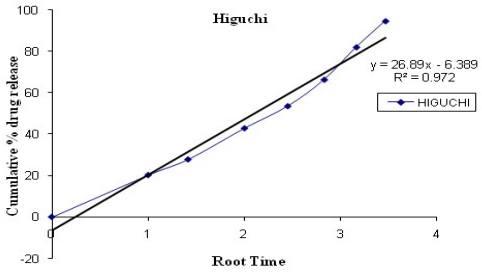

Figure 4: Higuchi plot

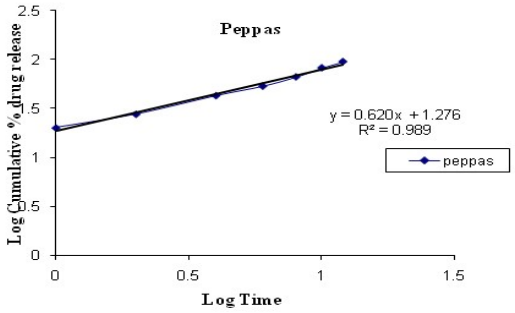

Figure 5: Peppas plot

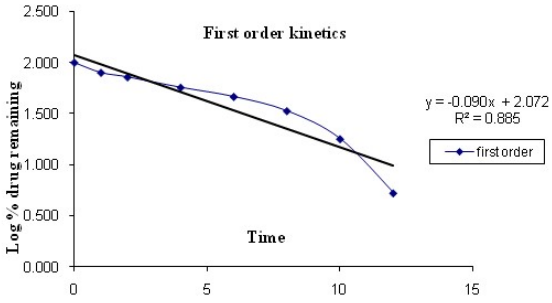

Figure 6: First order kinetics

The kinetics of In-vitro permeation studies using dialysis membrane for F6 formulation was plotted and the Regression coefficient value was found to be high for Korsmeyer-peppas release model i.e., 0.9892. And the n value was found to be 0.6203 which indicates the drug release pattern was found to be non-Fickian diffusion.

4. Conclusion

In present study buccal drug delivery of Cetylpyridinium was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Matrix type of buccal patches was developed by using polymers Eudragit-L100, HPMCk_4M and HPMCk15M.Buccal patches were prepared by employing solvent casting method. Propylene glycol and Tween80 were selected as permeation enhancer and plasticizer. Drug excipient

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