

Design, Development and *In Vitro* Evaluation of Novel Fast Disintegrating Tablet for Acetaminophen Delivery Using Direct Compression Method

Anil M. Pethe^{1*}, Arun T. Patil², Darshan R. Telange², Amol A. Tatode²

¹Department of Pharmaceutics, SVKM's, NMIMS (Deemed to be University), SPP School of Pharmacy and Technology Management, Mumbai Campus, Mumbai, Maharashtra, India, ²Department of Pharmaceutics, University Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, Maharashtra, India

Abstract

In this study, attempts were made to design and developed disintegrating drug delivery system; Acetaminophen fast disintegrating tablet (AFDT) by combining superdisintegrants and direct compression method. Acetaminophen is widely used as “over the counter (OTC)” and “common household drug” as analgesic and antipyretic along with poor absorption due to first pass metabolism. So, we aimed to use our novel delivery system to achieve rapid absorption in patients like mentally ill, bed ridden and those who do not have easy access to water. The AFDT were produced by combining three superdisintegrants like croscarmellose, crospovidone and sodium starch glycolate in 4% w/w as ratio of (1:1, 1:2, 2:1) using direct compression method. The optimized batch (A3) of tablet were evaluated for postcompression parameters like hardness (4.5 ± 0.75 kg/cm²), friability (0.76%), wetting time (42 ± 0.92 s), water absorption ratio (98.6%), disintegration time (24.00 ± 0.83 s) were found to be acceptable according to standard limits. The *in vitro* release rate of acetaminophen from AFDT was found to be more than that simple formulation in pH (5.8) using United State Pharmacopoeia dissolution test apparatus Type II. These results indicated that, the new AFDT formulation system combined advantage of faster release of acetaminophen, which had better effects of rapid oral absorption. Therefore, the AFDT may be used as fast disintegrating delivery system for OTC drug with poor absorption due to first pass metabolism.

Key words: Acetaminophen, direct compression, fast disintegrating tablet, postcompression parameters, superdisintegrants

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness and ease of manufacturing. For the past one decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually. Since the development cost of a new drug molecule is very high, efforts are now being made by pharmaceutical companies to focus on the development of new drug dosage forms for existing drugs with improved safety and efficacy together with reduced dosing frequency and the production of more cost-effective dosage forms.^[1,2] However, geriatric and paediatric patients experience difficulty

in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as “melt in mouth” or “mouth dissolve” or sometimes “dispersible” tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability for geriatric and paediatric

Address for correspondence:

Dr. Pethe M. Anil, SVKM's NMIMS (Deemed to be University), SPP School of Pharmacy and Technology Management, Mumbai Campus, Mumbai, Maharashtra, India. E-mail: anilpethe@gmail.com

Received: 01-08-2014

Revised: 07-01-2015

Accepted: 07-02-2015

patients. They are also suitable for the mentally ill, the bed-ridden and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market.^[3-5] Directly compressed tablet's disintegration and solubilisation depends on various factors such as single or combined action of disintegrant, water-soluble excipients, and effervescent agent. Disintegrant efficacy is based on force equivalent concept, which is the combined measurement of swelling force development and amount of water absorption and defines the capability of disintegrant to transform absorbed water into swelling force.^[6,7] Acetaminophen is considered to be the inhibition of cyclooxygenase (COX), and recent findings suggest that it is highly selective for COX-II while it has analgesic and antipyretic properties comparable to those of aspirin or other nonsteroidal anti-inflammatory drug (NSAIDs); its peripheral anti-inflammatory activity is usually limited by several factors, one of which is high level of peroxides present in inflammatory lesions. However, in some circumstances, even peripheral anti-inflammatory activity comparable to other NSAIDs can be observed. Clinically, NSAIDs are the most frequently prescribed by physicians for inflammatory disorders. NSAIDs exert their effect through inhibition of COX-II, the main form of isozyme associated with inflammation. But the simultaneous inhibition of COX-I and the resulting gastric and renal dysfunction limits their frequent use.^[8] In recent years, drug formulation scientists have recognized that single component excipients do not always provide the requisite performance to allow certain active pharmaceutical ingredients to be formulated or manufactured adequately. Hence, there is a need to have excipients with multiple characteristics built into them such as better flow, low/no moisture sensitivity, superior compressibility and rapid disintegration ability.^[9-14] The objective of this study was to achieve better concentration blends of superdisintegrants in the minimum concentration that will give best fast disintegrating tablet (FDT) formulation to achieve rapid absorption and fast disintegration, and to study the effects of different superdisintegrants in combination on *in-vitro* drug release and disintegration time.

MATERIALS AND METHODS

Materials

Acetaminophen was received as a gift from Shri Baalaji Medicare Pvt. Ltd., Mumbai, India. Croscarmellose was received as gift from Fischer Scientific Ltd.; Crospovidone was received as a gift from SD fine Chem. Ltd., Sodium starch glycolate was received as a gift from Central Drug House Laboratory, Mumbai, India. All other chemicals were of analytical grade.

Methods

Selection of excipient and optimisation of their concentrations

Disintegration time is the most important parameter to be optimized in design and development of FDT. The acetaminophen FDT (AFDT) were prepared using different excipient (blends) and superdisintegrants then evaluated for precompression parameters. The blends of excipients were selected for further study in Table 1.

Optimization of blends by precompression parameters

Before the formulation into final AFDT, the different excipient blends A1–C3 was prepared to study the type and effect of concentration of excipients along with superdisintegrants as shown in Table 2. According to concentration, weighed quantity of acetaminophen with different concentration of superdisintegrants, i.e., 4% w/w at ratio of (1:1, 1:2, 2:1) with excipients was mixed in geometric progression in clean and dry mortar. The blends were evaluated and Optimized on the basis of precompression parameters like compressibility index, bulk density, tapped density, Hausner's ratio and angle of repose.

Optimization of superdisintegrants (croscarmellose, crospovidone and sodium starch glycolate)

For tablets that require rapid disintegration is most important parameter for AFDT, the inclusion of the right superdisintegrant with its optimum concentration is a prerequisite for optimal bioavailability. Superdisintegrants decrease disintegration time along with absorption ratio, wetting time, dispersion time, hardness and friability that in turn enhances drug dissolution rate. Thus, the proper choice of superdisintegrants and its concentration of performance are of critical importance to the formulation of rapidly disintegrating dosage forms.

The composition of AFDT is shown in Table 1. In this composition the three superdisintegrants croscarmellose, crospovidone and sodium starch glycolate in combination because in most of the literature the single optimum concentration superdisintegrants was used and found that disintegration time less than the optimum level, by considering above problem we aimed to use combination of two superdisintegrants in optimum concentration, i.e., 4% at ratios of (1:1, 1:2, 2:1) can decrease the disintegration time more drastically for obtaining high bioavailability along with excipients and acetaminophen was mixed in geometric progression in a dry and clean mortar. The powder blend was then compressed into tablet.

Formulation of acetaminophen fast disintegrating tablet

The AFDT was prepared by direct compression technique according to the formula given in Table 1. Weighed quantity of acetaminophen along with optimized concentration of

Table 1: Different excipients composition for blends

Ingredients in mg/tablet	A1	A2	A3	B1	B2	B3	C1	C2	C3
Acetaminophen	325	325	325	325	325	325	325	325	325
Croscarmellose	20	40	20	-	-	-	20	40	20
Crospovidone	20	20	40	20	40	20	-	-	-
Sodium starch glycolate	-	-	-	20	20	40	20	20	20
Microcrystalline cellulose (pH 101)	133	113	113	133	113	113	133	113	113
Magnesium stearate	2	2	2	2	2	2	2	2	2

n=3

Table 2: Precompression evaluation results of blends

Blends	Compressibility index \pm SD* (%)	Bulk density (g/cm ³)	Tapped density (g/cm ³)	Hausner ratio	Angle of repose \pm SD* (degrees)
A1	22.73 \pm 1.06	0.4545	0.5882	1.29	31.42 \pm 0.89
A2	23.82 \pm 2.04	0.4761	0.6250	1.31	29.72 \pm 1.23
A3	18.18 \pm 1.09	0.4545	0.5555	1.22	30.12 \pm 1.24
B1	21.74 \pm 0.86	0.4347	0.5555	1.27	32.12 \pm 1.42
B2	20.84 \pm 1.52	0.4166	0.5263	1.26	30.12 \pm 1.34
B3	21.74 \pm 1.34	0.4347	0.5555	1.27	31.21 \pm 1.14
C1	22.75 \pm 1.85	0.4787	0.5880	1.23	32.12 \pm 1.56
C2	23.70 \pm 0.98	0.4882	0.6325	1.29	28.86 \pm 0.98
C3	22.69 \pm 1.07	0.4378	0.5567	1.27	30.16 \pm 1.12

n=3, *Represents the value as mean \pm SD. SD: Standard deviation

superdisintegrants and excipients was mixed in geometric progression in dry and clean mortar. The powder blend was then compressed into the tablet on a single punch Laboratory Scale Rotary Tablet (Karnavati Engineering, Rimek-II, India) at compression pressure 6 tons using 11.1 mm punch diameter.

Evaluation (acetaminophen fast disintegrating tablet) parameters

Postcompression parameters

Weight variation

The procedure described in United State Pharmacopoeia (USP-30) was employed to determine the weight variation of the tablets. Twenty tablets were randomly selected from each batch and weighed on an electronic balance and mean weight was taken. Each tablet was then weighed individually, and standard deviation in weight was calculated for each batch.^[15]

Hardness

Crushing strength of the tablet was measured using Monsanto hardness tester (Perfit). Five tablets were randomly selected from each batch, and average reading was noted. The mean values and standard deviation of each batch were calculated. The hardness is measured in kg/cm².^[16]

Friability

Friability indicates the ability of a tablet to withstand mechanical shocks while handling. Friability of the tablets

were determined using Roche Friabilator (Veego, India) and is expressed in percentage (%). Ten tablets were initially weighed (W_{initial}) and placed into the friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions and then the tablets were weight again (W_{final}). The loss in tablet weight due to abrasion or fracture was the measure of tablet friability. Percent friability (f) was calculated using the following formula:^[17]

$$f = \frac{W_0 - W_t}{W_0} \times 100\%$$

Where W_0 : Weight initial.

W_t : Weight final.

% friability of <1% is considered acceptable.

In vitro disintegration test

The disintegration time was determined using USP Tablet disintegration test apparatus (Veego, India) using 900 ml of distilled water without disk. The time in seconds taken for complete disintegration of the tablets until no mass remaining in the apparatus was measured in seconds.^[15]

Drug content uniformity

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.15 g of acetaminophen, add 50 ml of 0.1M sodium hydroxide, dilute with 100 ml of water, shake for 15 min and add sufficient water to produce 200.0 ml.

Mix, filter and dilute 10.0 ml of the filtrate to 100.0 ml with water. To 10.0 ml of the resulting solution add 10 ml of 0.1M sodium hydroxide, dilute to 100.0 ml with water and mix. Measure the absorbance of the resulting solution using double beam ultraviolet (UV)-spectrophotometer (UV-1800 Shimadzu) at the maximum at about 257 nm, respectively. Calculate the content of $C_8H_9NO_2$ taking 715 as the value of A (1%, 1 cm) at the maximum at about 257 nm.^[17]

Acceptance limits: Paracetamol tablets contain not <90.0% and not more than 110.0% of labeled amount of paracetamol.

Wetting time

The wetting time and capillarity of the oral dispersible tablets were measured by a conventional method. The tablet was placed in a petri dish of 6.5 cm diameter containing 10 ml water at room temperature and the times for complete wetting of tablets were recorded.^[18,19]

Water absorption ratio

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of distilled water. A tablet was put on the paper and the time required for complete wetting of the tablet was measured. The wetting tablet was then weighed. Water absorption ratio “R” was determined using the equation as follows:^[20-22]

$$R = 100 \times \frac{W_a - W_b}{W_b}$$

Where, W_a is Weight of tablet after water absorption.
 W_b is Weight of tablet before water absorption.

In vitro drug release study

The *in vitro* drug release study of AFDT was carried out using USP dissolution test apparatus Type II (Paddle type) (Lab, India), using 900 ml of phosphate buffer (pH 5.8) as the medium and rotating the paddle at 50 rpm for 30 min at $37 \pm 0.5^\circ\text{C}$. In this test, eight tablets from each batch was used for the studies. At specified time i.e., 0, 5, 10, 15, 20, 25, 30 min withdrawn a suitable volume of the sample and filter promptly through a membrane filter disc with an average pore diameter >1.0 mm. The absorbance of the resulting solution was measured at the maximum 257 nm using double beam UV-visible spectrophotometer (UV-1800 Shimadzu).^[15]

Drug – excipient compatibility studies

These studies were performed in order to confirm the drug-excipient interaction. These studies preferably include Fourier transform infrared spectroscopy (FTIR). FTIR spectra of acetaminophen and formulated FDT containing drug were recorded on FTIR spectrophotometer (Shimadzu 8101A). The scanning range was from 4000 to 400/cm, and the resolution was 1/cm. The scans were evaluated for the presence of principal peaks of drug, shifting and masking of drug peaks, and appearance of new peaks due to excipient

interaction. This spectral analysis was employed to check the compatibility of drugs with the excipients used.^[22]

Stability studies

Accelerated stability studies are conducted at three different conditions at $40^\circ\text{C}/75\%$ relative humidity (RH), $25^\circ\text{C}/60\%$ RH, 55°C and at ambient humidity as per ICH guidelines. The tablets were withdrawn on the 15th and 30th days and analysed for hardness, friability, drug content uniformity, and *in vitro* disintegration time which are the most important parameters for FDTs.^[23]

RESULTS

Selection of excipients concentration

The blend of different excipients for the formulation of AFDT was selected on the basis of the formulation of A1–C3 batches with different concentration of excipients along with superdisintegrants. The results [Table 1] shows that total six excipients were used for the preparation of blends of formulation where concentration of acetaminophen, microcrystalline cellulose and magnesium stearate was constant and concentration of superdisintegrants were changed.

Precompression parameters results

The acetaminophen drug with different concentration of excipients and superdisintegrants in formulation A1–C3 were optimized on the basis of pre- and post-compression parameters. The results [Table 2] shows that, the batch A3 was optimized with optimum concentration of croscarmellose and crospovidone superdisintegrants in 4% at ratio (1:2) was found to be satisfactory on the basis of compressibility index ($18.18 \pm 1.09\%$), bulk density (0.4545 g/cm^3), Hausner's ratio (1.22) and angle of repose (30.12 ± 1.24).

Formulation of acetaminophen fast disintegrating tablet

All AFDT tablet formulation was formulated by direct compression method according to the formula [Table 1]. After the optimization of blends of excipients, the formulation with same batches (A1–C3) were processed for direct compression technique and then evaluated for postcompression parameters.

Evaluation (acetaminophen fast disintegrating tablet) parameters

Postcompression parameters

The final AFDT were evaluated for postcompression parameters, i.e., official test and was found to be within the limits [Table 3] and on the basis of postcompression parameters

the A3 batch was optimized. The optimized batch A3 results shows that, the weight variation (498.0 ± 0.9), wetting time (42 ± 0.90 s), absorption ratio (98.6%), dispersion time (22 ± 1.08 s), hardness (4.5 ± 0.75 kg/cm²), friability (0.76%) and most important parameters for FDT is disintegration time (24.00 ± 0.83 s) was found to be within the acceptance limit.

Drug content uniformity

The content of acetaminophen present in the AFDT was 103.8 ± 2.28 as estimated by UV-visible spectrophotometer.

In vitro drug release study

In vitro dissolution studies showed that more than 45% of the drug was released from the formulation within 5 min. From *in vitro* dissolution data [Table 4], it was observed that $88.355 \pm 1.08\%$ of acetaminophen released in 30 min indicates that, the maximum amount of acetaminophen was released from tablet in stipulated period and it complies as per IP specifications, that is, 85–110% [Figure 1].

Drug – excipient compatibility studies

The results obtained with IR studies showed that there was no interaction between the acetaminophen and other excipients used in the formulation. The FTIR of acetaminophen has shown intense band at $3525.28/\text{cm}^{-1}$, $3426.69/\text{cm}^{-1}$, and $1650/\text{cm}^{-1}$ corresponding to the presence of functional groups such as primary amine group, hydroxyl group, and carbonyl group. The FTIR of AFDT formulation has shown intense bands at

$3528.32/\text{cm}^{-1}$, $3429.57/\text{cm}^{-1}$, and $1655.11/\text{cm}^{-1}$ which indicates no change in the functional groups such as primary amine group, hydroxyl group, and carbonyl group and confirmed undisturbed structure of acetaminophen, which indicates no drug-excipient interaction as shown in Figure 2a and 2b.

Stability studies

In the present study, accelerated stability studies were carried out on optimized A3 batch formulated AFDT wrapped in aluminium foil to prevent the formulation from exposure to light to simulate the aluminium packaging, and stored in air-tight containers which are impermeable to solid, liquid, and gases, under the following conditions $40^\circ\text{C}/75\%$ RH,

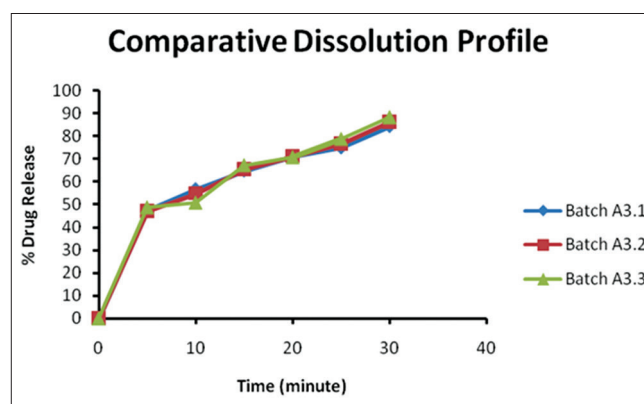


Figure 1: Dissolution profile of formulation batch A3.1–A3.3

Table 3: Composition of AFDT formulation

Ingredients in mg/tablet	A1	A2	A3	B1	B2	B3	C1	C2	C3
Acetaminophen	325	325	325	325	325	325	325	325	325
Croscarmellose	20	40	20	-	-	-	20	40	20
Crospovidone	20	20	40	20	40	20	-	-	-
Sodium starch glycolate	-	-	-	20	20	40	20	20	20
Microcrystalline cellulose (pH 101)	133	113	113	133	113	113	133	113	113
Magnesium stearate	2	2	2	2	2	2	2	2	2

n=3

Table 4: Results of postcompression evaluation parameters

Formulation code	Parameters						
	Wetting time* (s)	Absorption ratio (%)	Disintegration time* (s)	Dispersion time* (s)	Hardness* (kg/cm ²)	Friability (%)	Weight variation* (%)
A1	36±1.20	96.2	33.00±2.50	31.00±1.30	4.5±0.17	0.86	500.7±0.8
A2	38±0.90	98.2	35.00±2.18	34.00±1.18	4.6±0.25	0.43	500.2±1.3
A3	42±0.92	98.6	24.00±0.83	22.00±1.08	4.5±0.75	0.76	498.0±0.9
B1	55±1.30	87.7	42.33±1.69	44.11±0.90	4.7±0.23	0.92	500.0±1.2
B2	56±2.35	98.0	29.00±0.82	34.00±1.79	5.00±0.8	0.95	505.2±1.8
B3	55±2.70	91.8	37.00±1.29	36.00±2.18	4.5±0.35	0.86	499.0±1.9
C1	57±2.20	95.9	51.00±3.00	54.00±1.08	5.2±0.25	0.78	502.2±1.2
C2	52±1.20	99.7	52.33±2.05	49.85±1.98	4.5±0.18	0.69	500.0±1.4

n=6, *Represent as mean±SD; n=20, **Represent as mean±SD. SD: Standard deviation

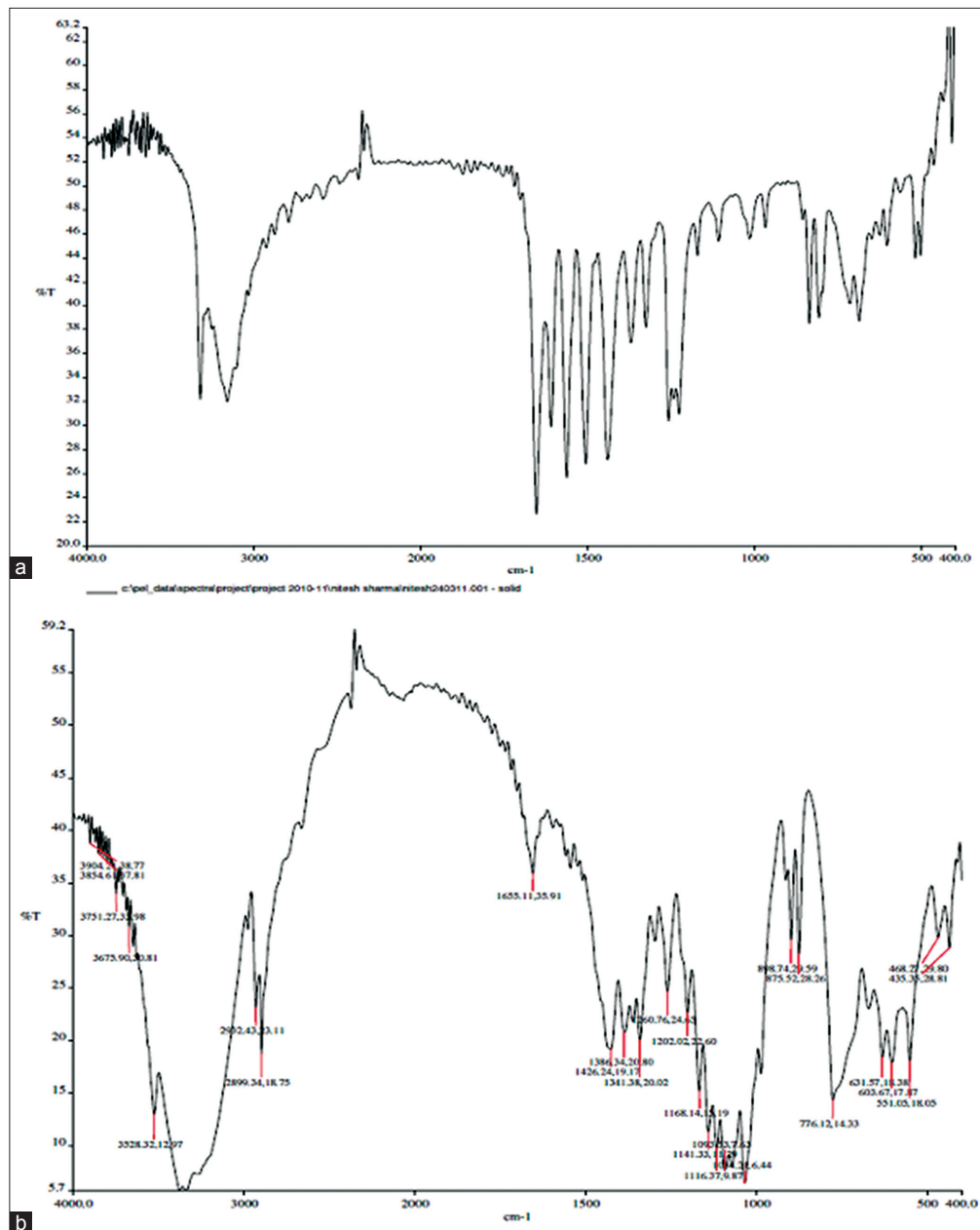


Figure 2: (a) Fourier transform infrared spectroscopy spectra of acetaminophen, (b) Physical mixture of acetaminophen and blends

25°C/60% RH, 55°C and at ambient humidity as prescribed by ICH guidelines for stability study. The stability data of formulation are shown in Tables 5 and 6.

DISCUSSION

In the present attempt, AFDT was prepared by direct compression method.

Before the formulation of AFDT, all batches of blends were optimized by evaluating their precompression parameter [Table 2] provides all data. The A3 batch was selected as optimized blend on the basis of flow and compressibility

properties like compressibility index, bulk density, tapped density, hausner's ratio and angle of repose. The optimized batch exhibiting good blends can be explained by (Shakar *et al.*, 2012, Chaturvedi *et al.*, 2012) using 4% superdisintegrants like croscarmellose and croscopolvidone in 4% at the ratio of (1:2) in formulation that could give better flow properties to blends.

The optimized blend batch, i.e., A3 along with other batches were further formulated as AFDT by direct compression method [Table 3] provides all data. All excipients including di-calcium phosphate, croscopolvidone, croscarmellose and acetaminophen exhibiting directly compressible properties instead of wet granulation that could lead to degradation of

Table 5: Stability data of AFDT at (25°C/60% RH) room temperature and at ambient humidity

Time interval	0 day	15 th day	30 th day
Evaluation parameters			
Hardness (kg/cm ²)±SD*	4.5±0.75	4.4±0.72	4.5±0.75
Friability (%)	0.76	0.78	0.76
Drug content uniformity (mg)±SD*	102.5±2.08	99.2±2.00	97.8±2.04
Disintegration time ±SD*	24.13±0.79	27.22±0.82	29.30±0.96

n=3, *Represents the value as mean±SD. SD: Standard deviation. AFDT: Acetaminophen fast disintegrating tablet, RH: Relative humidity

Table 6: Stability data of AFDT at (40°C/60% RH and 55°C) temperature and at ambient humidity

Time interval	0 day	15 th day	30 th day
Evaluation parameters			
Hardness (kg/cm ²)±SD*	4.5±0.75	5.7±0.74	6.2±0.75
Friability (%)	0.76	0.84	0.90
Drug content uniformity (mg)±SD*	102.5±2.08	98.3±2.20	98.9±2.14
Disintegration time (s)±SD*	24.13±0.79	35.22±0.91	43.12±0.96

n=3, *Represents the value as mean±SD. SD: Standard deviation, AFDT: Acetaminophen fast disintegrating tablet, RH: Relative humidity

excipients by the presence of moisture. The postcompression parameters of optimized batch A3, the weight variation, hardness, and friability were found to be within acceptable criteria resulted from the formation of tablet by directly compression method [Table 4] provides all data. As directly compressible excipients, the di-calcium phosphate, acetaminophen, crospovidone, croscarmellose given strong compactness to tablet may be responsible to be acceptable weight variation, hardness, and friability.

The most important parameters that to be optimized are disintegration time, wetting time, dispersion time and water absorption ratio as these are all related to exhibit FDT [Table 4]. The amount of drug and other excipients in each formulation was kept constant excluding superdisintegrants were changed at 4% w/w in different ratio of (1:1, 1:2, 2:1). In present attempt, all batches of tablet were fulfilled the official requirements (<3 min) for orodispersible tablet. Sodium starch glycolate, crospovidone and croscarmellose all these superdisintegrants in combination at different ratio (1:1, 1:2, 2:1) showed a steady fall in disintegration time as its concentration increased up to 4% and above its

concentration the disintegration time increased slightly, hence 4% w/w concentration of superdisintegrants in combination was selected as the most effective one [Table 1]. It was found that, the effect of a combination of two superdisintegrants at different ratio of batches (A1–C3) in disintegration time was found to be 24–52 s. The tablet formulations containing croscarmellose and crospovidone of batches (A1 and A2) at (1:1 and 2:1) ratio showed disintegration time reduced to 33 s and 35 s whereas the other formulations containing crospovidone and sodium starch glycolate of batches (B1, B2, B3) at (1:1, 2:1, 1:2) ratio disintegration time was found to be slightly higher and lower in above mention batches. In case of croscarmellose and sodium starch glycolate of batches (C1, C2, C3) at (1:1, 2:1, 1:2) ratio, the disintegration time was found to be much higher than previous batches but out of all these, when croscarmellose and crospovidone in combination batch (A3) at (1:2) ratio the disintegration time was reduced to 24 s resulted due to combination of superdisintegrants indicates synergistic effect. The reduced disintegration time also observed in the previous study (Swati *et al.*, 2010). In these studies found that the combination of two superdisintegrants at 4% reduced disintegration time drastically.

The wetting time is the minimum amount of time is required to wetting of tablet [Table 4] data shows that, the wetting time for nine batches were in range of 42–58 s in batch (A3) it observed that, the wetting time, water absorption ratio and dispersion time was found to be 42 s, 98.6% and 22 s. It resulted due to combine mechanism of swelling and wicking exhibited by croscarmellose and crospovidone at (1:2) ratio. Hence analysed all postcompression parameters indicates that, optimized tablet (A3) would be disintegrate rapidly even in a small amount of water/saliva. The above study is supported by (Patil *et al.*, 2011) in which similar results observed using a combination of superdisintegrants.

The cumulative % drug release from optimized batch has shown in Table 7 it was found that, all optimized batches (A3₁–A3₃) exhibited drug release up to 88% in phosphate buffer (5.8) to maintain pH of saliva. In phosphate buffer (5.8), the all three batches (A3₁–A3₃) showed excellent release of drug up to 88% in 30 min as compared to other batches. The drug release profiles of optimized batches containing a combination of superdisintegrants in ratio (1:2) are shown in Figure 1 respectively. Thus, the disintegration time and release rate of drug from the tablet was improved using a combination of superdisintegrants (croscarmellose and crospovidone) in ratio (1:2). The dissolution profile in FDT depend upon role of superdisintegrants in alone or in combination, concentration at which added to formulation etc. may help in improving the release rate of FDT (Shakar *et al.*, 2012; Priya *et al.*, 2009) superdisintegrants like croscarmellose and crospovidone behave as combine synergistic effect responsible for improving release rate of AFDT due to mechanism of swelling and wicking. The

Table 7: Dissolution profile of formulation batch A3.1-A3.3

Formulation batch number	A3.1*	A3.2*	A3.3*
Time (min)			
0	0	0	0
5	47.078±0.89	47.087±1.78	48.799±1.56
10	56.728±1.23	54.891±0.97	50.878±1.45
15	64.745±1.08	65.461±0.78	67.247±2.35
20	71.123±1.27	71.239±1.07	70.771±0.98
25	74.841±1.89	76.700±2.33	78.823±1.97
30	84.197±1.18	86.248±1.12	88.355±1.08

n=8, *Represents are expressed as mean±SD. SD: Standard deviation

IR study showed that, the absorption bands of different functional groups in AFDT formulation corresponds to somewhat parallel to the free acetaminophen which indicates no change in the functional groups such as primary amine group, hydroxyl group, and carbonyl group and confirmed undisturbed structure of acetaminophen, indicated no drug-exciipient interaction. The result of the stability study indicated that there were not much differences observed in hardness, disintegration time, drug content uniformity, and friability before and after the storage period at room temperature (25°C/60% RH) and at ambient humidity, but at temperature of (40°C/75°C and 55°C) and at ambient humidity, hardness was increased with time, prolonged the disintegration time of the tablet, and the probable reason was the loss of moisture from tablets, but in all cases, disintegration time is within the specified IP limit (within 3 min.). This indicates that the formulation is fairly stable at both storage conditions.

CONCLUSION

Fast disintegrating tablets of acetaminophen were prepared by direct compression method using croscarmellose, crosspovidone and sodium starch glycolate in combination of the ratios (1:1, 2:1, 1:2) respectively. From the observed pre- and post-compression parameters, it was concluded that, the optimized formulation of (A3) justified all the official requirements. The tablets exhibited acceptable hardness of average 4.5 kg/cm², friability of 0.86% and weight variation is <5% that is well within the acceptance criteria given by USP-30, dispersion time, wetting time and water absorption ratio was 22 s, 42 s and 98.6% respectively. The reduced *in vitro* disintegration time and improved *in vitro* drug release was due to a combination of superdisintegrants in ratio (1:2) at 4% along with fairly stable disintegration time at normal and extreme temperature would be very effective tool in providing fast onset of action without need of water.

ACKNOWLEDGMENTS

Author acknowledge his gratitude to SVKM's NMIMS (Deemed to be University) Shirpur Campus, Shirpur for accomplishing this research work. Authors also thankful to Shri Baalaji Medicare Pvt. Ltd., Mumbai for providing gift sample of Acetaminophen. Facilities provided by SPTM, NMIMS, Shirpur Campus, Department of Pharmaceutics and Quality Assurance, are fully acknowledged.

REFERENCES

- Aulton ME. Pharmaceutics: The Science of Dosage form Design. 1st ed. London: Churchill Livingstone; 1998. p. 247.
- Carter SJ. Copper and Gun's: Tutorial Pharmacy. 6th ed. New Delhi: CBS Publishers and Distributors; 1998. p. 225.
- Chang RK, Guo X, Burnside BA, Cough RA. Fast dissolving tablets. Pharm Tech 2000;24:52-8.
- Dobetti L. Fast-melting tablets. Developments and technologies. Pharm Tech 2001;(Suppl):44-50.
- Gissinger A, Stamm A. Comparative evaluation of the properties of some tablet disintegrants. Drug Dev Ind Pharm 1980;6:511-36.
- Shrivastava P, Sethi V. A review article on superdisintegrants. Int J Drug Res Tech 2013;3:76-87.
- Wayne R, Dipan D. Selecting superdisintegrants for orally disintegrating tablet formulations. Pharm Tech 2006;44:83-7.
- Shakar AA, Razzak SM, Hossain MM, Arif MH, Reza MS. Effect of superdisintegrants on some physical attributes and release profile of paracetamol immediate release tablets. Bangladesh Pharm J 2012;15:89-94.
- Chaturvedi S, Agrawal VK, Singh S. Impact of superdisintegrants on the release of oro – Dispersible tablets of losartan potassium: A comparative analysis. Sch Res Lib 2012;4:1768-76.
- Indhumathi D, Rathnam G. Design and optimization of orodissolving tablets of antidepressant drug by superdisintegrants addition method. Int J Pharm Sci Rev Res 2010;2:1-9.
- Khairnar DA, Chaudhari CS, Shelke PA. Superdisintegrants: An emerging paradigm in oro-dispersible tablets. Int J Biopharm 2014;5:119-28.
- Khinch MP, Gupta MK, Bhandar A, Agrawal D, Sharma N, Gupta S. Effects of various superdisintegrants on drug release of orally disintegrating tablets. Int J Pharm Res Dev 2010;2:1-8.
- Nagendrakumar D, Raju SA, Shirsand SB, Para MS. Design of fast dissolving granisetron HCL tablets using novel co-processed superdisintegrants. J Biosci Tech 2009;1:8-14.
- Patil C, Das S. Effect of various superdisintegrant on drug release profile and disintegration time of lamotrigine orally disintegrating tablets. Afr J Pharm Pharmacol 2011;5:76-82.

15. United State Pharmacopoeia-30. NF-27. Vol. 2. Rockville: The United State Pharmacopoeial Convention; 2009. p. 1266.
16. Lachman L, Lieber HA. Pharmaceutical Dosage Forms of Tablets. Vol. II. Bombay: Marcel Dekker; 1981. p. 241-243.
17. Government of India. Ministry of Health and Family Welfare. Indian Pharmacopoeia Vol. I, II. New Delhi: The Controller of Publication; 1996. p. 762-10.
18. Gorman EA, Rhodes CT, Rudnic EM. An evaluation of croscarmellose as a tablet disintegrant in direct compression systems. *Drug Dev Ind Pharm* 1982;8:397-410.
19. Kuchekar BS, Arumugam V. Fast dissolving tablets. *Indian J Pharm Edu* 2001;35:150-2.
20. Panagrahi D, Baghel S, Mishra SB. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. *J Pharm Res* 2005;4:35-8.
21. Swati C, Nisha C, Aniruddha R, Bhanudas S. Superdisintegrants selection for tramadol dispersible tablets. *J Basic Appl Pharm Sci* 2010;131:151-7.
22. Priya VA, Rao CG, Reddy DS, Reddy VP. The effect of different superdisintegrants and their concentrations on dissolution of topiramate immediate release tablets. *Int J Pharm Sci Nanotech* 2009;2:531-6.
23. Sharma D. Formulation development and evaluation of fast disintegrating tablets of salbutamol sulphate for respiratory disorders. *ISRN Pharm* 2013;2013:674507.

Source of Support: Nil. **Conflict of Interest:** None declared.