Pharmaceutical Sciences Asia

Pharm Sci Asia 2019; 46 (1), 25-32
DOI:10.29090/psa.2019.01.017.0068

Research Article

Effect of mode of superdisintegrant incorporation on tableting properties of metronidazole granules

Yonni Eshovo Apeji*,
Fidelis Dzarma Zechariah,
Sophie Nock Anyebe,
Babajide Tytler,
Adeniji Kehinde Olowosulu,
Avosuahi Rukayat Oyi

Department of Pharmaceutics and Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, Kaduna State, Nigeria

***Corresponding author:**
Yonni Eshovo Apeji
yeapeji@abu.edu.ng

KEYWORDS:
Croscarmellose sodium; Sodium starch glycolate; Disintegrant; Extragranular; Intragranular; Wet granulation

ABSTRACT

Superdisintegrants are a special class of excipients used in a tablet formulation to aid disintegration and possibly enhance the release kinetics of a drug. The intragranular and extragranular effect of sodium starch glycolate (SSG) or croscarmellose sodium (CCM) as superdisintegrants on tableting properties of metronidazole granules were investigated. The granules were characterized for particle size analysis, angle of repose, bulk and tapped densities as well as Carr's index (CI) and Hausner's ratio (HR). Tablets were prepared from each batch of granules weighing 500 mg on a single punch tablet press using 12 mm flat-faced punches and compressed at 57.5 MPa. The tablets were kept at 25 ± 2 °C/75 % RH for 24 h to allow for elastic recovery and the properties of weight variation, content uniformity, thickness, crushing strength (CS), disintegration time (DT), and drug-release were evaluated. The results showed that all the batches of granules exhibited good flow based on angle of repose < 30° , CI < 20 %, and HR ≤ 1.2. The evaluated tablet properties demonstrated that intragranular addition of either SSG or CCM lowered the CS and DT when compared to the extragranular effect. This indicates that the incorporation mode of superdisintegrant in a tablet formulation exerts an influence on tablet properties.

1. INTRODUCTION

Tablets remain the most common and preferred solid unit dosage form for delivering medicaments to patients [1]. The merits of tablets include the ability for accurate dosing, long shelf life, and cost-effective production[2,3]. Tablet formulations are usually composed of active pharmaceutical ingredients (APIs) and other supporting ingredients, collectively known as additives or excipients. Excipients play a vital role in the design of the tablet dosage form by determining its functionality and performance [4]. Among the tablet excipients, disintegrants are often considered as the most important as they ensure the break-up of the dosage form into smaller fragments upon ingestion, to allow the onset of drug dissolution and eventual absorption [5].

Disintegration plays a vital role in ensuring that the active drug component of a tablet is released when it comes into contact with the gastrointestinal fluid after oral administration. Failure of

the tablet to release the drug will lead to poor bioavailability and invariably therapeutic failure. There are several factors that influence the performance of disintegrants, one of which is the mode of incorporation of the disintegrant in the formulation. Disintegrants may be added intragranularly (endo-disintegrant), extragranularly (exo-disintegrant) or both. Several studies have evaluated the mode of incorporation of starches and their derivatives as disintegrant in tablet formulation. Odeku and Akinwande [6] evaluated the mode of incorporation of acid modified water and white yam starches on tableting properties of paracetamol. Tablets containing starches incorporated extragranularly showed faster disintegration but lower tensile strength than those starches incorporated intragranularly. In another study carried out by Adeoye and Alebiowu[7], they evaluated the disintegration potential of co-processed tapioca starch and mannitol prepared by co-fusion and co-grinding techniques. The results revealed that tablets produced with extragranular disintegrant exhibited a higher crushing strength compared to their intragranular counterpart. The focus of our study was to examine the effect of mode of incorporation of superdisintegrants on the tableting properties of metronidazole granules.

Superdisintegrants are a new generation of polymeric disintegrants that promote a rapid disintegration of tablets when used in low concentrations and thereby increase the dissolution rate of the drug [8]. They are chemically modified products of existing excipients which includes sodium starch glycolate, croscarmellose sodium and crospovidone [4]. Superdisintegrants are superior to the conventional disintegrants as they swell up to as much 300 – 400 times its original volume[9]. They have been employed in the formulation of orally disintegrating mini-tablets to facilitate rapid disintegration in the oral cavity for pediatric and geriatric patients who find it difficult to swallow[10]. Studies have shown that disintegration time improves remarkably when superdisintegrants are incorporated into insoluble systems as compared to soluble and partially soluble systems[11].

In this study, two superdisintegrants, sodium starch glycolate and croscarmellose sodium were incorporated either intragranularly or extragranularly in tablet formulations and the tableting properties of crushing strength, disintegration time, friability, disintegration efficiency ratio (DER) and drug release were evaluated. Crospovidone could not be used because it was not readily available as at the time the study was carried out.

2. MATERIALS AND METHODS

2.1. Materials

Metronidazole powder (Central Drug House (P) Ltd. New Delhi, India), Maize starch (Burgoyne Burbidge & Co. India, Mumbai), Colloidal silicon dioxide (Evonik Industries, Germany), Acacia gum (Kerry Ingredients and flavours Ltd, Ireland), Croscarmellose, Sodium starch glycolate, Lactose (DFE Pharma, Klever Strase 187, D-47574 Goch, Germany), Sodium stearyl fumarate (JRS Pharma GMBH CO.KG, 73494, Rosenberg, Germany). All other materials used were of analytical grade.

2.2. Preparation of metronidazole granules

Metronidazole granules were prepared by wet granulation using the superdisintegrants as an intragranular disintegrant and maize starch as an extragranular disintegrant. A powder mixture consisting of metronidazole powder, lactose and CCM or SSG was prepared in a mortar with the aid of a pestle and a solution of acacia gum was incorporated as a binder to mass the powder mix. The massed powder was screened by passing through a sieve (1.6 mm). The granules formed were dried in the oven at 40°C for 10 min. Subsequently, the granules were passed through a sieve (0.8 mm) and dried completely in the oven at 40 °C for 2 h. The entire process was repeated using maize starch as intragranular disintegrant and the superdisintegrants as extragranular disintegrants. The formula for preparing granules is given in Table 1.

2.3. Particle size analysis [12]

Particle size analysis was carried out using the sieving method. Test sieves ranging from 1000 µm to pan were arranged in a descending order; 1000 µm, 500 µm, 250 µm, 150 µm, 90 µm and pan. Ten grams of sample of each batch was placed on the 1000 µm sieve and allowed to vibrate for 10 min in the Endecott test sieve shaker. The amount retained on each sieve was weighed and the mean granule size calculated using the formula give below;

$$Mean\ granule\ size = \frac{\Sigma(\%weight\ of\ powder\ retained\ on\ each\ sieve\ X\ sieve\ size)}{100} \quad \text{Eq. 1}$$

Table 1: Granule formula for each batch

Ingredients	Quantity per tablet (mg)			
	Batch 1a	Batch 1b	Batch 2a	Batch 2b
Metronidazole (40 %)	200	200	200	200
Lactose (40 %)	200	200	200	200
MS (5 %)	25	-	25	-
CCM (5 %)	-	-	-	25
SSG (5 %)	-	25	-	-
Acacia (5%)	25	25	25	25

MS-Maize starch, **CCM**-Croscarmellose, **SSG**-Sodium starch glycolate

2.4. Angle of repose [13–15]

This was obtained using the fixed funnel method. A clean glass funnel was clamped on a retort stand such that the height from the tip of the funnel to the work bench surface was fixed at 8 cm and the outlet of the funnel was plugged. Ten grams of sample was poured into the funnel at 45 ° and the plug at the tip removed. The powder was allowed to flow freely under the influence of gravity. A conical heap of powder was formed. The dimensions of height and radius were measured and used to compute the angle of repose using Eq. 2 below. A mean of three measurements was obtained for each sample.

$$Tan\ \theta = \frac{h}{r} \qquad \text{Eq.2}$$

2.5. Flow rate determination [13–15]

To assess flow rate, 10 g of the sample was weighed and poured into the funnel of the flow rate apparatus. The time taken for the granules to flow out of the funnel was taken. This was repeated twice for each sample and the average value taken. The flow rate was calculated using the equation given below;

$$FR = \frac{weight\ of\ granules}{time\ of\ flow} \qquad \text{Eq. 3}$$

2.6. Bulk and tapped densities

Ten grams of sample were weighed using the electronic balance and transferred into a 50 mL measuring cylinder and the volume occupied was noted as V_o. The cylinder was tapped manually 50 times at constant rate and the tapped volume $V_{50,}$ was recorded. A mean of three replicates was recorded for each batch. The bulk and tapped densities were calculated using the equations given below;

$$BD = \frac{weight\ of\ granules}{bulk\ volume} \qquad \text{Eq. 4}$$

$$TD = \frac{weight\ of\ granules}{tapped\ volume} \qquad \text{Eq. 5}$$

The values obtained for bulk and tapped densities were used to calculate Carr's index (CI) and Hausner's ratio (HR) in triplicate using the equations given below

$$CI = \frac{T_D - B_D}{T_D} \times 100\ \% \qquad \text{Eq. 6}$$

$$HI = \frac{T_D}{B_D} \qquad \text{Eq. 7}$$

2.7. Tableting

The granules for each batch were mixed for 2 min with the extragranular excipients consisting of the extragranular disintegrant, lubricant and glidant before compression. Tablets weighing 500 mg were compressed at 57.5 MPa using the 12 mm punch and die set in the Single Punch Tablet Press. After compression, the tablets were stored for 24 h to allow for elastic recovery prior to evaluation of the tablet properties. The tableting formula is given in Table 2.

2.8. Uniformity of weight test

The uniformity of weight of twenty randomly selected tablets from each batch was determined according to the British Pharmacopoeia method [16].

2.9. Measurement of tablet thickness

The thickness of ten tablets selected at random from each batch was determined using a digital Vernier Calliper.

2.10. Content uniformity test

The metronidazole content of the tablets produced was determined using the procedure described in the British Pharmacopoeia [16]. The

Table 2: Tablet formula for batches 1a - 2b

Ingredients	Quantity per tablet			
	Batch 1a	**Batch 1b**	**Batch 2a**	**Batch 2b**
Metronidazole (40 %)	200	200	200	200
Lactose (40 %)	200	200	200	200
MS (5 %)	25	-	25	-
SSG (5 %)	-	25	-	-
CCM (5 %)	-	-	-	25
Acacia gum (5 %)	25	25	25	25
Extragranular excipients				
MS (5 %)	-	25	-	25
SSG (5 %)	25	-	-	-
CCM (5 %)	-	-	25	-
CSD (4 %)	20	20	20	20
SSF (1 %)	5	5	5	5
Total (mg)	**500**	**500**	**500**	**500**

Batch 1a: Formulation containing SSG as extragranular disintegrant
Batch 1b: Formulation containing SSG as intragranular disintegrant
Batch 2a: Formulation containing CCM as extragranular disintegrant
Batch 2b: Formulation containing CCM as intragranular disintegrant
MS: Maize starch, **SSG:** Sodium starch glycolate**, CCM:** Croscarmellose sodium**, CSD:** Colloidal silicon dioxide**, SSF:** Sodium stearyl fumarate

amount of drug in the tablet was estimated spectrophotometrically (UV – 1800 Spectrophotometer, Shimadzu Corporation, USA) at 277 nm using the regression data of the calibration curve ($y = 0.039x + 0.13$, $R^2 = 0.9983$) of metronidazole.

2.11. Disintegration time

Disintegration test was carried out on the four batches of tablets at 37 °C using a disintegration test apparatus. The time taken for the tablets to disintegrate and pass through the mesh was noted and the average disintegration time of six tablets was measured.

2.12. Crushing strength measurement

The breaking force required to crush the tablets was measured for the four batches of tablets using the Monsanto hardness tester. Each tablet was placed between the spindle and the anvil. The knob was screwed gradually from zero until the tablet was fractured. A mean of six replicates was recorded with the standard deviation determined.

2.13. Friability Test

Ten tablets were weighed and recorded before transferring into Erweka friabilator. It was allowed to rotate at 25 rpm for 4 mins. The tablets were collected, dedusted and reweighed collectively. Loss in weight was expressed as percentage of the initial weight calculated using the equation below:

$$\% \text{ friability} = \frac{initial\ weight - final\ weight}{initial\ weight} \times 100 \qquad \text{Eq. 8}$$

2.14. Disintegration Efficiency Ratio (DER)

The disintegrant efficiency ratio (DER) was determined using the relationship,

$$DER = \frac{CS/FR}{DT} \qquad \text{Eq. 9}$$

Where *CS*, *FR*, and *DT* are the crushing strength, friability, and disintegration time, respectively

2.15. Dissolution test

Dissolution studies were performed by using Erweka dissolution apparatus (Type DT6, GmbH, Heusenstamm, Germany) under sink conditions. Dissolution was determined in 900 mL 0.1N HCl at a rotating speed of 50 rpm and temperature of 37 ± 0.5 °C. A tablet was carefully placed into the vessel to exclude air bubbles from its surface. Five milliliters of samples were withdrawn at time intervals of 5, 10, 15, 20, and 30 min and replaced with equal volume of 0.1N HCl after each withdrawal. One milliliter from each sample withdrawn was diluted to 10 mL using the dissolution medium. The absorbance values were taken at 277 nm using the UV spectrophotometer (UV – 1800 Spectrophotometer,

Table 3: Physical properties of metronidazole granules

Batches	Mean granule size (µm)	Flow rate (g/s)	Angle of repose(°)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's Index	Hausner's ratio
1a	324.3	2.40(0.01)	25.6(0.1)	0.53(0.01)	0.64(0.01)	18(0.58)	1.20(0.01)
1b	274.1	2.50(0.01)	26.5(0.1)	0.50(0.02)	0.61(0.01)	18(0.58)	1.22(0.01)
2a	294.7	2.31(0.02)	25.2(0.1)	0.50(0.02)	0.61(0.01)	18(0.58)	1.22(0.01)
2b	263.9	2.52(0.02)	25.2(0.1)	0.51(0.01)	0.61(0.01)	16(0.58)	1.20(0.01)

Shimadzu Corporation, USA) and the amount of drug released at each time interval was calculated using the regression equation ($y = 0.039x + 0.13$, $R^2 = 0.9983$).

3. RESULTS

3.1. Physical properties of metronidazole granules

Table 3 displays the physical properties of metronidazole granules prepared for all the batches. The mean granule size (MGS) ranged from 263.9 – 324.3 µm with formulations containing the superdisintegrant as intragranular disintegrant (Figure 1b and 2b) having a lower MGS compared to their counterparts incorporating the superdisintegrant as an extragranular disintegrant in the formulation. The angle of repose did not exceed 30 ° implying that all batches of granules possessed good flow properties irrespective of the mode of incorporation of the superdisintegrant. However, it was observed that formulations containing the superdisintegrant as intragranular disintegrant had a slightly better flow rate compared to other batches. Bulk and tapped densities did not show any remarkable difference across the batches and the Carr's index and Hausner's ratio used as parameters to estimate flow properties were consistent with the angle of repose. The properties of the granules so examined did not yield much difference as a result of the mode of incorporation of the superdisintegrant apart from the MGS and a marginal difference in the flow rate.

3.2. Physical properties of metronidazole tablets prepared from the four batches

The physical properties of metronidazole tablets produced from the four batches are presented in Table 4. The mean weight of tablets ranged from 450 – 500 mg with formulations containing the superdisintegrant as extragranular disintegrant (1a & 2a) having a higher mean tablet weight. There seem to be a relationship between mean tablet weight and thickness as lower tablet weight corresponds to lower tablet thickness. Content uniformity was within the acceptable limit for all batches (95 – 105 %). The crushing strength (CS) of tablets was ranked in the following order: 1a > 1b > 2a > 2b, with formulations containing superdisintegrant as extragranular disintegrant (1a & 2a) having a higher crushing strength. The disintegration time (DT) of tablets was a reflection of the CS as lower values of CS produced shorter DT. The effect of mode of incorporation of superdisintegrant on CS and DT is presented in Figs. 1a & b respectively. The graphical relationship shows that CS and DT decrease when the superdisintegrant is incorporated intragranularly compared to the

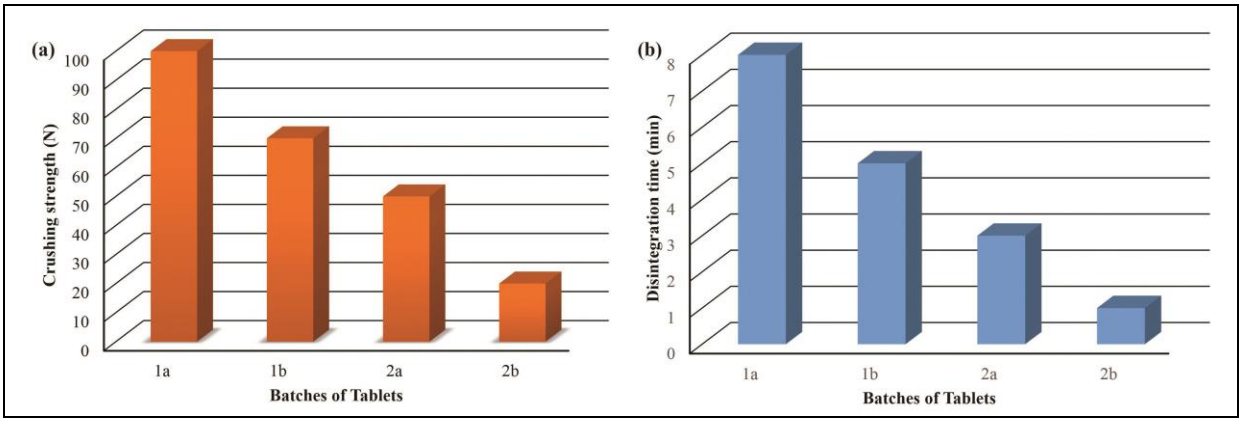

Figure 1. Effect of intragranular and extragranular addition of superdisintegrant on (a) crushing strength and (b) disintegration time of tablets for all the batches

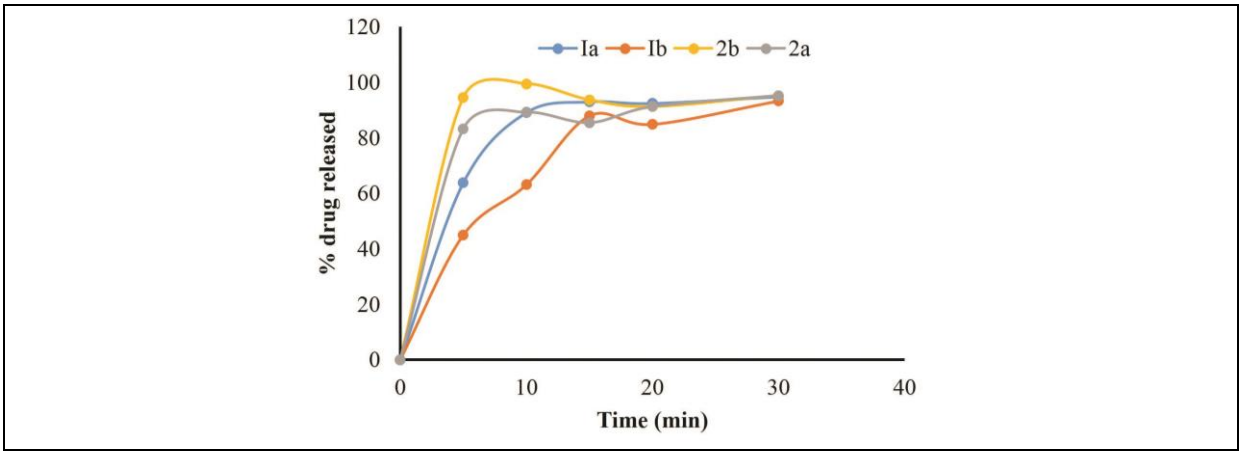

Figure 2. Drug release profile of the four batches of tablets showing the amount of drug released with time

extragranular addition of superdisintegrant to the formulation. Tablet friability exceeded 1 % for all the batches. Hence, none of the batches passed the test for friability according to the British Pharmacopoeia requirements. Disintegrant efficiency ratio (DER) is a measure of the balance between the mechanical and disintegration properties of tablets. Higher values suggest that a better balance between the two properties was achieved. It was observed that formulations containing the superdisintegrant as extragranular disintegrant (1a & 2a) had a better balance of mechanical and disintegration properties. The time taken to release 50 % of the drug ($T_{50\%}$) ranged from 3.7 – 5.3 min with batch 2b containing croscarmellose sodium (CCM) as intragranular disintegrant attaining the fastest release in 3.7 min. Maximum drug release of 100 % was attained in 10 mins by batch 2b correlating with its shortest disintegration time of 1 min.

4. DISCUSSION

The results from the study have shown that the intragranular addition of either SSG or CCM caused a lowering of the crushing strength and disintegration time of the tablets. This is consistent with the findings of Adeoye and Alebiowu [7] who observed that tablets produced with extragranular disintegrant exhibited a higher crushing strength compared to their intragranular counterpart, possibly due to the availability of more contact points for bonding. However, the effect was not the same with respect to disintegration time as the same study revealed that tablets containing extragranular disintegrants disintegrated faster than those prepared with intragranular disintegrants. Other studies have also reported that extragranular addition of disintegrants promotes faster disintegration compared to intragranular addition [6]. This has been attributed to the exposure of the larger amount of the extragranular disintegrant to the disintegration fluid resulting in a faster absorption of larger quantity of the disintegration fluid and the subsequent faster disintegration time[7]. The observed effect of lowering disintegration time due to intragranular addition as opposed to previous findings can be explained on the basis of the nature of the disintegrants. The superdisintegrants are known to swell to about 300 – 400 times its original volume. This is more likely to generate a greater disintegration force within the tablet that will facilitate rapid break-up of the tablet when it comes in contact with the disintegration medium. A higher value of DER was obtained with extragranular addition for both superdisintegrants implying that a better balance of mechanical and disintegration properties in

Table 4: Physical properties of metronidazole tablets from the four batches

Batches	Mean weight(g)	CU (%)	TN(mm)	CS(N)	DT(mins)	DER	$T_{50\%}$(min)	FR (%)
1a	0.50(0.01)	103.7	3.99(0.02)	100(0.8)	8(0.5)	27.17	4.5	0.46
1b	0.48(0.01)	100.3	3.92(0.07)	70(1)	5(0.4)	24.56	5.3	0.57
2a	0.47(0.01)	105.1	3.85(0.09)	50(0.7)	3(0.5)	22.83	4	0.73
2b	0.45(0.01)	102.3	3.81(0.09)	20(0.4)	1(0.5)	16.26	3.7	1.23

TN-Thickness, **CS**-Crushing strength, **DT**-Disintegration time, **CU**-Content uniformity, **FR**-Friability, **DER**-Disintegration efficiency ratio

tablets was attained [7,17,18]. Generally, tablets containing SSG either intragranularly or extragranularly produced tablets with higher crushing strength and longer disintegration time compared to those of CCM. This can be attributed to the mechanism by which both superdisintegrants exert their effect. SSG has been proposed to exert its disintegration ability by swelling while the combined mechanism of swelling, wicking and strain recovery have been proposed for the action of CCM. The nature of cross-linking with the presence of hydroxyl group which permits hydrogen bonding thereby increasing the hydrophilicity of CCM must have influenced its performance when incorporated intragranularly or extragranularly [19]. The drug release profile of CCM was a reflection of its rapid disintegration effect and this agrees with the findings of Gordon et al [20] who reported that croscarmellose sodium produced faster drug dissolution than sodium starch glycolate or crospovidone. Comparing the activity of the superdisintegrants with maize starch (MS), it was noted that formulations containing SSG and CCM as intragranular disintegrant had lower CS and DT in relation to formulations containing MS as intragranular disintegrant. This is because superdisintegrants are known to swell 300 – 400 times more than MS and so will exert a greater effect on CS and DT.

5. CONCLUSION

In conclusion, the mode of incorporation of superdisintegrant in tablet formulation was seen to influence the tablet properties. The intragranular addition of superdisintegrant caused a lowering of the crushing strength and disintegration time respectively for both materials investigated relative to the properties observed when added extragranularly. It will therefore be necessary for the formulator to carefully select the mode of incorporation of the superdisintegrant in order to attain a balance of tableting properties in a formulation.

6. ACKNOWLEDGEMENTS

The authors appreciate the following companies for the supply of gift samples of excipients: DFE Pharma (Germany) for sodium starch glycolate, croscarmellose sodium and lactose, JRS Pharma (Germany) for sodium stearyl fumarate, Evonik industries (Germany) for colloidal silicon dioxide and Kerry Ingredients and Flavours (Ireland) for acacia gum.

Conflict of Interest

The authors declare no conflict of interest.

Funding

None to be declared

Ethical approval

None to be declared

Article info:
Received November 14, 2017
Received in revised form February 16, 2018
Accepted March 3, 2018

REFERENCES

1. Kottke JM, Rudnic EM. Tablet dosage forms. In: Banker GS, Rhodes CT, editors. Modern pharmaceutics. 4th ed. New York, NY: Marcel Dekker, Inc; 2002. p. 287–333.
2. Alderborn G. Tablets and compaction. In: Aulton ME, editor. Pharmaceutics: The science of dosage form design. 2nd ed. Edinburgh, New York: Churchill Livingstone; 2001. p. 397–440.
3. Augsburger LL, Zellhofer MJ. Tablet formulation. In: Swarbrick J, editor. Encyclopedia of pharmaceutical technology. 3rd ed. New York, NY: Informa Healthcare USA, Inc; 2007. p. 3641–52.
4. Desai PM, Liew CV, Heng PWS. Review of disintegrants and the disintegration phenomena. J Pharm Sci. 2016;105(9):2545–55.
5. Moreton RC. Disintegrants in tableting. In: Augsburger, L. L, Hoag SW, editor. Pharmaceutical dosage forms: Tablets. 3rd ed. New York, NY: Informa Healthcare USA, Inc; 2008. p. 217–49.
6. Odeku OA, Akinwande BL. Effect of the mode of incorporation on the disintegrant properties of acid modified water and white yam starches. Saudi Pharm J. 2012;20(2):171–5.
7. Adeoye O, Alebiowu G. Dimensionless quantities in the evaluation of novel composite disintegrants. J Drug Deliv Sci Technol. 2014;24(2):222–8.
8. Srinarong P, Faber J, Visser M, Hinrichs W, Frijlink H. Strongly enhanced dissolution rate of fenofibrate solid dispersion tablets by incorporation of superdisintegrants. Eur J Pharm Biopharm. 2009;73(1):154–61.
9. Azad M, Afolabi A, Bhakay A, Leonardi J, Dave R, Bilgili E. Enhanced physical stabilization of fenofibrate nanosuspensions via wet co-milling with a superdisintegrant and an adsorbing polymer. Eur J Pharm Biopharm. 2015;94:372–85.
10. Stoltenberg I, Breitkreutz J. Orally disintegrating mini-tablets (ODMTs) - A novel solid oral dosage form for paediatric use. Eur J Pharm Biopharm. 2011;78:462–9.
11. Johnson J, Wang L, Gordon M, Chowhan Z. Effect of formulation solubility and hygroscopicity on disintegrant efficiency in tablets prepared by wet granulation, in terms of dissolution. J Pharm Sci. 1991;80(5):469–71.
12. Staniforth J, Aulton M. Particle Size Analysis. In: Aulton M, editor. Aulton's Pharmaceutics: The design and manufacture of medicines. 3rd ed. New York:

Churchill Livingstone Elsevier; 2007. p. 121–36.
13. Staniforth J, Aulton M. Powder Flow. In: Aulton M, editor. Aulton's pharmaceutics: The design and manufacture of medicines. 3rd ed. New York: Churchill Livingstone Elsevier; 2007. p. 168–80.
14. Pilpel N. Flow properties of non-cohesive powders. Chem Proc Eng. 1965;46:167.
15. Neumann B. The flow properties of powders. In: Bean H, Beckett A, Carless J, editors. Advances in pharmaceutical sciences. Volume II. London: Academic Press; 1967. p. 181–223.
16. British pharmacopoeia. British pharmacopoeia. Volume II. London, UK: Her Majesty's Stationery Office; 2013.
17. Adjei FK, Osei YA, Kuntworbe N, Ofori-kwakye K. Evaluation of the disintegrant properties of native starches of five new cassava varieties in paracetamol tablet formulations. J Pharm. 2017;2017:1–9.
18. Akin-Ajani OD, Itiola OA, Odeku OA. Evaluation of the disintegrant properties of native and modified forms of fonio and sweet potato starches. Starch/Starke. 2016;68:169–74.
19. Gohel MC, Parikh RK, Brahmbhatt BK, Shah AR. Preparation and assessment of novel coprocessed superdisintegrant consisting of crospovidone and sodium starch glycolate: a technical note. AAPS PharmSciTech. 2007;8(1):E1–7.
20. Gordon MS, Rudraraju VS, Kaushik D, Chowhan ZT. Effect of mode of superdisintegrant incorporation on dissolution in wet granulated tablets. J Pharm Sci. 1993;82:220–6.