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ORIGINAL ARTICLE

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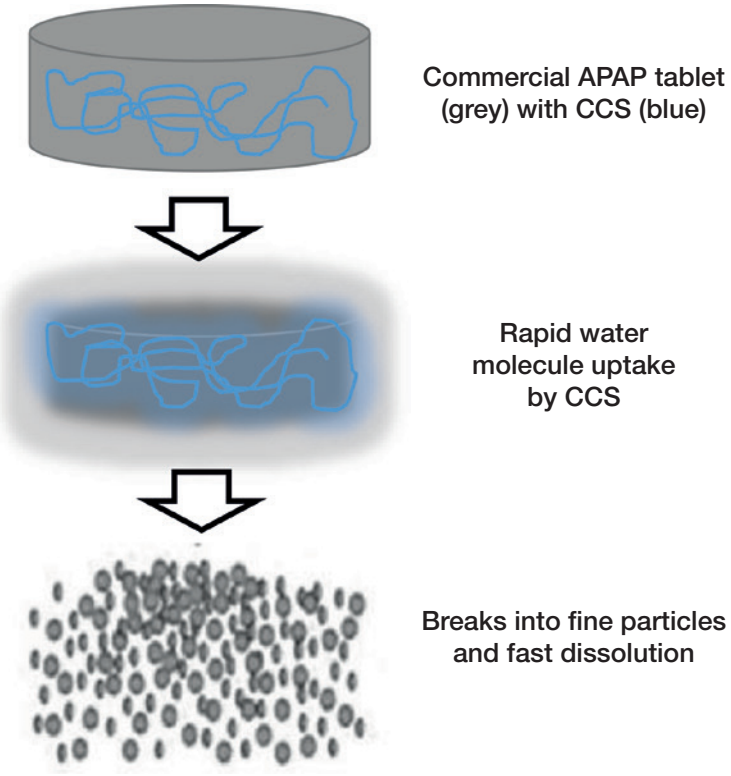
GRAPHICAL ABSTRACT



A simple approach to enhance dissolution of commercial paracetamol tablets for fast relief of pain

Uma abordagem simples para melhorar a dissolução de comprimidos comerciais de paracetamol para alívio rápido da dor

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ABSTRACT

BACKGROUND AND OBJECTIVES: Pain is considered a major clinical problem worldwide. Faster pain relief was reportedly achieved using a fast-dissolving paracetamol (APAP) tablet. Microcrystalline cellulose (MCC) is the most widely used excipient to produce fast-dissolving APAP tablet formulations, but it retards the dissolution of APAP. The present investigation reports incorporation of croscarmellose sodium (CCS) instead of MCC into APAP commercial tablet formulations to enhance the dissolution rate of APAP.

METHODS: A wet granulation method was used to prepare APAP tablets with various CCS concentrations, using a factorial design with 3^1 CCS concentrations as independent variables, while the dissolution percentage of the drug release at different time intervals was used as dependent variable. The disintegration time and dissolution rate of these APAP tablets were determined and compared with the dissolution rate of Amidol® and Panadol®, commercial APAP tablets available in Sudan.

RESULTS: The mean time to complete disintegration of the APAP tablets with CCS was faster than that for the commercial APAP tablets, both Amidol® (0.58 min vs. 2.43 min) and Panadol® (0.58 min vs. 1.32 min), and these differences were statistically significant for Amidol ($p \leq 0.001$) and Panadol® ($p \leq 0.01$). Moreover, the dissolution rate for the APAP tablets with CCS was significantly faster than those for Amidol® and Panadol®.

CONCLUSION: The dissolution of APAP from Amidol® and Panadol® can be successfully enhanced by incorporating CCS in their formulation and can be considered as a simple approach for fast-pain relieving using APAP.

Keywords: Croscarmellose sodium, Disintegration time, Factorial design, Fast-dissolving tablets, Microcrystalline cellulose, Pain, Paracetamol, Tablet dissolution rate.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor é considerada um grande problema clínico em todo o mundo. O alívio mais rápido da dor foi obtido com o uso de um comprimido de paracetamol (APAP) de dissolução rápida. A celulose microcristalina (CMC) é o excipiente mais amplamente usado para produzir formulações de comprimidos de APAP de dissolução rápida, mas retarda a dissolução do APAP. A presente pesquisa relata a incorporação de croscarmelose sódica (CCS) em vez de CMC em formulações comerciais de comprimidos de APAP para aumentar a taxa de dissolução do APAP.

MÉTODOS: Um método de granulação úmida foi usado para preparar o APAP com várias concentrações de CCS, sendo usado um desenho fatorial de 3^1 concentrações de CCS como variáveis independentes, enquanto a porcentagem de dissolução da liberação do fármaco em diferentes intervalos foi usada como variável dependente. O tempo de desintegração e a taxa de dissolução desses comprimidos de APAP foram determinados e comparados com a taxa de dissolução de Amidol® e Panadol®, comprimidos comerciais de APAP disponíveis no Sudão.

RESULTADOS: O tempo médio para a desintegração completa dos comprimidos de APAP com CCS foi mais rápido do que o dos comprimidos comerciais de APAP, tanto Amidol® (0,58 min vs. 2,43 min) quanto Panadol® (0,58 min vs. 1,32 min), e essas diferenças foram estatisticamente significativas

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HIGHLIGHTS

- A simple 3^1 factorial design was applied to prepare new APAP tablets for quick pain relief.
- APAP tablets with CCS disintegrate quicker than Panadol® and Amidol® tablets.
- Significantly, APAP tablets with CCS dissolve much faster than Panadol® and Amidol® tablets.

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para o Amidol® (p≤0,001) e o Panadol® (p≤0,01). Além disso, a taxa de dissolução dos comprimidos de APAP com CCS foi significativamente mais rápida do que as taxas de Amidol® e Panadol®.
CONCLUSÃO: A dissolução do APAP para Amidol® e Panadol® pode ser aprimorada com sucesso pela incorporação da CCS em sua formulação e pode ser considerada uma abordagem simples para o alívio rápido da dor usando APAP.
Descritores: Celulose microcristalina, Comprimidos de dissolução rápida, Croscarmelose sódica, Dor, Paracetamol, Projeto fatorial, Taxa de dissolução do comprimido, Tempo de desintegração.

INTRODUCTION

Pain is considered a major clinical issue and represents a socio-economic burden on healthcare systems globally. It was estimated that about 20% of the adults suffer from pain globally and 10% are newly diagnosed with chronic pain each year[1,2]. Pain management includes several approaches, such as pharmacologic therapy, lifestyle management, and behavioral therapy. Pharmacological therapy for pain includes non-steroidal anti-inflammatory drugs (e.g. paracetamol - APAP), opioids, and central nervous system-acting drugs[3,4]. APAP had been considered as the front-line drug for the symptomatic treatment of mild-to-moderate pain. The suitability of this drug depends on the type of pain and patient risk factors (e.g., age, presence of comorbidities related to metabolism, gastrointestinal - GI - tract or cardiovascular tract)[5].
APAP is included on the World Health Organization List of Essential Medicines. The use of APAP as a self-medication is highly prevalent in the different communities around the world. Many previous studies showed that up to 65% of students practiced self-medication with APAP to treat mild-to--moderate pain[6]. Self-medication can be defined as obtaining and consuming drugs without the advice of a physician for the surveillance of treatment. In Sudan in a community based cross-sectional study about self-medication in Khartoum State with a sample of 1,200 adult persons, the prevalence of self-medication was of about 28.3%, including analgesics containing APAP in 9.7% of them[7].
Following oral administration, APAP is absorbed within few hours from the GI tract, mainly from the small intestine[5]. Its absorption rate is directly dependent upon of patient's gastric emptying rate. It was found that reducing patient's gastric emptying rates may result in delayed absorption of APAP into the blood system. Studies had reported impaired APAP absorption rate in diabetic and aging patients, wherein aging was found to be associated with modest slowing of gastric emptying[8,9]. Thus, these events could impede effective pain relief in the elderly or diabetics.
The aim of this study was to enhance the dissolution rate of Amidol® and Panadol® tablets using a simple 3^1 factorial design approach of changing the original disintegrant system of microcrystalline cellulose (MCC) in their formulation with the super-disintegrant system croscarmellose sodium (CCS). Considering that Amidol® and Panadol® are commercial APAP tablets available in the Sudan, this study hypothesized that replacing MCC with CCS in the tablet formulations of Amidol® and Panadol® would enhance tablet dissolution rate and drug bioavailability and finally would give a rapid and consistent onset of drug action for pain management.

METHODS

Two popular APAP tablet brands with a level claim of 500 mg were collected from local pharmacies in Omdurman city, Sudan. One is a local item, Amidol® (Amipharma Ltd, Sudan) and the other is an imported item, Panadol® (Glaxo SmithKline group, UK). The product information such as manufacturer name, date of manufacturing, and expiry date at the time of procurement was coded by number for each brand.
APAP powder was a gift from Shanghai-Sudan Co., Ltd, Sudan. Potassium di-hydrogen orthophosphate was purchased from BDH Laboratory supplies, U.K. Disodium hydrogen phosphate was purchased from CDH fine chemicals, India. Hydrochloric acid was obtained from Thomas Baker, India. All other reagents and solvents were of the highest analytical grade commercially available.

Preparation of APAP tablets

Three batches of APAP tablets were prepared using a wet granulation method of tablet manufacturing and the quantity of CCS *per* tablets was selected as *per* 3^1 factorial design (Tables 1 and 2). Briefly, APAP, starch paste (binder), starch (filler) and MCC were blended thoroughly in a dry mortar and granulated using water as granulating fluid to form a wet mass. The wet mass formed was then pressed through a mesh No. 40 to obtain wet granules, which dried at 60°C for 24 h. The dried granules were passed through a mesh No. 500 to break the aggregates formed and to obtain discrete granules with a suitable particles size. Finally, magnesium stearate (lubricant) was passed through a mesh No. 80 and thoroughly blended with the granules to obtain the final granules that are suitable for compressing to tablets. The granules were transferred into a tablet punching machine (Rimek, USA) employing 9 mm flat punches.

Table 1. Composition of the three batches of APAP tablets

Batch Code	Composition of tablet			
	APAP (mg)	CCS%	MCC %	Other excipient
B1	500	25	75	q.s.
B2	500	50	50	q.s.
B3	500	100	0	q.s.

Table 2. Coding of the actual values for 3^1 factorial design

Independent variable: Concentration of CCS used		
Low %	Medium %	High %
25	50	100

Dependent variables: % APAP dissolve at different time intervals

Determination of tablet weight variation

A weight variation test is applicable to demonstrate the uniformity of dosage unit for tablets containing 25 mg or more of a drug substance comprising 25% or more, by weight, of the dosage unit. Ten tablets from each formulation were chosen and then weighed individually, followed by calculation of the mean weight and standard deviation. According to the USP monographs for tablet weight determination, the deviation should not be more than 15% for each tablet to be accepted[10].

Determination of tablet hardness

A sample of 10 tablets were held between a fixed and a moving jaw of hardness test apparatus (Erweka TBH 30 MD, Germany) and reading of the indicator is adjusted to zero. The screw knob was moved forward until the tablet breaks and the force required breaking the tablet was noted[11].

Determination of tablet friability

A sample of 20 tablets was taken and carefully de-dusted prior to testing. The tablet sample was accurately weighed and placed in the drum of apparatus. The drum was rotated 100 times, removed the tablets, the loose dust from the tablets was removed as before, and accurately reweighed. The test was repeated three times, and the mean of the three tests was determined. A maximum mean weight loss from the three samples of not more than 1.0% is considered acceptable for most products[10].

Determination of tablet disintegration rate

A sample of 1 tablet from all batches of APAP tablets, Amidol® and Panadol® was place in each of the six tubes of the basket in the apparatus (Erweka type TZ 121, Germany). The apparatus then was operated using water as medium maintained at 37±2ºC. The time taken for the complete disintegration of the last tablet was recoded, and the tablets were examined at the end of the experiment[12].

Determination of tablet dissolution rate

Dissolution tests of APAP tablet batches (B1, B2 and B3) and reference commercial APAP tablets (Amidol® and Panadol®) were performed in phosphate buffer of pH 5.8 (900 mL), using eight station dissolution rate test apparatus (Erweka TZ 121, Germany) with paddle stirrer at 50 rpm and at a temperature of 37°C ± 1°C. To perform the test, a sample of one tablet from each type was used. Samples of dissolution fluid (5 ml) were withdrawn through a filter at different time intervals (5, 10, 15, 30, 4 and 60 min) and assayed for APAP at 243 nm. The sample of dissolution fluid withdrawn at each time was replaced with fresh drug free dissolution fluid and a suitable correction was made for drug present in the samples withdrawn. Each dissolution experiment is run in triplicates (n =3)[13].

Statistical analysis

The results was expressed as mean of three determinations ± standard deviation (S.D.). Statistical analysis was performed using one-way analysis of variance (ANOVA) (SPSS software, version 22.0, SPSS Inc.). *Post-hoc* comparisons of the means were performed using Tukey's Honestly Significance Difference test. In all tests, a probability value of $p<0.050$ was considered statistically significant.

RESULTS

Weight variation of APAP tablets

The weight variation which is the key to controlling the crushing strength and friability of the tablet was firstly assessed in this study. The results of weight variation test for all batches of APAP tablets, Amidol® and Panadol® tablets are shown in table 3. The obtained values for all batches of APAP tablets are within acceptable range according to USP monographs for tablet weight. Thus, incorporation of CCS to the formulation MCC did not affect in tablet weight appreciably.

Hardness of APAP tablets

The hardness values for all batches of APAP tablet, Amidol® and Panadol® are shown in table 4 and figure 1. Mean tablet hardness for all batches were observed to be in the range of 5 to 6.5 kg, which were in the acceptable range according to the USP monographs for tablet hardness. The tablet hardness exhibited the following order: B3>B1>B2. There was significant difference ($p<0.010$) in tablet hardness between batches

Table 3. Weight variation results for all APAP batches, Amidol® and Panadol® tablets (n=20, ± SD)

No	Tablet weight in g				
	B1	B2	B3	Amidol®	Panadol®
1.	0.669	0.529	0.772	0.529	0.669
2.	0.671	0.505	0.75	0.505	0.671
3.	0.668	0.614	0.760	0.614	0.668
4.	0.666	0.649	0.719	0.649	0.666
5.	0.687	0.557	0.738	0.557	0.687
6.	0.618	0.558	0.742	0.558	0.618
7.	0.719	0.553	0.799	0.553	0.719
8.	0.649	0.557	0.775	0.557	0.649
9.	0.697	0.560	0.753	0.560	0.697
10.	0.676	0.558	0.791	0.558	0.676
11.	0.620	0.555	0.778	0.555	0.620
12.	0.618	0.658	0.781	0.658	0.618
13.	0.729	0.549	0.772	0.549	0.729
14.	0.679	0.589	0.763	0.589	0.679
15.	0.667	0.651	0.785	0.651	0.667
16.	0.666	0.628	0.78	0.628	0.666
17.	0.744	0.575	0.781	0.575	0.744
18.	0.690	0.624	0.796	0.624	0.690
19.	0.676	0.661	0.794	0.661	0.676
20.	0.698	0.651	0.789	0.651	0.698
Mean	0.669	0.579	0.767	0.580	0.669
SD	4.790	8.020	2.786	8.020	4.790

B3 and B2, while there is no significant difference between batches B3 and B1 (Figure 1). In this study, the incorporation of CCS to the tablet formulation did not affect the tablet hardness appreciably. The low hardness value may be the result of the improper type and/or amount of disintegrant system used in the tablet formulation[10].

Figure 1 shows the hardness test result for batches B3, Amidol® and Panadol®. The hardness values of batch B3, Amidol® and Panadol® were 6.54 kg, 5.52 kg and 8.72 kg respectively. There was significant difference in hardness value between batch B3 and Amidol® while there was statistical difference ($p<0.050$) between batch B3 and Panadol® tablets.

Friability of APAP tablets

Results for the friability test for all batches of APAP tablet, Amidol® and Panadol® are shown in table 5 and figure 2. Mean tablet friability for all batches were observed to be in the range of 0.2 to 0.5, which were in the acceptable range according to the USP specification (not losing more than 1% of their initial weight). Tablet of batch B2 was the most friable one followed by B1 and lastly batch B3. Tablets should be hard enough to resist abrasion when subjected to stresses from collision or during sliding towards one another[11].

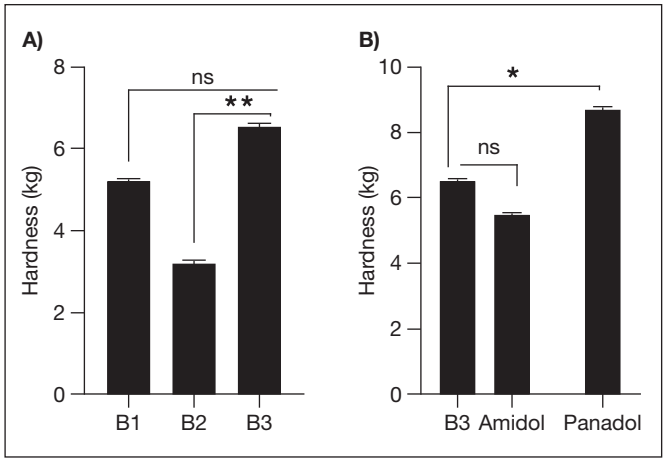

Figure 1. Hardness test results for all APAP, Amidol® and Panadol® batches

(A) The hardness values of batches B1, B2 and B3. (B) The hardness values of B3, Amidol® and Panadol® . Data are presented as mean ± SD (n=3). Where: ns: statistically insignificant; * and **: p< 0.050 and 0.01.

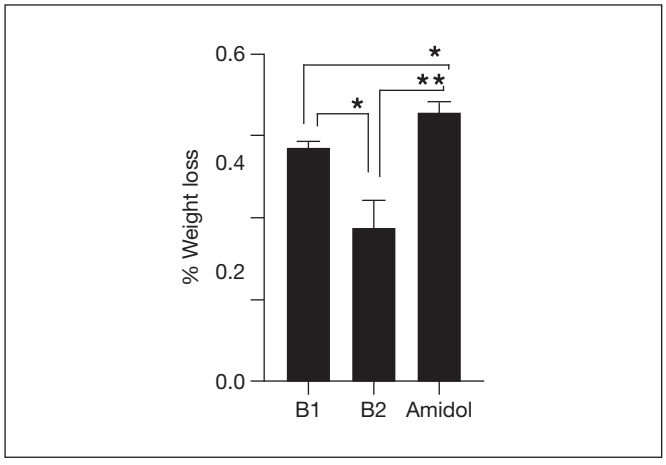

Figure 2. Friability test results for APAP tablet batches B1 and B2 and Amidol®

Data are presented as mean ± SD (n=3). Where: * and **: p<0.050 and 0.01.

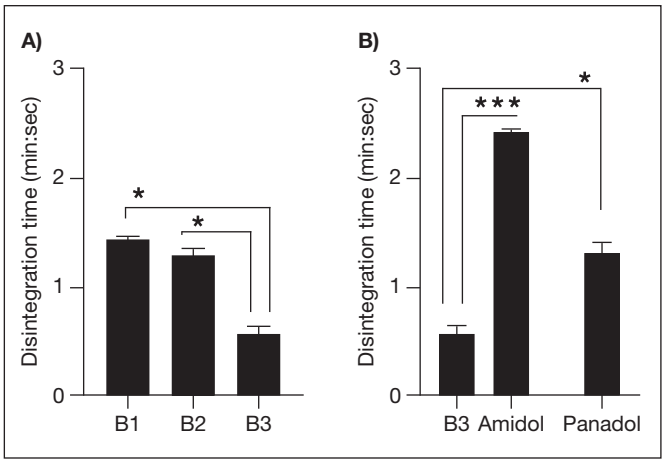

Figure 3. The disintegration time for all APAP tablet batches, Amidol tablets and Panadol tablets.

(A) The disintegration time of tablets of batches B1, B2 and B3. (B) The disintegration time for tablets of batch B3, Amidol® and Panadol® tablets. Data are presented as mean ± SD (n = 6). Where: ns; statistically insignificant, *, ***: p< 0.050, 0.001.

Table 4. Hardness test results for all APAP tablet batches, Amidol® tablets and Panadol® tablets (n = 20, ± SD)

No	Tablet hardness in kg				
	B1	B2	B3	Amidol®	Panadol®
1.	16.14	18.12	23.12	12.23	9.29
2.	18.01	19.09	22.53	11.66	7.57
3.	18.16	19.42	23.88	11.82	8.64
4.	18.03	19.63	22.78	12.65	9.16
5.	19.97	19.50	22.54	11.77	7.48
6.	17.45	19.70	20.21	12.53	7.51
7.	18.30	19.64	21.35	11.39	8.07
8.	18.14	19.41	19.12	11.64	9.16
9.	19.79	19.52	20.14	10.63	7.27
10.	18.03	18.21	23.51	10.89	7.65
11.	18.45	19.73	22.65	11.7	8.63
12.	19.09	19.19	23.75	12.56	9.01
13.	18.46	17.88	21.45	11.32	7.56
14.	17.35	19.20	20.85	10.7	7.47
15.	19.53	19.35	22.14	11.94	8.46
16.	18.15	19.96	23.67	12.47	8.35
17.	17.45	18.75	19.96	11.66	7.57
18.	19.79	19.56	20.15	10.8	9.23
19.	19.20	19.92	22.71	12.46	8.7
20.	19.30	19.20	23.46	11.32	9.2
Mean	18.32	19.22	22.12	11.74	8.21
STD	0.96	0.62	1.45	0.65	0.72
RSD	5.23	3.20	6.54	5.52	8.72

Disintegration time of APAP tablets

Table 6 shows disintegration time for all tablet batches, Amidol® and Panadol®. The disintegration time of batch B1, B2 and B3 was 1:45 min, 1:30 min and 0.58 min respectively. There was significant difference in disintegration time of tablet of batches B1 and B2 with respect to batch B3 ($p<0.0050$ - Figure 3). In addition, the disintegration time of tablet of batch B3 was significantly lower compared to the disintegration time of Amidol® and Panadol® tablets. There was significant difference ($p<0.001$) in disintegration time between tablets of batch B3 and Amidol® and ($p<0.050$) between tablets of batch B3 and Panadol® (Figure 3).

Dissolution rate of APAP tablets

In this study, desired results were obtained in batch B3 which contained the highest concentration of CCS (Table 6) and by increasing CSS concentration in the formulation, the disintegration time was largely decreased. Water wicking and swelling are the two possible mechanisms of disintegrant action of CCS. The exposure to water causes CCS to swell and exerts pressure against surrounding of formulation ingredients, which, in turn, results into disintegration of the formulation[14,15]. Table 7 and figure 4 show dissolution data results for tablet batches B1, B2 and B3, Amidol® Panadol® tablets. Mean dissolution rates for all batches were observed to be in the range according to the USP monographs for tablet dissolution. The tablet dissolution rate exhibited the following order: B3>B2>B1. However, there was significant difference ($p<0.010$) in dissolution rate in different time intervals between the three batches (Figure 4A). As the concentration of CCS was increased in tablet formulation, the tablet dissolution rate was increased. This corroborates the previous findings reporting the improvement in dissolution and disintegration behavior with MCC tablets and poorly-water soluble drugs through inclusion of polyethylene glycol, polysorbate and CCS[16].

In addition and more interestingly, the dissolution rate of tablet of batch B3 was significantly faster compared to the disintegration rate of Amidol® and Panadol® tablets. There was significant difference ($p<0.001$) in dissolution rate between tablets of batch B3 and Amidol® and Panadol® (Figure 4B).

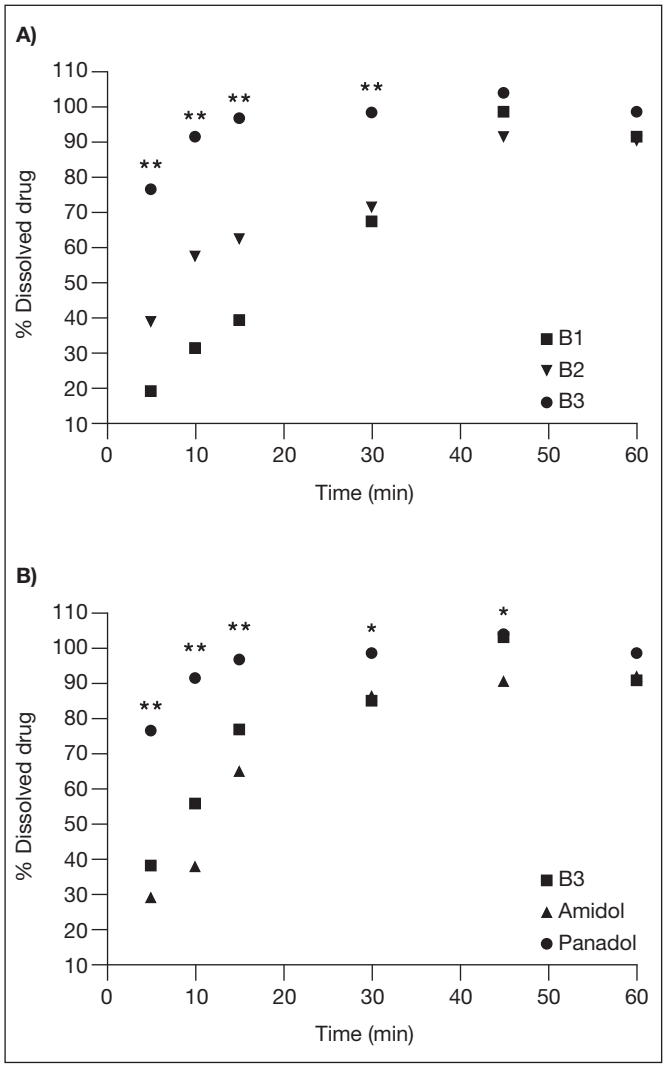

Figure 4. The cumulative dissolution curves for all APAP batches, Amidol® and Panadol®

(A) The cumulative dissolution curves for batches B1, B2 and B3. (B) The cumulative dissolution curves for batch B3, Amidol® and Panadol® . Data are presented as mean ± SD (n = 3), where: *, **: $p < 0.050$ and 0.010.

Table 5. Friability test results for all APAP tablet batches, Amidol® tablets and Panadol® tablets (n=10, ± SD)

Test No	Tablet weight in g				
	B1	B2	B3	Amidol®	Panadol®
Weight of 20 tablet before test	15.21	16.12	15.79	11.25	13.45
Weight of 20 tablet after test	15.15	16.08	15.79	11.20	13.45
	0.6	0.4	0	0.5	0
% Weight loss	0.433	0.285	0	0.497	0

Table 6. Disintegration test results for all APAP tablet batches, Amidol® tablets and Panadol® tablets (n=6, ± SD)

Disintegration time (min.sec)				
B1	B2	B3	Amidol®	Panadol®
1.45	1.30	0.58	2.43	1.32

Table 7. Dissolution test results of tablets of all batches, Amidol® tablet and Panadol® tablets

Time intervals	% drug dissolution				
	B1	B2	B3	Amidol®	Panadol®
After 5 min	39.15	19.53	76.85	29.34	38.07
After 10 min	57.69	31.86	91.62	38.07	56.07
After 15 min	62.55	39.87	97.02	65.07	76.85
After 30 min	71.73	67.77	98.82	85.77	85.32
After 45 min	91.62	98.82	104.22	90.72	103.30
After 60 min	90.72	91.62	98.82	91.62	90.72

DISCUSSION

CCS is cross-linked carboxymethylcellulose sodium and it is used as a super disintegrant in tablet formulation. The functionality of CCS as a disintegrant is related to its fluid uptake and shellability characteristics. In this study, the independent factor affecting dissolution of APAP tablets was the CCS. Both APAP tablet disintegration and dissolution rate were significantly increased with increasing CCS content. So, it is reasonable to believe that when CCS is present at higher concentrations in APAP tablets drug release would be favored by faster dissolution compared to a lower CCS content. Furthermore, this study observed that release of the drug from APAP tablets was largely by dissolution rather than diffusion out of the tablet matrix. There was a notable increase in the tablet size over the experiment time rather than eroded.

The effective pain management might be achieved by faster APAP tablet disintegration and dissolution rates, especially in the case of patients with a slow gastric emptying rate, e.g., the elderly or diabetic individuals[17,18]. In fact, numerous studies have been conducted to enhance APAP tablet formulations to effectively control mild-to-moderate pain. These include enhancing tablet disintegration rate, enhancing tablet dissolution rate by utilizing amino acid salts or alkali metal salts of APAP and addition of calcium carbonate or antacids to APAP tablets[19]. However, there is a certain degree of difficulty in formulation and preparation technologies to improve the dissolution of APAP tablets by the methods mentioned above, which brings a great challenge to the preparation production in industry. Therefore, a simple approach that would not only improve the dissolution of APAP tablets, but also be suitable for industrial production was introduced in this study.

APAP is a white crystalline powder, odorless with a bitter taste. With a low water solubility and high lipophilicity, APAP is a Biopharmaceutical Classification System (BCS) type III drug. Therefore, APAP bioavailability is limited by permeation rate and not solubility. This study was based on the dissolution parameters that are considered safe determinants of the efficacy of APAP tablets in pain control[12,20]. Dissolution of APAP tablets is a critical step leading to the release of active drug in the absorption site of the gatro intestinal tract.

Determination of cumulative dissolution profile at a different time intervals has become an important means of gauging the intrinsic quality of tablets. Therefore, in this study, cumulative dissolution at 5 time intervals were used for studying the dissolution of the tested APAP tablets and compared with the dissolution of standard APAP tablets namely Amidol® tablet and Panadol®. From the results of dissolution experiments that were shown in table 4, it was found that the cumulative dissolution of all APAP batches (B1 and B2), Amidol® tablet and Panadol® tablet reached 95% of APAP within time ranged between 30 to 40 min. However, it was entirely different in tablet of batch B3 that reached cumulative dissolution of 95% of APAP within 15 min (Figure 4), which might indicate high potential to fastest drug absorption and bioavailability for the pain management.

A previous survey study reported that the majority of consumers read over-the-counter drug package labels prior to purchase. This positive behavior might suggest that marketing claims like “rapid” or “fast release” may impact purchasing decisions[20,21]. In this study, the obtained results showed that the incorporation of CCS, instead of original MCC used in APAP commercial tablets, would enhance the solubility and dissolution of commercial tablet significantly. In more details, it has been proven that the dissolution rate of APAP tablets could be enhanced 3-fold in relation to the dissolution rate of commercial tablets of Amidol® and Panadol® (Figure 4).

In this study, a simple APAP tablet formulation with faster drug release was successfully prepared using a wet-granulation method and a 3^1 factorial design method. The best tablet formulation batch (B3) was found to be the “High Percentage”, that consisted of 100% CCS in the tablet formulation. The independent variable, concentration of CCS, exhibited a positive effect upon the dependent variable, tablet dissolution rate at different time intervals. Incorporation of CCS into Amidol® and Panadol® formulation instead of the original disintegrant system, MCC, exhibited a significant enhancement in tablet dissolution rate. Such an approach might be exploited as a simple and effective method for developing fast-dissolving APAP tablets for effective pain management[20,23,24].

CONCLUSION

In this work, a simple APAP tablet formulation with quicker drug release was produced successfully utilizing a wet-granulation method and a 3^1 factorial design. The batch (B3) with 100% CCS was the most effective tablet formulation. The independent variable, CCS concentration, had a positive influence on the dependent variable, tablet dissolving rate, at various time intervals. The incorporation of CCS into Amidol® and Panadol® formulations, rather than the traditional disintegrant system, resulted in a considerable increase in tablet disintegrating and dissolving rate. Such an approach might be used as a simple and efficient method for creating fast-dissolving APAP tablets for effective pain treatment.

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AUTHORS’ CONTRIBUTIONS

Alaa A. Abdulla

Research, Methodology, Data Collection, Writing - Preparation of the original

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Conceptualization, Resource Management, Project Management, Writing - Review and Editing, Supervision, Visualization.

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