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Research Article

Formulation and Evaluation of Novel Aceclofenac Matrix Tablet Using Natural Polymers

Rajesh Kumar[1], Dr. Vijay Sharma[2], Sunil Kumawat[3]

[1]Research Scholar, Goenka College of Pharmacy, Lachhmangarh, Sikar, Rajasthan.
[2]Professor, Goenka College of Pharmacy, Lachhmangarh, Sikar, Rajasthan.
[3]Associate Professor, Goenka College of Pharmacy, Lachhmangarh, Sikar, Rajasthan.

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Address for Correspondence: Rajesh Kumar
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Abstract:
The current study attempted to design and create Aceclofenac sustained release matrix tablets employing different proportions of *Hibiscus rosa-sinensis* mucilage, *Mimosa Pudica* mucilage as natural polymers and povidone.Aceclofenac is widely used as a centrally acting muscle relaxant; therefore, have been selected to prepare sustained release dosage forms.Different types of evaluation parameters were evaluated like appearance, thickness, diameter, weight variation, hardness, friability, drug content, in-vitro dissolution studiesand stability studies.Sustained release matrix tablets can improve patient compliance by lowering the total dose and dosing schedule, which can be extremely beneficial in the treatment of chronic illnesses.
Key words: Sustained release matrix tablet, friability, muscle relaxant.

Introduction

Matrix tablets is a promising approach for the establishment of extended-release drug therapy as tablets offer the lowest cost approach to sustained and controlled release solid dosage forms. Matrix tablets may be defined as the "oral solid dosage forms in which the drug or active ingredient is homogeneously dispersed throughout the hydrophilic or hydrophobic matrices which serves as release rate retardants".[1]

These systems release drug in continuous manner by dissolution-controlled and diffusion-controlled mechanisms. Two different release mechanisms are operative, either of which is zero-order erosion and decreasing surface area, and dissolution of coated particles, but the overall tablet release profile comprising the two mechanisms in sequence is nearly linear for most of the dose in the tablet.[2]

Aceclofenac

Aceclofenac is from the class of Non-Steroidal Anti-Inflammatory Drug (NSAID). It is a derivative of aryl acetic acid.The usual dose of aceclofenac is 100mg given orally twice daily. One tablet in the morning and the other in the evening. There is some evidence that the dose of aceclofenac should be reduced in patients with hepatic impairment and it is suggested that an initial daily dose of

100mg be used. Aceclofenac is a potent inhibitor of the enzyme Cyclooxygenase (COX), which is involved in the production of prostaglandins. Aceclofenac has shown to exert effect on a variety of mediators of inflammation. The drug inhibits the synthesis of inflammatory cytokines interleukin (IL)-1β and inhibits Prostaglandin E2 (PGE2) production.[3,4]

Materials and Methods

Aceclofenac, *Mimosa Pudica, Hibiscus rosa-Sinensis*, Micro crystalline cellulose, Povidone, Magnesium stearate, Talc, Iso propyl alcohol, Hydrochloric acid, these were the ingredients which were used in the formulation of aceclofenac matrix tablets.

Evaluation Parameters of Matrix Tablets[5,6,7,8,9]

After formulation of tablets, they are evaluated for various parameters. Prepared matrix tablets were evaluated for following parameters:

Appearance, Shape and Size

Appearance of prepared tablets was observed visually.

Dimension (thickness and diameter):

The thickness and diameter of tablets were important for uniformity of tablet size. The thickness and diameter of the tablets was determined using a vernier caliper. Ten tablets from each type of formulation were used and average values werecalculated.

Weight variation

This test is performed to check the uniformity of weight of the prepared tablets, as drug content is directly related to the weight of tablet. In this process, 20 tablets were weighed individually. The average weight of one tablet was calculated by taking average mean.

Hardness

Hardness of tablets is the amount of force needed to split them. Both Monsanto and Pfizer type hardness tester were used to determine the hardness of the formulated tablets. Tablets placed between the avanils and pressure applied. The hardness was calculated as kg/cm^2. Three tablets from each formulation were taken and average was calculated.

Friability

The friability of the tablet is determined using the friability test instrument. Friability is used to determine the amount to which tablets break during physical stress situations such as packaging, handling, transportation, and so on. The % weight reduction is estimated by comparing the pre- and post-operative weight of 20tablets.

The Roche friabilator was used to measure friability of the formulated tablets. Weight of 20 tablets was measured and placed in the friabilator chamber. The friabilator was rotated at speed of 25 rpm for 4 min. After completion of 100 revolutions, the tablets were weighted again and % weight loss is calculated, which corresponds to friability.

$$\%\, Friability = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

Drug content

The drug content was calculated by triturating ten tablets in a mortar with pestle to get fine powder. Powder equivalent to weight of one tablet was taken and was dissolved in distilled water. Measure the absorbance (after dilution, if required) of Aceclofenac at λmax using UV-Visible Spectrophotometer. The drug content was calculated by using standard calibration curve.

*In-vitro*Dissolution Studies

Dissolution studies of matrix tablets are performed to ensure sustained release of the drug (Aceclofenac) for longer duration. Dissolution studies of prepared matrix tablets were performed in two steps. Initially, Acid buffer pH 1.2 (corresponding to gastric environment) was used as dissolution media for initial two hours. Then, the dissolution media was replaced with Phosphate buffer pH 6.8 (corresponding to intestinal environment) as dissolution media for next ten hours. Paddle apparatus was used for dissolution studies at 50 RPM and $37^0 \pm 0.5^0$C.

Stability study:

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated sability studies are adopted.

ICH specifies the length of study and storage conditions

- Long-Term Testing: 25^0 C ± 2 C at 60% RH ± 5% for 12 Months
- Accelerated Testing: 40^0 C ± 2 C at 75% RH ± 5% for 6 Months

Result and Discussion

Appearance

Appearance of prepared tablets was observed visually and did not show any defect such as capping, chipping and lamination.

Table 1: Evaluation parameters: shape, diameter and average weight

Formulation	Shape	Diameter	Thickness	Average weight (mg) (Mean±S.D.*)
F1	Round	8.0 mm	4.0 mm	302.92±0.86
F2	Round	8.0 mm	3.9 mm	298.83±0.56
F3	Round	8.0 mm	4.0 mm	302.12±0.67
F4	Round	8.0 mm	4.0 mm	300.61±0.52
F5	Round	8.0 mm	4.0 mm	301.98±0.51
F6	Round	7.9 mm	4.0 mm	299.98±0.75
F7	Round	8.0 mm	3.9 mm	301.86±0.62
F8	Round	8.0 mm	4.0 mm	299.76±0.68
F9	Round	8.0 mm	4.0 mm	300.02±0.50

All the tablets prepared were round in shape. Diameter was found to be range in 7.9 to 8.0 mm and range thickness were found to be 3.9 to 4.0 mm for all the formulations.A tablet is designed to contain a specific amount of drug. When the average mass of the tablet is 300 mg the pharmacopeial limit for percentage deviation is ± 5%. The percentage deviation from average tablet weight for all the tablet was found to be within the specified limits and hence all formulations complied with the test for weight variation according to the pharmacopeial specifications.

Table 2: Evaluation parameters: average hardness, friability and drug content

Formulation	Average Hardness (kg/cm^2) (Mean± S.D.*)		Friability (%)	Drug content(%w/w)
	Monsanto type	Pfizer type		
F1	5.7±0.3	5.4±0.2	0.67±0.30	98.86±0.06
F2	5.8±0.2	5.8±0.3	0.64±0.20	98.55±0.09
F3	6.0±0.2	6.1±0.3	0.62±0.30	98.25±0.15
F4	6.3±0.5	6.3±0.3	0.61±0.10	98.85±0.05
F5	5.9±0.3	5.9±0.2	0.64±0.30	98.64±0.16
F6	6.0±0.2	6.0±0.2	0.63±0.20	98.17±0.11
F7	6.1±0.2	6.1±0.3	0.61±0.20	98.88±0.23
F8	6.2±0.3	6.2±0.5	0.58±0.10	99.09±0.12
F9	6.5±0.2	6.5±0.4	0.51±0.10	99.85±0.14

The hardness of tablets was found to be in the range of 5.4±0.2 kg/cm^2 to 6.5±0.4 kg/cm^2. This indicates good tablet strength.The friability of prepared tablets was found to be 0.51±0.10 to 0.67±0.30 which are less than the standard limits (1%). It may be concluded that the prepared matrix tablets pass the friability test.The % drug content of prepared tablets was found to be 98.17±0.11 - 99.85±0.14 %, which is within the prescribed limits. Therefore, the prepared matrix tablets pass the test for drug content (content uniformity).

***In-vitro* Dissolution Studies**

Table 3: Dissolution profile of Aceclofenac matrix tablet formulations

Time (Min.)	Cumulative % Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	6.43	7.71	6.43	5.57	9.86	8.14	7.29	5.57	4.29
2	17.15	12.44	11.15	8.58	22.73	14.15	13.29	13.29	7.72
3	27.03	23.17	23.16	15.87	29.61	26.6	23.17	21.02	12.87
4	41.20	35.62	29.19	22.75	41.64	37.77	28.33	24.90	17.60
5	66.10	42.94	36.93	31.77	55.4	45.95	38.22	31.79	23.19
6	77.75	51.99	43.83	37.81	64.46	54.15	44.69	37.82	26.64
7	84.69	61.05	52.02	48.99	69.68	61.92	52.03	49.01	31.39
8	92.50	67.97	59.80	57.19	77.47	67.13	58.94	54.63	36.14
9	96.03	74.48	66.29	61.97	84.41	72.35	65.01	61.12	40.46
10	98.60	80.48	72.72	68.82	91.70	77.06	71.44	67.98	44.32
11	99.24	88.79	78.44	72.40	94.89	84.94	78.45	73.69	49.13
12	99.78	93.18	84.96	80.62	97.57	91.47	83.68	78.06	52.18

In case of F1, the release profile, it was showing 99.78% release in 12 hours. In case of F2, the release profile, it was showing 93.18% release in 12 hours. In case of F3, the release profile, it was showing 84.96% release in 12 hours. In case of F4, the release profile, it was showing 80.62% release in 12 hours. It observed that increasing the *Mimosa Pudica* mucilage concentration resulted in significant

decrease in the percentage Aceclofenac released.

In case of F5, the release profile, it was showing 97.57% release in 12 hours with slower release. In case of F6, the release profile, it was showing 91.47% release in 12 hours with slower release than F5. In case of F7, the release profile, it was showing 83.68% release in 12 hours. In case of F8, the release profile, it was showing 78.06% release in 12 hours. It observed that increasing the *Hibiscus rosa-Sinensis* mucilage concentration resulted in significant decrease in the percentage Aceclofenac released. In case of F9, the release profile, it was showing 52.18% release in 12 hours it concludes F9 has better sustained release than the other formulations. And it was observed that higher polymer levels result in slower release rates as evident from the in-vitro drug release profile of batches when compared to other formulations. Based on the in-vitro drug release data, the formulation F9 was selected as the optimized formulation. Hence the formulation F9 was selected for the further stability study.

Stability study:

Table 4:- Stability study of best formulation F9.

Characteristic	Initial	1st Month	2nd Month	3rd Month
Hardness (kg/cm2)	6.5±0.2	6.5±0.3	6.4±0.2	6.3±0.3
% Friability	0.51±0.10	0.50±0.10	0.50±0.20	0.49±0.20
Drug content (%)	99.85±0.14	99.24±0.08	98.92±0.08	98.81±0.13
***In vitro* drug release after 12 hrs**	52.18	52.18	51.75	51.33

After 3 months of stability studies at 40°C ± 2°C / 75% RH ± 5%, the results in the above table given that the optimized formulation F9 had shown satisfactory stability. Only there were minimal deviations which are acceptable.

Conclusion

In present investigation an attempt has been made to design and develop Aceclofenac sustained release matrix tablets using various percentages of *Mimosa Pudica* mucilage, *Hibiscus rosa-sinensis* mucilage as natural polymers and povidone, as release retarding polymers. After compression parameters like Appearance, Thickness, Hardness, Weight variation, Friability, content uniformity and In-Vitro release studies were evaluated. Result of the present study demonstrated that hydrophilic polymers could be successfully employed for formulating sustained release matrix tablets of Aceclofenac. The investigated sustained release matrix tablet was capable of maintaining constant plasma concentration. This can be expected to reduced the frequency of administration and decrease the dose dependent side effects. The efficacy and safety of Aceclofenac tablet dosage form are expected to offer optimum therapeutic efficacy and improved patient compliance.

According to stability study it was found that there was no significant change in hardness, friability, drug content and in vitro dissolution of optimized formulation (F9). From the overall studies, it can be concluded that the formulation F9 was considered as best formulation by using data of evaluation parameters.

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