JOPAT Vol 19(1), 375 – 386, Jan – June 2020 Edition
ISSN2636 – 5448, https://doi.org/10.4314/jopat.v19i1.3

A Comparative Evaluation of Fast Dissolving Tablets of Acetaminophen Using Super-disintegrant Blends and Sublimation Method

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ABSTRACT

Fast disintegrating tablets (FDTs) are gaining prominence as drug delivery systems and emerging as one of the popular and widely accepted dosage forms, especially for the peadiatric and geriatric patients. This study aims to evaluate and compare the tablet properties of fast disintegrating tablets of acetaminophen prepared by super-disintegrant blends and sublimation methods. Two groups of tablets comprising various batches were prepared by wet granulation. Granules batches of one group of tablets (A-G) were prepared with different concentrations of sodium starch glycolate and croscarmellose sodium while the other group of tablets (H-N) were incorporated with varying concentrations of menthol into the batches. The granules were subjected to analysis and compressed into tablets. The post-compression parameters of the tablets such as weight uniformity, crushing strength, friability, wetting and disintegration times, as well as dissolution studies were evaluated. Drug-excipient compatibility studies using Fourier transform infrared (FTIR) analysis was also carried out. Granules were fair to good in flow with Carr's indices ≤ 20.14 and angles of repose ranging from 21.34 to 35.00°. Tablets crushing strength values were between 3.44 to 8.26 kp while their friability values were < 1.52%. They showed wetting and disintegration times that were ≥ 0.18 and ≥ 0.25 min. Dissolution studies showed that four batches of tablets (two from each method used in formulation) achieved 100% drug release within 30 min. FTIR analysis shows no interactions between acetaminophen and excipients used in formulation. Tablets from both methods were comparable in their tablet properties but the disintegrant blend tablets exhibited superior crushing strengths, hence formed harder tablets, while the sublimation method tablets were superior in their wetting and disintegration times.

Keywords: acetaminophen, super-disintegrants, sublimation, tablet parameters

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INTRODUCTION

Oral dosage forms are the most popular form of drug delivery with tablet formulations accounting for about 70 - 80% of all pharmaceutical drug formulations [1]. The popularity enjoyed by the oral route is based on its numerous advantages such as precise dosage, self-medication, inexpensive therapy, non-invasiveness and ease of administration [2]. These advantages culminates in patient's high compliance and therapeutic success. An important disadvantage to this dosage form is difficulty in swallowing or dysphagia, experienced by a wide range of persons especially the elderly [3]. About 50% of the world's population experience this problem which can lead to a high level of non-compliance and therapeutic failure [4]. In order to overcome this problem and achieve better compliance, an alternative dosage form like the fast disintegrating tablets was developed [5,6].

The United States' FDA defined fast disintegrating/dissolving tablets as solid oral dosage form with drug substances, that when placed on the tongue would disintegrates rapidly within seconds. The tablets are also known as orally disintegrating, oro-dispersible tablet, fast dissolving, mouth dissolving, rapid-dissolve, quick disintegrating, melt-in-mouth, quick dissolving, porous tablets etc [7]. They all have the unique advantage of disintegrating instantaneously when placed on the tongue, releasing their drug which dissolves or disperses in the saliva causing quicker the absorption and onset of clinical effect [8]. Drugs formulated as FDT have the advantage of improved bioavailability as a result of pre-gastric absorption in the mouth and oesophagus as well as a reduced amount of drug undergoing first-pass metabolism [9,10].

Acetaminophen is a widely used over-the-counter analgesic, antipyretic and a mild anti-inflammatory drug [2,11]. A number of acetaminophen formulations in various forms such as dispersible tablets, fast disintegrating tablets, suspensions and syrups are available in the market. Various approaches have been employed in the formulation of fast disintegrating tablets and two of such methods are the combination of two or more super-disintegrants and the incorporation of a sublimating agent into the tablet formulation. Since disintegrants aids tablet breakup when in contact with fluid, a combined system of super-disintegrants can act additively to effect fast disintegration. A sublimating agent on the other hand, when incorporated into a tablet mass can create a network of pores in the tablet upon sublimation, making it possible for quick uptake of fluid by the tablet for fast breakup or disintegration. As these two methods have been successfully employed in many research works [12-14], this study aims to evaluate and compare the post compression properties of tablets formulated with both methods with the view to ascertain the best or superior method in the preparation of acetaminophen FDTs.

MATERIALS AND METHODS

Materials

Acetaminophen powder, lactose and maize starch BP (Qualikens Chemical Industries, New Delhi, India.). Hydroxypropyl methylcellulose (HPMC), sodium starch glycolate, croscarmellose sodium, sodium lauryl sulphate and menthol (Edo Pharmaceuticals, Benin City, Edo State, Nigeria). Talc and magnesium stearate (Nomagbon Pharmaceuticals, Benin City, Edo State, Nigeria). Sweetener (Sweetex®) (Reckitt Benckiser, UK), Strawberry flavour (Foster Clark Products Limited, Malta). Water was double distilled in our laboratory. All sieves were British Standard Sieves (Endecotts Ltd. London, England).

Methods

Granulation

Using the formula shown in Tables 1a and b, fourteen (14) batches (A-N) of acetaminophen granules were prepared by wet granulation and compressed into tablets. Tablets of seven batches (A-G) were prepared with a combination of super-disintegrants while the other seven batches (H-N) were incorporated with a sublimating agent. For each batch, the required quantity of acetaminophen powder, lactose and maize starch BP sufficient to produce 100 tablets was dry mixed in a mixer (Moulinex, France) for 5 min. Half of the required amounts of sodium starch glycolate, croscarmellose sodium and sodium lauryl sulphate or menthol was incorporated intragranularly to the powder mix in geometric proportions during the mixing process. Sufficient quantities of the binder mucilage (5.0 %w/v HPMC) required to form a wet mass was gradually added to the dry powder mix. The wet mass was passed through an 850 µm sieve and the resulting granules dried at 60 ºC for 30 min in a hot air oven (Gallenkamp, UK). The other half of the ingredients, flavour and sweetener were added to the dried granules, mixed thoroughly and further dried for 30 min. The resulting granules were rescreened through a 710 µm sieve before the glidant (talc) and lubricant (magnesium stearate) previously weighed and mixed in a mortar was added in geometric proportion and mixed with the dry granules. The granules were kept in an airtight container until analyses and compression.

Table 1: Formula for the preparation of acetaminophen granules and tablets by super-disintegrant blends method

Ingredients	Batches						
	A	B	C	D	E	F	G
Acetaminophen (mg)	500	500	500	500	500	500	500
Lactose (mg)	74.49	49.49	49.49	49.49	49.49	49.49	49.49
Maize starch BP (mg)	50	50	50	50	50	50	50
Sodium starch glycolate (mg)	-	25	20	15	10	5	-
Croscarmellose sodium (mg)	-	-	5	10	15	20	25
Sodium lauryl sulphate (mg)	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Sweetener (mg)	0.01	0.01	0.01	0.01	0.01	0.01	0.01
HPMC (5.0 %w/v)	qs	qs	qs	qs	qs	qs	qs
Talc (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Table 1b: Formula for the preparation of acetaminophen granules and tablets by sublimation method

Ingredients	Batches						
	H	I	J	K	L	M	N
Acetaminophen (mg)	500	500	500	500	500	500	500
Lactose (mg)	76.94	51.94	39.44	26.94	14.44	1.94	126.94
Maize starch BP (mg)	50	50	50	50	50	50	-
Menthol (mg)	-	25	37.5	50	62.5	75	-
Flavour (ml)	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Sweetener (mg)	0.01	0.01	0.01	0.01	0.01	0.01	0.01
HPMC (5.0 %w/v)	qs	qs	qs	qs	qs	qs	qs
Talc (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Granule analysis

Bulk and tapped densities

A 30 g quantity of the acetaminophen granules was poured gently into a 100 ml graduated cylinder and the volume occupied by the granules noted. The ratio of the weight of the granules to the volume of the granules was calculated as the bulk density. Then the measuring cylinder still containing the granules was tapped 100 times on a wooden platform to a constant volume. The new volume was noted and used in calculating the tapped density.

Carr's index and Hausner's ratio

The difference between the tapped and bulk densities of the acetaminophen granules divided by the tapped density and the ratio expressed as a percentage was calculated as the Carr's index while the ratio of the tapped density to the bulk density of the starch powder was calculated as the Hausner's ratio.

Flow rate and angle of repose

Using the method of Carstensen and Chan [15], a funnel clamped by a retort stand over a clean paper was filled with 10.0 g of granules with the efflux tube of the funnel closed. The efflux was opened and the granules allowed to fall freely under gravity. The time taken for the granules to flow out was noted. The flow rate was calculated as the ratio of the weight of granule to the time of flow. The height and base diameter of the heap of granules was measured and used in calculating the angle of repose using Equation 1.

$$\theta = tan^{-1}(h/r) \quad \ldots . \quad (1)$$

Where h is the height of the heap of granules and r is the radius of the circular base

Compression of granules

Batches of the granules were compressed into tablets using a 12 stations rotary tableting machine (F-3 Manesty Machines, UK) fitted with 10.5 mm round punches at compression pressure of 40 tonnes. The die volume was adjusted to compress tablets of uniform weight by using granules weighing 630 mg. Batches I-M tablets were dried at 60 °C for 6 h (for the sublimation of menthol) until a constant weight was obtained. The tablets made were then kept in air tight containers and stored in a desiccator until evaluation.

Tablet evaluations

Weight uniformity

The weight of each of 20 tablets was determined from each batch using an electronic balance (Tianfu - DT-1000, China). Their mean values and standard deviations were computed and recorded.

Crushing strength

The crushing strength of ten individual tablets per batch was determined. The force required to break a tablet by diametric compression of the tablet placed in a motorized tablet hardness tester (Campbell Electronics, Model HT-30/50, India) was recorded. The mean and standard deviation values were calculated and recorded.

Friability

Twenty tablets selected randomly from each batch were weighed and placed in the drum of a friabilator (Erweka GmbH, Germany) set to revolve at 25 rpm for 4 min. At the end, the tablets were brought out, de-dusted and re-weighed. Friability was calculated as a percentage loss in weights of the tablets.

Wetting time and water sorption ratio

A folded piece of tissue paper saturated with water was placed in a petri dish. A tiny amount of amaranth powder was placed on the top surface of a weighed tablet weighed tablet and then placed on the soaked tissue paper. The time taken for a red colour to appear on the top surface of the tablet was taken as the wetting time [16]. The wetted tablet was then reweighed and the difference between the final and initial weights with respect to the initial weight and expressed as a percentage was taken as the water sorption ratio of the tablet. The mean of triplicate determinations and their standard deviations were calculated [17].

Disintegration time

The disintegration times of six tablets per sub-batch of the tablets were determined in distilled water at 37 ± 0.5 °C using the disintegration apparatus (Erweka, DT-D, Germnay). The time taken for each tablet to break down into its particles that passed through the mesh of the apparatus was recorded and used to calculate the average time and standard deviation of disintegration.

Dissolution studies

The dissolution profiles of the various batches of tablets were determined using the USP Type II (paddle) method. A dissolution apparatus (Erweka, DT-D, Germnay) containing 900 ml of 0.1 N HCl solution maintained at 37 ± 0.5 °C with a paddle speed of 50 rpm was used. The apparatus was operated for 30 min and at various time intervals, a 5 ml volume of the dissolution fluid was withdrawn and replaced with an equivalent volume maintained at the same temperature (37 ± 0.5 °C). The withdrawn samples were filtered and diluted with an equal volume of 0.1 N HCl and their absorbances determined at λmax of 245 nm with a UV-Visible Spectrophotometer (T70, PG Instruments Ltd, USA). The concentration and the percentage of drug released at each time interval was determined using the equation from the standard calibration plot earlier obtained from the pure acetaminophen.

Drug-excipient interaction studies

FTIR compatibility studies was carried out on pure acetaminophen powder, granules, tablets and the physical mixture of the ingredients to investigate any interaction between the drug and the excipients during the mixing and tableting processes. Analysis of sample was carried out using FTIR-4100 Spectrophotometer (Shimadzu Co. Japan). The potassium bromide (KBr) tablet method was used; five milligrams of the sample was blended with KBr to 200 mg. The powder was compressed using a Sigma KBr press into a tablet shape. The tablet was placed in the sample compartment and scanned at a range of 4000 - 750 cm^{-1}.

Statistical analysis

Evaluations were carried out in triplicates and mean values reported with standard deviation. Differences between means were subjected to student's t-test at 5.0% level of significance using GraphPad InStat 3.10.

RESULTS

Granule properties

Results from the granule analysis are shown in Table 2. Granules formulated with disintegrant blends (Batches A-G) had bulk and tapped densities ranging from 0.44-0.57 g/ml and 0.56-0.67 g/ml, respectively while those from sublimation method (Batches H-N) were 0.40-0.60 g/ml and 0.48-0.71 g/ml, respectively. Their Carr's indices were ≤ 20.14 for batches A-G granules and ≤ 18.70 for batches H-N granules while their Hausner's ratios were ≥ 1.25 and ≥ 1.23 respectively. Disintegrant blend granules exhibited the highest granule flow of 10.35 g/s as against 9.31 g/s for sublimation method granules. Their angles of repose fell within the range of 21.34° to 35.00º, indicative of granules with good to fair flowability.

Table 2: Pre-compression parameters of the batches of acetaminophen granules

Batches	Bulk density (mg/ml)	Tapped density (mg/ml)	Carr's index (%)	Hausner's ratio	Flow rate (g/s)	Angle of repose (°)
A	0.54 ± 0.013	0.61 ± 0.002	10.89 ± 0.48	1.12 ± 0.06	10.30 ± 0.56	21.60 ± 1.10
B	0.50 ± 0.014	0.56 ± 0.003	10.07 ± 0.08	1.11 ± 0.09	6.67 ± 0.98	26.65 ± 1.15
C	0.47 ± 0.003	0.56 ± 0.014	15.45 ± 0.03	1.18 ± 0.08	5.34 ± 1.15	25.21 ± 1.03
D	0.44 ± 0.002	0.56 ± 0.003	20.14 ± 0.31	1.25 ± 0.07	6.03 ± 0.32	27.51 ± 0.90
E	0.51 ± 0.001	0.63 ± 0.006	18.08 ± 0.68	1.22 ± 0.02	5.04 ± 1.21	21.34 ± 1.11
F	0.57 ± 0.011	0.67 ± 0.009	14.39 ± 0.07	1.17 ± 0.04	6.82 ± 1.10	26.73 ± 1.04
G	0.53 ± 0.009	0.59 ± 0.002	10.20 ± 0.92	1.11 ± 0.06	10.35 ± 2.89	24.21 ± 1.06
H	0.53 ± 0.011	0.61 ± 0.010	13.26 ± 0.24	1.15 ± 0.04	8.54 ± 1.44	22.60 ± 1.04
I	0.42 ± 0.021	0.50 ± 0.019	16.00 ± 0.22	1.19 ± 0.05	7.54 ± 1.88	25.64 ± 1.42
J	0.43 ± 0.013	0.49 ± 0.014	12.25 ± 0.58	1.14 ± 0.02	6.68 ± 0.50	27.47 ± 1.06
K	0.40 ± 0.022	0.50 ± 0.030	18.70 ± 0.46	1.23 ± 0.04	5.59 ± 1.10	34.20 ± 1.28
L	0.60 ± 0.012	0.71 ± 0.020	15.10 ± 0.44	1.18 ± 0.04	6.54 ± 1.80	34.80 ± 1.06
M	0.53 ± 0.011	0.65 ± 0.010	18.40 ± 0.27	1.23 ± 0.05	6.50 ± 1.40	35.00 ± 1.16
N	0.41 ± 0.005	0.48 ± 0.015	14.50 ± 0.47	1.17 ± 0.03	9.10 ± 0.93	24.21 ± 1.18

All readings were taken in triplicate ± standard deviation

Tablet properties

Results from the evaluation of the tablets are shown in Table 3. All the formulated tablets exhibited tablet weights ranging from 620.0-641.0 mg with minimal weight variation within batches. The crushing strengths of the entire tablets were within the range of 3.44 to 8.26 kp with the tablets prepared by disintegrant blends exhibiting higher values. Similarly, the friability values of the entire tablets were within the range of 0.98 to 1.52% with the disintegrant blends tablet formulations having lower values. The tablets exhibited variable wetting times and water sorption capacity of 10.05 - 910.65 sec and 18.10-91.20%, respectively. Tablets formulated with sublimation method showed a decrease in wetting time and an increase in water sorption with increase in the amount of menthol used in the formulation. The tablets showed a range of disintegration times from 0.25-18.00 min with batches of tablets formulated by disintegrant blends showing variable disintegration times while tablets formulated with sublimation method showed decrease in disintegration times with increase in the amount of menthol used in the formulation.

Table 3: Post-compression parameters of the batches of acetaminophen tablets

Batches	Weight (mg)	Crushing strength (kp)	Friability (%)	Wetting time (sec)	Water sorption (%)	Disintegration time (min)
A	0.632 ± 0.013	8.26 ± 1.24	0.99 ± 0.48	460.54 ± 0.66	24.15 ± 0.65	8.00 ± 0.06
B	0.627 ± 0.014	5.41 ± 0.54	1.06 ± 0.08	160.04 ± 0.54	41.44 ± 0.18	3.00 ± 0.02
C	0.629 ± 0.003	7.00 ± 0.38	1.10 ± 0.03	43.97 ± 0.42	52.22 ± 0.71	0.64 ± 0.03
D	0.631 ± 0.002	6.86 ± 0.34	1.18 ± 0.31	33.35 ± 0.17	84.43 ± 1.01	0.48 ± 0.02
E	0.625 ± 0.001	6.72 ± 0.43	1.20 ± 0.68	34.47 ± 0.76	58.49 ± 0.87	0.51 ± 0.03
F	0.627 ± 0.011	7.24 ± 0.49	1.14 ± 0.07	40.05 ± 0.56	62.32 ± 0.54	0.57 ± 0.03
G	0.628 ± 0.009	6.86 ± 0.49	1.08 ± 0.22	220.65 ± 0.42	31.60 ± 1.67	4.00 ± 0.03
H	0.626 ± 0.021	7.45 ± 0.59	1.00 ± 0.24	584.45 ± 0.52	22.85 ± 0.56	10.00 ± 0.03
I	0.635 ± 0.032	4.89 ± 0.57	1.18 ± 0.46	105.40 ± 0.45	44.24 ± 0.81	2.01 ± 0.02
J	0.641 ± 0.011	4.40 ± 0.45	1.24 ± 0.22	63.70 ± 0.24	51.21 ± 0.70	1.31 ± 0.05
K	0.620 ± 0.040	4.04 ± 0.39	1.32 ± 0.44	40.35 ± 0.20	66.30 ± 0.90	0.92 ± 0.02
L	0.625 ± 0.022	3.85 ± 0.47	1.44 ± 0.47	30.47 ± 0.60	85.45 ± 0.44	0.43 ± 0.04
M	0.636 ± 0.041	3.44 ± 0.39	1.52 ± 0.12	10.05 ± 0.25	91.20 ± 0.14	0.25 ± 0.03
N	0.632 ± 0.015	5.72 ± 0.65	0.98 ± 0.32	910.65 ± 5.55	18.10 ± 2.62	18.00 ± 0.09

All readings were taken in triplicate ± standard deviation.

Figures 1a and b shows the dissolution profiles of the acetaminophen tablets. Each batch of tablet displayed a drug release pattern that correlates with its disintegration time. Not all the batches released 100 % of their drug content within the 30 min of dissolution testing. Batches D and E tablets prepared with a disintegrant blend ratio of 3:2/2:3 achieved almost 100 % drug release in 10 min while batches L and M tablets formulated with 12.5 and 15.0 % menthol achieved this same drug release among the tablets formulated with sublimation method.

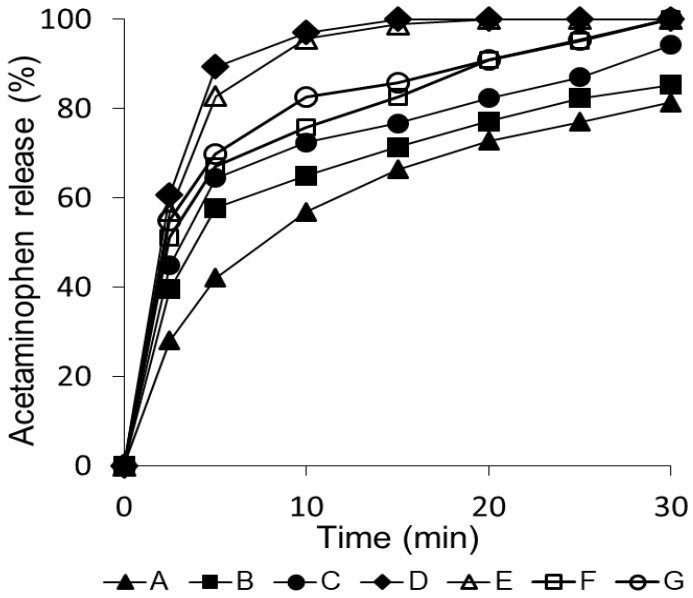

Figure 1a: Dissolution profiles of acetaminophen batches of tablets (A-G) prepared by disintegrant blends

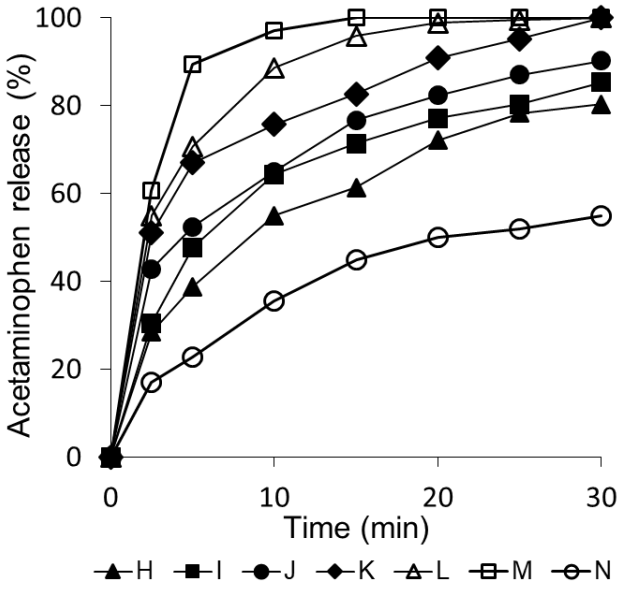

Figure 1b: Dissolution profiles of acetaminophen batches of tablets (H-N) prepared by sublimation method

Compatibility studies

Figure 2 shows the FTIR spectra of pure acetaminophen powder (a), granules (b), tablet (c) and a physical mixture of all the ingredient used in the formulation by disintegrant blends (Figure 2a) and sublimation method (Figure 2b). The spectrum of pure acetaminophen powder showed characteristic peaks at 1227.00, 1636.42 and 3171.00 cm^{-1}. These peaks observed for acetaminophen remained unchanged in the spectral data of the granules, tablet and a physical mixture of ingredient from both methods used in tablet formulation. This observation ruled out the possibility of a chemical interaction or complex formation between acetaminophen and all other formulation ingredients during the mixing and tableting processes.

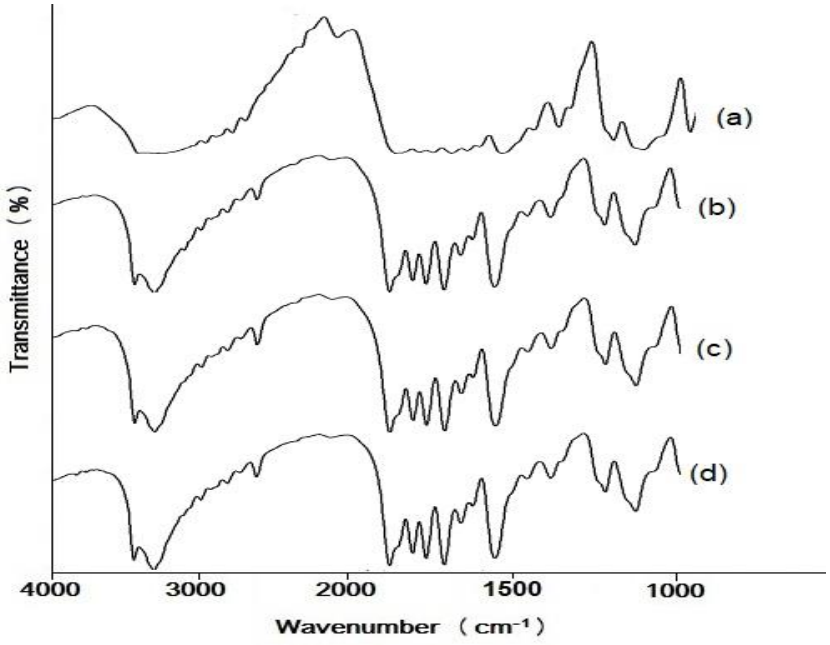

Figure 2a: FTIR spectra of pure acetaminophen powder (a), physical mixture of ingredients (b), formulated granules (c) and compressed tablet (d) prepared with disintegrant blends

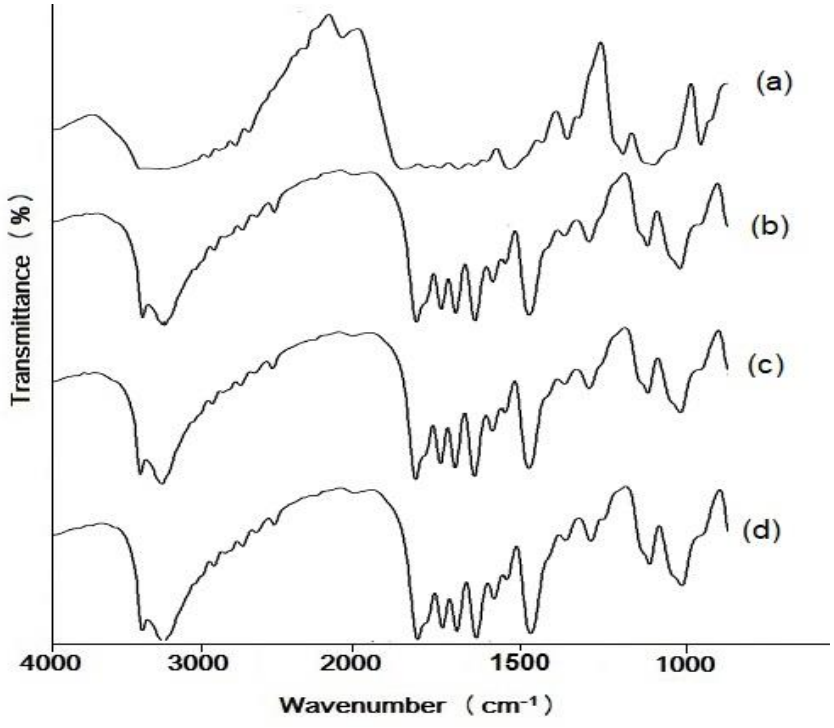

Figure 2b: FTIR spectra of pure acetaminophen powder (a), physical mixture of ingredients (b), formulated granules (c) and compressed tablet (d) prepared with sublimation method

DISCUSSION

A comparative evaluation of the post compression parameters of fast disintegrating tablets formulated with both disintegrant blends and sublimation methods have been carried out. The micromeritic properties of the granules prepared by wet granulation method using both methods indicates a gradation in flowability from good to fair flowing granules.

Although no observable pattern can be discerned in granule batches of both the disintegrant blends and sublimation methods, the former had superior values to the latter. These superior values may be attributable to the higher number of formulation ingredients with different particle sizes and shapes, conferring on the granule particles less inter-particulate friction and ease of flow [18].

The tablets formulated with both methods showed minimal weight variation ($p > 0.05$) within and among the batches, therefore in compliance with the British Pharmacopoeia specification of not more than two of the individual weights of tablets deviating from the average weight by more than ± 5.0 % and none should deviate by more than ± 10.0 %. The uniform die filling during the compaction process of the tablets would have been responsible for the minimal weight variations exhibited by the tablets. The crushing strength values of the tablets did not meet the British Pharmacopoeia specification of 5.0 - 8.0 kp as acceptable crushing strength values for optimal tablet hardness [19]. Though others have postulated crushing strength values above 4.0 kp as satisfactory for tablet hardness [20], the low values of batches L and M tablets containing 12.5 and 15.0 %w/w of menthol, respectively, can be traced to the micro-porous nature of the tablets. The high amounts of menthol used in the formulation of these batches of tablets,

will on sublimation make the tablet porous thereby weakening inter-particle bonds within the tablet and consequently decreasing the ability of the tablet to withstand diametrical compression.

The friability test results of the formulated tablets showed that practically all the batches of tablets formulated did not meet the 0.8 - 1.0 % tablet weight loss specified by the British Pharmacopoeia [19] except the control batches A and H tablets, containing only maize starch as disintegrant and batch M tablets containing neither disintegrant nor sublimating agent. The superior low friability values of the disintegrant blend tablets were not significantly different from those prepared with the sublimating agent. Also, the friability of the sublimating agent tablets increased with the increase in the amounts of menthol and this observation seems to be linked with the hardness of the tablets as the least hard tablets of batches L and M were also the most friable tablets.

Though it may be safe to say that the low crushing strengths of the tablets with sublimating agent was responsible for their high friability values but that cannot be said of the disintegrant blend tablets with high crushing strength values. A combination of factors may be responsible for this observation and these includes the binder and the amounts of binder used, since binders are the key determinants of a tablet's hardness and friability [17,21]. Another factor playing a role here is the amounts of the super-disintegrants added extra-granularly. While the quantity of binder used in the formulation may have been enough for the inter-particle and inter-granular adhesion in the granulation and compaction processes respectively, giving tablets of good hardness, the quantities of extra-granular super-disintegrants added to the granulates on the other hand will compromise inter-granular interaction and bonding leading to enhanced friability.

Results from the wetting times, moisture sorption and disintegration times of the tablets reveals a correlation between them. The faster the wetting time, the higher the moisture sorption and the faster the disintegration of the tablet. Therefore the ability of the tablets to take up moisture instantaneously is crucial to fast disintegration. Though tablets made with disintegrant blend ratios 3:2 and 2:3 gave acceptable wetting and disintegration times, those made with 12.5 and 15.0 %w/w of menthol were superior in their wetting and disintegration times. This further proves the important role played by fluid uptake and the rate of that uptake in tablet disintegration, as the micro-porous network afforded by the sublimating agent in the tablets facilitates quick fluid intake by capillary action or wicking, generating enough swelling force within the tablet to cause disintegration. Whereas, fluid uptake for the disintegrant blend tablets will require fluid penetrating the micro crevices of the tablet compact before effecting disintegration, a wicking or capillary action that will not be as fast as that taking place in a micro-structured porous tablet [22]. However, it is generally accepted that FDTs should disintegrate within a few seconds or in less than a minute, when placed in the mouth, but the US Food and Drug Administration stipulates a time frame of approximately 30 sec while the European Pharmacopoeia states that a disintegration time of less than 3.0 min is indicative of a fast disintegrating tablet [23,24].

The dissolution studies of the tablets revealed that there was an initial burst of drug release from most of the tablets in the first 5 min of dissolution testing. This release was highest with batches D and E tablets prepared with a disintegrant blend ratio of 3:2/2:3 and batches L and M tablets formulated with 12.5 and 15.0 % menthol. These tablets achieved over 70.0 % drug release within 5 min and also they were the tablets with shorter

disintegration time. Therefore, the burst of drug release can be traced to the fast disintegration times of the tablets as disintegration determines to a great extent the area of contact between the solid tablet and the dissolution fluid facilitating the dissolution process.

CONCLUSION

Results from the study revealed that fast disintegrating tablets of acetaminophen prepared by disintegrant blend were comparable to those prepared by sublimation method in all tablet parameters investigated. Though the disintegrant blend tablets exhibited superior values in the crushing strengths of the tablets hence formed harder tablets, the sublimation method tablets were superior in their wetting and disintegration times. This shows that both methods have their merits and demerits and the method of choice falls on the formulator, who decides based on the most desired qualities expected in a formulated fast disintegrating tablet.

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