Available online on 15.03.2025 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

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Research Article

Formulation and Evaluation of Solid Dispersion Tablets of Aceclofenac

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Article Info:

Article History:

Received 23 Dec 2024
Reviewed 27 Jan 2025
Accepted 19 Feb 2025
Published 15 March 2025

Cite this article as:

Ghosh B, Das S, Basu S, Bhunia SN, Biswas U, Mandal A, Formulation and Evaluation of Solid Dispersion Tablets of Aceclofenac, Journal of Drug Delivery and Therapeutics. 2025; 15(3):15-20 *DOI: http://dx.doi.org/10.22270/jddt.v15i3.7016*

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Abstract

Formulating the solid dispersion (SD) of the weakly water-soluble medication aceclofenac using various matrix types and creating tablets from the prepared SD of aceclofenac were the goals of this work. The solution approach was used to prepare the SD of aceclofenac utilizing a variety of matrices, including lactose, mannitol, and urea. The HPMC E15 LV polymer was used in the direct compression method to create the tablets. The granules were assessed by measuring their Carr's index, Hausner ratio, bulk density, tapped density, and angle of repose. The results are satisfactory. The tablets' hardness, friability, drug content, and *in-vitro* release were measured and examined. A pure drug's release study was carried out. It was evident from the results that pure aceclofenac dissolved relatively slow. The time at which aceclofenac dissolved was extremely quick when it was produced in SD form. Aceclofenac SD tablets were made, and a release analysis was conducted based on the different matrices employed in the process, such as urea, lactose, and mannitol. The SD of aceclofenac tablets with urea produces noticeably better results in the release studies compared to lactose and mannitol. Thus, long-term stability research is necessary for this formulation's future development.

Keywords: Solid Dispersion, Aceclofenac, Lactose, Urea, Mannitol

INTRODUCTION:

Among the many alternatives available for the delivery of different pharmaceuticals, the oral route is the most commonly utilized due to its affordability, ease of use, patient friendliness, and simplicity of administration. This kind of distribution method serves as an illustration of a traditional drug delivery system, and these Conventional dosage forms can help the medication release instantly[1]. This means that the drug is absorbed more quickly when using these formulations. Combining medications, however, raises the possibility of toxicity and leads to patients who are noncompliant. There are numerous ways to get around the disadvantages of standard dose formulations of this kind. The idea of a cutting-edge medication delivery system among them turns out to be the best method for creating matrix tablets. One important strategy for the development of improved medication delivery is the use of matrix tablets systems. The term "matrix tablets" refers to oral dosage forms where the active component is evenly distributed across hydrophilic or hydrophobic matrices[2].

A popular prescription for treating osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis is aceclofenac, a strong non-steroidal anti-inflammatory medicine. Aceclofenac is a chemical that has Analgesic action is shown by [2-(2, 6-dichlorophenyl) amino] phenylacetyl oxyacetic acid. Low gastrointestinal side effects are associated with this derivative of diclofenac. The material is crystalline and white in color. It dissolves easily in ethanol and acetone but not in water. It is highly bioavailable (nearly 90–95%) and well absorbed when taken orally. About 70–80% of the medication is eliminated by the renal route, and aceclofenac has a half-life of 4-6 hours[3].

Aceclofenac, a medication belonging to BCS class II, has limited bioavailability and poor drug dissolution due to its high permeability and low water solubility. Therefore, increasing solubility and dissolving rate seems to be a challenging step. Thus, several strategies have been employed to improve the solubility and rate of dissolution of poorly soluble drugs, including as micronization, polymorphism, and solid dispersion techniques. One of the most practical and effective methods for improving the drug release profile of poorly soluble medications is solid dispersion[4]. Sekiguchi and Obi presented the solid dispersion theory for the first time in 1961. A solid dispersion is defined as "A group of solid items, especially pharmaceuticals that are hydrophobic, consist of a hydrophilic matrix containing two or more different moieties[5].

An assortment of solid materials made up of two or more separate components, namely a hydrophobic drug and a hydrophilic matrix, with the drug evenly dispersed in either crystalline or amorphous particles, is called a solid dispersion[6].In order to increase the bioavailability and solubility of drugs that are poorly soluble, the solid dispersion method is often used. The current work formulates and evaluates matrix tablets using a solid dispersion technique in an effort to increase the solubility and rate of dissolution through the use of various polymers[7].

A lower frequency of dosage leads to a longer duration of drug release, reduction of drug buildup, enhancement patient adherence, reduction of medical expenses are the advantages of solid dispersion[8].

MATERIALS AND METHODS:

MATERIALS:

Aceclofenac was purchased from Yarrow chem product, Mumbai. Urea, mannitol, lactose monohydrate, HPMC E 15 LV, magnesium stearate, and talc were purchased by Loba Chemie Pvt. Ltd. (Mumbai). Micro Crystalline Cellulose was purchased from Merck speciality Pvt. Ltd.

METHODS:

Preparation of solid dispersion by solution method:

In solution method, hydrophilic matrix (urea, Mannitol, Lactose Monohydrate) is first dissolved in adequate amount of water and melted in water bath with gradual increase in temperature until it completely melts. Now, drug is added in the melted urea or mannitol or lactose monohydrate with constant stirring and leaves this mixture to cool at room temperature. The ratio of drug and hydrophilic matrix taken is 1:1. The mixture was dried, crushed, pulverized and passed through sieve number #60 and stored in desiccators[9].

Preparation of Tablets:

The solid dispersion of Aceclofenac tablets were prepared by direct compression method. Required quantity of solid dispersion of Aceclofenac, HPMC and MCC are weighted and mixed uniformly using pestle mortar. Then talc and magnesium Stearate are added with it.

Table 1: Various composition of Aceclofenac SD Tablets

Ingredients	F1	F2	F3
Aceclofenac (SD)	100mg	100mg	100mg
Urea	100mg	---	---
Mannitol	---	---	100mg
Lactose Monohydrate	---	100mg	---
HPMC E 15 LV	100mg	100mg	100mg
Micro Crystalline Cellulose	15mg	15mg	15mg
Magnesium Stearate	5mg	5mg	5mg
Talc	5mg	5mg	5mg

All ingredients are mixed uniformly. After that, the powders are punched in a tablet compression machine and get tablets[9].The various composition of Aceclofenac SD tablet shown on the table 1.

Characterization of granules flow characteristics:

Bulk Density:

A precise amount (m) of granules was carefully added to the measuring cylinder. The granules were read to the closest graded unit to determine the unsettled apparent volume (V) after being leveled without compacting if required. The bulk density was determined using the formula m/V and represented as grams per ml[10].

Tapped Density:

A predetermined amount of granules was placed in a measuring cylinder and tapped for five minutes using a mechanical tapping device[10]. Both the first and last volumes were mentioned.

$$Tapped\ Density = \frac{Weight\ of\ Granules}{Final\ Volume\ after\ tapping}$$

Angle of Repose:

The angle of repose measures the frictional forces in loose powder or granules. The angle between the surface of a pile of granules or powder and the horizontal plane is as large as it can be. The funnel method is used for this[11]. The following formula is used to determine the angle of repose value:

$$\theta = \tan^{-1} h/r$$

Where,

Θ =Angle of repose, h =Height of the pile, r =Radius of the pile

Compressibility Index and Hausner ratio:

A powder's tendency to consolidate is measured by its compressibility index (CI), which is a measure of the relative significance of interparticulate interactions.

A measure of a material's flowability that accounts for the resistance a bed of particles encounters as a result of their interactions is called the Hausner ratio (HR)[11]. Compressibility index and hausner ratio were calculated by using the following formula:

$$Compressibility\ Index = \frac{Tapped\ Density - Bulk\ Density}{Tapped\ Density} \times 100$$

$$Hausner\ Ratio = \frac{Tapped\ Density}{Bulk\ Density}$$

The results of bulk density, tapped density, angle of repose, compressibility index and hausner's ratio are noted on table 2.

Evaluation of Tablets:

Hardness Test: A tablet's hardness is an indicator of its strength and capacity to withstand mechanical shocks during processing and handling. Using a Monsanto hardness tester, the tablets' hardness was assessed for each formulation. kg/cm-2 is the unit of measurement[12].

Friability Test: Friability tests are used to evaluate the impact of shocks and friction, which frequently result in tablets breaking, chipping, or capping. Roche Friabilator was employed to assess the tablets' friability[12].

Drug Content: Ten tablets were chosen at random from each batch for this test, and they were ground up in a mortar. The powder was dissolved in 10 ml phosphate buffer pH 7.4 by sonication for 15 min and filtered through Whatman filter paper. Suitable dilutions were made, and the drug content was analysed spectrophotometrically at 276 nm using a UV-VIS spectrophotometer (model Jasco V730)[13,14].

Dissolution Test: *In vitro* dissolution study of tablets were conducted using USP dissolution apparatus II at 50 rpm, using phosphate buffer pH 7.4 as a dissolution media maintaining at 37 ± 0.5° C[15].

The results of hardness, friability, drug content are shown in table 3.

Drug Release Kinetic:The following formulas were used to assess the data from the *in vitro* release study using the linear regression method:

i) Zero Order:

$$Qt = K0\ t$$

Where, Q= Amount of drug release in time t

K0 = Zero order rate constant expressed in unit of concentration/ time

t = Release time

ii) First Order:

$$Log\ Q = Log\ Q0 - Kt/2.303$$

Where, Q0 = The initial concentration of drug

K= The first order rate constant

t = Release time

iii) Higuchi Model:

$Q = Kt_{1/2}$

Where, K= Release rate constant

T= Release time

iv) Hixon- Crowell model:

$W_0^{1/3} - W_t^{1/3} = kt$

Where, W0 = Initial amount of drug in the pharmaceutical dosage form

W_t = Remaining amount of drug in the pharmaceutical dosage form at time t

K = Rate Constant incorporating the surface volume relation

V) Kormeseyer- Peppas model:

$$\frac{Mt}{M\infty} = Kt\ n$$

Where, Mt = Amount of drug release at time t

M∞ = Amount of drug released after infinite time

Mt/M∞ = Fraction solute release

t= Release time

K= Kinetic constant incorporating structural and geometric characteristics of the polymer system

n= Diffusion exponent that characterizes the mechanism of the release of traces [16,17]

The results are shown in table 5 and figs 2-6.

RESULTS:

The granules were assessed by using the following parameters: angle of repose which ranges from 25.80 ± 0.135 to 28.44 ± 0.198, bulk density ranges from 0.38 ± 0.005 to 0.45 ± 0.008 kg/ cm^3, tapped density ranges from 0.42 ± 0.003 to 0.51 ± 0.006 kg/ cm^3, Carr's index ranges from 9.52 ± 0.004 to 16.32 ± 0.009 and hausner's ratio 1.10 ± 0.02 to 1.19 ± 0.04.

Table 2: Precompression Evaluation [Characterization of Granules]

Formulation	Angle of Repose	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio
F1	25.75±0.423	0.38±0.005	0.42±0.003	9.52 ± 0.004	1.10±0.02
F2	28.44±0.198	0.41±0.012	0.49±0.007	16.32±0.009	1.19±0.04
F3	26.80±0.135	0.45±0.008	0.51±0.006	11.76±0.007	1.13±0.06

*Mean± SD (n=3)

The hardness of the tablet's ranging from 3.8 ± 0.03 to 5.4 ± 0.06 kg/ cm^2, friability ranges from 0.56 ± 0.03 to 0.71 ± 0.04 % and drug content ranges from 81.2 ± 0.032 to 83.38 ± 0.028 %.

Table 3: Postcompression Evaluation

Formulation	Hardness (Kg/ cm^2)	Friability (%)	Drug Content (%)
F1	5.4 ± 0.06	0.56±0.04	83.38±0.028
F2	4.9± 0.08	0.71±0.03	81.2±0.032
F3	3.8±0.03	0.67±0.02	82.09±0.025

*Mean± SD (n=3)

Table 4: Comparative release study of three formulations

Formulation	% of Drug Release
F1	94.616
F2	76.687
F3	57.694

Table 5 : Kinetic study of *in-vitro* release data of Aceclofenac

Formulation Code	Zero Order	First Order	Higuchi Model	Hixon – Crowell Model	Korsmeyer Peppas Model
Correlation Coefficient					
F1	0.954	0.711	0.997	0.994	0.952
F2	0.977	0.829	0.982	0.961	0.976
F3	0.979	0.743	0.989	0.9759	0.974

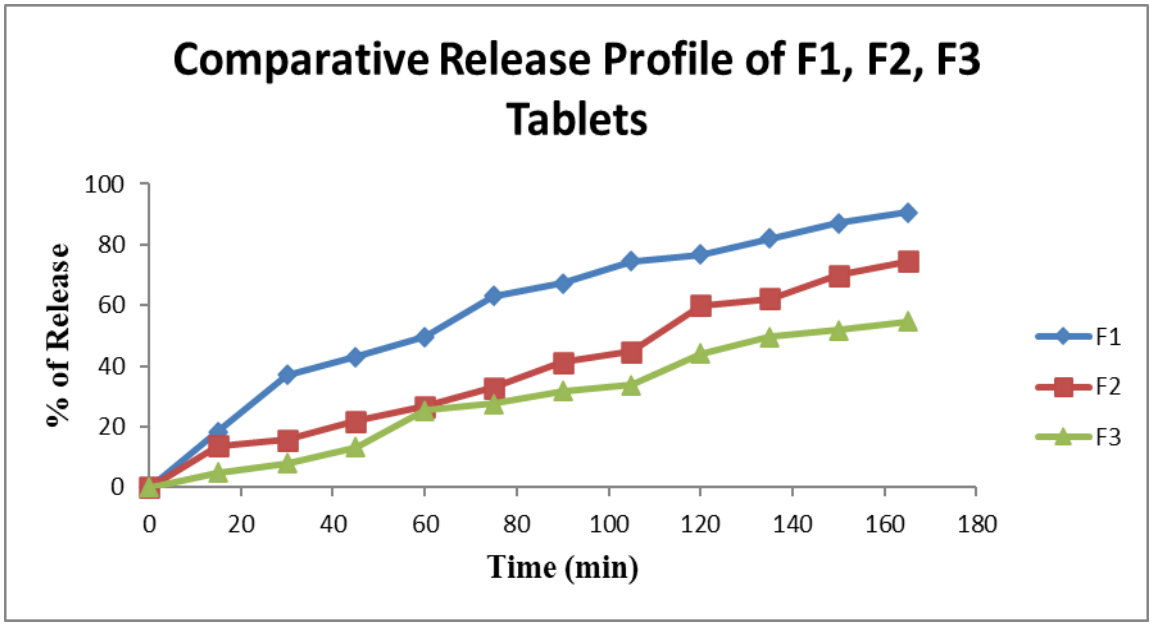

Figure 1 : Comparative Release Profile of various formulation

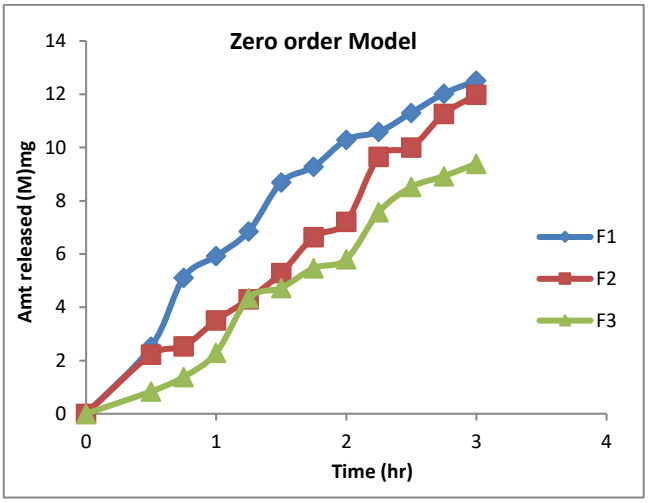

Figure 2: Zero order release plot for prepared solid dispersion tablets

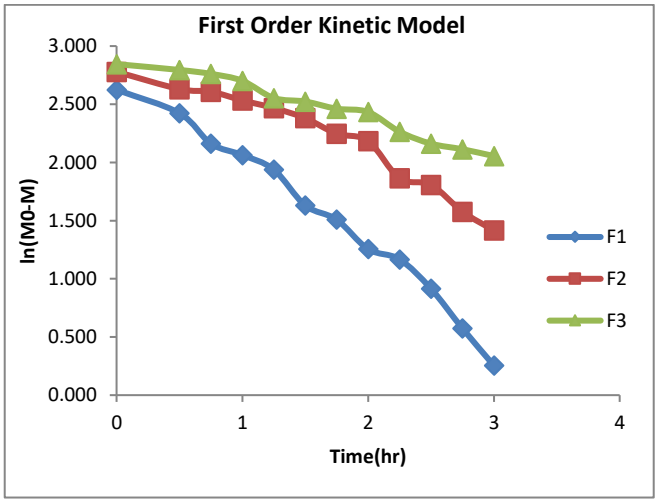

Figure 3: First order release plot for prepared solid dispersion tablets

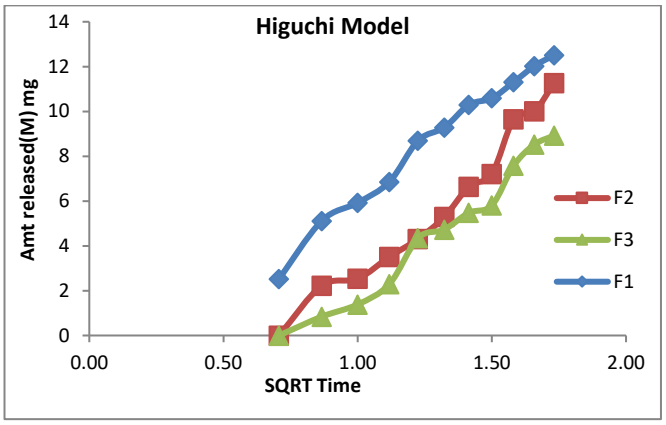

Figure 4: Higuchi release plot for prepared solid dispersion tablets

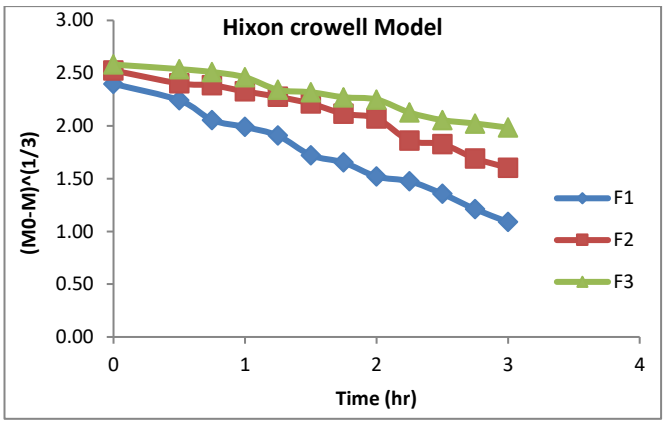

Figure 5: Hixon Crowell release plot for prepared solid dispersion tablets

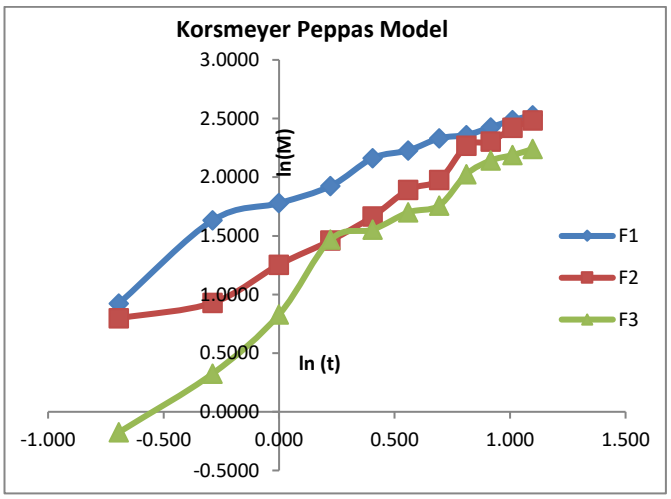

Figure 6 : Korsmeyer Peppas release plot for prepared solid dispersion tablets

DISCUSSIONS:

A variety of precompression experiments, including angle of repose, tapped density, bulk density, Carr's index, and Hausner's ratio, were conducted after the aceclofenac was produced in SD form utilizing a variety of matrix, including urea, mannitol, and lactose. Upon examining these outcomes, it was decided that the results are within standard limit and highly satisfactory. After preparing the SD of aceclofenac tablets, it was found that the F1 batch had superior hardness and friability compared to the other two batches. The F1 batch had a drug content of 83.38 ± 0.028 percent, which is significantly higher than the other two formulations. After three hours, the dissolution study for formulations F1, F2, and F3 reveals that they release 94.616%, 76.687 %, and 57.694 % of the medication, respectively. Consequently, after the discussion, it has been determined that, out of the three formulations, F1 is the best batch. The release data was analyzed using various kinds of kinetic models, including zero order, first order, Higuchi model, Hixon-Crowell model and korsmeyer Peppas model as illustrated in figs 2-6. The value of R2 was reported in table 5. All of the above formulations fit the Higuchi model the best.

CONCLUSION:

Pure aceclofenac had an extremely sluggish rate of dissolution. The rate of dissolution was quite rapid when the aceclofenac was produced in SD form. Aceclofenac SD tablets were made, and a release study was performed. When compared to tablets made with mannitol and lactose, the release of aceclofenac SD tablets made with urea was superior. Aceclofenac SD tablets' bioavailability improved in conjunction with their rate of dissolution. For this formulation's future development, a long-term stability study is also necessary.

Conflict of Interest: The authors declare no potential conflict of interest with respect to the contents, authorship, and/or publication of this article.

Author Contributions: All authors have equally contributed.

Source of Support: Nil

Funding: The authors declared that this study has received no financial support.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Ethics approval: Not applicable.

REFERENCES:

1. Mondal N: The role of matrix tablet in drug delivery system. International Journal of Applied Pharmaceutics 2017; 10(1): 1-6 https://doi.org/10.22159//ijap.2018v10i1.21935

2. Kala S and Juyal D: Pre-formulation and characterization studies of aceclofenac active ingredient. The Pharma Innovation 2016; 5(9): 110-19.

3. Singh N and Sarangi MK: Solid dispersion - a novel approach for enhancement of bioavailability of poorly soluble drugs in oral drug delivery system. Global Journal of Pharmacy & Pharmaceutical Science 2017; 3(2): 1-8. https://doi.org/10.19080/GJPPS.2017.03.555608

4. Sukanya M, Sai Kishore V, Design and Development of Solid Dispersions of Simvastatin for Enhancing the Solubility, Am. J. PharmTech Res. 2012; 2(4): 733-740.

5. Agarwal P and Akthar S: A comprehensive review on sustained release matrix tablets: A promising dosage form. Universal Journal of Pharmaceutical Research 2018; 3(6): 49-54. https://doi.org/10.22270/ujpr.v3i6.222

6. Venkates KK, Arunkumar N, Verma PRP, Rani C. Preparation and In vitro characterization of valsartan solid dispersions using

skimmed milk powder as carrier. Int. J. Pharma Tech Res. 2009; 1 (3): 431-437.

7. Bhise S, Mathure D, Patil MVK and Patankar RD: Solubility enhancement of antihypertensive agent by solid dispersion technique. International Journal of Pharmacy & Life Sciences 2011; 2(8): 970-995.

8. Farago PV, Raffin RP, Pohlmann AR, Guterres SS, Zawadzki SF. Physicochemical characterization of a hydrophilic model drug-loaded PHBV Microparticles obtained by the double emulsion/solvent evaporation technique. J Braz Chem Soc 2008; 19:1298-1305. https://doi.org/10.1590/S0103-50532008000700011

9. Singh P, Shrivastava AK, Kumar S and Dwivedi MD:Formulation and evaluation of sustained release matrix tablets of aceclofenac. Borneo Journal of Pharmacy 2021; 4(2): 99-109. https://doi.org/10.33084/bjop.v4i2.1854

10. Gupta A, Kataria MK, Bilandi A. Formulation and evaluation of solid dispersion of glipizide for solubility and dissolution rate enhancement. Int J Pharm Drug Anal 2014; 2:74-87.

11. Kalman H. Quantification of mechanisms governing the angle of repose, angle of tilting, and Hausner ratio to estimate the flowability of particulate materials. Powder Technology. 2021 Apr 1; 382:573-93. https://doi.org/10.1016/j.powtec.2021.01.012

12. Sahu S, Dangi R, Patidar R, Rukhsaar, Rathi J, Asati V. Formulation and evaluation of sustain released matrix tablet of atenolol. Journal of Drug Delivery and Therapeutics 2019; 9(1): 183-89. https://doi.org/10.22270/jddt.v9i1.2281

13. Reddy KY and Nagaraju A: Formulation and in-vitro evaluation of sustained release matrix tablets of azathioprine. Asian Journal of Pharmacy and Technology 2020; 10(2): 65-70. https://doi.org/10.2174/1872211314666210604120619 PMid:34086557

14. Kamal Dua, Ramanna MV, Sara UVS, Himaja M, Garg V et al Dissolution enhancement of aceclofenac through solid dispersions. Indian Pharmacist 2006; 70-72.

15. Das S, Mandal PR. Design, formulation, and evaluation of solid dispersion tablets of poorly water-soluble antidiabetic drug using natural polymer. Asian J. Pharm. Clin. Res. 2019;12:195-207. https://doi.org/10.22159/ajpcr.2019.v12i4.32035

16. Sakore S, Chakraborty B. Formulation and evaluation of enalapril maleate sustained release matrix tablets. Int J Pharm Biomed Res. 2013;4(1):21-26.

17. Das S, Samanta AR, De HS. Formulation, in vitro release kinetics and stability interpretation of sustained release tablets of metformin hydrochloride. Int J Pharm Pharm Sci. 2015;7(3):418-22.