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A Novel Approach of Formulation & Evaluation of Tablet in Capsule Device for GI Protection Pain Management

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Abstract

This research article presents a novel approach in the formulation and evaluation of a tablet in capsule device aimed at providing GI protection and effective pain management. Key aspects include the development of Aceclofenac Extended-Release tablets and Misoprostol Immediate Release tablets, enclosed in a hard gelatin capsule. The study covers preformulation, formulation development, in-process quality control checks, and stability studies. Results indicate the combination dosage form offers advantages in safety, patient compliance, and therapeutic efficacy.
Keywords: tablet, capsule, formulation, aceclofenac, misoprostol

1. INTRODUCTION

Historically, the most convenient and commonly employed route of drug delivery has been by oral ingestion. Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. It is considered the most natural, uncomplicated, convenient, and safe route. Among the different oral dosage forms, tablets and capsules stand out as the most preferred options by pharmaceutical manufacturers, physicians, and patients (1). Tablets, which are solid dosage forms containing medicinal substances with or without suitable diluents, offer several advantages such as excellent physicochemical stability, accurate dosing, and ease of mass production with robust quality controls. Similarly, capsules, which are solid dosage forms where the drug is enclosed within a hard or soft soluble shell, provide versatile drug delivery options for powders and non-powder fillings such as tablets, capsules, and pellets (1, 2).

Solid oral dosage forms, such as tablets and capsules, have distinct advantages over other forms of medication. They are the most stable dosage form in terms of physical, chemical, and microbiological attributes, providing accurate, stable doses with the greatest precision and least content variability. They are also user-friendly, easy to handle, and carry, and have an attractive, elegant appearance. The manufacturing cost of tablets is relatively low, and their production speed is quite high, making them suitable for large-scale production. Furthermore, the packaging and shipping of tablets are comparatively easy and cost-effective. Tablets and capsules can also mask the unpleasant taste and odor of medications, reduce incompatibilities and deterioration due to environmental factors, and offer various branding possibilities through colored film coatings, different shapes, sizes, or logos (3).

However, solid oral dosage forms also come with certain disadvantages. Drugs that are amorphous in nature or have low-density characteristics are difficult to compress into tablets. Hygroscopic drugs are not suitable candidates for compressed tablets, and drugs with poor wetting properties, slow dissolution profiles, and high optimal gastrointestinal absorption may be challenging to formulate as tablets (4). Additionally, drugs with bitter tastes and objectionable odors require special treatments like coating or encapsulation, which may increase production costs. Capsules are not suitable for extremely soluble materials such as potassium chloride or highly efflorescent or deliquescent fill materials. Despite these challenges, the continued development and optimization of tablet and capsule formulations ensure that they remain a cornerstone of effective and reliable drug delivery systems (5).

The aim of this study is to formulate a combination dosage form of Aceclofenac Extended-Release tablets (200 mg) and Misoprostol Immediate Release tablets (200 mcg) enclosed in Size '0' elongated Hard Gelatin Capsules. This involves conducting a preformulation study to assess the compatibility of Aceclofenac and Misoprostol with various excipients, followed by the preparation of compact Aceclofenac ER tablets using hydrophilic polymers HPMC and Ceolus KG 1000, and Misoprostol IR tablets by direct compression. Comprehensive quality control checks and an accelerated stability study will be performed to ensure the efficacy, safety, and stability of the combination product under specified conditions.

2. METHODOLOGY

2.1 PRE-FORMULATION STUDIES

Preformulation studies is the first step in the rational development of dosage forms of a drug substance, It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of preformulation studies is to generate information useful to the formulator in developing stable and bioavailable dosage forms that can be mass produced (6).

2.1.1 Drug-Excipient Compatibility Study

The drug and the excipients chosen for the formulation were screened for compatibility by physical and assay methods.

2.1.2 Physical Compatibility Study

The physical compatibility studies were conducted to provide valuable information in selecting the appropriate excipients for the formulation. It was done by mixing the drugs and the excipients, taken in 2 ml glass vial and kept at 40±2ºC/75±5% RH. Any change in colour of the physical mixture was observed visually (6).

2.1.3 Compatibility Study by Assay and Water Content

Assay and Water by KF can be used to investigate the Drug-excipient interactions.

2.2 PREPARATION OF BUFFER SOLUTIONS

2.2.1 Preparation of 0.1N Hydrochloric Acid (1.2pH) 70

8.5 ml of the hydrochloric acid was taken and dissolved in water and made upto 1000 ml to get 0.1N hydrochloric acid.

2.2.2 Preparation of Phosphate buffer solution (6.8pH) 70

50 ml of 0.02 M Potassium dihydrogen phosphate was taken in a 200 ml volumetric flask. 22.4 ml of 0.02 M sodium hydroxide solution was added and the volume was made up to 200 ml using distilled water (7).

2.2.3 Preparation of 1% sodium lauryl sulphate 45

1 g of sodium lauryl sulphate was dissolved in 100 ml of distilled water.

2.3 STANDARD PLOT FOR ACECLOFENAC

2.3.1 Standard plot in 0.1 N Hydrochloric Acid Buffer pH 1.2 30

100 mg of Aceclofenac was weighed and dissolved in 10ml of methanol and made up to 100 ml with 0.1 N Hydrochloric Acid buffer pH 1.2 to get a concentration of 1mg/ml. From the stock solution 10ml was taken and diluted to 100 ml to get a concentration of 100 mcg/ml. The above solution was further diluted with 0.1N Hydrochloric acid buffer pH 1.2 to get a concentration of 2, 4, 6, 8 and 10 mcg/ml. The absorbance of the resulting solutions was measured at 275 nm using UV-Visible spectrophotometer taking 0.1 N HCl as blank (7).

2.3.2 Standard plot in Phosphate Buffer pH 6.8 30

100 mg of Aceclofenac was weighed and dissolved in 10 ml of methanol and made up to 100 ml with phosphate buffer pH 6.8 to get a concentration of 1mg/ml. From the stock solution 10 ml was taken and diluted to 100 ml to get a concentration of 100mcg/ml. The above solution was further diluted with phosphate buffer pH 6.8 to get a concentration of 2, 4, 6, 8 and 10 mcg/ml. The absorbance of the resulting solutions was measured at 275 nm using UV-Visible spectrophotometer taking pH 6.8 phosphate buffer as blank (8).

2.4 PRECOMPRESSION STUDIES OF DRUG AND BLEND

2.4.1 Flow Property Measurements

The flow properties of powders are critical for an efficient tabletting operation. A good flow of the powder or granulation to be compressed is necessary to assure efficient mixing and acceptable weight uniformity for the compressed tablets. The flow property measurements include Bulk Density, Tapped Density, Compressibility index, Hausner's ratio and Angle of Repose. The flow property measurements of drug and blend were determined to select the type of granulation technique to be carried out for the formulation (8).

2.5 FORMULATION DEVELOPMENT

2.5.1 Formulation of Immediate Release Blend of Misoprostol

The immediate release tablets of Misoprostol were prepared by direct compression technique.47 Crospovidone was used as the superdisintegrant (2%, 3% and 4% concentrations). The blends were compressed by 16 station tablet compression machine using 6.25mm round concave punches.

The immediate-release tablet of Misoprostol was formulated and optimized. The optimized formulation was used for the final filling in the capsule (9).

2.5.2 Formulation Of Aceclofenac Extended-Release Tablet

The extended release granules were prepared by Non aqueous wet granulation technique. Different grades of hydrophilic polymer HPMC such as HPMC E50, HPMC K100LV CR, HPMC K4M CR, HPMC K15M CR and HPMC K100M CR were used in

different ratios. The tablets were compressed by 16 station compression machine using 17 X 4.5mm caplet punch tooling. The optimized batch of extended release tablets were finally filled in the capsule along with the optimized batch of Misoprostol.

2.6 POST COMPRESSION STUDIES

2.6.1 Physical Parameters

2.6.1.1 General appearance

The general appearance of the tablets from each formulation batch was observed. The general appearance parameters are shape, colour, presence or absence of odour and taste were evaluated visually (9).

2.6.1.2 Uniformity of Weight

Twenty tablets were selected at a random and weighed individually. The average weight was calculated. The percentage deviation of tablets was calculated and compared with the standard specifications.

2.6.1.3 Thickness

The thickness was measured to determine the uniformity of size and shape. Thickness of the tablets was measured using vernier caliper.

2.6.1.4 Hardness

Hardness is defined as the force required for breaking a tablet at diametric compression test and it is termed as tablet crushing strength. Hardness of the prepared formulations was determined using Dr. Schleuniger Pharmatron model 5Y tablet tester. It was expressed in kp.

2.6.1.5 Friability

Friability of the prepared formulations was determined by using Roche friabiltor. Pre- weighed sample of tablets was placed in the friability tester, which was then operated for 25 revolutions for 4 min, tablets were dedusted and reweighed (10).

2.7 IN VITRO DISINTEGRATION STUDIES FOR IR TABLETS

The disintegration time was determined using disintegration test apparatus. The tablets were placed in each of the six tubes of the basket. The assembly was suspended in water maintained at a temperature of 37ºC ± 2ºC and the apparatus was switched on. The time taken to disintegrate the tablets completely was noted.

2.8 IN VITRO DISSOLUTION STUDIES Misoprostol Tablets

The release of Misoprostol was determined using USP Type II paddle dissolution apparatus under sink condition. 500ml of de-aerated water was used as dissolution medium at a temperature of 37ºC ±0.5ºC. The paddle was stirred at a speed of 50 rpm. The release studies were carried out for 30 min. 10 ml of sample was withdrawn at regular intervals of 10 min and the percentage of drug dissolved were determined using HPLC method.

2.9 STABILITY STUDY

Stability study of optimized formulation of tablet in capsule was carried out according to ICH guidelines. Accelerated stability study of encapsulated formulation can be performed by packing 30 units of capsules in 60cc HDPE Bottle and 33mm PP Child Resistant closure with induction seal liner and 1 g per bottle of 6 g/yard Cotton as dunnage. Then these bottles are kept at and 40°C ±2ºC/75±5% RH. The samples were withdrawn at 1st, 2nd and 3rd month and analyzed for the following raiders (10),

- Thickness
- Assay
- Disintegration for IR tablets only
- Dissolution

3. Results and Discussion

The present investigation was to formulate tablets for immediate release of Misoprostol and extended release of Aceclofenac enclosed in a capsule for pain management with GI protection. The drug-excipient study was conducted to reveal the excipient compatibility with the drug. The physical and chemical compatibility of drug and excipients are given in Table 1 and 2.

3.1 PREFORMUALTION STUDIES

3.1.1 Drug -Excipient Compatibility Study

Table 1: Drug– Excipient Compatibility

S.No	Drug-Excipient	Ratio	Initial		Appearance
			Assay %	WC	
1	MI-MCC Type 102	1:1	97.29	4.75	White powder
2	MI-Crospovidone	1:0.25	98.90	3.81	White powder
3	MI-Cabosil	1:0.25	96.58	2.79	White powder
4	MI-Stearic acid	1:0.25	98.05	1.25	White to off white powder
5	AC-MCC KG 1000	1:0.5	98.05	4.32	White powder
6	AC -HPMC E50	1:0.5	96.07	3.12	White powder
7	AC-Stearic acid	1:0.25	99.30	0.10	White to off white powder

Table 2: Drug– Excipient Compatibility (Accelerated Stability Studies)

S.No	Drug-excipient	40± 2° C/75±5% RH-2W			40± 2° C/75±5% RH-4W		
		Assay%	WC	Appearance	Assay%	WC	Appearance
1	MI-MCC PH 102	93.0	3.90	NC	96.0	4.62	NC
2	MI-Stearic Acid	95.0	0.81	NC	93.0	1.14	NC
3	MI-Colloidal silicon dioxide	94.0	2.43	NC	94.0	2.56	NC
4	MI-Crospovidone	91.0	3.68	NC	97.0	3.77	NC
5	AC-MCC KG 1000	95.0	3.75	NC	95.7	4.21	NC
6	AC-HPMC E50	96.08	2.78	NC	94.03	3.00	NC

7	AC-Stearic acid	97.0	0.05	NC	95.0	0.07	NC

NC- No change, WC- Water content, MI- Misoprostol, AC- Aceclofenac

Inference

The excipients were found to be compatible with the drug.

3.2 STANDARD PLOT FOR ACECLOFENAC

The concentration and absorbance for Aceclofenac in 0.1N HCl (pH 1.2) and Phosphate buffer (pH 6.8) at wavelength 275 nm was measured using UV Visible Spectrophotometer. The results are given in Table 3; Figure 1-2.

Table 3: Standard plot for Aceclofenac

S. No	Concentration (mcg/ml)	Absorbance at λ_{275nm}	
		pH 1.2	pH 6.8
1	0	0	0
2	2	0.024	0.061
3	4	0.049	0.122
4	6	0.074	0.187
5	8	0.097	0.243

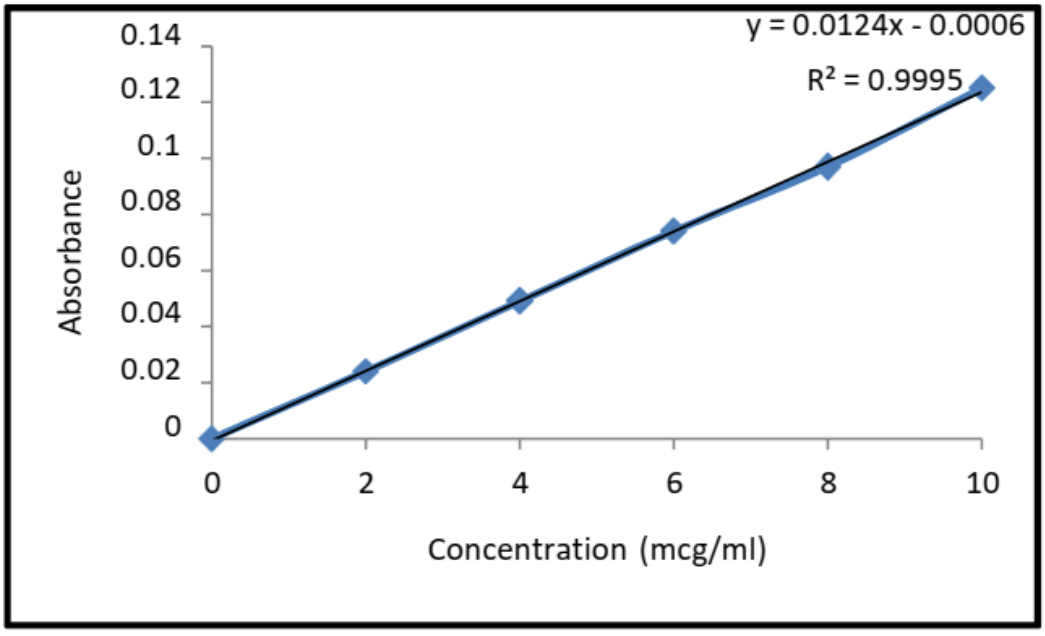

Figure 1: Standard plot of Aceclofenac in pH 1.2

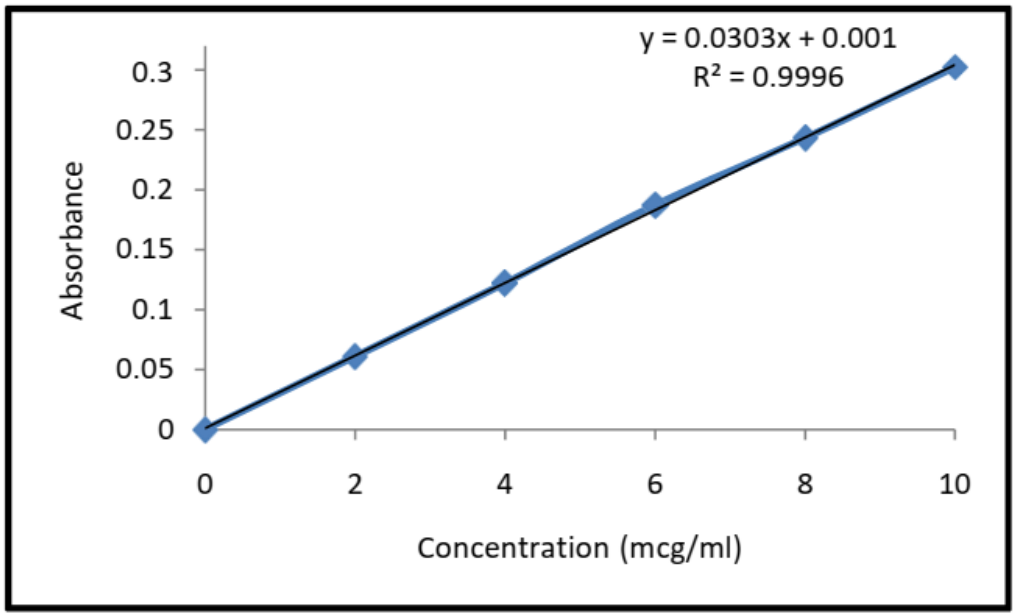

Figure 2: Standard plot of Aceclofenac in pH 6.8 Phosphate Buffer

3.3 EVALUATION OF IR FORMULATION PRECOMPRESSION STUDY

The drug and the formulated blends were evaluated for precompression parameters. The results are given in Table 4.

Table 4: Precompression study of drug and formulated blends

Drug and Formulation	Bulk Density g/cm^3 *	Tapped Density g/cm^3 *	Compressibility index (%)*	Hausner's Ratio*	Angle of Repose (Degree)
MI	05848± 0.0091	0.6754 ± 0.0072	13.42 ± 0.4430	1.15 ± 0.0072	21.50
M1	0.4987± 0.0078	0.5361 ± 0.0056	8.52 ± 1.02	1.09 ± 0.01	22.36
M2	0.5018± 0.0021	0.5590 ± 0.018	10.24 ± 1.75	1.11 ± 0.0220	23.45
M3	**0.4863± 0.0143**	**0.5317 ± 0.0025**	**8.53 ± 2.62**	**1.09 ± 0.0280**	**23.05**

*** Mean ± S.D (n = 3)**

The bulk density of the IR blends ranged from 0.4863 to 0.5018 g/cm3 and the tapped density ranged from 0.5317 to 0.5590 g/cm3. The compressibility index of the IR blends ranged from 8.52% to 10.24% and Hausner's ratio ranged from 1.09 to 1.11. The angle of repose of the IR blends ranged from 22.36 to 23.45. The formulated blend shows good flow property so direct compression was employed.70 The IR blends were evaluated for bulk density, tapped density, compressibility index, Hausner's ratio and Angle of Repose.

3.4 POST COMPRESSION STUDY FOR TABLETS UNIFORMITY OF WEIGHT

The uniformity of weight of the formulated tablets is given in Table 5

Table 5: Uniformity of weight of the formulated tablets

Formulation	**Uniformity of weight (mg) ***
M1	125.28±0.3382
M2	125.36±0.4852
M3	**125.58±0.5263**

*** Mean± S.D (n=20)**

The tablets comply with the test for uniformity of weight.

3.5.1 Tablet Thickness

The thickness of the formulated tablets is given in Table 6

Table 6: Thickness of formulated tablets

Formulation	**Thickness (mm) ***
M1	3.114±0.0219
M2	3.112±0.0109
M3	**3.114±0.0308**

*** Mean± S.D (n=5)**

The tablets possess uniform thickness.

3.5.2 Hardness

The hardness of the formulated tablets is given in Table 7

Table 7: Hardness of formulated tablets

Formulation	**Hardness (kp) ***
M1	5.16±0.0547
M2	5.18±0.0457
M3	**5.17±0.0358**

*** Mean± S.D (n=5)**

All the formulated tablets showed sufficient mechanical strength to resist the transportation and handling.

3.5.3 Friability

The friability of the formulated tablets are given in Table 8.

Table 8: Friability of formulated tablets

Formulation	**% Friability**
M1	0.34
M2	0.42
M3	**0.40**

The percentage friability of all the formulations was within acceptable limits.

3.5.4 Drug Content

The drug content of the IR tablets is given in Table 9.

Table 9: Drug content of formulated IR tablets

Formulation	**% Drug Content**
M1	98.76 ± 0.1300
M2	97.48 ± 0.0100
M3	**98.56**± 0.1201

All the formulated tablets showed sufficient mechanical strength to resist the transportation and handling.

3.5.5 Friability

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3.5.6 **Drug Content**

The drug content of the IR tablets is given in the Table 9.

Table 9: Drug content of formulated IR tablets

Formulation	**% Drug Content**
M1	98.76 ± 0.1300
M2	97.48 ± 0.0100
M3	**98.56**± 0.1201

3.5.7. DISINTEGRATION TIME

The disintegration time of the IR tablets is given in the Table 10.

Table10: Disintegration time of IR tablets

Formulation	**Disintegration time (minutes)**
M1	8.50 ± 0.012
M2	4.29 ± 0.0004
M3	**2.10** ± 0.0020

3.6 **IN VITRO DISSOLUTION STUDY**

The in vitro dissolution of immediate release formulations of Misoprostol aregiven in the Table 11.

Table 11: In vitro Dissolution study of IR formulation of Misoprostol

Time (Min)	**Cumulative % drug release**		
	M1	**M2**	**M3**
0	0	0	**0**
10	20.39±0.7112	30.35±1.22	**60.28±0.7**
20	48.38±0.6515	60.78±1.988	**85.02±0.5178**
30	69.99±1.5076	73.49±1.817	**98.94±0.4564**
40	78.42±0.7616	87.52±0.4659	
50	87.81±0.9269	98.27±0.3463	
60	96.95±0.5162		

The formulation M3 containing 4% of Crospovidone released the drug faster when compared to M1 and M2 formulations. The formulation M3 released 98.94% of Misoprostol at the end of 30mins. Therefore formulation M3 was optimized and selected for filling in capsule.

3.7 EVALUATION OF ER FORMULATION PRECOMPRESSION STUDY

The drug and the formulated blends of ER formulation were evaluated for precompression parameters. Formulations A9 to A13 don't have stability the broke up in the compression process. So, no further parameters are not able to carry for those formulations. The results are given in Table 12.

Table11.12: Precompression study of drug and formulated blends

Drug and formulation	**Bulk density g/cm^3 ***	**Tapped density g/cm^3 ***	**Compressibility Index (%)**	**Hausner's Ratio**	**Angle of Repose (Degree)**
AC	0.6511± 0.0012	0.8326± 0.0010	21.79 ± 0.0907	1.27 ± 0.0000	37.99
A1	0.5916± 0.0018	0.7682± 0.0023	22.99 ± 0.5831	1.30 ± 0.0000	32.45
A2	0.5886± 0.002	0.7693± 0.0011	23.48 ± 0.3329	1.30 ± 0.0057	33.06
A3	0.589± 0.0024	0.7711± 0.0019	23.62 ± 0.4635	1.31 ± 0.0057	32.12
A4	0.5880± 0.0024	0.7689± 0.0011	23.54 ± 0.1563	1.31 ± 0.0058	34.36
A5	0.5883± 0.0025	0.7695± 0.0013	23.55 ± 0.1674	1.30 ± 0.0057	31.58
A6	0.5898± 0.0009	0.7696± 0.0006	23.37 ± 0.2271	1.31 ± 0.0058	32.10
A7	0.5894± 0.0001	0.7708± 0.0057	23.52 ± 0.7000	1.31 ± 0.01525	33.42
A8	0.5897± 0.0019	0.7705± 0.0024	23.47 ± 0.1053	1.30 ± 0.0057	33.36

The bulk density of the formulated blends ranged from 0.5880 to 0.5916 and tapped density ranged from 0.7682 to 0.7711. The compressibility index ranged from 22.99 to 23.62 and Hausner's ratio ranged from 1.30 to 1.31. The Angle of repose ranged from 31.58 to 34.36. The formulated blends did not show adequate flow properties for compression. Hence Non aqueous wet granulation method was employed. The formulated ER granules were evaluated for bulk density, tapped density, compressibility index, Hausner's ratio and Angle of Repose. The results are given in the Table 13

Table 13: Precompression study of Extended release granules

Formulation	**Bulk density g/cm^3**	**Tapped density g/cm^3**	**Compressibility Index (%)**	**Hausner's Ratio**	**Angle of Repose (Degree)**
A1	0.5852± 0.0046	0.7316± 0.0009	20.0 ± 0.6560	1.24± 0.0115	25.25
A2	0.5889± 0.0018	0.7395± 0.0008	20.35 ± 0.3000	1.25 ± 0.0057	25.12
A3	0.5912± 0.0011	0.741± 0.0008	20.21 ± 0.2402	1.25 ± 0.0057	24.29
A4	0.5905± 0.0056	0.7393± 0.0004	20.11 ± 0.862	1.25 ± 0000	23.22
A5	0.5906± 0.0005	0.7392± 0.0004	20.09 ± 0.0400	1.25 ± 0000	22.78
A6	0.5916± 0.0008	0.7414± 0.0011	20.19 ± 0.2371	1.25 ± 0.0057	25.11
A7	0.5904± 0.0003	0.7405± 0.0015	20.25 ± 0.1404	1.25 ± 0.0000	26.0
A8	**0.5911± 0.0006**	**0.7328± 0.0048**	**19.32 ± 0.6178**	**1.23 ± 0000**	**27.26**

The bulk density of the ER granules ranged from 0.5852 to 0.5916 g/cm^3 and the tapped density of ranged from 0.7316 to 0.7410 g/cm^3. The compressibility index of the ER granules ranged from 19.32 to 20.35% and Hausner's ratio ranged from 1.23 to 1.25. The Angle of Repose of the ER granules ranged from 22.78 to 27.26. The formulated granules shows good flow property.

3.8 IN VITRO RELEASE KINETICS

The values obtained from in vitro dissolution of Aceclofenac Extended release tablets were fitted to kinetic models. The results are given in table 14.

Table 14: In vitro release kinetics of Aceclofenac ER tablets

Time (Hr)	% Cum Drug Release	% Cum Drug Remaining	Log % Cum Drug Remaining	Square root of time	Log time	Log % cum drug release	Cube root of % drug remaining
0	0	100	2	0	0	0	4.6415
2	9.14	90.86	1.9583	1.4142	0.3010	0.9609	4.4956
4	20.69	79.31	1.8993	2	0.6020	1.3157	4.2964
6	47.97	52.03	1.7162	2.4494	0.7781	1.6809	3.7332
8	63.25	36.75	1.5652	2.8284	0.9030	1.8010	3.3246
10	85.27	14.73	1.1682	3.1622	1	1.9307	2.4513
12	98.1	1.9	0.2787	3.4641	1.0791	1.9916	1.2385

The kinetic parameters revealed that release data of optimized formula A8 showed r^2 value of 0.985 which is close to 1, indicating that release of drug follows **zero order kinetics** and the release is independent of concentration.

3.9 STABILITY STUDY

The optimized tablets were subjected to stability studies and the results are given in Table 15.

Table 15: Stability study of physical parameters of the optimized formulations Misoprostol

Parameter	**Initial**	**1st month**	**2nd month**	**3rd month**
Uniformity of weight (mg)*	125.58± 0.5263	125.21± 0.3796	125.02± 0.5225	124.99± 0.4083
Thickness(mm)**	3.114± 0.0308	3.11± 0.0054	3.11± 0.0054	3.11± 0.0044
Disintegration Time (min)	2.10± 0.0152	2.23± 0.1369	2.18 ± 0.1158	2.21 ± 0.0790

Water content of finalized formulation	4.72	5.16	5.37	5.62

A Tablet in Capsule device containing Aceclofenac ER tablet and Misoprostol IR tablet for pain management with gastroprotection was successfully formulated. The rationale for combining a nonsteroidal anti-inflammatory drug (NSAID) and a prostaglandin analogue was well justified, and the design of the drug delivery system was simplified by encapsulating two different tablets (Aceclofenac and Misoprostol) in a single capsule, offering advantages in terms of gastrointestinal (GI) protection, patient compliance, and chronotherapeutics. Aceclofenac extended release tablet (200 mg) was formulated using various grades of hydrophilic polymer such as HPMC E50, HPMC K100 LV CR, HPMC K4M CR, and HPMC K15M CR to prolong the release over 12 hours. Misoprostol immediate release tablet (200 mcg) was formulated using Crospovidone as a superdisintegrant at concentrations of 2%, 3%, and 4%. Formulation characteristics, including precompression and postcompression studies, were conducted as per standard procedures, and the tablets met the required limits for uniformity of weight, hardness, thickness, diameter, friability, and drug content. In vitro dissolution studies were conducted separately, and Aceclofenac ER formulation A8 was optimized based on its ideal 12-hour release profile following zero-order kinetics, while Misoprostol IR formulation M3 was optimized based on disintegration time (11, 12). The optimized formulations of Aceclofenac A8 and Misoprostol M3 were filled in size '0' elongated capsules, and stability studies under accelerated conditions (40 ± 2°C / 75 ± 5% RH) were satisfactory.

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