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Formulation and Characterization of Buccal Mucoadhesive Patch of Chlorhexidine Gluconate

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Abstract: Buccal Mucoadhesive patch of Chlorhexidine gluconate were prepared using HPMC K100M, HEC and PVA as mucoadhesive polymers. Glycerol was added as plasticizer. Preparation of all the patches using above mentioned polymers was done by solvent casting technique. The formulations were evaluated for various parameters like weight variation, patch thickness, folding endurance, surface pH, *in vitro* mucoadhesive and *in vitro* release study. The prepared patches were exhibiting good thickness, weight and content uniformity. The folding endurance was also satisfactory. The patches showed good mucoadhesion characteristics and sustained drug release. Patches with HPMC K100M released the drug over a period of 3 hr, while HEC and PVA sustained the release up to 4 hrs. Thus the patches can be helpful for the effective management of oral hygiene with sustained and localized release of Chlorhexidine Gluconate.
Key Words: Chlorhexidine Gluconate, Buccal patch, Mucoadhesion, HPMC.

1. Introduction:

Extensive efforts have recently been focused on targeting a drug or drug delivery system in a particular region of the body for extended period of time, not only for local targeting of drugs but also for the better control of systemic drug delivery. The unique environment of the oral cavity offers its potential as a site for drug delivery. Because of the rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach or which are extensively metabolized in the liver. But the limitations of buccal drug delivery include continuous secretion of saliva, resulting in rapid removal of released drug. Conversely, mucoadhesive drug delivery system provides an opportunity to retain drug in contact with the mucosa for prolonged period.[1]

Chlorhexidine gluconate (CHG) is a bisbiguanide antiseptic and disinfectant effective against wide range of bacteria, fungi and some viruses. It is also used for gingivitis and prevention of plaque.[2] In market, it is mainly available in the form of oral Rinse (Hexidine, Peridex). Clinical pharmacology shows antibacterial activity during oral rising. Microbial sampling of plaque has shown a general reduction in counts of certain

assayed bacteria, both aerobic and anaerobic, ranging from 54 to 97% through six month use and without any significant changes in bacterial resistance. Pharmacokinetics studies with oral CHG oral rinse shows that approximately 30% of the drug is retained in the oral cavity following Rinsing. This retained drug is slowly released into the oral fluids.[3,4]

The aim of the present investigation was to design sustained release bucco-adhesive patch of CHG for reduced wastage of drug and improved residence time for prolonged anti-microbial action.

2. Experimental:

2.1 Materials

Chlorhexidine gluconate was kindly provided as gift sample from Shalaks Pharma, Mumbai. Hydroxy Propyl Methyl Cellulose K100M was obtained as gift sample from Colorcon Lab, Mumbai. Hydroxy Ethyl Cellulose, Polyvinyl Alcohol and Glycerol were obtained from Loba Chemie. All other chemicals were used of analytical grade.

2.2 Methods

2.2.1 Preparation of Buccal mucoadhesive patches

Buccal mucoadhesive patches of Chlorhexidine gluconate were prepared using HPMC K100M, HEC and PVA as mucoadhesive polymers. Glycerol was added as plasticizer. Preparation of all the patches using above mentioned polymers was done by solvent casting technique. [5,6]

A required quantity of polymer was gradually added, with constant stirring to the required volume of hot distilled water and the final volume was made by adding cold water. CHG and glycerol were incorporated in the polymeric solution. The medicated gels were left overnight in sonicator at room temperature to ensure clear, bubble-free gel. The gels were casted into glass Petri dish (9cm diameter) and allowed to dry at room temperature till a flexible film was formed. The dried films were cut into patches of 20mm diameter and packed in aluminium foil and stored in glass container maintained at room temperature.

2.2.2 Evaluation of Formulation

a. Mass uniformity and patch thickness [7]

Assessment of mass uniformity was done in five different randomly selected patches from each batch and thickness of the film was measured at ten different randomly selected spots using a digital micrometer screw gauge having least count 0.01 m (10 μm). The mean and the standard deviation were calculated. It is desirable that measured patch should have nearly constant and uniform thickness.

b. Content uniformity [7]

The patches were taken randomly from the batch and it is allowed to dissolve in 100 ml of distilled water contained in a 200 ml beaker. The beaker was stirred at a temperature controlled magnetic stirrer maintained at 37^0C for 3 hrs. The resultant suspension was filtered and analyzed for the drug content against the reference standard at 254 nm.

c. Mucoadhesive strength:[8]

The force required to detach the patch from the mucosal surface was expressed the mucoadhesive strength. The lab scale apparatus previously reported by Parodi et.al with sheep small intestine mucosa was used.

For determination of mucoadhesive strength, the mucoadhesive patch was fixed to a platinum lamina using cynoacrelate adhesive. A piece of sheep intestinal mucosa, 3 cm long was also glued to the platform. The exposed patch surface was moistened with distilled water and left for 30 sec. for initial hydration and swelling. The platform was then raised upward until the hydrated patch was brought into contact with the mucosal

surface. On the right pan, a constant weight of 5 g as added at 2 min interval the total weight required for complete detachment of the patch was recorded and the mucoadhesive strength was calculated.

d. Moisture absorption [1]

The patches were sharply cut using fabricated mould in 2 cm^2 area. These circular pitches of patch were stored in clean desicators for 48 hrs. These pieces were weighed accurately and weight was noted as initial dry water of the patch. This patch pieces were transferred in the desicators containing saturated solution of sodium bromide, ammonium chloride and potassium dichromate having (58%, 79% and 98% relative humidity) respectively and were weighed every 24 hours for few days to calculate the percent moisture content.

e. Surface pH [5]

Surface pH of the patch is essential to study expected mucosal irritation after application of patch to buccal mucosa. The randomly selected buccal patches from each batch were selected and were let to swell for 2 hrs. on the surface of agar plate prepared by dissolving 2% m/v agar in warm isotonic buffer of pH 6.75 under stirring and then pouring the solution into a petri dish till gelling at room temperature. The surface was measured by means of a pH paper placed on the surface of the swollen patch.

f. Folding endurance test [5]

Folding endurance of the patch is essential to study elasticity of the patch during storage. The folding endurance of the patches was determined by repeatedly folding one patch at the same place till it broken or folded upto 300 times which is considered to reveal good film properties.

g. *In vitro* release study [5]

The in vitro drug release study was performed using Keshary-chain diffusion cell using distilled water as dissolution medium maintained at 37 ± 0.5^0C. Cellophane membrane was used as the semi permeable diffusion membrane.1 ml of sample was withdrawn at the interval of 2 hrs from receptor compartment maintaining sink condition. The samples were analyzed by UV spectrophotometry at 254 nm after suitable dilutions.

Table 1: Formulations of Buccal Mucoadhesive Patches of CHG

Batch No.	**Quantity %w/v**								
	A1	**A2**	**A3**	**B1**	**B2**	**B3**	**C1**	**C2**	**C3**
CHG	2	2	2	2	2	2	2	2	2
HPMC K 100M	0.5	1	1.5	-	-	-	-	-	-
HEC	-	-	-	10	10.5	11	-	-	-
PVA	-	-	-	-	-	-	9.5	10	10.5
Glycerol	1	1	1	5	5	5	5	5	5
Distilled water	Up to 30 ml								

3. Result and Discussion:

a. Mass uniformity and patch thickness

As depicted in table 2, formulations buccal mucoadhesive patches of CHG exhibit good uniformity in the mass as well as thickness. The thickness of patches varied from 0.2 mm to 0.88 mm which can be considered as a comfortable thickness for better patient compliance.

b. % Drug Content:

All the formulations were showing percent drug content ranging from 96 to 102%. Thus the prepared batches comply for the content uniformity.

Table No. 2: Evaluation Parameters of Buccal Mucoadhesive Patches of CHG

Batch Code	Mucoadhesive strength (gm)	Weight mg/2cm^2	Thickness (mm)	% drug content	Surface pH	Moisture uptake	Folding endurance
A1	139.25±0.96	74.17±0.04	0.2±0.01	97±1.2	5.52±0.13	27.66	270.5±0.55
A2	155.5±1.29	106.3±0.09	0.25±0.00	101±0.55	5.46±0.05	28.12	272±0.45
A3	172.75±2.06	107.9±0.05	0.28±0.01	102±0.18	5.34±0.05	29.16	274±0.45
B1	250.5±2.38	203.8±0.04	0.8±0.01	98±1.1	5.50±0	24.03	293.8±1.1
B2	274.5±2.06	265.1±0.04	0.79±0	101±0.45	5.46±0.05	27.07	296.6±0.89
B3	285.25±2.36	290.1±0.08	0.82±0	96±0.55	5.42±0.11	29.57	298.6±0.89
C1	513±2.45	203.1±0.08	0.79±0	99±0.25	5.40±0.11	14.77	282.2±0.45
C2	535.5±3.11	240.1±0.09	0.81±0.01	98±1.24	5.50±0	19.58	286.4±0.89
C3	545.25±4.35	280.9±0.05	0.88±0.01	96±2.15	5.50±0.05	16.72	289.4±0.55

c. Mucoadhesive strength:

The most important parameter for the preparation of buccal mucoadhesive patch is mucoadhesive strength. The batches showed force of mucoadhesion varying in a range of 155.5 gm to 545.25 gm. It can be observed that the maximum mucoadhesive strength is exhibited by PVA. HPMC K100M shows satisfactory but less mucoadhesion compared to other polymers which can be attributed to its lower concentration in the formulation than that of other polymers. But the use of higher concentration is having limitations in preparation of patches like patch molding, integrity and drying. The results of mucoadhesion of all three polymers also show that the mucoadhesion is proportionately dependent on the concentration of polymer used.

d. Moisture absorption

The mechanism of mucoadhesion is dependent on the hydration of the mucoadhesive polymer. Hence it is important to study the moisture sorption capacity of the mucoadhesive polymer. Also the parameter influences the drug release pattern of the formulation. It was observed that the moisture uptake of the polymers was ranging between 14.77 to 29.57 %. PVA showed minimum while HPMC K100M is having maximum moisture sorption.

e. Surface pH

Surface pH of the patch is essential to study expected mucosal irritation after application of patch to buccal mucosa. The surface pH values of the prepared formulations were ranging from 5.4 to 5.52, which is non irritant at buccal environment.

f. Folding endurance test

Folding endurance of the patch is essential to study elasticity of the patch during storage. All the patches demonstrated a good folding endurance varying from 270.5 to 298.6.

g. *In vitro* release study

Fig no.1 shows *in vitro* drug release profiles of the prepared formulations. It was observed that patches with HPMC K100M released the drug over a period of 3 hr, while HEC and PVA sustained the release upto 4 hrs. The sustained release effects were proportionately dependent on the polymer concentration.

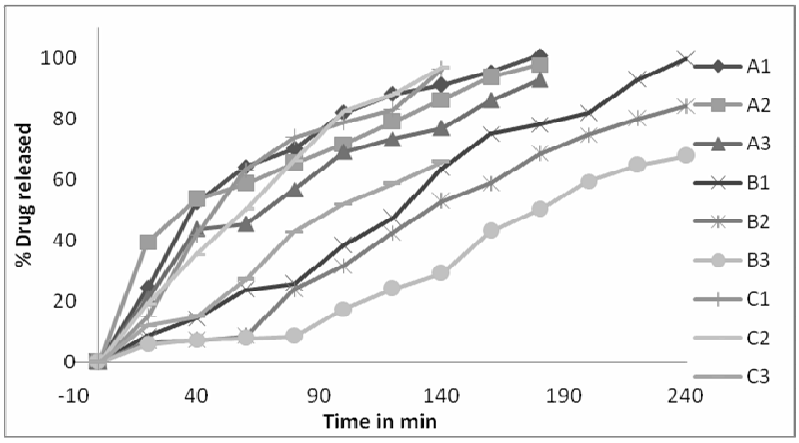

Fig. 1: Dissolution profile of buccal mucoadhesive patches

4. Conclusion:

Buccal mucoadhesive patch of CHG was prepared with the objective of better oral care. The patches were formulated with three mucoadhesive polymers vz. HPMC K100M, HEC and PVA. It was observed that the prepared patches were exhibiting good thickness, weight and content uniformity. The folding endurance was also satisfactory. The patches showed good mucoadhesion characteristics and sustained drug release. Thus it can be concluded that the patches can be helpful for the effective management of oral hygiene with sustained and localized release of Chlorhexidine Gluconate.

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