Journal of Advanced Scientific Research

Available online through https://sciensage.info

ISSN 0976-9595

Research Article

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ACECLOFENAC BY DIRECT COMPRESSION METHOD

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Received: 05-11-2021; Revised: 10-03-2022; Accepted: 12-03-2022; Published: 31-03-2022

 https://doi.org/10.55218/JASR.202213219

ABSTRACT

Nowadays, Oro dispersible tablets are gaining much importance because it is easily approachable and due to its patient compliance. In this study, Formulation and evaluation of one such tablets of Aceclofenac by direct compression method using super disintegrants like Cross carmellose sodium (CCS) was performed.

Due to low water soluble property of aceclofenac, it has poor dissolution and bioavailability. In order to minimize this property OTD's are prepared. ODT's were prepared by direct compression method using super disintegrant i.e Cross Carmellose Sodium (CCS) in different concentrations. The prepared powder blend was subjected to various evaluation studies like pre compression parameters like angle of repose, tapped density, and bulk density. Post compression parameters like weight variation, hardness, friability, drug content, wetting time, disintegration and dissolution studies were performed. The drug excipients compatibility was verified by FTIR.

The precompression evaluation studies showed that the prepared powder blend has good flow property. The hardness and friability revealed that it has good mechanical strength with acceptable disintegration time. The optimized formulation indicated good *in vitro* drug dissolution profile with maximum drug being released at all the time intervals indicates an ideal profile for the development of ODT's. The results of pre compression studies and post compression along with FTIR are presented.

Keywords: Oro dispersible tablets, Aceclofenac, FTIR, Super disintegrant, Cross carmellose sodium.

1. INTRODUCTION

Novel drug delivery system (NDDS) aims to improve safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance; one such approach is orodispersible tablets [1]. Oral medication delivery methods, particularly tablets, are the most frequently used dosage forms because they are small, provide a consistent dose, and are painless to administer [2]. Dysphagia is more common in the elderly and children due to physiological abnormalities associated with both populations. Dysphagia affects approximately one-third of the population and is linked to a variety of diseases such as parkinsonism, diabetes mellitus (DM) [3], mental impairments, motion sickness, unconsciousness, and lack of water [4,5]. Because of benefits in dosage, stability, storage, cost, and transportation, the World Health Organization (WHO) now advises that dispersible tablets be preferred over suspensions wherever available. Patient compliance may be enhanced using dispersible tablets and Orally Disintegrating Tablets (ODTs), especially in juvenile, geriatric, and institutionalised patients [6].

Orodispersible tablets (ORDs), sometimes known as "mouth dissolving tablets," are solid dosage forms that dissolve rapidly in the oral cavity in less than 1 minute [7] and combine the benefits of both liquid and traditional tablet formulations, making it easier to consume the medicine in a liquid dose form. ORDs breakdown quickly in the mouth with the assistance of saliva [8] to create dispersion that may be readily ingested without the need for water [9]. Other benefits of ODTs that have been studied include their capacity to improve the bioavailability of medicines that are poorly water soluble by improving dissolution profiles [10].

An ideal ODT has a pleasing mouth feel, sufficient hardness, and an appropriate friability limit, and is manufactured using traditional methods [11].

Superdisintegrants, which improve the disintegration efficiency of tablets at low concentrations, have been introduced because of advancements in tableting technology. Superdisintegrants help ODTs generated by direct compression disintegrate and dissolve better [12]. In addition, flavouring agents, sweetening agents may also be added to provide an acceptable taste. Suitable sweetening agents include sucrose, fructose, glucose, sodium saccharin, aspartame. Colour is a vital means of identification for many pharmaceutical tablets and is also usually important for consumer acceptance [13].

Aceclofenac is a phenyl acetic acid-based Non-Steroidal Anti-Inflammatory Drug (NSAID) with anti-inflammatory and analgesic effects that may be taken orally. It is one of the most well-tolerated NSAIDs, having a reduced rate of gastrointestinal side effects. Unfortunately, because its limited water solubility (0.058g /ml), it has poor dissolving and oral bioavailability. It is a Biopharmaceutical Classification System (BCS) class II drug, with oral bioavailability assessed by gastrointestinal tract dissolution rate. As a result, improving Aceclofenac solubility is critical to increasing its bioavailability and therapeutic efficacy [14].

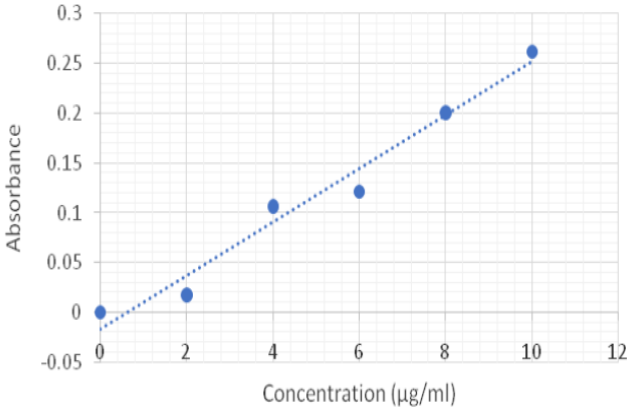
Oral fast dissolving tablets can be made using a variety of ways. To produce quick tablet disintegration, direct compression is one of the ways that requires the addition of super disintegrant or highly water soluble excipients to the formulation. Direct compression, which does not utilize water or heat during the formulation process, is the best technique for moisture and heat-sensitive medications [14]. The goal of this study was to develop and evaluate aceclofenac fast-dissolving tablets using optimization approaches for drug dissolution and absorption using a superdisintegrant, cross carmellose sodium.

2. MATERIAL AND METHODS

Aceclofenac was a gift sample from Hetero Drugs Pvt. Ltd (Hyderabad). Cross carmellose sodium, magnesium stearate, talc, MCC, sodium saccharin and lactose were obtained from SD Fine Chemicals. All the other used were of analytical grade.

2.1. Estimation of Aceclofenac

Aceclofenac was estimated by Spectrophotometric method at 276nm in phosphate buffer of. Accurately weighed amount of Aceclofenac was dissolved in 3-4ml of methanol and stirred until the drug was dissolved and volume was made upto 100ml using phosphate buffer to prepare 1mg/ml solution. 1ml of this solution is was taken out and dissolved in 100ml of buffer solution which forms secondary stock solution. From this solution, dilutions were made with pH 6.8 phosphate buffer to prepare a series of standard solutions containing 2, 4, 6, 8 and 10 µg/ml of Aceclofenac. The solutions were analyzed in the region 200-400nm using UV spectrophotometer (Lab India UV) and the absorbance was measured at 276nm using phosphate buffer as blank. The calibration curve of aceclofenac was plotted as shown in the graph.



Graph 1: Calibration curve of the drug

2.2. Formulation of Orodispersable tablets

The orodispersable tablets were prepared by direct compression method according to the formula given in Table 1.

Table 1: Formulation table of Aceclofenac orodispersable tablets

Ingredients (mg)	F1	F2	F3	F4	F5
Aceclofenac	100	100	100	100	100
Microcrystalline sodium	184	186	184	182	179
Cross carmellose sodium	5	10	15	20	25
Lactose	184	186	184	181	179
Sodium saccharin	10	10	10	10	10
Talc	2	2	2	2	2
Magnesium stearate	5	5	5	5	5
Total	500	500	500	500	500

A total number of five formulations were prepared, each formulation batch comprised of 30 tablets. Tablets were formulated using cross carmellose sodium as superdisintegrating agent at concentrations of 5%, 10%, 15%, 20% and 25%. Weighed quantities of Aceclofenac, CCS, Lactose, sodium saccharin, MCC, Talc and Mg stearate were taken. Drug along with the other excipients were passed through sieve 60 except talc and magnesium stearate, which were passed through sieve 40. All the excipients along with drug were taken in a mortar and pestle and triturated to form a uniform mixture of the blend. The prepared blend was compressed into 500mg tablets using 8mm round flat punches on single station rotary tablet machine. The composition of each formulation is given in Table 1.

2.3. Precompression evaluation of powder blend

2.3.1. Angle of repose

Using the funnel method, the angle of repose of the powder blend was calculated. The powder blend was placed in a funnel and allowed to flow freely over the surface after being precisely weighed. The angle of repose was estimated by measuring the diameter of the powder cone and repeating the process three times.

2.3.2. Bulk density

A measured quantity of powder blend was taken in a measuring cylinder and volume occupied by the powder was noted as bulk volume(v_b) and mass as (m). The bulk density was calculated as

Bulk density=mass of the powder(m)/tapped volume of the powder(v_t)

2.3.3. Tapped density

In a 25ml measuring cylinder, a weighed quantity of powder was added. The cylinder was allowed to fall under its own weight onto a hard surface from a height of 2.5 cm at 2 sec intervals after the initial volume was determined, mechanically for 50 times i.e 50 tappings. The volume of powder retained in the cylinder is noted as final volume (v_t). Tapped density was calculated as follows:

Tapped density=mass of the powder/ tapped volume of powder (v_t)

2.3.4. Compressibility index (Carr's index)

Carr's granules' flow property features are determined by the compressibility index. The potential powder arch and stability are directly measured by the % compressibility of granules. The following formula may was used to compute the Carr's index.

% Carr's index=et -eb /et ×100

Where, 'et' is the tapped density of granules and 'eb' is bulk density of granules

2.4. Post compression evaluation of tablets

2.4.1. Weight variation

Each batch had twenty tablets chosen at random, and the average weight was determined. The individual weights of the tablets were then compared to the average weight to determine the weight variance of the tablets.

2.4.2. Friability

The Roche Friabilator was used to assess tablet friability at 25 rpm for 4 minutes. The weight of twenty tablets was recorded before and after the test, and friability was estimated using the following formula:

% friability = [(initial weight-final weight) ÷ initial weight] x 100

2.4.3. Hardness

Monsanto hardness Tester was used to determine the breaking strength of the tablets. It was measured in terms of kg/cm^2. The tablet was placed in between the two jaws of tester and rotated until the tablet was broken. The hardness was measured by reading the scale of the tester. The hardness limits for tablets should be within the range of 4-6kg/cm^2.

2.4.4. Wetting Time and absorption ratio

In a petri plate containing 10mL of water, round tissue sheets were put. Six pills were then put on the tissue paper's surface one after the other each time. The wetting time was defined as the time it took for water to reach the tablet's top surface. Time taken for wetting of tablet was noted and wetted tablet was noted. Water absorption ratio R was determined using the following equation [15]:

$R= W_a-W_b/W_b$ x 100[9]

Where W_b and W_a are the weights of the tablet before and after water absorption, respectively.

2.4.5. Drug content

In this method, one tablet from each formulation was taken in a mortar and pestle and crushed to fine powder. From the crushed tablet take 5mg of aceclofenac was taken and dissolved in 20ml of ethanol. The solution was filtered and 0.1ml of the filtrate was

taken and diluted in 10ml of ethanol. The absorbance of resultant solution was measured by spectrophotometric method at 276 nm in UV spectrometer (UV LAB INDIA). The drug content was measured using the standard calibration curve and the average percentage drug content was calculated using the formula:
Drug content=concentration x dilution factor÷1000

2.4.6. Disintegration Time

Using an Electro lab disintegration device, an in vitro disintegration test was performed on six tablets from each batch. Each tablet was put in a disintegration device with 900 mL of distilled water and kept at 37±2 °C. The disintegration time was calculated as the time it took for the tablet to completely disintegrate with no particle matter left in the mesh.

2.4.7. Dissolution Studies

An electro lab dissolution test device was used to conduct an in vitro dissolution investigation of tablets at a rotation speed of 100 rpm. The dissolution research used six tablets from each batch at random. Each tablet was put in a beaker with 900 mL of pH 6.8 phosphate buffer. The temperature was kept constant at 37±0.5 C. For the single-point dissolving test on the preliminary tablets, a sample of 5 mL was withdrawn at 30 minutes, and equivalent quantities of samples were withdrawn at 5, 10, 15, 20, 25 and 30 minutes to investigate the release profile of the optimised table.

2.4.8. Fourier transform infrared spectroscopy (FT-IR)

FTIR was used to investigate the drug-polymer interaction. The medication and polymer must be compatible in order to create a stable result. As per the technique, drug and polymer interactions were investigated using FT-IR (Bruker Alpha Model). Lactose, pure acyclofenac, Mg stearate, talc and microcrystalline cellulose were analysed using infrared spectroscopy. There is no difference in the peaks of the combination when compared to the pure medication, indicating that there are no interactions.

3. RESULTS AND DISCUSSIONS

3.1. Precompression Evaluation

All the precompression evaluation studies like Angle of Repose, Bulk density, Tapped density, and Carr's compressibility index are given in table 2. Angle of repose defines the flow property of powder blend. Those with low angle of repose have good flow property than those with high angle of repose values [16]. All the formulation blends were shown good flow property showing angle of repose within the range of 24.93°-30°. All the formulation powders were found within the range of 0.41-0.43. All the formulation powder blend were also found within the range of 0.59-0.65. Carr's index values were also found within the range of 12.78-28.61 indicating all the formulation blend were having acceptable flow property [17].

Table 2: Precompression parameters of powder blend

Formulation Code	Bulk density (gm/cc)	Tapped density (gm/cc)	Angle of repose (degrees)	Carr's index (%)
F1	0.4214	0.59	28.81	28.61
F2	0.4190	0.65	30.0	13.36
F3	0.4217	0.61	26.56	12.78
F4	0.4213	0.64	26.43	13.78
F5	0.4330	0.62	24.93	23.43

3.2. FT-IR Study

The use of spectroscopic methods such as FT-IR in Pre-formulation has contributed significantly for the early prediction and possibility of physical and chemical interactions between the drug and excipient and to assist in the rationalized selection of the most appropriate excipients in the design of dosage forms. The drug sample showed characteristic functional group peaks at 3442.23cm^{-1} due to N-H stretching, 3181.05cm^{-1} due to O-H stretching, 1716.22 cm^{-1} due to C=O stretching, 1547.60 cm^{-1} due to skeleton vibration of aromatic C-C stretching, 1259.26 cm^{-1} C-N aromatic amine, 1419.37 cm^{-1} O-H in plane bendin. Lactose showed characteristic functional group peaks at 3460.12-3696.13 cm^{-1} due to stretching vibrations of C-O-H bonds of lactose alcohol. Two sharp bands were found at 3045-2958.84 cm^{-1} due to C-H stretching vibrations [18]. Talc showed characteristic vibrations of hydroxyl groups linked to Si(Si-OH) and Mg(Mg-OH) at 3441-3671.54cm^{-1}. Then bands with intense peaks at 1040 cm^{-1} are contributed by the siloxane group (Si-O-Si) stretching vibrations while bands found at 669.16 cm^{-1} are due to Si-O-Mg bond [19]. Magnesium stearate shows characteristic twin peaks at 1540.22 and 1463.55

cm^{-1} that are attributed by asymmetric carboxylate (COO) stretching vibration and symmetric vibrations of carboxylate group respectively. The peaks at 2916.03 and 2840.34 cm^{-1} are due to the C-H stretching vibrations [20]. The FT-IR spectrum of MCC shows characteristic band of O-H stretching vibrations of hydroxyl group at 3566.42cm^{-1}. C=O bands of aldehyde were found at 1771.27cm^{-1}. Peaks at 1507.62cm^{-1} are associated with CH_2 bending vibrations. C-O stretching vibrations at 1362.80 were associated with the CH_2 -OH group. C-O-C bands were focused at 1051.22cm^{-1} [21]. Sodium saccharin showed characteristic peaks at 1647.40cm^{-1} due to C=O bonds. C-C bond stretching vibrations were found at 1558. 40cm^{-1}. Peaks found at 1251.48$cm^{-1}$and 1145.93cm^{-1} were attributed to SO_2-N- stretching vibrations.

All the characteristic peaks of aceclofenac were found in their original range in the optimized formulation indicating that there was no interaction between the drug and other excipients.

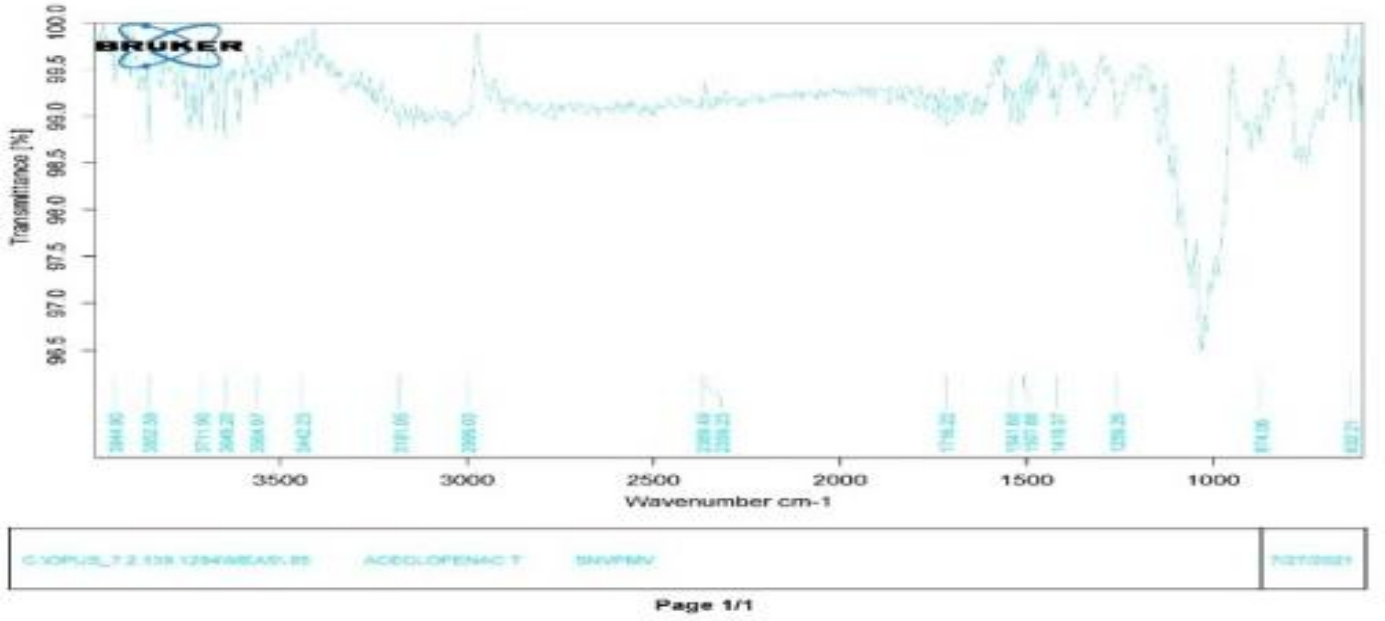


Fig. 2: FTIR spectrum of Aceclofenac

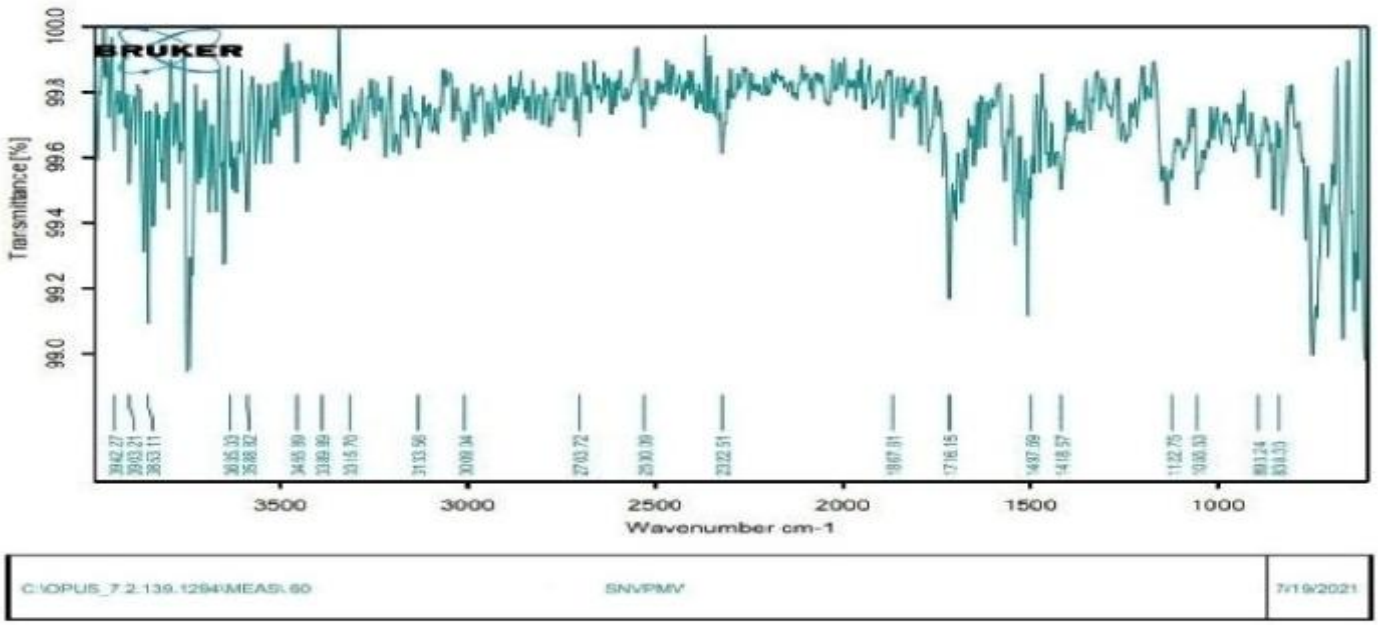


Fig. 3: FTIR spectrum of optimised formulation

3.3. Post compression parameters

All the post compression parameters results like Hardness, Thickness, Friability and Weight variation are given in following table 3.

Other parameters like disintegration, wetting time, water absorption ratio, drug content are given in table 4.

3.3.1. The wetting time and water absorption ratio

It is one of the important parameter that determines the ability of tablet to disintegrate and absorption capability in the presence of small amount of water. The wetting time was found to be within the range of 22-34 sec. The gradual decrease in the wetting time is due to increase in the concentration of super disintegrant that absorbs water and swells resulting in dispersion of the tablet. The results are tabulated in the table 5. Disintegrating time is a very important factor which should be less than 60 sec. There was decrease in disintegrating time with increase in the concentration of super disintegrator that is from 54sec in F1 with 5% to 37sec in F5 with 25% which shows that disintegration is inversely proportional to the concentration of super disintegrator CCS. The optimized formulation was found to be within the limits that is 37 sec.

3.3.2. In vitro dissolution studies

Dissolution studies of the ODTs clearly indicate the drug release as per specifications, optimized formulation F5 showed best drug release of 100.8% in 30 min. The results are shown in fig 4 [21].

Table 3: Post compression studies of aceclofenac tablets

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation
F1	2.38	4.0	0.42	480
F2	2.45	3.5	0.84	470
F3	2.34	3.0	0.41	470
F4	2.36	4.0	0.61	481
F5	2.42	3.5	0.42	475

Table 4: Post compression studies of aceclofenac tablets

Formulation code	Disintegration time (sec)	Wetting time (sec)	Water absorption ratio	Drug content
F1	54.8	34	58.69	92.75
F2	46.8	32	60.75	93.95
F3	45.8	29	63.65	95.67
F4	44	25	68.79	97.54
F5	37	22	74.65	99.93

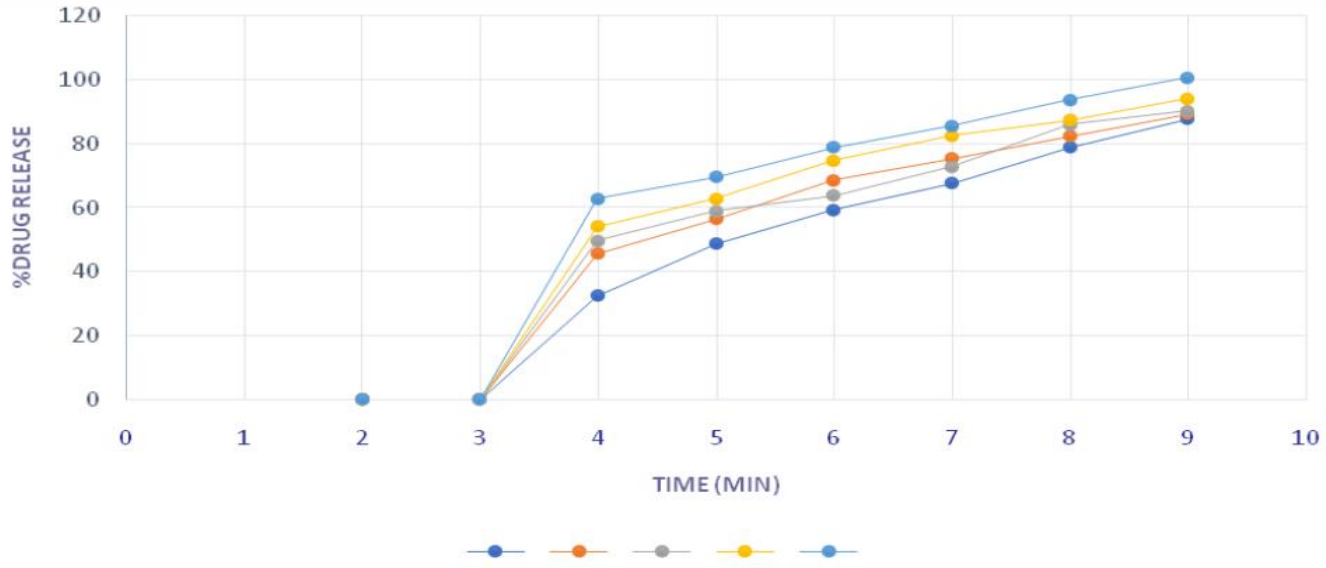


Fig. 4: In vitro drug release studies of Aceclofenac formulations

4. CONCLUSION

The oral dispersible tablets of aceclofenac were successfully prepared by direct compression method. The various evaluation tests like pre compression studies, FTIR, post compression studies like weight variation, hardness, drug content, disintegration, dissolution were performed and results were found to be within the limits. Formulation F5 with 25% of CCS has shown the results that satisfies the acceptance criteria for OTD'S. Hence, it is considered as optimized formulation. From the above study, we can conclude that Formulation F5 can be prepared as aceclofenac ODT's for better patient compliance than the conventional forms that are available in the market.

Conflict of interest

The authors declare no conflict of interest.

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