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Formulation & evaluation of muccoadhesive buccal patches for delivery of atenolol

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ABSTRACT

Mucoadhesive buccal patches of Atenolol for local delivery of the drug to the oral cavity were formulated by Solvent casting technique. Mucoadhesive polymer, namely sodium carboxymethyl cellulose (NaCMC) of different grade were incorporated into the patches to modify their mucoadhesive properties as well as the rate of drug release, using glycerol as plasticizer. Different concentrations of polymer were used for the preparation of patches. The patches were evaluated on the basis of their physical characteristics like surface pH, folding endurance, mucoadhesive performance, and release rate. The in-vitro drug release was carried out in Franz diffusion cell, with commercially available dialysis membrane. Formulation P-10 (10 % Sodium carboxy Methyl Cellulose (NaCMC), 5 % glycerol and 2 % Atenolol) showed sustained release upto 10 hours.

Keywords: Mucoadhesive Buccal Patch, Atenolol, sodium carboxymethyl cellulose (NaCMC), Franz diffusion cell.

INTRODUCTION

Amongst the various routes of administration tried so for novel drug system lacalized delivery to tissues of the oral cavity has been investigated for a number of applications including the treatment of toothaches, periodontal disease, bacterial /& fungal infections, apthous & dental stomatitis[1]. Buccal cavity has a wide variety of functions & it acts as an excellent site for absorption of drugs[2]. It provides direct entry of drug molecules in to the systemic circulation. Thus, avoiding hepatic first pass effect[3].

Atenolol is a Beta blocker widely used in the treatment of Hypertension & cardiac disease. Atenolol 50% of a dose is absorbed oral administration[4]. Buccal route by pass the hepatic first pass effect the dose of atenolol could be reduced. The half life is about 6-7 hrs & low molecular weight i.e.266.3 make it a good candidate for administration by the buccal route[2].

Polymer sodium carboxy methyl cellulose is used in different concentration with drug (Atenolol). It is a synthetic polymer. It has a ph 6 to 8 & it is a suspending agent, its melting point is approx 227^{o}c & its molecular weight is 90000-700000.

Mucoadhesion or the attachment of a natural or synthetic polymer to a biological substrate is a practical method of drug immobilization or localization & important new aspects of controlled drug delivery[5].

There are different theories of Mucoadhesions[6]

(1) Electronic Theory- The polymer and mucous membrane having the different electronic structure when these two comes in contact then transfer of electrons occur which causing the formation of double layer at the interphase by which adhesion between polymer & mucous membrane take place.
(2) Adsorption Theory- This theory states that bond formation between polymer and mucous membrane is due to the vanderrwall forces, hydrogen bond or any other weak bond.
(3) Wetting theory- According to this theory the interaction between polymer & mucous membrane depends upon surface tension of

polymer & mucous & also form the interfacial tension between these two & calculated as

F = Sp+Sm-Ipm

Where F= is the strength of Mucoadhesion

Sp= Surface tension of Polymer

Sm= Surface tension of Mucous

Ipm= Interfacial tension of Polymer & Mucous.

(4) Diffusion Theory- The concept that interpenetration of polymer chain & mucous chain produce adhesion bonds is supported by diffusion theory. The depth of the penetration of one chain in to another is calculated as

L = 1/(tDp)

Where L = Penetration Depth

t = time of depth

Dp = Diffusion constant

(5) Fracture Theory- This theory analyse the force require to separate two surfaves of polymer & mucous after adhesion & calculate as-

S = F/A

Where S = tensile stress

F = Force of detachment

A = Constant area

Objective- Objective of the work is to prepare Muco adhesive buccal patches containing Atenolol & Evaluate the prepared batches of Atenolol.

Plan of Work is to prepare the standard curve, Prerparation of Atenolol buccal patches, Evaluation of buccal patches, compilation of data.

METHOD OF PREPARATION

Formulation of Muccoadhesive buccal patches

Muccoadhesive buccal patches were prepared by "Solvent casting techniques". The polymer sodium carboxy methyl cellulose were used in concentration of 3%, 2%,1% respectively. In all cases 5% v/v glycerol was added as plasticizer. For the preparation of sodium carboxy methyl cellulose patches with atenolol 1%,2%,3% (NaCMC) was dissolved in distilled water & stirrer by means of Magnetic stirrer then added 5% v/v glycerol & 1% w/v Atenolol in all cases with continuous stirring. The resultant viscous solution was filtered & left to stand until all the air bubbles disappeared. The solution was poured in a clean,dry,glass petridish & allowed to dry in an oven at 40^0C till a flexible film was formed. Patches were cut & packed in aluminium foil for evaluation.

The evaluation parameters are

Patch thickness[2]- The thickness of 19 patches was measured using screw gauge. The data were analysed for sample mean.

Mass Uniformity[7]- The mass of each 10 individual patches was determined by placing it an electronic balance. The mass data from the patches were analysed for sample mean.

Surface ph[3]- The patches were left to swell for 1hr on the surface of agar plate, prepared by dissolving 1% agar in buffer solution (ph 6.8) under stirring. The surface ph was measured by means of a ph paper placed on the surface of swollen patches.

Radial Swelling[1]- The radial swelling of patches were determined by weighing patch (w_1) & placed separately in petridish containing phosphate buffer (ph 6.8). The petridish were stored at room ttemperature, after 10min the patch were removed & excess water on their surface was carefully absorbed using filter paper & weighed (w_2). The percentage radial swelling was calculated as-

Radial Swelling (%) = $(w_2-w_1/w_1)x100$

Folding Endurance[8]- Folding endurance of the patches was determined normally by repeatedly folding the patch at the same place till it broken or folded up to 300 times, patches without breaking game the value of folding endurance.

Drug Content[1]- Three patches of each formulation were taken in separate 10ml of ph 6.8 phosphate buffer was added & continuously stirred for 1hr. The solution were filtered, diluted suitably & analysed at 2.25nm in a UV spectrophotometer. The average of drug contents of three patches was taken as final reading.

In-vitro release study[2]- Commercially available cellophane membrane was employed for the study, which were permeable to low molecular weight substances. The in vitro release study was done in Franz diffusion cell. The diffusion call consists of two parts upper donar compartment and a bottom receptor compartment. The receptor compartment was enclosed by water jacket to control the temperature. An O-ring seal couple with a membrane & a patch to separate the top & bottom compartment, for allowed 10mm of diffusion area. In the receptor compartment the phosphate buffer (ph 6.8) was filled, cell were placed on magnetic stirrer & maintained at $37^o\pm0.5^0$C.

RESULT & DISCUSSION

The drug content of formulation 1 (C_1) was 98.6%, C_2 was 98.5% and for C_3 was 98.3% were given in table 1.The folding endurance was more than 300 in all cases (C_1, C_2, & C_3) were given in table 2. The

mass uniformity of formulation 1 (C_1) was (-0.0004 to 0.0106), C_2 was (-0.003 to 0.016) & C_3 was (-0.01 to 0.007) Surface ph was approx 7.0 in all formulations as shown in Table 2(a). Radial swelling of formulation 1 (C_1) was 1.282%, C_2 was 1.298% & C_3 was 1.315% were given in table 2. Percentage drug release after 6 hrs from formulation 1 (C_1) was 35.7%, C_2 was 27.1% & C_3 was 25.6% were given in table 2 (b) Patch thickness of C_1 was 3.30mm, C_2 was 4.45mm & C_3 was 5.19mm were given in table 2

CONCLUSION

The study was aimed at preparation of mucoadhesive buccal patches of Atenolol. We conclude that the **drug content** was uniformity with a maximum variation of 0.4% this indicates that the drug was dispersed uniformly throughout the patches. All the patches showed a **folding endurance** more than 300 which shows a good flexibility. **Surface pH** of all formulations was nearer to neutral i.e.7 hence no nasal irritation was expected. The **radial swelling** on all the cases shows no any specific change. In case of **In-vitro release study** as the concentration of polymer increase the percentage drug release decrease which shows sustained release of drug from dosage form. In **patch thickness** as the concentration of polymer increase the thickness of Patches also increase. The buccal muco-adhesive drug delivery system is used to avoid gastro-intestinal tract difficulties as in oral route. It is suitable in case of vomiting during oral administration. Is avoid first pass metabolism. The therapy can be quickly terminated in case of toxicity. Due to rich vascularity the absorbance of drug is better. It is easily administrated to unconscious patient. No degradation of drug occurs.

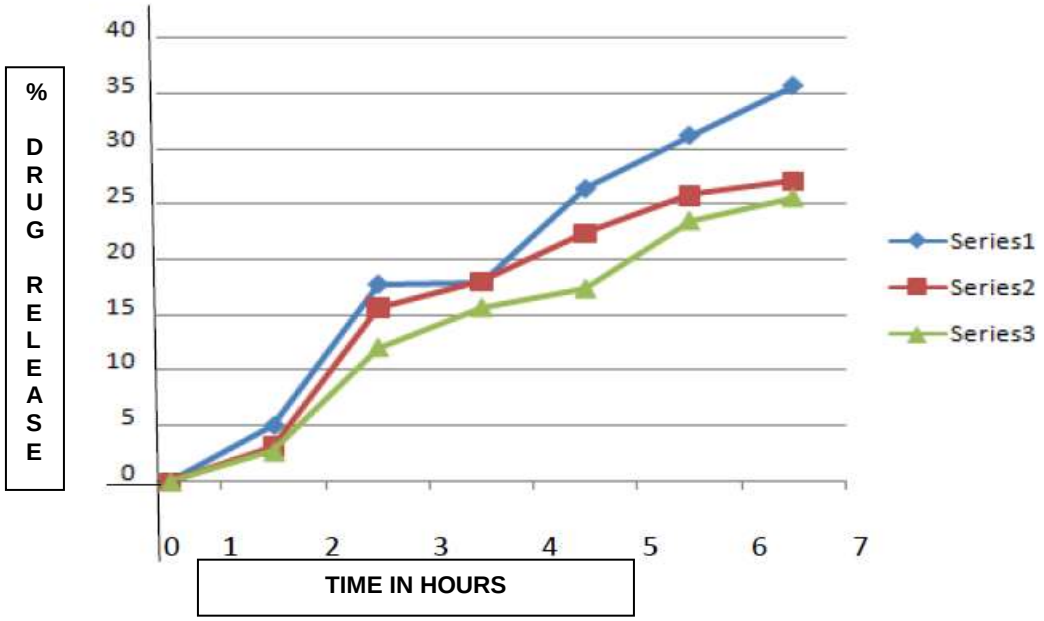

Figure No 1: PERCENTAGE DRUG RELEASE FROM PATCHES C_1 (Blue), C_2 (Red), C_3 (Green)

Table No 1. DRUG CONTENT OF DIFFERENT PATCHES

S.No.	Percentage Drug Formulations		
	C_1 (Blue)	**C_2 (Red)**	**C_3 (Green)**
1.	99.1	98.3	98.2
2.	98.0	98.5	99.7
3.	98.7	98.7	97.2
Average	**98.6**	**98.5**	**98.36**

Table No 2. RESULTS OF DIFFERENT BUCCAL PATCHES

S.No.	Evaluation Parameter	C_1 (1%)	C_2 (2%)	C_3 (3%)
1.	Drug Content (%)	98.6	98.5	98.3
2.	Folding Endurance	> 300	> 300	> 300
3.	Mass Uniformity	[-0.0004 to 0.016]	[-0.003 to 0.016]	[-0.01 to 0.007]
4.	Surface ph	Approx 7.0	Approx 7.0	Approx 7.0
5.	Radial Swelling (%) in 10 min	1.282%	1.298%	1.315%
6.	Percentage Drug Release (%) After 6hrs	35.7%	27.1%	25.6%
7.	Patch thickness (mm)	3.30mm	4.45mm	5.19mm

Table 2 (a) MASS UNIFORMITY

For C_3 (3%) Weight of 20 patches= 1.639, Average weight= 1.639/20= 0.08

For C_2 (2%) Weight of 20 patches= 1.482, Average weight= 1.482/20= 0.0743

FOR C_3 (3%)				FOR C_2 (2%)			
S.No.	**Single patch Weight**	**Avg. Weight**		**S.No.**	**Single patch Weight**	**Avg. Weight**	
1.	0.096	0.08	0.016	**1.**	0.073	0.074	-0.001
2.	0.077	0.08	-0.003	**2.**	0.078	0.074	0.004
3.	0.072	0.08	-0.008	**3.**	0.081	0.074	0.007
4.	0.076	0.08	-0.004	**4.**	0.068	0.074	-0.006
5.	0.072	0.08	-0.008	**5.**	0.076	0.074	0.002
6.	0.088	0.08	0.008	**6.**	0.077	0.074	0.003
7.	0.074	0.08	-0.006	**7.**	0.077	0.074	0.003
8.	0.088	0.08	0.008	**8.**	0.078	0.074	0.004
9.	0.088	0.08	0.008	**9.**	0.074	0.074	0
10.	0.076	0.08	-0.004	**10.**	0.073	0.074	-0.001
11.	0.072	0.08	-0.008	**11.**	0.078	0.074	0.004
12.	0.088	0.08	0.008	**12.**	0.068	0.074	-0.006
13.	0.096	0.08	0.016	**13.**	0.067	0.074	-0.007
14.	0.088	0.08	0.008	**14.**	0.073	0.074	-0.001
15.	0.077	0.08	-0.003	**15.**	0.081	0.074	0.007
16.	0.072	0.08	-0.008	**16.**	0.076	0.074	0.002
17.	0.074	0.08	-0.006	**17.**	0.081	0.074	0.007
18.	0.088	0.08	0.008	**18.**	0.077	0.074	0.003
19.	0.077	0.08	-0.003	**19.**	0.074	0.074	0
20.	0.076	0.08	--0.004	**20.**	0.073	0.074	-0.001
Max. 0.007mg				**Max. 0.016mg**			
Min -0.01mg				**Min -0.003mg**			

For C_1 (1%) Weight of 15 patches= 1.146, Average weight= 1.146/15= 0.0764

FOR C_1 (1%)			
S.No.	**Single patch Weight**	**Avg. Weight**	
1.	0.074	0.0764	-0.002
2.	0.081	0.0764	0.004
3.	0.084	0.0764	0.007
4.	0.087	0.0764	0.0106
5.	0.076	0.0764	-0.004
6.	0.078	0.0764	0.0016

7.	0.082	0.0764	0.005
8.	0.074	0.0764	-0.002
9.	0.078	0.0764	0.0016
10.	0.087	0.0764	0.0106
11.	0.081	0.0764	0.004
12.	0.076	0.0764	-0.0004
13.	0.075	0.0764	-0.002
14.	0.074	0.0764	-0.002
15.	0.076	0.0764	-0.0004
	Max 0.016mg		
	Min -0.0004mg		

Table 2 (b) In-Vitro Percentage Drug Release

S.No.	Time (Hrs)	Percentage Drug Release		
		C_1 (Series 1)	**C_2 (Series 2)**	**C_3 (Series 3)**
1.	0 hr	0 %	0 %	0 %
2.	1 hr	5.1 %	3.2 %	2.7 %
3.	2 hrs	17.8 %	15.7 %	12.1 %
4.	3 hrs	18.0 %	18.1 %	15.7%
5.	4 hrs	26.4 %	22.4 %	17.4 %
6.	5 hrs	31.2 %	25.8 %	23.5 %
7.	6 hrs	35.7 %	27.1 %	25.6 %

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