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DEVELOPMENT AND EVALUATION OF HARD GELATINE CAPSULE OF ACECLOFENAC DRUG

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ABSTRACT

The oral route is the one most frequently used for drug administration. Oral dosage forms are usually intended for systemic effects resulting from drug absorption through the various epithelia and mucosa of the gastrointestinal tract. Capsules are solid dosage forms containing drug and usually appropriate filler(s), enclosed in a hard or soft gelatin shell. Aceclofenac, Empty hard gelatin capsules, PEG 4000 and all other materials were obtained through commercial sources. Aceclofenac granules were prepared by wet granulation method. Specified quantity of Aceclofenac, micro crystalline cellulose and PEG 4000 will be weighed and mixed uniformly. Required quantity of alcohol drop wise incorporated to the blend. Wet granules will be passed through sieve #10 & air dried for 15 minutes. The dried granules will then be passed through sieve #22. Required quantity of magnesium stearate & talc were added to the granules. The prepared granules were then added to the Size #3 empty hard gelatine capsule. The formulation of granules of Aceclofenac is shown in Table 2. Aceclofenac was planned to formulate as an immediate release system. The prepared granules were evaluated for percentage yield, angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index. The hard gelatin capsule containing granules of aceclofenac were also evaluated for disintegration time, drug content and *in-vitro* drug release. Stability study shows that there was no significant change in disintegration time, drug content and *in-vitro* drug release of the formulation. Thus, formulation was considered optimized formulation for immediate release of Aceclofenac.

KEYWARDS: Aceclofenac, Hard Gelatin Capsules, PEG 4000.

INTRODUCTION

The oral route is the one most frequently used for drug administration. Oral dosage forms are usually intended for systemic effects resulting from drug absorption through the various epithelia and mucosa of the gastrointestinal tract. Compared with other routes, the oral route is the simplest, most convenient and safest means of drug administration. Disadvantages of this route include the relatively slow onset of action, the possibilities of irregular absorption and the destruction of certain drugs by the enzymes and secretions of the gastrointestinal tract. The most popular oral dosage forms are tablets, capsules, suspensions, solutions and emulsions.[1] Capsules are solid dosage forms containing drug and usually appropriate filler(s), enclosed in a hard or soft gelatin shell. The gelatin shell readily ruptures and dissolves following oral administration, and in most cases the drug is released from a capsule faster than from a tablet.[2] Hard gelatin capsules consist of two pieces in the form of cylinders closed at one end: the shorter piece, called the 'cap', fits over the open end of the longer piece, called the 'body. Both soft and hard gelatin capsules contain gelatin, water, colorants and optional materials such as process aids and preservatives; in addition, soft capsules contain various plasticizers. Capsules may also be manufactured from hydroxypropyl methylcellulose in order to produce a shell with low moisture content.[3]

The aim of the present study is to develop Hard gelatine capsule of Aceclofenac.

The purpose of the present work was aimed at the following objectives:

- ✓ The main objective of the present study is to produce the sustained release Aceclofenac capsules (75mg) of 8h release to reduce the dosing frequency.
- ✓ Optimization of procedure for sustaining drug delivery.
- ✓ Comparison of release profiles of capsules with the market formulations.

MATERIALS AND METHOD

Aceclofenac was obtained as a gift sample from Astron Pharma, Ahmedabad. Empty hard gelatin capsules were generous gift sample form Ligo Capsules, China. PEG 4000 and all other materials were obtained through commercial sources.

Formulation of granules of aceclofenac[4]

Aceclofenac granules were prepared by wet granulation method. Specified quantity of Aceclofenac, micro crystalline cellulose and PEG 4000 will be weighed and mixed uniformly. Required quantity of alcohol drop wise incorporated to the blend. Wet granules will be passed through sieve #10 & air dried for 15 minutes. The dried granules will then be

passed through sieve #22. Required quantity of magnesium stearate & talc were added to the granules.

Formulation of hard gelatine capsules of aceclofenac

The prepared granules were then added to the Size #3 empty hard gelatine capsule. The formulation of granules of Aceclofenac is shown in Table 1.

Table 1: Formulation of granules of aceclofenac.

S. No	Ingredients	Quantity Given (mg/capsule)
1.	Aceclofenac	50 mg
2.	Micro-crystalline cellulose	38 mg
3.	PEG 4000	6 mg
4.	Magnesium stearate	4 mg
5.	Talc	2 mg
6.	Alcohol	q.s.

Evaluation parameters

Evaluation of micromeritic properties of granules

1. Percentage yield[5]

The percentage yield of the granules was determined for drug and was calculated using the following equation:

$$\text{percent yield} = \frac{\text{actual yield}}{\text{theoretical yield}} \times 100\%$$

2. Angle of repose[5]

Angle of repose (α) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (*h*) was obtained. The radius of the heap (*r*) was measured and angle of repose was calculated:

$\alpha = \tan^{-1}(h/r)$

3. Bulk density[6]

Apparent bulk density (ρb) was determined by placing presieved drug excipients blend into a graduated cylinder and measuring the volume (Vb) and weight (M) “as it is”

$\rho b = M/Vb$

4. Tapped density[7]

The measuring cylinder containing a known mass of blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using following formula:

ρt = M/ Vt

5. Hausner's ratio[7]

Hausner's ratio is an index of ease of powder flow; it is calculated by following formula:

Hausner's ratio = ρt\ ρb

Where, ρt = Tapped density and ρb = Untapped bulk density

6. Carr's index[8]

The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility which is calculated as follows:

C = (ρt – ρb) / ρt * 100

Where, ρt = Tapped density and ρb = Untapped bulk density

Evaluation of hard gelatin capsule

1. Disintegration time[9]

One capsule was placed in each of six tubes of assembly and assembly was suspended in water. Discs were added to each tube, temperature was maintained at 37 ± 2°C and assembly was operated for 60 min.

2. Drug content[10]

Weigh an amount of the granules equivalent to 50 mg of aceclofenac was dissolved in 100 ml of phosphate buffer pH 6.8, filtered, diluted suitably and analyzed for the drug content at 246 nm using UV-visible spectrophotometer.

3. *In-vitro* drug release study[10]

The release rate of losartan potassium from granules was determined using IP Dissolution Test Apparatus Type II (basket type). Granules were first incorporated in empty hard gelatin capsule of size #3 and then placed in a dry basket at the beginning of each test. Lower the basket in the dissolution medium and apparatus was run at 50 rpm, The dissolution test was

performed using 900 ml of phosphate buffer pH 6.8, at 37 ± 0.5^{0}C and 50 rpm. 5 ml were withdrawn at time intervals of five minute for 60 minutes. This was maintained at same temperature, was added to the bulk. The samples were filtered through Whatman filter paper no. 41. Absorbance of these solutions was measured at 246 nm using UV-Visible spectrophotometer**.** Cumulative percentage drug release was calculated using an equation obtained from a standard curve (Figure 2).

4. Stability Study as Per ICH Guideline

Stablity study as per ICH guidelines were performed for one month under the conditions of 40°C ± 2°C 75 % RH ± 5%. The formulation was evaluated for disintegration time, drug content and *in-vitro* drug release.

RESULTS AND DISCUSSION

Spectroscopic studies

Aceclofenac standard graph: - A solution of 0.1mg/ml Atenolol was prepared and UV scan was taken between 200 to 400 nm. The absorption maximum was found to be 275 nm in simulated gastric fluid pH 1.4 and had good reproducibility.

Table No. 2: Standard graph of aceclofenac.

Concentration (µg/ml)	Absorbance (nm)
0	0
2	0.093
4	0.161
6	0.245
8	0.331

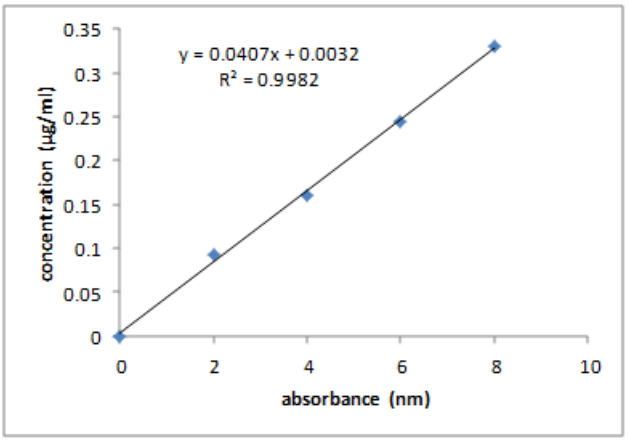

Figure no. 1: Standard curve of aceclofenac.

In the present study, hard gelatin capsules containing granules of aceclofenac were prepared by wet granulation method. For each batch, blend of drug and excipients were prepared and evaluated for micromeritic properties shown in Table 3.

The percentage yield was found to be in the range of 79.72 ± 0.402 to 79.89 ± 0.382. Angle of repose was found to be in the range of 18.23 ± 0.106 and 19.22± 0.856. Bulk density was found to be between 0.456± 0.012 and 0.490± 0.008 gm/cm3 and tapped density between 0.516± 0.003 and 0.576± 0.012 gm/cm3 for all formulations. From density data % compressibility was calculated and was found to be between 12.603 ± 1.671% and 14.963 ± 3.010%. Hausner's ratio was found to be between 1.128± 0.022 and 1.170± 0.030. All the batches show the good micromeritic properties for wet granulation and hence granules were prepared by using wet granulation method.

Table 3: Evaluation of micromeritic properties of granules.

Batch No.	Percentage Yield (%)	Angle of Repose (θ)	Bulk Density (gm/cm3)	Tapped Density (gm/cm3)	Hausner's Ratio	Carr's Index (%)
1	79.89 ± 0.382	19.22 ± 0.856	0.456 ± 0.012	0.517 ± 0.003	1.128 ± 0.022	12.603 ± 1.671
2	78.84 ± 0.490	18.23 ± 0.106	0.463 ± 0.016	0.545 ± 0.005	1.163 ± 0.032	14.310 ± 2.407
3	79.72 ± 0.402	19.10 ± 0.92	0.490 ± 0.008	0.576 ± 0.012	1.170 ± 0.030	14.963 ± 3.010

All the readings are expressed as mean ± standard deviation (n=3)

Disintegration time

The disintegration time for hard gelatin capsule was found to be in the range of 2.54 ± 0.816 to 3.33 ± 0.471 min.

Table 4: Evaluation of fast disintegrating time.

Batch No.	Disintegration Time (sec)
1	2.60 ± 0.106
2	3.33 ± 0.471
3	2.54 ± 0.816

Drug content

The percentage drug content of all the optimized formulations were found to be between 98.59 ± 0.633% to 99.16 ± 0.575%, which was within the acceptable limits as per IP.

Table 5: Evaluation of drug content.

Batch No.	Drug Content (%)
1	99.03 ± 0.392
2	99.12 ± 0.575
3	98.59 ± 0.633

***In- vitro* drug release**

The % cumulative drug release of all the batches were shown in Figure 2. The results of disintegration time, drug content and *in-vitro* drug release were shown in Table 6.

Table 6: Evaluation of % cumulative drug release at 60 min.

TIME(Mins)	B1	B2	B3
0	0	0	0
10	16	15	18
15	26.2	27.1	27
20	31.8	43.2	39.1
30	48.9	62.8	51
40	66.1	71.6	62.2
50	85.3	89.9	80.5
60	99.7	99.6	99.4

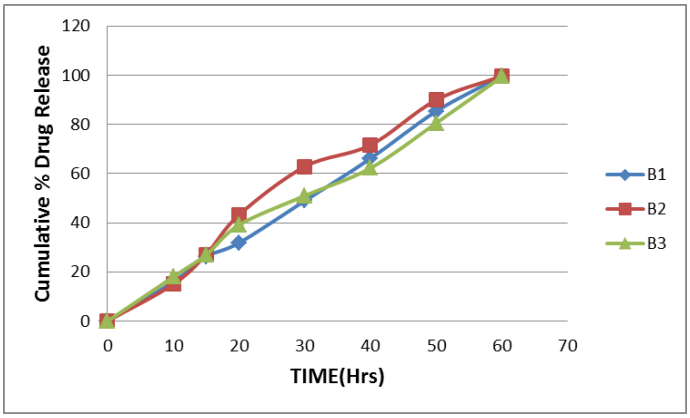

Figure no. 2: Dissolution graph for formulations B1, B2, B3.

Stability Study as per ICH Guideline

Stability study of hard gelatin capsule containing granules of Aceclofenac was done to see the effect of temperature and humidity on capsules during the storage time. Capsules were evaluated periodically (0 and 1 months) for disintegration time, drug content and *in-vitro* drug release. Stability study results show that there was no significant change in disintegration time, drug content and *in-vitro* drug release of the formulation shown in Table 7.

Table 7: Stability study results of formulation.

Test After Time (Months)	Disintegration TIME (Seconds)	Drug Content (%)	*In-vitro* Drug Release (%)
0	2.57	98.76	98.86
1	3.25	97.88	96.67

CONCLUSION

The aim of the present study was to develop an optimized formula for hard gelatin capsule containing granules of Aceclofenac. Aceclofenac was planned to formulate as an immediate release system. The prepared granules were evaluated for percentage yield, angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index. The hard gelatin capsule containing granules of aceclofenac were also evaluated for disintegration time, drug content and *in-vitro* drug release. Stability study shows that there was no significant change in disintegration time, drug content and *in-vitro* drug release of the formulation. Thus, formulation was considered optimized formulation for immediate release of Aceclofenac.

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