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Development and Evaluation of Mucoadhesive Tablet of Acelofenac by using Different Mucoadhesive Polymer

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ABSTRACT

The objective of this study is to design and evaluate the mucoadhesive tablet prepared by different mucoadhesive polymer. In the present work, the mucoadhesive tablet of Acelofenac was prepared by using HPMC, sodium carboxy methyl cellulose, and combination of both polymers. The nine formulations were prepared in drug polymer ratio of 1:25, 1:50, 1:75 the results of angle of repose were ranged between 15.05-27.47, which indicates good flow properties of powder, carr's index values were found to be in the range of 4.16 % to 10.48 %. These findings indicated that the powder mixture of all 9 batches of formulation exhibited good flow properties. Tablets were subjected for evaluation of uniformity of weight, hardness, friability, drug content uniformity, swelling behavior, release rate study, mucoadhesive study. The in-vitro drug release of F8formulation exhibits complete release of Acelofenac with nonfiction first order release kinetic. The formulation F8 exhibited good mucoadhesion property. From the study it can be concluded that the combination of HPMC and sodium CMC used as mucoadhesive sustained release tablet.

Keywords: *HPMC, Sodium CMC, Mucoadhesive tablets.*

INTRODUCTION

Acelofenac is Non-Steroidal Anti-Inflammatory Drug (NSAID). It is a phenylacetic acid derivative showing anti-inflammatory and analgesic properties, is mainly used in the treatment of osteoarthritis, rheumatoid arthritis, post-traumatic pain, unclosing spondylitis, etc. Acelofenac is rapidly and efficiently absorbed after oral administration, but has short biological half-life of 4-4.3 h. Thus frequency dosing is necessary to sustain the drug also improves the safety and efficacy of the medication, adverse effects like gastrointestinal disturbances, peptic ulceration and gastrointestinal bleeding also. To overcome the demerits of a conventional dosage form, a suitable mucoadhesive drug delivery system was designed [1-4]. The present study was aimed to formulate and evaluate oral controlled release mucoadhesive tablets of Acelofenac by using different mucoadhesive polymer in different concentration. The aim of any research is to deliver a bioactive fraction to exact location of body and shows its maximum therapeutic response. Mucoadhesive formulations have a vast scope of applications, for controlled drug and site-specific drug delivery have made rapid advances. Though it is rapidly absorbed after oral administration, while it is completely absorbed from the gastrointestinal tract. Mucoadhesive drug delivery systems are delivery systems, which utilize the property of bioadhesion of certain polymers Bioadhesion is defined as an ability of a material to adhere a particular region of the body for extended period of time not only for local targeting of drugs but also for better control of systemic delivery [5]. Controlled release formulation describes sustained action along with its predictability and reproducibility of release of drug ingredients from the drug delivery system. Out of drug delivery systems, the mucoadhesive drug delivery system is more reliable than traditional drug delivery systems. Bioadhesive microspheres have advantages such as efficient absorption and enhanced bioavailability of drugs owing to a high surface-to-volume ratio, a much more intimate contact with the mucus layer, and specific targeting of drugs to absorption site [6]. Mucoadhesion, an interfacial phenomenon, is based on two materials, one of which is mucus layer of mucosal tissue to which the drug is held together by means of interfacial forces for prolonged period of time. Control release system ensures localization of drug in a particular site to improve and increase the bioavailability [7]. Mucoadhesion as a means of influencing the duration of contact of medicinal formulations with mucous membranes immediately became a subject of interest to technologists. Hence, in the present investigation an approach was made to the development of mucoadhesive Acelofenac dosage forms which will sustained the drug action at the exact target site.

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MATERIALS AND METHOD

Materials:

Acelofenac was gifted by Fine Lab as a free gift sample. Microcrystalline Cellulose, Hydroxy Propyl Methyl Cellulose, Sodium Carboxyl Methyl Cellulose was purchased from research lab fine chem. industry. All other reagents and chemicals used were of analytical reagent grade

Methodology: [8]

Mucoadhesive tablet of Acelofenac was prepared by wet granulation method by using HPMC, sodium carboxymethyl cellulose and combination of both polymers. Weigh the intracellular ingredient (HPMC, Sodium CMC, and Microcrystalline Cellulose) accurately of required quantity. Pass the Acelofenac through mesh no 80. Mix the intracellular ingredients with Acelofenac in a geometric proportion. Add a starch paste as binder. Pass it through mesh no.10 & air dry the granules. Pass the granules through mesh no. 20, supported on mesh no. 40.Mix 15% fine & other extra granular ingredient (TALC & MAGNESIUM STEARATE) with the granules. Formulation with various mucoadhesive polymers is given in **Table 1**.

Table No. 1: Formulation of Acelofenac sodium using different mucoadhesive polymer

	HPMC			Sodium CMC			HPMC+Sodium CMC		
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Acelofenac	7gm	7gm	7gm	7gm	7gm	7gm	7gm	7gm	7gm
Polymer	1.75gm	3.5gm	4.5gm	1.75gm	3.5gm	4.5gm	3.5gm	7gm	9gm
MCC	8.54gm	6.93gm	5.39gm	8.54gm	6.93gm	5.39gm	17.08gm	13.86gm	10.78gm
Talc	0.07gm	0.07gm	0.07gm	0.07gm	0.07gm	0.07gm	0.07gm	0.07gm	0.07gm
Magnesium stearate	0.14gm	0.14gm	0.14gm	0.14gm	0.14gm	0.14gm	0.14gm	0.14gm	0.14gm

Evaluation Test Procedure:

Flow Properties:

I. Flow rate:

Tip of the funnel is closed with butter paper supported by finger tip & funnel is filled with 5 gm of powder. Finger is then removed, & the time required for powder to pass through funnel completely is noted down.

Formula:- ***Flow rate= weight(gm)\ time(sec.)***

II. Percentage compressibility: (CARR'S INDEX):

Take the 5gm powder in dry measuring cylinder is mechanically tapped on plain uniform surface at constant velocity. Note the poured volume & also after 3 times & 50 times tapped volume of powder & calculate density.

Formula:- ***% Compresibility=tapped bulk density- initial bulk density\tapped bulk density*100***

Table No. 2: Standard value of powder flow of CARR'S index test

S. No.	CARR'S index	Type of flow
1	5-15	Excellent flow
2	12-18	good
3	18-23	satisfactory
4	23-35	poor
5	36-38	Very poor
6	More than 40	Extremely poor

III. Compressibility index: (porosity):

Take 5 gm of powder in dry measuring cylinder & placed on mechanical device. Note the poured volume & tapped volume after 50 times tapped.

Formula:- ***Compressibility index (I) = (1-vol. after tapping\vol. before tapping)*100***

IV. Hausner's ratio:

Hausner's ratio is calculated by using poured &tapped volume of powder in dry measuring cylinder.

Formula:- ***Tapped density\ Poured density***

V. Angle of repose: [9]

Take 2 gm of powder in dry funnel, attach at a height top 2cm of a paper, and remove the finger from tip in order to fall of powder. Then carefully make outline to the pile, take 3 diameters &calculated mean diameter, divide by 2 we get the radius(r). Also find out the height of pile.

Formula:- ***Tan θ = 2h\D***

Post Compression Parameters: [8]

Tablet Thickness:

Thickness was measured using a calibrated screw gauge. Three tablets of each formulation were picked randomly and thickness was measured individually.

Hardness:

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling, the hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets was determined.

Friability:

Roche friabilator was used for testing the friability. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm. After 4 min., the tablets were weighed and the percentage loss in tablet weight was determined.

$$\% \text{ loss} = \frac{\text{Intial wt. of tablet} - \text{Final wt. of tablet}}{\text{Intial wt. of tablet}}$$

Weight Variation:

Twenty tablets were weighed individually and the average weight was determined. Then percentage deviation from the average weight was calculated. Deviation should not exceed the values given in **Table 3**.

Table No. 3: Standard IP limit

Average weight of tablet	Percentage deviation
80 mg or less	±10
>80 mg < 250 mg	±7.5
250mg or more	±5

value in weight variation test

Determination of drug content: [11]

20 tablets was taken and powdered accurately. Powdered containing about 50mg of Acelofenac was taken and shake it with 50 ml methanol in volumetric flask .5ml of this solution was taken and diluted upto 100ml with methanol and absorbance was noted at 276nm.

Swelling Index: [12]

Swelling of tablet excipients particles involves the absorption of a liquid resulting in an increase in weight and volume. Liquid uptake by the particle may be due to saturation of capillary spaces within the particles or hydration of macromolecule. The liquid enters the particles through pores and bind to large molecule, breaking the hydrogen bond and resulting in the swelling of particle. The extent of swelling can be measured in terms of % weight gain by the tablet. For each formulation batch one tablet was weighed and placed in a Petri plate containing 25ml of 1.2 pH buffer solution. After each interval the tablet was removed from beaker, removes excess of buffer by using filter paper and weighed again up to 12 hours. Swelling index was calculated by using the following formula.

$$\text{Swelling index} = (w2.\ w1)/\ w$$

Mucoadhesion Test: [13, 14]

The mucoadhesive strength of tabletwas measure on the modified physical balance. The apparatus consist of the modified double beam physical balance in which the right pan has been replaced by glass slide with copper wire and additional weight, to make right side equal with left side pan. A taflone block of 3.8 cm diameter and 2 cm height was fabricated with an upward portion of 2 cm height and 1.5 cm diameter on one side. This was kept in beaker fill with buffer media 0.1 N HCl pH 1.2, which was then placed below right side of balance. The goat gastric mucus membrane was used as model membrane and pH a 1.2 solution was used as the moistening fluid. The goat stomach mucosa was kept in Tyrode solution at 37 C for 2 hours. The underlying mucus membrane was separated and washed thoroughly with a pH 1.2 buffer solution. It was then tied to Teflon-coated glass slide and thus slide was fixed over the protrusion in Teflon block using a thread. The block was then kept in beaker containing pH 1.2 buffer solution at the level that just touches the membrane. By keeping a 5g weight on the right pan, the two sides of the balance were made equal. The beaker with the Teflon block was kept below the left hand set up of the balances. The tablet was shrunk on to the lower side of the left hand side pan. The 5g weight from the right pan was then removed. This lowered the left pan along with the tablet over the membrane with the weight of 5g. This was kept undisturbed for 3 minutes. Then, the weight on the right hand side was slowly added in an

increment of 0.5g till the tablet just separated from the membrane surface. The excess weight on right pan i.e., total weight minus 5g was taken as a measure of the mucoadhesive strength. From the mucoadhesive strength, force of adhesion was calculated.

***In –Vitro* Dissolution Studies:** [12]

The release rateof Acelofenac from tablets were determined using USP dissolution testing apparatus (paddle type). The test was performed using 900 ml of phosphate buffer P^h7.2 at 37 ± 0.5°C and 50rpm for study. Aliquot volume of 5 ml was withdrawn at regular intervals. The samples were replaced with fresh dissolution medium. After filtration, the amount of drug release was determined from the standard calibration curve of pure drug.

RESULT AND DISCUSSION

Acelofenac mucoadhesive tablet were prepared by using different mucoadhesive polmer in different polymer concentration given in **Table 1**.

Evaluation of Mucoadhesive tablet of Acelofenac:
Micromeritic Properties:
Angle of Repose: The results of angle of repose were ranged between 15.05-27.47, which indicatesgood flow properties of powder.

Carr's Index: The carr's index values were found to be in the range of 4.16 % to 10.48 %. These findings indicated that the powder mixture of all batches of formulation exhibited good flow properties.

Table No. 4: Precompression evaluation of mucoadhesive tablets

Formulation	Flow Rate	Compressibility %	Compressibilt index	Hausner's Ratio	Angle of repose
F1	8gm/sec	6%	5.7%	1.063	26.10
F2	6.29gm/sec	8.23%	8.3%	1.089	23.94
F3	7.19gm/sec	10.48%	10.34	1.117	27.47
F4	8.29 gm/sec	4.16%	5.55	1.043	22.29
F5	8.30gm/sec	8%	8.33	1.08	19.29
F6	9.49gm/sec	8.85%	8.88	1.097	15.64
F7	9.54gm/sec	5.35%	5.55	1.056	15.05
F8	9.06gm/sec	10.20%	9.75	1.113	17.43
F9	5gm/sec	8.80%	7.7	0.923	20.25

Evaluation of Post Compression Parameters:
Tablet Hardness:

Hardness of the developed formulations F1 to F9 varied from 2.5 kg/cm2 to 3.00kg/cm2.

Friability:

Friability of the developed formulations varied from 0.004 % to 0.48 % loss which was less than 1% as per official requirement of IP.

Weight Variation:

The average weight of twenty tablets was calculated for each formulation which varied from 0.22gm to 0.26gm that complied the official requirement as per IP.

Uniformity of Drug Content: The drug content varied from 97.69 ± 0.13 % to 98.98 ± 0.43 % which was within the required limits.

Table No. 5: Post compression parameters

Formulation Code	Hardness Kg/cm²	Friability (% loss)	Weight variation (Gm)
F1	3	0.38	0.23-0.25
F2	2.5	0.40	0.23-0.25
F3	3	0.32	0.23-0.26
F4	3	0.40	0.23-0.25
F5	2.5	0.45	0.23-0.26
F6	2.5	0.48	0.23-0.26
F7	2.5	0.084	0.22-0.22
F8	3	0.004	0.23-0.25
F9	3	0.01	0.22-0.24

***Swelling index*:**

The swelling index was good when polymer in combination was used, swelling index of nine formulation was given in **Table 6**.

***Mucoadhesive test*:**

As the concentration of two combined mucoadhesive polymer increased the adhesion property of tablets were increase and mucoadhesive strength of 9 formulation was given in **Table 7**.

Invitro drug release:

From the invitro dissolution data, it was found that the drug release studies from all formulations containing HPMC and sodium carboxy methyl cellulose polymer was 80.21%, 90.45% and 90.31% hence the combination showed faster drug release and more mucoadhesioive property

Table No. 6: In vitro swelling study of prepared mucoadhesive tablets of Acelofenac:

F (Hrs)	1	2	3	4	5	6
1	24.81	26.11	30.9	39.9	45.0	50.2
2	25.20	27.21	32.2	40.1	47.0	52.3
3	27.90	35.40	39.0	45.2	50.0	55.4
4	26.10	30.20	35.0	41.2	48.25	51.45
5	27.30	29.41	33.4	42.2	50.2	54.4
6	30.20	39.56	45.5	50.4	55.1	59.0
7	30.40	35.20	37.0	44.9	51.4	55.6
8	28.40	33.20	37.48	45.2	51.2	56.20
9	35.20	40.44	47.28	52.00	55.0	58.4

Table No. 7: Ex-vivo mucoadhesive strength determination of Acelofenac

Formulation code	Mucoadhesive strength
1	15.50
2	16.80
3	19.10
4	20.20
5	25.91
6	30.11
7	34.20
8	40.1
9	45.20

DISCUSSION

The mucoadhesive property of Acelofenac was increased by using different mucoadhesive polymer. As the concentration of mucoadhesive polymer increases the mucoadhesion property also increases. The percent yield, swelling index were high for all nine formulations. The mechanism of the release of drug from mucoadhesive tablet was first order and nonfiction. Hence Sustain release oral mucoadhesive tablets of Acelofenac can reduce dosing frequency and patient compliance.

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