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DEVELOPMEMENT OF MUCOADHESIVE BUCCAL PATCH CONTAINING ACECLOFENAC: IN VITRO EVALUATIONS

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ABSTRACT: Mucoadhesive buccal patch of Aceclofenac were prepared using polymer like Gelatin, Poly Sodium CMC and Poly Vinyl Alcohol. Eight formulations were prepared with varying the concentration of Poly Sodium CMC and evaluated for various parameters like weight variation, patch thickness, volume entrapment efficiency %, and measurement of % elongation at break, folding endurance, i*n vitro* mucoadhesive time, *in vitro* release and stability study. The formulations showed a sustained release. The F5 formulation containing Aceclofenac 6%, Gelatin 4.5%, Poly Sodium CMC 5.5%, Propylene Glycol 5%, Poly vinyl Alcohol 2.5% and Distilled Water up to 100%, showed a release of 88.4% after 8 hours. The Aceclofenac stability studies were performed at 40 ± 2 ^{0}C / 75 ± 5% RH. Among the eight formulation, F5 formulation showed maximum desired properties release.
Key words: Aceclofenac, Buccal patch, Mucoadhesion, Gelatin.

INTRODUTION

The interest in novel rout of drugs administration occurs from their ability to inhance the bioavaibility of the drugs impaired by narrow absorption windows in the gastrointestinal tracts .Drugs delivery via the buccal routs using bioadhesive dosage forms offers such a novel routs of drugs administration. This route has been used successfully for the systematic delivery of number of drugs candidates[1-5] .Problems such as high first pass metabolisms and drugs degradation in the gastrointestinal tract can be circumvented by administrating the drug buccal routes[6,7]. Moreover, buccal drug delivery offers safe and easy method of drugs utilization, because drug absorption can be promptly terminated in case of toxicity by removing buccal dosage form from buccal cavity.

Aceclofenac, a new NSAID posses good anti-inflammatory, analgesics and anti-pyretic, used for treatment of treating condition like osteoarthriritis, rheumatoid arthritis, dental pain and other rheumatoid disorder. Its is highly protein bound and posses short biological half life of 4-5 hours, which makes it's an ideal candidate for administration by buccal routs the effectiveness of mucoadhesive formulation is greatly determined by the nature the polymer composition used[8].

In the presented study, an attempted was to formulate mucoadhesive patch of Aceclofenac using PEG, PVA, and gelatin by solvent casting method.

MATERIALS AND METHODS

MATERIALS

Aceclofenac was gifted by Alkem Laboratories Limited, Mumbai. Gelatin, Poly-Sodium CMC and Polyvinyl Alcohol was purchased from Loba Chemicals. All chemicals used were of analytical grade.

METHODS

Preparation of Mucoadhesive Patches

Mucoadhesive patch were prepared by solvent casting method. All ingredients were accurately weighed and mixed by trituration in glass pestle and mortal. The mixture was then added gradually to magnetically stir solvent system containing the plasticizer. Stirring was continued until a clear solution was obtained. The solution was then transferred quantitatively to petri-dish (glass) diameter 6cm .The petri-dishs were covered with inverted funnels to allow controlled evaporation of the solvents. These were lefts undisturbed upon temperature (20-25^{0}C) for one to two days depending upon the solvent system used. Small patches of size 15 mm and 20mm diameter, 0.2 to 0.3 mm thick were carefully pull out from the petri-dishes.

Table 1- Various Formulation for Mucoadhesive Buccal Patches

Sr. No.	Ingredient (w/v)	Formulation code							
		F1	F2	F3	F4	F5	F6	F7	F8
1	Aceclofenac	6%	6%	6%	6%	6%	6%	6%	6%
2	Gelatin	4.5%	4.5%	4.5%	4.5%	4.5%	4.8%	5%	5.5%
3	Poly Sodium CMC	3%	3.5%	4%	4.5%	5.5%	6%	6.5%	7%
4	PEG	5%	5%	5%	5%	5%	5%	5%	5%
5	PVA	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
6	Distilled water	78%	77.5%	77%	76.5%	76%	75.2%	75%	74%

EVALUATION OF MUCOADHESIVE PATCHES.

Weigh variation

Weigh variation was tested by comparing the averages weighed of 10 different randomly selected patches from each batch with individual patch

Patch thickness

Patch thickness was measured at 5 different randomly selected spots using a screw gauge.

Volume entrapment efficiency %

Volume entrapment efficiency % is volume uptake by capacity by buccal capacity of fluid (saliva) by buccal patches after adhesion into the buccal cavity. Mucoadhesive patch were weighed individually (X_0) and placed separately in 2% agar gel plates and incubated at $37^0C \pm 1^0C$. After 90 min. the final weight of the patch (X_T) were noted and the volume entrapment efficiency was using the following formula (Nafee N A.; et al 2003).

Volume entrapment efficiency % = $(X_T - X_0)\ 100/X_0$

Where X_0 = initial weight of patch, X_T = final weight of patch (after 90min.)

Measurement of the % elongation at break

The initial length of the patch was measured on scale and applying the force the patch unit the patch was broken and calculated the % elongation of patch by using the following formula

% Elongation at break = Increase in length x 100/ Initial length

Surface pH

The patches was allowed to swell then in contact with 0.5 ml of distilled water (pH 6.5±0.5) for one hour at room temperature and pH was noted down by bringing electron in contact the surface the pH , allowing it equilibrate for 1 minute[9].

Folding endurance

Folding endurance of the patches was determined by repeatedly folding one patch at 180^0 angle of plane at same plane till it broke or folded to 200 time without breaking[10] .

***In vitro* mucoadhesive time**

In vitro mucoadhesive time was measured (n=3) after application of the patches onto freshly cut sheep buccal mucosa. The fresh buccal mucosa was fixed in the inner side the beaker, above 2.5 cm from the bottle, with cynoacrylate glue. One side of the each patch was wetted with one drop of isotonic phosphate buffer pH 6.8 and pasted to the sheep buccal mucosa by applying the small force with a fingertip for 30 seconds. The beaker was filled with 500ml of isotonic phosphate buffer 6.8 and was kept at 37 ± 1^0C. After 2 min, a 50 rpm string rate was applied to simulate the buccal cavity environment. The time required for the patch to detach from the sheep buccal mucosa was recorded as mucoadhesive time[11].

***In vitro* release**

In vitro permeation studies were carried out in an all glass modified two-chambered diffusion cells. The lower side of upper compartment was completely closed tied membrane of goat was kept at 34^0C[7].

The buccal mucosa was kept in saline solution for the prevention of damage the cells. The appropriate size 2 cm^2 was cut down and fixed in between the lower surface the diffusion cell i.e. on the mouth of receptor compartment and was kept fixed with in donor compartment , thus by incorporating the PBS solution in the donor compartment which is having 1 ml capacity the drug release phenomenon was yet started . the lower chamber of the apparatus had small volume compartment (60ml) and liquid in it was string using a steel coated needle at 100 rpm , the two chamber were tightly and cell connected by flow maintaining the temperature at 37 ± 1^0C.

Stability study

The stability study of optimized mucoadhesive patch formulation was performed at 40^0C 37 ± 5^0C & 75±5% RH for three months. The value of all parameter after three months remain same as their values and minor changes occur in value of volume entrapment efficiency, % elongation & %drug release after 8 hour which was considerable(Jean T.G. et al)

RESULT AND DISSSION

The various formulation of mucoadhesive patches prepared by varying the concentration of one or more ingredients (Table -1) and evaluated for various parameter .All the eight mucoadhesive patch formulation

comply with referred values excepts F1 &F2 for %elongation parameter (Table-2). The folding endurance, mucoadhesive time, %drug release (after 8hrs) were maximum i.e. 325, 268, 88.4 respectively in F5 formulation. Based on this parameter F5 formulation was as optimized formulation.

The surface pH of all mucoadhesive patch formulation with in the range 5.83 to 7.2 but F1, F2, F3, F4 formulation does not comply with referred values i.e. 6.2 to 7.2. The F5 formulation had pH 6.73 that was almost near to pH (7.0) & hence expected to be non-irritant to buccal mucosa (Table -2)

Conclusion

On the basis of above studies patch formulation F5 comprises of galtin 4.5 %, poly sodium CMC 5.5%, Propylene glycol 5%, Poly vinyl Alcohol for stability drug release, folding endurance and mucoadhesive time.

Table 2: Optimization of Mucoadhesive Patch formulation (*Optimized formulation)

Sr. No.	Parameter	Referred value	F1	F2	F3	F4	F5*	F6	F7	F8
1	Weight variation	Average ± 25mg	200	203	201	203	209	206	200	201
2	Patch thickness(mm)	Uniform	0.90	0.93	0.95	0.97	0.98	0.92	0.94	0.92
3	Volume entrapment efficiency (%)	Not less than 1.5%	3.2	2.9	3.19	3.6	2.8	2.6	2.6	3.0
4	%Elongation at break	Not less than 25%	11.2	18	22.5	22.5	36	37.6	38	34
5	pH	6.2 - 7.0	6.16	6.06	5.83	7.2	6.73	6.23	6.3	6.7
6	Folding endurance	Not less than 250	224	255	275	300	325	311	289	260
7	Mucoadhesive time (min.)	Above 180 min	186	213	230	248	268	240	214	197
8	% Drug release after 8 hrs	Above 75%	76	83	85.6	87	88.4	82.5	80	77.5

Drug release study was performed for various mucoadhesive patch formulation and results are show in Fig no.1. All formulation showed more then 75% of drug release after 8hrs. Among them, F5 formulation shows maximum %release i.e. 88.4% as compared to other.

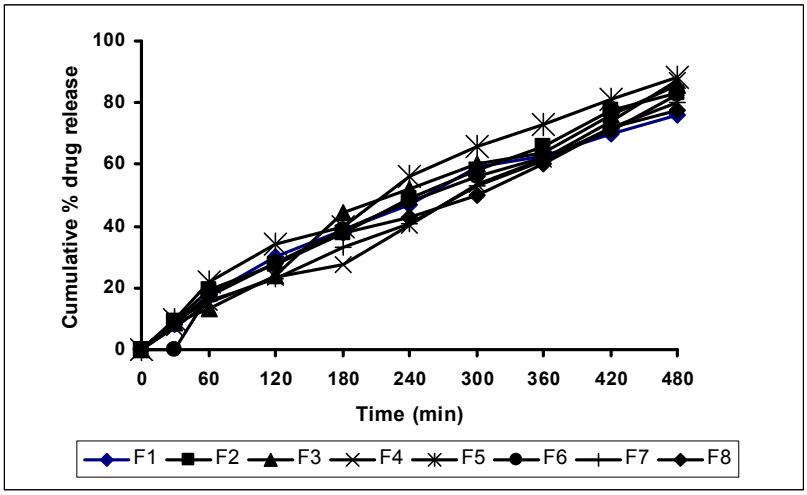

Fig no.1: Cumulative % Drug Release of Various Mucoadhesive Patch

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