



FORMULATION AND EVALUATION OF BILAYER TABLET CONTAINING DICLOFENAC SODIUM AS SUSTAINED RELEASE

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ABSTRACT:

Objective: The objective of the present investigation is to design formulate and characterized the bilayer tablet containing Diclofenac sodium and Aloe Vera gel powder. In which diclofenac sodium is sustained release and Aloe Vera gel powder is immediate release. In order to produce a single dosage form containing two different classes, drug are widely prescribed by the physician to have better patient compliance.

Methods: Bilayer tablet was prepared by direct compression, The immediate release layer of Aloe Vera gel powder was prepared by using different excipients such as starch, sodium starch glycolate, lactose, talc etc. sustained release layer of diclofenac sodium was prepared by using HPMC K4M, lactose, Talc Magnesium stearate, talc etc. for preparation of bilayer tablet sodium starch glycolate are use as super disintegrants in immediate release tablet and HPMC K4M are use as controlled release polymer. Various Preformulation parameter i.e. Identification, melting point, compatibility study, solubility are checked. Micromeritics properties of powder blend such as bulk density, tapped density, hausner's ratio, Carr's index, angle of repose are performed. Post-compression parameter was done such as hardness, friability, weight variation, drug content uniformity, thickness, in vitro drug release.

Results: Result was found within the limit of the standard of optimized formulation. The drug release of the tablet was in the range of 82 to 92% in 8 h.

Conclusion: Bilayer tablet was prepared by optimized batches of both layers. The prepared tablets showed satisfactory results for various evaluation parameters. The optimized formulation based on all the parameter A1 (Sodium starch glycolate) is selected for the immediate release layer and D3 (HPMC K4M) was selected for the controlled release layer. The drug release mechanism was found to be zero order release depends upon diffusion.

Keywords: Bilayer tablet, Diclofenac sodium, Aloe Vera gel powder, HPMC K4M, Immediate release, Sustained release, Direct compression

Introduction:

The purpose of any drug delivery system is to provide a therapeutic amount of the drug to the proper site of action in the body to maintain the desired drug concentration. Oral route is most convenient route of the administration dosage form. Tablet is a convenient dosage form acceptable by patients and physicians. Bilayer tablet is suitable for sequential release of two drugs in which one is immediate release and another is sustained release. The fixed-dose Combinations of two or more active drugs produced in a single dosage form. The advantages of combination therapy to reduce the number of the dosage form in prescription and maintain administrative cost as well as improving patient compliance. The present study is about to find out the solution to reduce the incidence of diclofenac sodium-induced GI injury and other severe GI problems. This problem is overcome by preparing the bilayer tablet of diclofenac sodium with Aloe vera gel powder. Diclofenac sodium is a non-steroidal anti-inflammatory drug which has analgesic and antipyretic activity. Diclofenac is used to treat pain, menstrual pain, dysmenorrhea, ocular inflammation, osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. The primary mechanism responsible for its analgesic, anti-inflammatory and antipyretic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase and it appears to inhibit DNA synthesis. Inhibition of COX also decreases prostaglandins in the epithelium of the stomach, making it more sensitive to corrosion by gastric acid, which is responsible for the cause of ulcer. Diclofenac is absorbed 100% orally, 99% protein bound, metabolized and excreted both in urine and bile. The elimination half-life is 1.2 to 2 h hence, diclofenac is suitable for sustained release layer. Both layers are compressed by direct compression methods. To evaluate blends in terms 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.

MATERIALS AND METHODS

Material

Sample was procuring from Diclofenac sodium (), HPMC K4M, Talc (Thermosil fine chem.) Aloe vera gel powder (maple biotech pvt ltd bhosari, Pune) starch, sodium starch glycolate, (research lab) Lactose, (Sahyadri scientific supply) Magnesium Stearate (Hilab chemicals) were sample is analytical grade.

Method

Formulation of bilayer tablet was prepared by direct compression method. Immediate release layer was prepared by using different super disintegrants (sodium starch glycolate).

Drug and above super disintegrants were passed through the 40# sieve and transfer into polybag and mix up to 3 min. Then add other excipients to the above mixture. Finally, add (glidant) talc into the blend.

Another layer was also prepared by direct compression; drug and polymer (HPMC k4M) were pass through the 40# sieve transfer into polybag and mixed properly up to 3 min. Other excipients were mixed well and finally added Magnesium Stearate in the above blend and were mixed for 2 min.

Finally above optimized batch blends were compressed by rotary tablet compression machine (Make-CREATE INDUSTRIES, MODEL-LP-8GMP).

Table 2: Formulation of sustained release diclofenac sodium

S. No.	Ingredients	Weight (mg)		
		D1	D2	D3
1	Diclofenac sodium	50	50	50
2	HPMC K4M	12	20	28
3	Lactose	128	120	112
4	Talc	5	5	5
5	Magnesium stearate	5	5	5
	Total	200	200	200

Preformulation study:

Identification test by U. V vis.

spectrophotometer A. For diclofenac sodium:

25 mg of diclofenac sodium was weighed accurately and transferred it to 25 ml volumetric flask. Dissolved it in ethanol and make the volume up to 25 ml with respective solvent. This was considered a stock solution (1000 mcg/ml). Further dilutions were made with this stock solution and scanned in the range of 400-200 nm using respective blank in UV spectrophotometer (SHIMADZU U. V 1800).

Melting point determination

Melting point of diclofenac sodium and aloe vera gel powder was determined by using melting point apparatus by capillary method.

Determination of solubility

Qualitative Solubility

Qualitative solubility analysis of drugs was done by dissolving 5 mg of drug in 5 ml solvent such as distilled water, methanol, ethanol, chloroform, phosphate buffer (7.4), ether.

Compatibility study, by FT-IR spectroscopy

The powdered substance of the tablet was mix, dried potassium bromide (IR grade) ratio of sample is should be 1:100 mg, i. e 1 mg sample: 100 mg KBr. are compressed to form transparent pellets. The sample was scanned from 4000 to 400 cm^{-1} at ambient temperature. (Perkin Elmer Spectrum-65)

Pre-compression evaluation**Bulk density**

Bulk density was determined by introducing the powder blend into measuring cylinder and the total volume was measured and also total powder weight was measured. The bulk density was calculated by using formula.

Bulk density (BD) = weight of powder/bulk volume.

Tapped density

Tapped density was determined by tapping the cylinder by using the tapped density apparatus. Tapped the cylinder up to 100 times and then measure the tapped volume and calculate the tapped density by using formula.

Tapped Density (TD) = weight of powder/tapped volume.

Hausner's ratio

Hausner's ratio bulk density as to tapped density is the number that is correlated to the flowability of a powder or powder blend. It is calculated using formula,

Hausner's ratio = tapped density/bulk density.

Compressibility index

Compressibility index was calculated by formula,

Carr's index (%) = $\frac{\text{Tapped density} - \text{bulk density}}{\text{bulk density}} \times 100$

Angle of repose

The angle of repose of powder blend of each layer of each formulation was determined by fix funnel method. The blend was poured through funnel separately until apex of pile so formed just touch the tip of the funnel. The angle of repose was calculated by using formula

θ
 $= \tan^{-1}h/r$ h is height of pile; r is the radius of pile.

Post-compression evaluation

Uniformity weight

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

Friability

Friction and shock are the forces that most often cause tablets to chip, cap or break. 10 tablets are 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. The loss due to abrasion is a measure of the tablet friability. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked. The percentage friability was determined by the formula:

$$\% \text{ friability} = [\text{initial weight} - \text{final weight} / \text{initial weight}] * 100$$

RESULTS AND DISCUSSION

Pre-formulation studies

The UV absorption of 10 µg/ml in methanol for Aloe vera gel powder is 262 nm in the range of 200-400 nm exhibit maximum and in case of Diclofenac sodium at 275 nm.

Melting point, solubility and compatibility study of both drugs are carried out and the result is including in table 4.

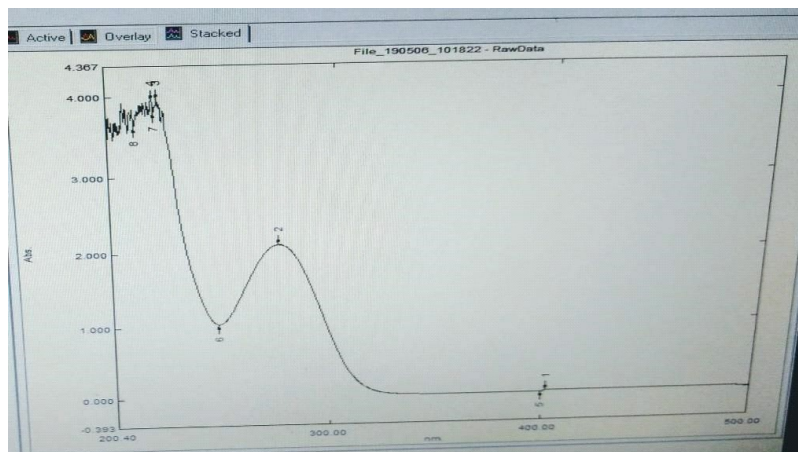


Fig. 2: Absorbance maxima of diclofenac sodium

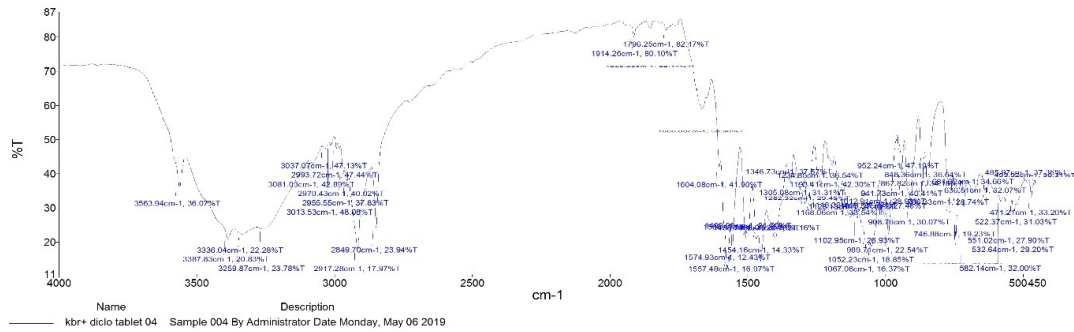


Fig. 6: FTIR of diclofenac sodium tablet

Pre-compression evaluation

The micromeritic properties such as of bulk density, tapped density, Angle of repose, compressibility index, and Hausner's of Aloe vera gel powder immediate release layer blend and Diclofenac sodium sustained release layer were studied. The overall results were shown in table No5. The value of bulk density indicates good packing characteristics. 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 6: Pre-compression evaluation of sustained release powder blend, (diclofenac sodium)

S. No.	Parameter	D1	D2	D3
1	Bulk density (g/ml)	56.67	60.5	58.20
2	Tapped density (g/ml)	68.1	69.6	66.70
3	Compressibility index (%)	16.1%	13.07%	12.87%
4	Hausner's ratio	1.20	1.16	1.14
5	Angle of repose (degree)	20 °	21.5 °	24.2 °

Post-compression evaluation of tablet

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

The hardness of each batch of the tablet was checked by using Monsanto hardness tester. The hardness was measured in terms 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), which was rotated for 4 min at 25 rpm. After dusting, the total remaining mass of tablet was recorded and the percent friability was calculated.

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

Table 7: Post-compression evaluation of immediate release tablet

S. No.	Parameter	A1	A2	A3
1	Uniformity weight(mg)	149 mg	147 mg	153 mg
2	Thickness(mm)	3.0	3.1	3.0
3	Hardness(kg/cm ²)	3.2 kg/cm ²	3 kg/cm ²	3.5 kg/cm ²
4	Friability (%)	0.84%	0.67%	0.91%

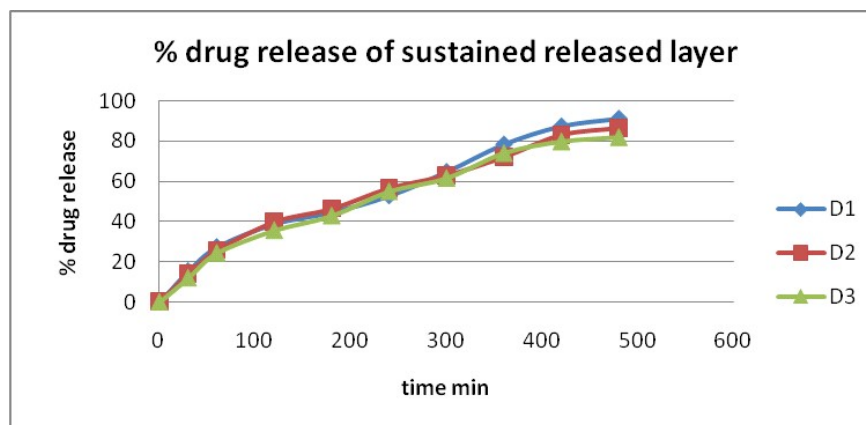
5	Drug content	97.54	98.10	96.92
6	% Drug release	90.21%	89.75%	87.82%

Table 8: Post-compression evaluation of sustained release tablet

S. No.	Parameter	A1	A2	A3
1	Uniformity weight(mg)	199 mg	203 mg	201 mg
2	Thickness(mm)	3.5	3.5	3.7
3	Hardness(kg/cm ²)	6.5 kg/cm ²	7 kg/cm ²	6.2 kg/cm ²
4	Friability (%)	0.54%	0.91%	0.80%
5	Drug content	95.40	91.50	96.92
6	% Drug release	91.21%	86.35%	82.12%

Table 9: Post-compression evaluation of bilayer tablet of A1 and D3 Optimized batch

S. No.	Parameter	A1D3
1	Uniformity weight(mg)	349 mg
2	Thickness(mm)	3.5 mm
3	Hardness(kg/cm ²)	5.2 kg/cm ²
4	Friability (%)	0.90%
5	Drug content (immediate release)	97.21
	Drug content (Sustained release)	95.49
6	% drug release (immediate release)	93.80%
	% drug release (Sustained release)	84.26%

**Fig. 8: % Drug release of the sustained released layer (diclofenac sodium)**

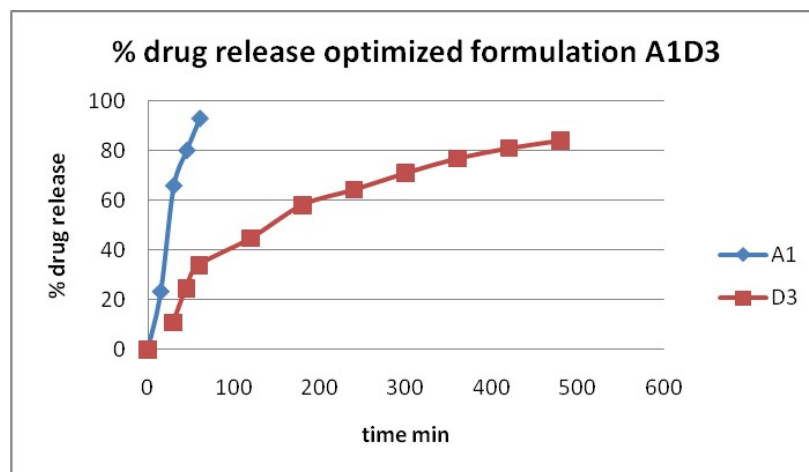


Fig. 9: % Drug release optimized formulation A1, D3

CONCLUSION:

The prepared tablets showed satisfactory results for various evaluation tests such as tablet dimension, hardness, friability, weight uniformity, drug content and in vitro dissolution study. The optimized formulation based on all the parameter A1 (Sodium starch glycolate) is selected for the immediate release layer and D3 (HPMC K4M) was selected for the controlled release layer. The drug release mechanism was found to be zero order release; dependent on both drug diffusion and polymer relaxation. The bilayer tablets of Aloe vera gel powder and Diclofenac sodium useful for NSAID with antiulcer Aloe vera gel powder.

REFERENCES:

1. B Prabakaran, K Elango, K Ramesh Kumar, D Jaison. Formulation development and evaluation of gastroretentive bilayer floating tablets of simvastatin and telmisartan. *Int J Pharma Res Rev* 2016;5:9-18.
2. Prabhakar Shirse. Formulation and evaluation of bilayer tablets of diclofenac sodium with ranitidine HCL for sustained and immediate release. *J Appl Pharm Sci* 2012;2:136-41.
3. <https://en.wikipedia.org/wiki/Diclofenac>. [Last accessed in 10 Mar 2019]
4. Bharath Kumar N, S Bharath, R Deveswaran, BV Basavaraj, V Madhavan, Extended drug release retarding effect of aloe vera gel in the design of tablet dosage form. *IJPBS* 2012;2:54-9.
5. Karthik Varma V. Excipients used in the formulation of the tablet. *Res Rev J Chem* 2016;5:143-5.
6. Lachman L, Lieberman HA, Kanig JL. The theory and practice of Industrial pharmacy, Varghese Publishing House Bombay; special Indian edition; 2009.
7. Gurdeep R Chatwal, Sham K Anand. Instrumental methods of chemical analysis. 3rd ed Himalaya Publishing House, Mumbai; 2011. p. 244.
8. Shivani Kala, Divya Juyal. Preformulation and characterization studies of aceclofenac active ingredient. *Pharma Innovation J* 2016;5:110-9.
9. Indian Pharmacopoeia. Ministry of Health and Family Welfare. Ghaziabad, India: The Indian Pharmacopoeia commission; 2010. p. 3.
10. United States Pharmacopoeia. 30th edition NF 25-2007, The Official Compendia of Standards. 643, Pharmacopoeial forum; 2007. p. 28.