Advances in Bioresearch
Adv. Biores., Vol 12 (3) May 2021: 91-103

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.12.3.91103

Advances in Bioresearch

ORIGINAL ARTICLE

Formulation and Evaluation of Bilayer Tablet Containing Mefenamic acid As Sustained Release and Aloe Vera Gel Powder as Immediate Release

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ABSTRACT
The objective of present study is to formulate and evaluate Bilayer tablet containing Mefenamic acid as sustained release layer and aloe Vera is immediate release layer. Mefenamic acid is a NSAID it can causes ulceration in stomach by increasing ph of stomach but anta acid not given with mefenamic acid because anta acid decreases absorption of mefenamic acid. aloe vera gel powder have positive impact on this condition. Aloe vera gel powder has cyto-protective and healing properties it will help the sustained release layer of Mefenamic acid was formulated by using HPMC K15, HPMC K4 controlled release polymer. Immediate release layer of aloe vera gel powder was formulated by using various excipient such as crospovidone, starch, talc, lactose etc. various pre-formulation parameter such a organoleptic characteristics was checked. Micro-meritics properties of both layer powder such as a bulk density, tapped density, hausners, ratio, carŕsindex, angle of repose are performed. Post compression evaluation parameter was checked such as hardness, friability, weight variation, drug content uniformity, thickness, in vitro drug release of all batches was found in range of 95.38 to 93.56 within 8hr.Bilayer tablet of optimized batch of both layers (A3, M1). Optimized batch of both layer showed satisfactory result for different evaluation parameter. The optimized formula contain of immediate release layer A3 (crospovidone) batch and sustained release layer of M1 (HPMC k4M) batch. The drug release mechanism was found to be zero order release found to be diffusion
Keywords: *Bilayer tablet, Mefenamic acid, Aloe vera gel powder, HPMC K15, K4M, Immediate release, direct compression, Sustained release.*

Received 19.02.2021 Revised 22.04.2021 Accepted 03.05.2021

How to cite this article:
S L. Jadhav, R K. Bhalerao, S M. Dhobale, D D. Gaikwad, R M. Thorat. Formulation and Evaluation of Bilayer Tablet Containing Mefenamic acid As Sustained Release and Aloe Vera Gel Powder as Immediate Release. Adv. Biores. Vol 12 [3] May 2021. 91-103

INTRODUCTION

The purpose of any drug delivery system is to supply a therapeutic quantity of the drug to the proper site of action in the body to maintain the desired drug concentration. Oral rout is most suitable route of the administration dosage form. Tablet is a convenient dosage form acceptable by patients and medical practitioner. Bilayer tablet is suitable for sequential release of two drugs in single dosage form which one is immediate release and another is sustained release. [1]

Single dosage form containing two different category drugs. The benefit of combination therapy to reduce the number of the dosage form in prescription and maintain administrative cost as well as improving patient compliance.[2]

Mefenamic acid is an NSAID its mechanism of action by inhibiting the cyclooxygenase (COX). Mefenamic acid is used to treat Acute, moderate, severe Pain, Moderate Pain in dysmonoheral disease Mefenamic acid is rapidly and almost completely absorbed by oral route, 500 mg of single oral mefenamic acid absorbed extent of 30mcg/hr/ml Long term use of a Mefenamic acid can cause negative effect on gastric system in body it can cause gastric ulceration. Aloe vera with Mefenamic acid lower the side effect of Mefenamic acid it has cytoprotective, healing capacity. [4]

Present study is to prepared Bilayer tablets of Mefenamic acid (Sustained Release) by using HPMC as controlled release polymer in sustained release layer along with other excipients and aloe Vera gel powder (Immediate release) using crosprovidone super disintegrate in an immediate release . [5] Tablet layer was manufactured separately using 8 station CREATE compression machine. To evaluate blends (powder) for pre-compression terms such as a of Angle of repose, Bulk and tapped density, Carr's index, Hausner's Ratio and to evaluate Bi-layer matrix tablets in terms of hardness, weight variation, friability, thickness, drug content uniformity, In vitro dissolution studies in 1.2 and 6.8 pH. [6]

MATERAIL AND METHODS

MATERAIL

Sample was gifted from Mefenamic acid (enaltec), HPMC K15M, Talc (Thermosil fine chem.) Aloe Vera gel powder (maple biotech pvt ltd bhosari, Pune, Maharashtra) sodium starch glycolate, (research lab,pune) Lactose, (Sahyadri scientific supply,pune) Magnesium Stearate (Hilab chemicals) starch, were sample is analytical grade.

METHODOLOGY

Formulation of two layer tablet was prepared by using direct compression technique. Immediate release layer was prepared by using different super disintegrates (Crossprovidone). Drug and above super disintegrates were passed through the 40# sieve and transfer into polybag and mix up to 5 min. Then add remaining excipients to the above mixture. Then, add (glidant) talc into the blend. Another layer was also prepared by direct compression; drug and polymer (HPMC k4M)and other exicipent (expect mag sterate) were pass through the 40# sieve transfer into polybag and mixed properly up to 5 min. Other excipients were mixed well and finally added Magnesium Sterate in the above powder and were mixed for 8 min. Finally above optimized batch blends were compressed by rotary tablet compression machine (Make-CREATE INDUSTRIES, MODEL-LP8GMP) [6, 7]

Table 1 Formulation of immediate release layer of aloe Vera gel powder

Ingredients	A1	A2	A3	A4	A5	A6	A7	A8	A9
Aloe veragel powder	100	100	100	100	100	100	100	100	100
Crospovidone	02	05	08	-	-	-	1	2.5	4
SSG	-	-	-	02	05	08	1	2.5	4
lactose	93	90	87	93	90	87	93	90	87
Talc	5	5	5	5	5	5	5	5	5
Colour	qs.	qs.	qs.	qs.	qs.	qs.	qs.	qs.	qs.
Total (Mg)	200	200	200	200	200	200	200	200	200

Table 2:Formulation of sustained release Mefenamic acid

Ingredient	M1	M2	M3	M4	M5	M6	M7	M8	M9
Mefenamic acid	250	250	250	250	250	250	250	250	250
HPMC K4M	67.5 (15%)	112.45 (25%)	157 (35%)	-	-	-	33.75	56	78.5
HPMC K15M	-	-	-	67.5 (15%)	112 (25%)	157 (35%)	33.75	56	78.5
Lactose	118	73	28	118	73	28	18	73	28
talc	10	10	10	10	10	10	10	10	10
Mag sterate	5	5	5	5	5	5	5	5	5
total	450mg	450mg	450mg	450mg	450mg	450mg	450mg	450mg	450mg

Preformulation study: [8, 9]

Identification test by U. V vis. Spectrophotometer

For Mefenamic acid:

Accurately Weigh Mefenamic acid was dissolved in methanol to obtained solution of 25 µg /ml solution. UV spectrum was recorded in the wavelength between 200-400 nm ranges using UV spectrophotometer against blank methanol. Wavelength for maximum absorbance was recorded.

For Aloe Vera gel powder

Accurately Weigh Aloe veragel powder Dissolved in methanol to obtained solution of 25 µg /ml solution. UV spectrum was recorded in the wavelength between 200-400 nm ranges using UV spectrophotometer against blank methanol. Wavelength for maximum absorbance was recorded.

Melting point determination

Melting point of Mefenamic acid and Aloe veragel powder was performed by melting point apparatus using capillary method. Small amount of sample is place in capillary tube which having 1mm diameter with one end is closed. The capillary was placed in melting point apparatus and start heating smoothly, when sample starts melting at that time temperature is note down in frequent time.

Determination of solubility [10]

Qualitative Solubility

solubility of drugs were determined by dissolving 4 mg of drug in 4 ml of different solvents such as distilled water methanol, ethanol, HCl (0.1N), phosphate buffer ph 6.8 acetone were used to determine the solubility of drug.

Compatibility study, by FT-IR spectroscopy [8]

The drugs and Excipients (of both layer separately) with KBr (1:1:100) ratio, KBr pellet were prepared and subjected to storage at dry box at elevated temperature 400C for one day and then take IR spectra by FTIR spectrophotometer (PerkinElmer). The identified peaks were compared with the standard peaks of reported IR spectrum pure drugs and Excipients.

Pre-compression evaluation [8]

Bulk density

It is the ratio of the total weight of powder with exipient to the volume it occupied and expressed in gm/ml. bulk density is affect while calculating the size of container needed for handling, shipping, and storage of row material. It should be considered in hopper design and received for milling equipment and for sizing blending equipment in the scale up to pilot and to commercial production.

The bulk density is directly proportional particle size distribution, size of particle and tendency of particle for adhesion. The bulk density and bulkiness were determined by following method.

A sample of about 20 gm of both powder blend (sustained release and immediate release blend) was carefully transferred in to 100ml volume containing measuring cylinder and cylinder dropped on to the hard wooden surface three times from height of 1 inch at two second interval.

Bulk density was determined by following formula.

Bulk density = Weight of powder/volume

As per particle size directly proportional to the bulk density. The bulk density of irregular shape particle has lower bulk density and spherical particle have higher density.

Tapped density

After calculating the bulk volume the same measuring cylinder was put into tapped density apparatus. The tapped density apparatus was set to 300 taps dropped per min and the opened operated for 500 taps. Volume was noted by (Va) and then again tapped for 750 times at that time volume was noted as (Vb)

If the difference between Va and Vb not more than 2% then Vb is consider as final tapped volume. If the difference between Va and Vb is greater than 2%, so we go through tapping for 1250 times. Tapped density is calculated by this formula is given below.

Tapped density = weight of power (gm)/ tapped volume (ml)

Hausner's ratio

Hausner's ratio is a very important parameter to measure the flowing property of powder and also granules. This can be calculate by following formula –

< 1.25 indicate good flow (=20% Carr)

> 1.50 indicate poor flow (=35%Carr)

Between 1.25 and 1.5, adding glident will improve flow property. Carr,s index is one point determination and does not reflect ease or speed with which consolidation occur. some powder blend have high index suggesting poor flow but may consolidate rapidly, which is essential for uniform filling of tablet machine when powder flows at nearly equal to bulk density into the die and consolidate to approaching tapped density prior to compression.

Hauser's ratio is calculated by this formula.

Hauser's ratio = tapped density/ bulk density.

Compressibility index

Compressibility index was calculated by formula,

Carr's index (%) = Tapped density–bulk density/tapped density* 100

Angle of repose

It is maximum angle between surface of pile and horizontal plane. This angle universally proportional to free flowing properties of powder.

Angle of repose was calculated by using Neumann's technique and calculated using formula, for a lubricated as well as lubricated powder.

Tan ɵ = h/r

I.e. tan-1 (h/r)

Where, ɵ is angle of repose

h is height

r is radius of pile base.

Post-compression evaluation [5]

Uniformity weight

Uniformity weight of the tablet was determined by selecting 20 tablets randomly. This selected tablet weighing individually and the weight of individual tablet was correlated with average weight.

Table 3:Limits for tablet weight variation test

Average weight of tablet (mg)	% Difference allowed
130 or less	10 %
From 130 to 324	7.5 %
>324	5%

Thickness

Thickness of the tablet was measured by using vernier caliper. 6 tablets were accurately selected and thickness was measured in unit (mm).

Hardness

Hardness is one of the very important evaluation parameter of tablet. The resistance of tablet to shipping or breakage, under condition of storage transportation and handling before usages depends on its hardness. Hardness directly proportional to the drug release pattern of the tablet. The hardness of tablet of each formulation was determined using Monsanto hardness tester. It is expressed in kg/cm3.

Friability

Friability is the measure of tablet strength. Roche friabilator is generally used to determine the friability of tablet. Friction and shock this are forces that can cause tablets to chip, cap or break. 10 tablets are accurately weighed and placed in the (roche friabilator) apparatus they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight of tablet. Abrasion is directly proportional to the tablet friability.

A maximum weight loss of 1% is allowed if weight loss is more than 1% then this tablet will not pass the friability test any broken or smashed tablets are not picked. The percentage friability was determined by the formula:

% friability = [initial weight – final weight/initial weight] ×100

Content uniformity

1) For Mefenamic acid

10 tablets were taken and crushed into mortar to form powder. From that, sample equivalent to 10 mg of drug was taken and transferred to 100ml volumetric flask. Phosphate buffer ph 6.8 (20ml) was added dissolve the drug and volume was made up to mark with phosphate buffer ph 6.8 this was filtered. From the filterate 1ml was taken and diluted with pH phosphate buffer ph 6.8 and absorbance of this solution was measured by using U.V-spectrophotometer at 285 nm (SHIMADZU; U.V1800).

2) For aloe Vera gel powder

Tablets were taken and crushed into morter to form powder. From that, sample equivalent to 25 mg of drug was taken and transferred to 100ml volumetric flask. 0.1 N HCl (20ml) was added dissolve the drug and volume was made up to mark with 0.1N HCl, this was filtered. From the filterate 1ml was taken and diluted with 0.1N HCl and absorbance of this solution was measured by using U.V-spectrophotometer at 262.5 nm (SHIMADZU; U.V1800)

In vitro drug dissolution studies

***In vitro* drug release was studied for immediate release tablet (Aloe Vera gel powder)**

The In-vitro dissolution study for the Aloe veragel powder immediate release tablets were carried out in USP type-II dissolution test apparatus (Electrolab TDT-08L) (Paddle type) using 900 ml of 0.1 N HCL at 50 rpm and temperature 37±0.5°C. At predetermined time intervals, 5 ml of the samples were withdrawn by means of a syringe fitted with a pre-filter, the Volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium. The resultant samples were analyzed by measuring the absorbance at 262.5 nm using UV Visible spectrophotometer and calculate the percentage drug release.

***In vitro* drug release was studied for sustained release tablet (Mefenamic acid)**

The In-vitro dissolution study for the Mefenamic acid floating sustained released tablet were carried out in USP type-II dissolution test apparatus (Electrolab TDT-08L) (Paddle type) using 900 ml of phosphate buffer ph 6.8 at 50 rpm and temperature 37±0.5°C. At predetermined time (1 hr.) intervals up to 8 hrs, 5 ml of the samples were withdrawn by means of a syringe fitted with a pre-filter; the volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium (phosphate buffer 6.8). The resultant samples were analyzed by measuring the absorbance at 285 nm using UV Visible spectrophotometer and calculate the percentage drug release.

In vitro drug release was studied for Bilayer tablet

The In-vitro dissolution study for the Mefenamic acid and Aloe veragel powder Bilayer tablet were carried out in USP type-II dissolution test apparatus (Electrolab TDT-08L) (Paddle type) using 900 ml of 0.1 N HCl at 50 rpm and temperature 37±0.5°C. At predetermined time (1 hr.) intervals up to 12 hrs, 5 ml of the samples were withdrawn by means of a syringe fitted with a pre-filter; the volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium (0.1 N HCl). The resultant samples were measuring the absorbance by simultaneous estimation at 285 nm and 262.5 nm using UV Visible spectrophotometer and calculate the percentage drug release.

RESULTS AND DISCUSSION

Pre-formulation studies [8, 9]

The UV absorption of 100 ppm solution in methanol for Aloe Vera gel powder is 285.5 nm in the range of 200-400 nm exhibit maximum and in case of Mefenamic acid at 285 nm. The absorbance maxima of Aloe vera gel powder and mefenamic acid was found to be 261.5nm and 285 nm respectively. Melting point, solubility and compatibility study of both drugs are carried out and the result is including in table 4.

Figure 1: Absorbance maxima of Mefenamic acid.

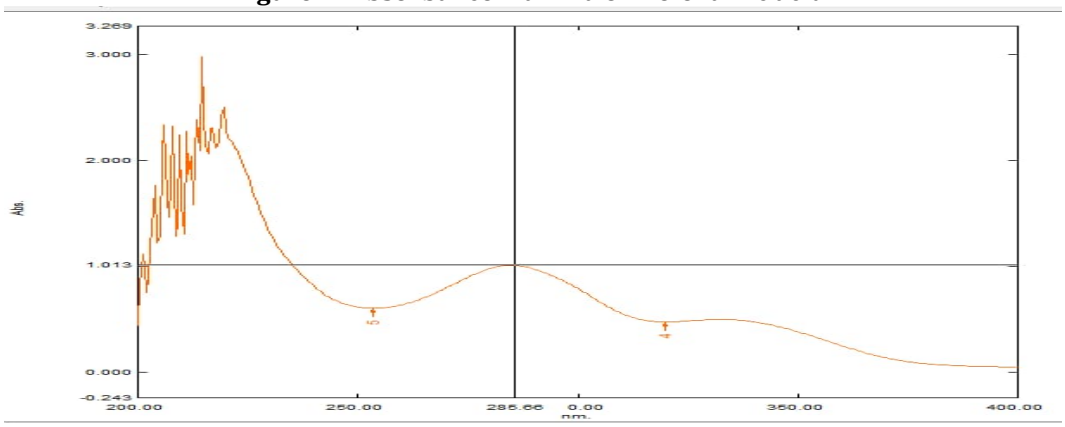
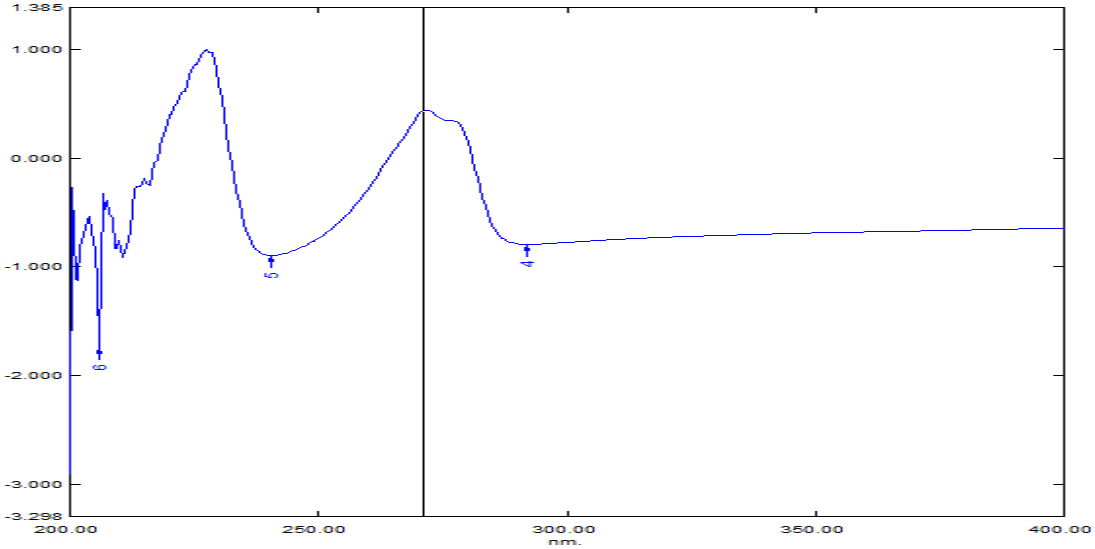


Figure 2: Absorbance maxima of aloe Vera gel powder



Compatibility study by FTIR [8]

Drug polymer interaction was studied by FTIR spectroscopy. The spectra were recorded for mefenamic acid with polymer mixture. Also the spectra were recorded for aloe Vera gel powder and physical mixture of drug with polymers using FTIR. And polymers are found compatible with the drugs.

Figure 3: FTIR of Mefenamic acid and excipient

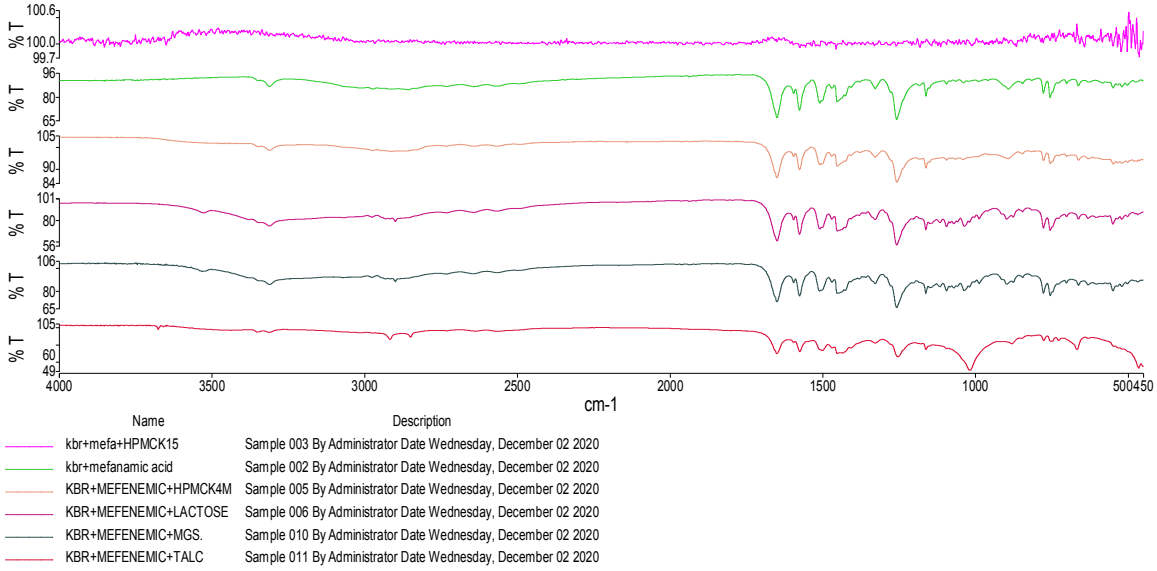


Figure 4: FTIR of Aloe vera gel powder and excipient

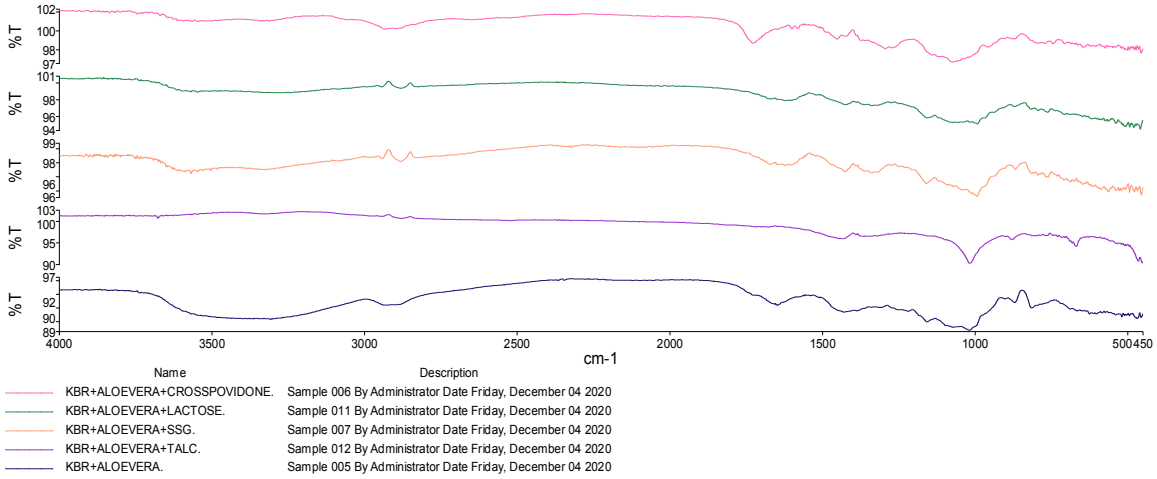


Table 4 : Preformulation study of aloe Vera gel powder and Mefenamic acid

Sr. No.	Parameter	Aloe Vera gel powder	Mefenamic acid
1	Identification by U. V Vis -spectrophotometer.	261.5 nm (λ max)	285 nm (λ max)
2	Melting Point	224 °C	183 °C
3	Solubility	Highly Soluble in water, ethanol, methanol, Phosphate buffer, poorly soluble in chloroform.	In Soluble in water, Slightly soluble in methanol soluble in ether sparingly soluble in acetone.
4	Compatibility study	compatible	Compatible

Pre-compression evaluation [8]

The micrometrics properties such as of bulk density, tapped density, Angle of repose, compressibility index, and Hausner's ratio of Mefenamic acid sustained release layer and Aloe Vera gel powder immediate release layer blend and were studied separately. The overall results were shown in table No :5 the value of bulk density shows that good packing properties. The compressibility index of the formulation Indicating poor flow properties of powder which were further confirmed by determining the angle of repose, it is in the range of 16 ° to 26 ° which indicates good flow properties.

Table 5:Pre-compression evaluation of immediate release layer blend (Aloe Vera gel powder)

parameter	Batches								
	A1	**A2**	A3	**A4**	**A5**	**A6**	**A7**	**A8**	**A9**
Bulk density	0.4115	0.3893	0.4496	0.4085	0.4696	0.3963	0.4303	0.4285	0.3797
Tapped density	0.5696	0.5445	0.5741	0.5302	0.5966	0.5027	0.5576	0.5365	0.5637
Carr's index	27.75	28.44	21.68	22.95	21.28	21.16	22.82	23.85	25.69
Hausner's ratio	1.38	1.39	1.27	1.32	1.28	1.28	1.29	1.26	1.51
angle of repose	25.2	24.45	25.78	23.67	27.02	24.57	22.81	24.22	22.81

Table 6: Pre-compression evaluation of sustained release powder blend, (Mefenamic acid)

parameter	Batches								
	M1	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**	**M9**
Bulk density	**0.4096**	0.4269	0.3701	0.3689	0.3765	0.3743	0.4155	0.4023	0.4063
Tapped density	**0.5363**	0.5366	0.5362	0.5643	0.5586	0.5407	0.5297	0.5296	0.5643
Carr's index	**23.62**	20.07	31.56	35.25	29.54	31.21	24.86	27.29	29.57
Hausner's ratio	**1.30**	1.25	1.44	1.50	1.48	1.44	1.27	1.31	1.38
angle of repose	**27.21**	27.95	34.04	31.38	30.15	26.28	29.51	30.08	28.5

Post-compression evaluation of tablet [5]

The prepared tablets were evaluated for weight variation test, dissolution test, thickness, hardness uniformity of dosage units and friability. The weight variation test is performed by weighing 20 tablets separately, calculating the average weight and comparing the individual weights of each tablet to the average.

The hardness of each batch of the tablet was determined by using Monsanto hardness tester. The hardness was measured in unit of kg/cm2. The hardness of 6 tablets was determined using The Friability was determined by first weighing 10 tablets after dusting and placing them in a friability tester ,Roche friabilator will be used, which was rotated for 4 min at speed 25 rpm. After complication of dusting, the total remaining weight of tablet was recorded and the % friability was calculated by using formula.

The thickness of the each 10 tablets was calculated by using Vernier Caliper. All test value is included. Drug content uniformity and *In vitro* drug release determined according to the USP guidelines. Test values are including in table 9.

Table 7 :Post-compression evaluation of immediate release layer tablet

Batches	thickness	diameter	wt variation	Hardness	DT	friability	drug content	%release
A1	4 mm	6 mm	200.6±2.61	3.0	1	0.654	95.23	88.93
A2	4 mm	6 mm	201.05±2.57	2.5	1.15	0.585	91.34	92.14
A3	4 mm	6 mm	200.1±3.3	2.5	1.37	0.0.449	95.63	95.38
A4	4 mm	6 mm	199.7±2.72	2.0	1.3	0.796	96.63	77.85
A5	4 mm	6 mm	198.3±2.41	3.0	1.5	0.574	93.45	80.12
A6	4 mm	6 mm	199.9±2.7	2.5	1.3	0.449	94.16	83.27
A7	4 mm	6 mm	198.8±2.52	2.0	1.2	0.456	90.72	82.92
A8	4 mm	6 mm	199.7±2.3	2.5	1.26	0.469	92.86	85.31
A9	4 mm	6 mm	200.7±2.23	3.0	1.57	0.498	95.63	93.89

Table 8: Post-compression evaluation of sustained release layer tablet

Batches	Height	Diameter	hardness	friability	Drug content	%release
M1	**5mm**	**10mm**	**4.5**	**0.7509**	**96.91**	**93.56**
M2	5mm	10mm	4.5	0.7736	91.45	88.63
M3	5mm	10mm	4.0	0.7102	95.87	81.23
M4	5mm	10mm	3.8	0.747	88.09	82.78
M5	5mm	10mm	4.0	0.7836	99.36	78.09
M6	5mm	10mm	3.8	0.7843	99.23	71.06
M7	5mm	10mm	4.5	0.8052	94.77	87.02
M8	5mm	10mm	4.3	0.8185	88.66	82.36
M9	5mm	10mm	4.0	0.8741	98.44	78.32

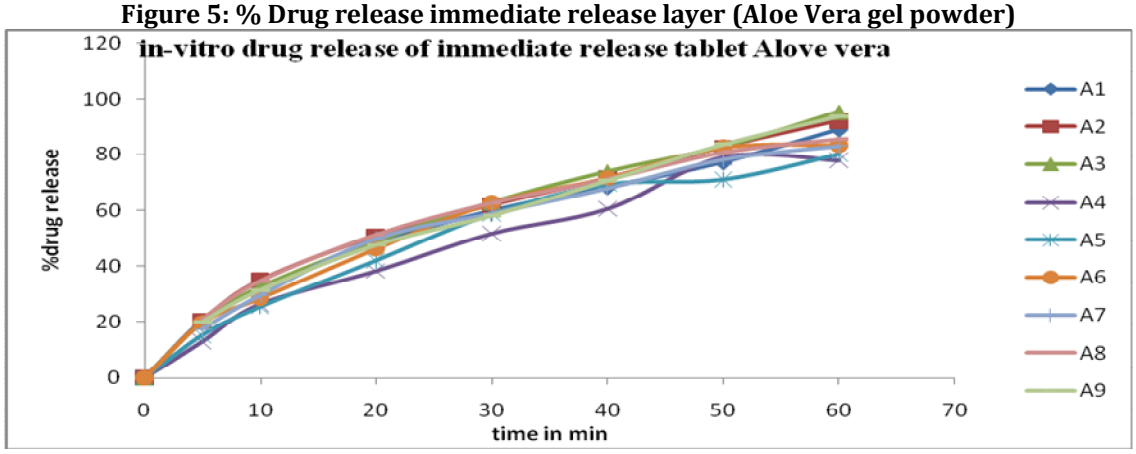
Table 9: Post-compression evaluation of bilayer tablet of A3 and M1 Optimized batch

Evaluation Parameter	Result
Thickness Bilayer tablet (mm)	4 mm
Weight Variation(mg)	648± 2.63
Average Tablet Hardness(kg/cm^2)	4 kg/cm^2
% Friability	0.60
Disintegration time of immediate release layer	1.2 min
Floating lag time of floating matrix layer	3 min
% drug content of Immediate release layer	95.31%
% drug content of floating matrix layer	98.09%
% drug release of immediate release layer	95.21%
% drug release of floating matrix layer	93.34%

***In vitro* drug release was studied for immediate release tablet (Aloe Vera gel powder)**

The In-vitro dissolution study for the Aloe veragel powder immediate release tablets were carried out in USP type-II dissolution test apparatus (Electrolab TDT-08L) (Paddle type) using 900 ml of 0.1 N HCL at 50 rpm and temperature 37±0.5°C. At predetermined time intervals, 5 ml of the samples were withdrawn by means of a syringe fitted with a pre-filter, the Volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium. The resultant samples were analyzed by measuring the absorbance at 262.5 nm using UV Visible spectrophotometer and calculate the percentage drug release.In the present study the formulation A3 has shown cumulative percent drug release of about 94.88% in 01 h as shown in figure.

Figure 5: % Drug release immediate release layer (Aloe Vera gel powder)



***In vitro* drug release was studied for sustained release tablet (Mefenamic acid)**

The In-vitro dissolution study for the Mefenamic acid floating sustained released tablet were carried out in USP type-II dissolution test apparatus (Electrolab TDT-08L) (Paddle type) using 900 ml of phosphate buffer ph 6.8 at 50 rpm and temperature 37±0.5°C. At predetermined time (1 hr.) intervals up to 8 hrs, 5 ml of the samples were withdrawn by means of a syringe fitted with a pre-filter; the volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium (phosphate buffer 6.8). The resultant samples were analyzed by measuring the absorbance at 285 nm using UV Visible

spectrophotometer and calculate the percentage drug release. In the present study the formulation M1 has shown cumulative percent drug release of about 92.36% in 08 h as shown in figure.

Figure 6: % Drug release of the sustained released layer (Mefenamic acid)

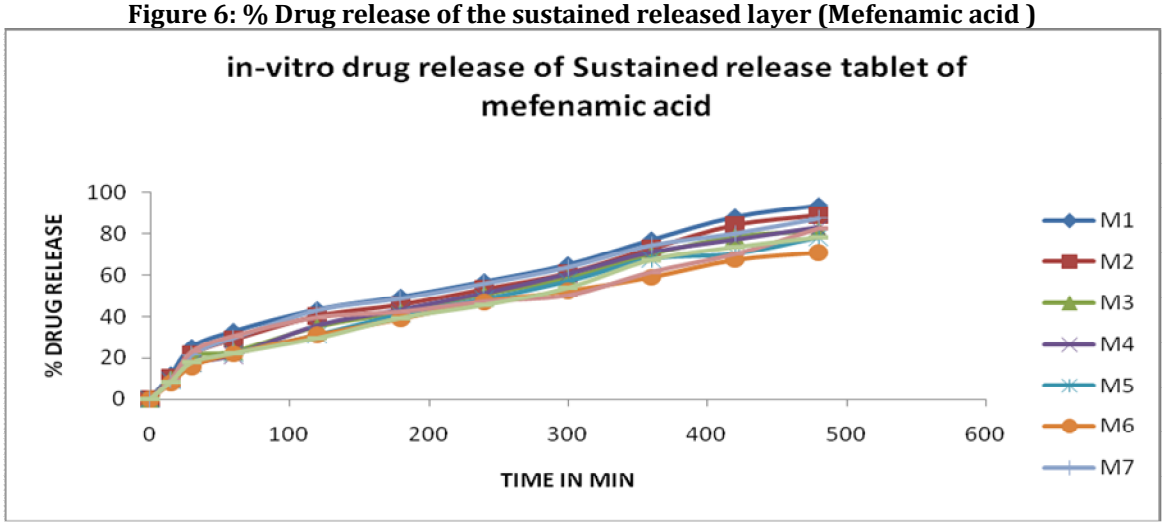


Figure 7: % Drug release of the optimized formulation A1, T3.

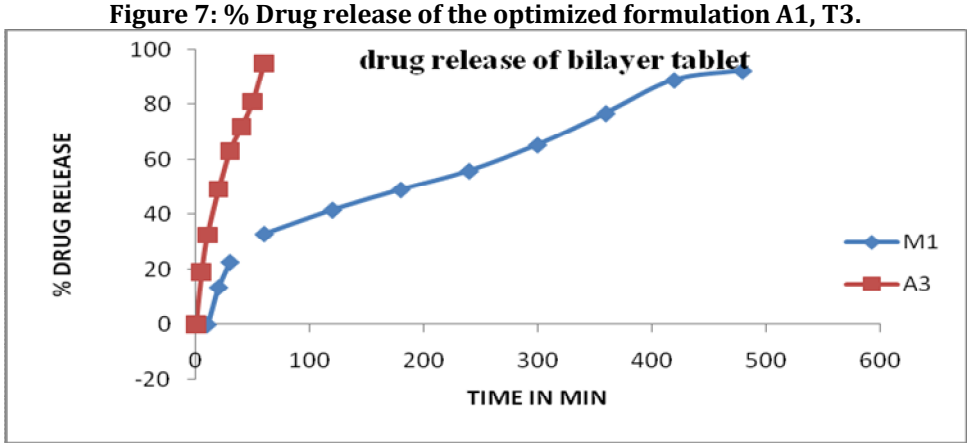


Table 10: Drug release kinetics of Aloe vera gel powder tablet

Time (min)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining (Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
5	18.93	81.07	2.236	1.909	0.699	1.277	18.93	4.328	0.314
10	32.45	67.55	3.162	1.830	1.000	1.511	13.52	4.073	0.569
20	48.99	51.01	4.472	1.708	1.301	1.690	16.54	3.709	0.933
30	62.96	37.04	5.477	1.569	1.477	1.799	13.97	3.333	1.309
40	71.85	28.15	6.325	1.449	1.602	1.856	8.89	3.042	1.600
50	80.96	19.04	7.071	1.280	1.699	1.908	9.11	2.670	1.972
60	94.88	5.12	7.746	0.709	1.778	1.977	13.92	1.724	2.918

Fig. 08: Drug release kinetic of immediate release layer (Aloe vera gel powder)

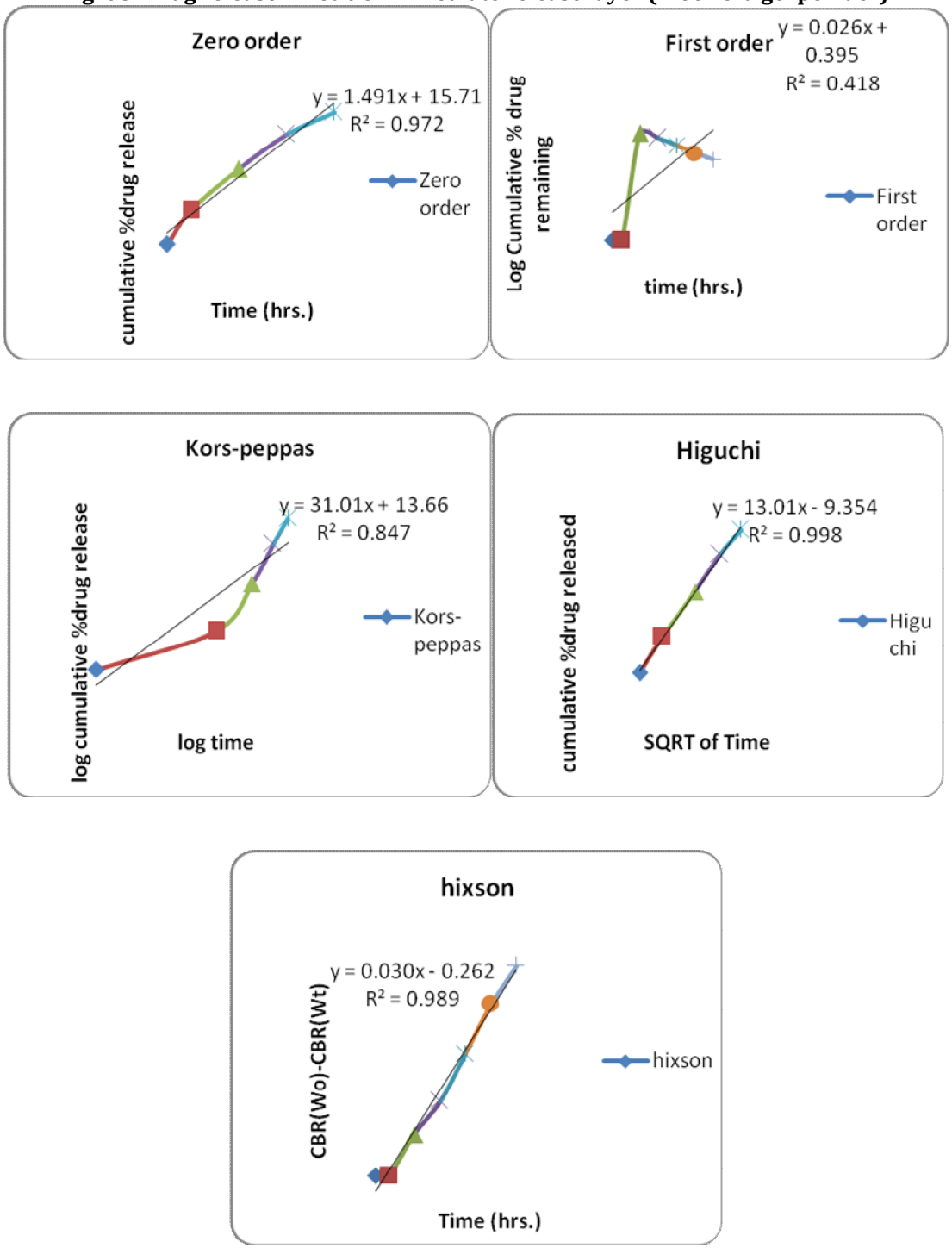
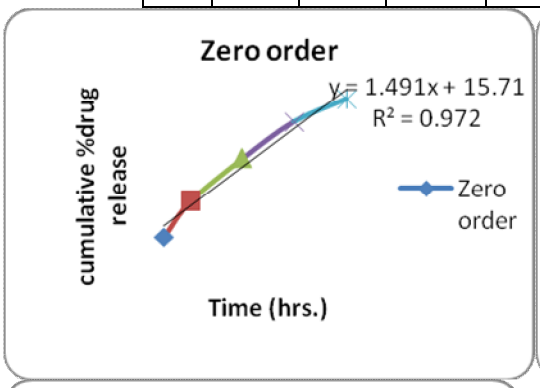
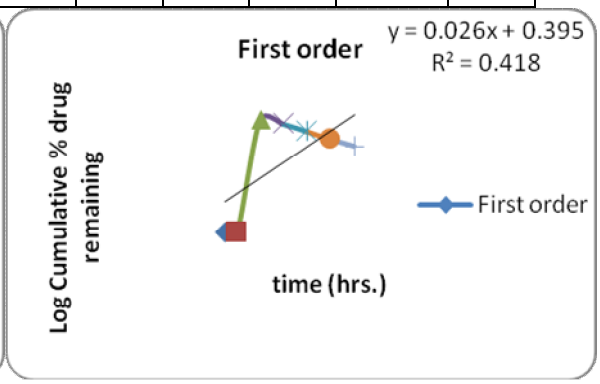
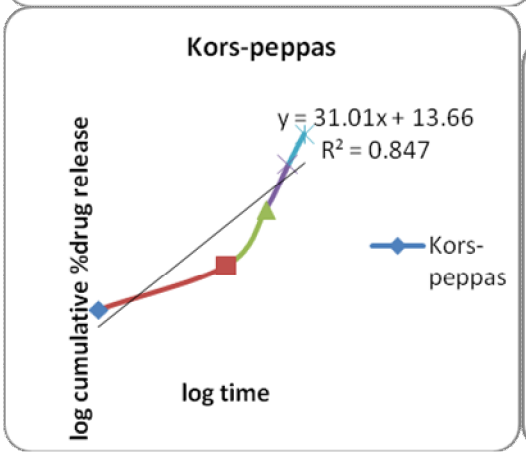


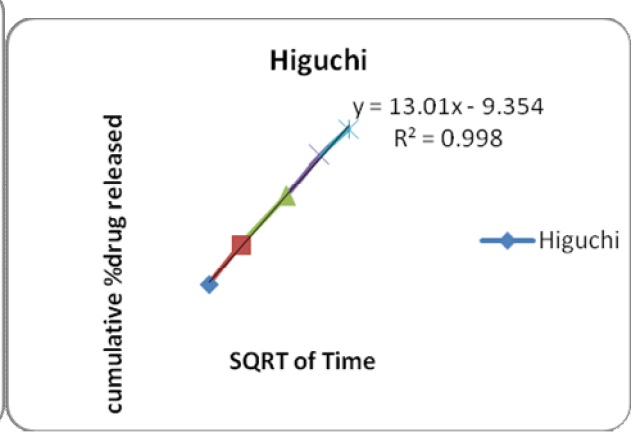
Table 11: Drug release kinetics of Mefenamic acid

Time(min)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
15	11.45	88.55	3.873	1.947	1.176	1.059	11.45	4.457	0.185
30	22.63	77.37	5.477	1.889	1.477	1.355	11.18	4.261	0.381
60	32.99	67.01	7.746	1.826	1.778	1.518	10.36	4.062	0.580
120	41.63	58.37	10.954	1.766	2.079	1.619	8.64	3.879	0.763
180	48.96	51.04	13.416	1.708	2.255	1.690	7.33	3.709	0.933
240	55.85	44.15	15.492	1.645	2.380	1.747	6.89	3.534	1.108
300	65.35	34.65	17.321	1.540	2.477	1.815	9.5	3.260	1.382
360	76.85	23.15	18.974	1.365	2.556	1.886	11.5	2.850	1.792
420	88.85	11.15	20.494	1.047	2.623	1.949	12	2.234	2.408
480	92.36	7.64	21.909	0.883	1.000	1.965	3.51	1.970	2.672









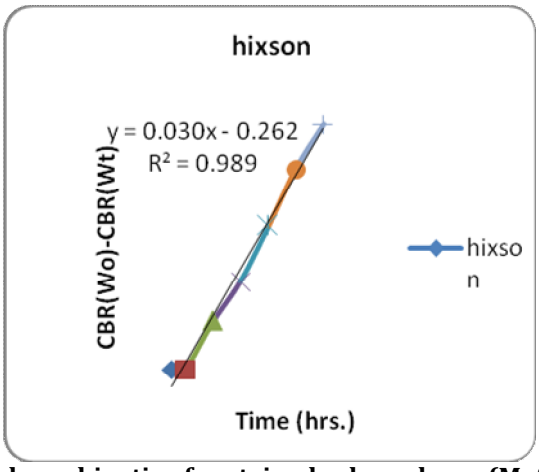


Fig. 9: Drug release kinetic of sustained release layer (Mefenamic acid)

Kinetic models

Dissolution data of above bi-layered tablet was perfectly fitted in, Hixon, and Higuchi equations. The mechanism of drug release pattern was determined by using Higuchi equation.

CONCLUSION

It is proved from this study that the bilayer tablet of Analgesic drug mefenamic acid as sustained release and antiulcer drug aloe vera gel powder as immediate release can be formulated. Formulated tablets showed satisfactory results for various evaluation parameters such as tablet dimension, hardness, thickness, friability, weight uniformity, drug content and in vitro dissolution study. The optimized formulation based on all the parameter A3 (Crospovidone) is selected for the immediate release layer and M1 (HPMC K4M) was selected for the sustained release layer, where A3 formulat ion shows % drug release 94.88 % within one hour and M1 formulation shows % drug release 92.36% within 08 hours.Thus the objective of formulating the bilayer tablets of Aloe Vera gel powder and Mefenamic acid useful for relief pain with antiulcer property has been achieved.

ACKNOWLEDGMENT

Authors are thankful to Vishal Institute Pharmaceutical Education and Research, Ale for providing the raw materials and instrument to carry out this research work successfully

AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

Declare none

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