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Original Research Article

Effect of superdisintegrant type and concentration on dissolution behaviour of Ondansetron orodispersible tablets

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Abstract

Purpose: *To investigate the effect of various superdisintegrants on disintegration time and early-phase dissolution in ondansetron hydrochloride orodispersible tablets (ODTs).*
Methods: *A total of 12 formulations were prepared by direct compression using a 3×4 full factorial design. Crospovidone (CPV), sodium starch glycolate (SSG), and croscarmellose sodium (CCS) were each tested at 2, 4, 6, and 8 % w/w. Primary responses were disintegration time, 5-minute drug release, dissolution similarity (f_2), and Korsmeyer–Peppas exponent (n).*
Results: *All blends had acceptable flow properties. At 8 % w/w, CPV released 77.2 % within 5 min compared to SSG ($p < 0.01$), f_2 = 45.3 between CPV and SSG indicated dissimilar profiles, and f_2 = 90.8 between SSG and CCS confirmed equivalent swelling-polymer behaviour. Korsmeyer–Peppas modelling gave n = 0.33 for CPV (Fickian diffusion) and n = 0.45, 0.44 for SSG and CCS, respectively, consistent with partial gel-layer resistance. Korsmeyer–Peppas rate constant showed kKP = 40.09 min^{-n} for CPV compared to 7.13 min^{-n} and 28.50 min^{-n} for SSG and CCS, respectively. Furthermore, CPV produced faster early drug release compared to SSG and CCS at all concentrations.*
Conclusion: *Crospovidone shows significantly superior early-phase dissolution at all concentrations compared with SSG and CCS*

Keywords: *Crospovidone, Korsmeyer–Peppas model, Ondansetron hydrochloride, Orodispersible tablets, Superdisintegrants*

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INTRODUCTION

Orodispersible tablets (ODTs) represent one of the specialized oral solid dosage forms specifically designed to disintegrate rapidly within the oral cavity without requiring water or chewing. This system improves patient compliance of extreme age groups (paediatrics and geriatrics), and is suitable for patients with dysphagia. Such advantages have attracted many reputable manufacturers to target such dosage forms. Orodispersible tablets (ODT) have great benefits in emergencies and when rapid therapeutic response is critical. This is attributed to the rapid disintegration and dissolution of the system which is followed by rapid systemic absorption and bioavailability [1]. A rapid onset of drug action is important for the treatment of many medical conditions, particularly vomiting. Ondansetron (Ond) is a widely used antiemetic

drug. It is a potent and selective serotonin (5-HT3) receptor antagonist commonly prescribed for the prevention and management of chemotherapy-induced nausea and vomiting [2].

Rapid onset formulations are required in such conditions, since the episodes of nausea and vomiting are usually not predictable with the associated need to provide rapid relief. The rapid drug release from ODT *in vivo* and clinical efficacy depend strongly on efficient, rapid tablet disintegration and subsequent drug release. Disintegration step is a complex physicochemical process that precedes dissolution. Disintegration occurs in a sequence that is characterized by liquid penetration into the porous tablet matrix (weakens inter-particulate bonds), followed by particle separation and dispersion into smaller particles [3]. Therefore, drug dissolution from tablets is accelerated by reducing the time required for disintegration. Superdisintegrants are incorporated into tablets to make disintegration time within seconds. Superdisintegrants are a special type of excipient added to tablets in low concentrations (< 10 %) to enhance drug release and bioavailability via several mechanisms. These excipients act by capillary (wicking) action governed by Washburn flow dynamics, swelling-induced volumetric expansion, and deformation recovery [4]. In the capillary wicking, superdisintegrants create a hydrophilic network that absorbs water into the matrix via capillary pressure. The rapid hydration of crosslinked polymer chains generates expansion forces that physically resist the tensile strength of the compacted tablet. The inherent chemistry of selected polymer superdisintegrants would specify the mechanism by which and the speed at which the rupture occurs. The most common types of superdisintegrants that are used in tablets are crospovidone (CPV), crosscaramellose (CCS), and sodium starch glycolate (SSG) [3].

Crospovidone is a synthetic crosslinked polyvinylpyrrolidone derivative that swells rapidly and forms a porous network-like structure without formation of a gel layer. Crospovidone (CPV), when in contact with water, causes capillary-driven water uptake and immediate particle separation, which causes the matrix to break apart without forming viscous barriers [4]. Sodium starch glycolate (SSG) and croscarmellose sodium (CCS) are highly crosslinked hydrophilic polymers that expand significantly upon hydration. Because they are anionic sodium salts composed primarily of repeating glucose units, they act differently compared to CPV. Although the mechanisms of different superdisintegrants are diverse, their behaviour in compacted tablets depends on several variables, such as polymer amount, compaction pressure, excipient distribution, and overall microstructural porosity [4]. Increasing the concentration does not always result in direct proportional reduction in disintegration time [5,6]. Different studies have reported that swelling-based disintegrants may exhibit paradoxical effects at higher concentrations rather than the expected improvement in disintegration [7]. Beyond an optimal concentration threshold, certain superdisintegrants like CPV no longer reduce disintegration time [3]. This plateau level is possibly due to localized gel formation, increased fluid viscosity, or blockage of pores during the rapid hydration phase, which creates a barrier preventing further water wicking into the tablet [7]. At plateau concentration, the swollen superdisintegrant polymer fuses upon contact with saliva, creating a viscous gel layer on the surface of the tablet. This phenomenon, known as gel-blocking, prevents water from interacting with the tablet matrix and prolongs the disintegration and dissolution process [3]. Many studies have examined single-factor designs, which failed to quantify the effect of the complex interaction between polymer structure and concentration. Conventional approaches explore the synergistic or antagonistic effect of combination systems of two or more superdisintegrants. Several published works ignore the kinetics of early phase dissolution (0-5 min.). Determination of drug release within the first 5 min provides evidence on rapid onset characteristics. This study used a 3×4 full factorial design experiment to quantify the interaction effects between superdisintegrant type and concentration using two-way ANOVA. The study specifically focused on early phase kinetic similarity and dissimilarity (using the similarity factor (f_2) to identify significant variations in the first 5 min of drug release), and characterization of the drug release (Higuchi and Korsmeyer–Peppas models to determine the release exponent (n) and identify diffusion mechanisms).

EXPERIMENTAL

Materials

Ondansetron hydrochloride (USP grade, ≥ 99.8 % purity) was obtained as a gift sample from Sama Alfayhaa Drug Industry, Basra, Iraq. The superdisintegrants evaluated were crospovidone (CPV; Polyplasdone™ XL), sodium starch glycolate (SSG; Explotab®), croscarmellose sodium (CCS; Ac-Di-Sol®), microcrystalline cellulose (Avicel® PH-102), and spray-dried mannitol (Pearlitol® 200 SD). Additional

excipients included aspartame (taste-masking sweetener), colloidal silicon dioxide (Aerosil® 200), and magnesium stearate. All other reagents, including the 0.1 N HCl used for dissolution media, were of analytical grade and used as received.

Factorial design

A 3 x 4 full factorial design was employed to evaluate the effect of the main formulation variables on the tablet critical quality attributes (CQAs). Two independent variables were investigated, which include superdisintegrant type (X1: CPV, SSG, CCS) and concentration (X2: 2, 4, 6, and 8 % w/w), yielding 12 distinct formulations (F1 – F12; Table 1). The evaluated dependent responses included pre-compression micromeritic properties, post-compression mechanical strength, *in vitro* disintegration time (Y1), 5-min cumulative drug release (Y2), similarity factor (Y3), and diffusion release exponent (Y4).

Preparation of orodispersible powder blends

Ambient conditions in the formulation suite were maintained at 22 ±2 ℃ and a relative humidity (RH) of <40 %. Ondansetron (8 mg) was mixed with diluent (microcrystalline cellulose). Then the premix was subsequently passed through a standard ASTM 60-mesh stainless steel sieve to deagglomerate any cohesive primary particles. The selected superdisintegrant (CPV, SSG, or CCS) and spray-dried mannitol were similarly passed through a 40-mesh sieve and sequentially integrated into the powder bed. The sieving process was repeated to ensure complete mixing. Then the glidant (colloidal silicon dioxide) and lubricant (magnesium stearate) were passed through an 80-mesh sieve, added to the blend, and mixed for 3 min to prevent over-lubrication, which reduces wetting and delays disintegration [8].

Pre-compression micromeritic characterization

Before compression, the flow and compressibility of the 12 powder blends were evaluated to confirm they had suitable rheological properties for tablet production using direct compression.

Bulk, tapped density, *compressibility index and Hausner ratio*

The formulation (50 g) was transferred into a 100 mL graduated cylinder. The initial volume (V_0) was recorded to calculate bulk density ($D_b = M/V_0$). To calculate the tapped density ($D_t = M/V_t$), the final volume (V_t) was recorded after successive tapping (< 2 % difference) using tapped density tester [9]. Carr's Compressibility Index (CI) and Hausner Ratio (HR) were calculated as shown in Eqs. 1 and 2.

$$CI\ (\%) = (D_t – D_b)/D_t)100 \quad \ldots\ldots\ldots\ldots (1)$$

$$HR = D_t/D_b \quad \ldots\ldots\ldots\ldots (2)$$

Carr's index < 15 % and HR < 1.15 indicate excellent flowability and uniform tablet die filling

*Angle of repose (*θ)

The Fennel method was used to measure angle of repose (θ). The height (h) and radius (r) of the formed powder cone after allowing the powder to flow from a funnel installed at 10 cm above the base were recorded. The angle of repose was calculated using Eq 3 [6].

$$\theta = \tan^{-1}(h/r) \quad \ldots\ldots\ldots\ldots (3)$$

DIRECT COMPRESSION TABLETING PARAMETERS

The final mixture was compressed using a single-punch tableting machine.

Table 1: Constituents of ondansetron orodispersible formulations

Constituents (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Ondansetron HCl	8	8	8	8	8	8	8	8	8	8	8	8
Crospovidone (CPV)	3	6	9	12	-	-	-	-	-	-	-	-
Sodium starch glycolate	-	-	-	-	3	6	9	12	-	-	-	-
Croscarmellose sodium	-	-	-	-	-	-	-	-	3	6	9	12
Mannitol (Pearlitol)	30	30	30	30	30	30	30	30	30	30	30	30
Aspartame	3	3	3	3	3	3	3	3	3	3	3	3
Colloidal silicon dioxide	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Microcrystalline cellulose	103	100	97	94	103	100	97	94	103	100	97	94
Total tablet weight	150	150	150	150	150	150	150	150	150	150	150	150

The machine was adjusted to produce a consistent 150 mg tablet size. The compression force was adjusted to produce mechanically intact tablets for each formulation.

Post-compression physicochemical evaluation

Following a 24 h relaxation period after compression (to allow for the dissipation of residual elastic strain), the compressed ODTs were subjected to post-compression evaluation.

Weight variation and dimensional uniformity

A total of 20 randomly selected tablets per formulation were weighed individually using an analytical balance to ascertain compliance with USP tolerance limits (±7.5 % for 130 – 324 mg tablets).

Tablet thickness and diameter (n = 10) were measured with a calibrated digital vernier calliper to verify physical reproducibility [10].

Mechanical integrity (hardness and friability)

Tablet hardness was measured using a Monsanto-type tester. Friability was evaluated using a Roche friabilator. A pre-weighed sample of 20 dedusted tablets was rotated at 25 rpm for 4 min (100 rev), then dedusted and reweighed. The percentage of mass loss was calculated to ensure compliance with < 1 % pharmacopeial limit [6].

***In vitro* wetting time**

The wetting time of the formulations was evaluated to quantify capillary action and moisture penetration kinetics. Five circular tissue papers (10 cm diameter) were layered within a matching Petri dish. Distilled water (10 mL) impregnated with a water-soluble dye to enhance visual contrast was added to the dish.

A single tablet was positioned onto the surface of the moistened paper. Time required for the dye solution to completely permeate the matrix and reach the upper surface of the tablet was recorded as the wetting time [11].

***In vitro* wetting volume assessment**

The volume of water required to cause tablet disintegration was recorded as the wetting volume. Water was added dropwise to the tablet, which was placed in dry Petri dish to record wetting volume [11].

***In vitro* disintegration time assessment**

Disintegration time was recorded according to USP. Six randomly selected tablets from each formulation were placed in disintegration tester baskets under *in situ* conditions (900 mL of distilled water at 37 ± 0.5 °C) [10,12].

In vitro dissolution studies

In vitro drug release was evaluated using the paddle type dissolution tester under *in situ* conditions (900 mL 0.1 N HCl (pH 1.2; 37 ± 0.5 °C), 50 rpm to simulate gastric fluid). Aliquots of 5 mL were withdrawn at 1, 2, 5, 8, 10, 15, and 20 min with replacement of fresh volume of dissolution medium. The withdrawn samples were passed through 0.45 µm syringe filter, filtered and diluted. Thereafter, the absorbance was measured using UV-Vis spectrophotometer at 310 nm [10].

UV-Vis spectrophotometric calibration curve

Stock solution (A; 250 µg/mL) was prepared by dissolving 25 mg of the ondansetron in 0.1 N HCl, and diluted using 1 in 9 serial dilution. The absorbance was read at 310 nm to obtain the calibration curve with an equation ($y = 0.0392x + 0.0217$; $R^2 = 0.9985$).

Mathematical modelling of release kinetics

To elucidate mass transport mechanisms, dissolution data (up to 60 % fractional release) were analysed via the DDSolver add-in for Microsoft Excel. Profile equivalence was evaluated using the similarity factor (f_2), where values between 50 and 100 denote equivalence. Release kinetics were fitted to Higuchi and Korsmeyer-Peppas models. The Korsmeyer-Peppas diffusional exponent (n) characterized the transport mechanism, distinguishing Fickian diffusion ($n \leq 0.45$) from non-Fickian release kinetics ($0.45 < n < 0.89$) [13].

Data analysis

Data were expressed as the mean ± standard deviation (SD; n = 6) of independent samples. A two-way analysis of variance (ANOVA) was utilized to evaluate the primary effects of superdisintegrant type, concentration, and synergistic interactions on disintegration and dissolution kinetics. Tukey's multiple comparisons post hoc test was used to identify

discrepancies among examined formulations. $P < 0.05$ was considered statistically significant.

RESULTS

Flow properties

The formulations had excellent to good flow properties (Table 1).

Post-compression characteristics

Weight variation complied with the official standards and < 1 % friability (Table 3).

In vitro wetting kinetics and concentration

Formulations F4, F8, and F12 had significantly higher wetting times, demonstrating a concentration-dependent effect ($p < 0.05$; Figure 1).

Disintegration kinetics

In vitro disintegration time (Y1) served as the primary macroscopic response variable, revealing significant differences across formulations (Figure 2). Crospovidone (CPV; F1–F4) exhibited progressively linear reduction in disintegration time with increasing concentration, reaching a minimum of 22 sec at 8 % concentration (F4). Conversely, SSG (F5–F8) and CCS (F9–F12) demonstrated a paradoxical effect. For SSG, disintegration time did not decrease significantly between 6 % (F7: 29.2 ± 2.1 sec) and 8 % (F8: 29.8 ± 2.5 sec; $p > 0.05$).

In vitro dissolution kinetics

While all formulations achieved > 95 % release at 20 min, they differed significantly during the first 5 minutes (Y2). Formulation F4 (CPV 8 %) liberated 77.2 % of its content within 5 min, F8 (SSG 8 %) released only 59.3 %, which differs significantly ($p < 0.01$; Figure 3).

Mathematical modelling

Formulation F4, F8, and F12 demonstrated Fickian diffusion, anomalous transport, and Fickian-anomalous kinetic behaviour, respectively (Table 4).

Table 2: Micromeritic evaluation and rheological characterization (mean ± SD, n = 3)

Code	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner Ratio	Angle of Repose (θ°)
F1	0.49±0.01	0.56±0.02	12.50±1.2	1.14±0.01	26.8±0.5
F2	0.50±0.02	0.57±0.01	12.28±0.9	1.14±0.02	27.1±0.4
F3	0.48±0.01	0.55±0.02	12.72±1.1	1.15±0.01	27.5±0.6
F4	0.51±0.01	0.58±0.01	12.06±0.8	1.13±0.01	26.4±0.3
F5	0.50±0.02	0.58±0.02	13.79±1.4	1.16±0.02	28.2±0.5
F6	0.49±0.01	0.57±0.01	14.03±1.2	1.16±0.01	28.5±0.4
F7	0.51±0.01	0.60±0.02	15.00±1.5	1.18±0.02	29.1±0.7
F8	0.52±0.02	0.61±0.01	14.75±1.1	1.17±0.01	29.8±0.6
F9	0.49±0.01	0.56±0.02	12.50±1.3	1.14±0.02	27.3±0.5
F10	0.48±0.02	0.56±0.01	14.28±1.0	1.17±0.01	27.9±0.4
F11	0.50±0.01	0.59±0.02	15.25±1.4	1.18±0.01	28.6±0.8
F12	0.51±0.01	0.60±0.01	15.00±1.2	1.18±0.02	28.9±0.5

F1 – F4 (CPV 2, 4, 6, and 8 % respectively), F5 – F8 (SSG 2, 4, 6, and 8 % respectively), F9 – F12 (CCS 2, 4, 6, and 8 % respectively); CPV (crospovidone), CCS (croscarmellose), SSG (sodium starch glycolate).

Table 3: Post-compression characteristics of the optimized ODTs (Mean ± SD)

Code	Weight variation (mg, n=20)	RSD (%)	Thickness (mm, n=10)	Hardness (kg/cm^2, n=10)	Friability (%, n=20)
F1	149.8±1.2	0.8	3.12±0.04	5.4±0.3	0.42
F2	150.1±1.5	1	3.11±0.05	5.2±0.4	0.48
F3	149.5±1.4	0.94	3.13±0.03	5.3±0.2	0.50
F4	150.4±1.6	1.06	3.10±0.06	5.1±0.4	0.53
F5	148.9±1.8	1.21	3.14±0.04	5.5±0.3	0.55
F6	150.2±1.3	0.87	3.12±0.05	5.4±0.5	0.62
F7	149.7±1.7	1.14	3.15±0.03	5.2±0.4	0.78
F8	150.5±1.4	0.93	3.13±0.06	5.0±0.3	0.85
F9	149.3±1.5	1	3.11±0.05	5.6±0.2	0.58
F10	150.6±1.2	0.8	3.12±0.04	5.5±0.4	0.65
F11	149.8±1.9	1.27	3.14±0.05	5.2±0.5	0.81
F12	150.1±1.6	1.07	3.15±0.06	4.8±0.4	0.84

F1 – F4 (CPV 2, 4, 6, and 8 % respectively), F5 – F8 (SSG 2, 4, 6, and 8 % respectively), F9 – F12 (CCS 2, 4, 6, and 8 % respectively); CPV (crospovidone), CCS (crosscaramellose), SSG (sodium starch glycolate)

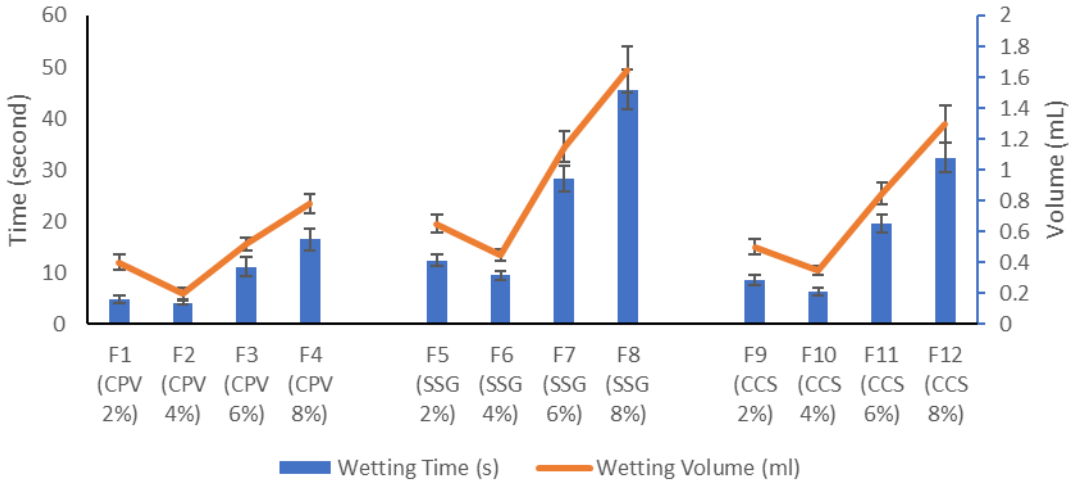

Figure 1: Wetting kinetics for ODT Ondansetron HCl (mean ± SD), CPV (crospovidone), CCS (croscarmellose), SSG (sodium starch glycolate)

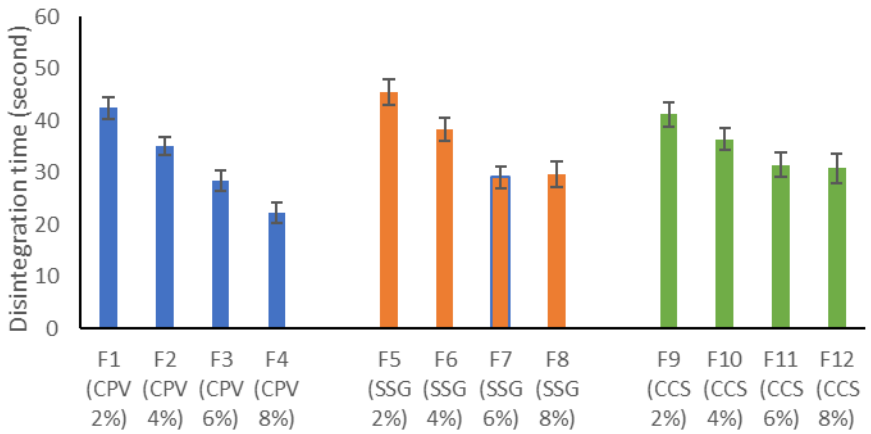

Figure 2: *In vitro* disintegration time of the factorial ODT formulations (Mean ± SD, n = 6), CPV (crospovidone), CCS (crosscaramellose), SSG (sodium starch glycolate)

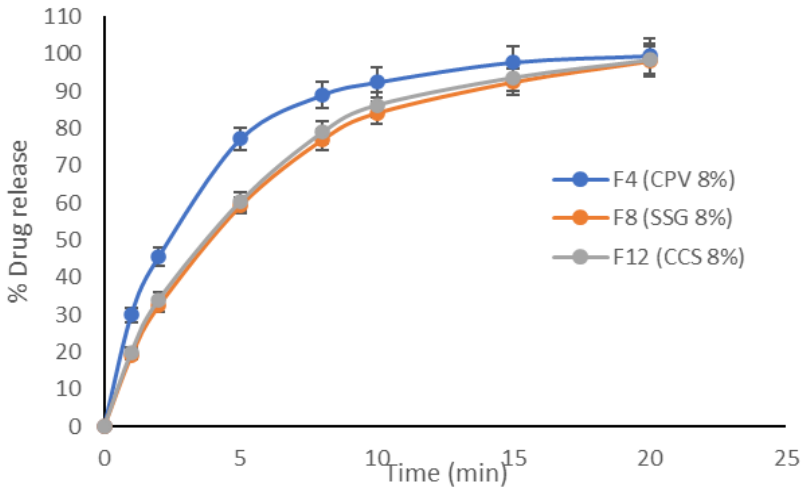

Figure 3: *In vitro* dissolution profiles of selected formulations (F4, F8, F12; mean % ± SD, n = 6), CPV (crospovidone), CCS (croscarmellose), SSG (sodium starch glycolate)

Table 4: Kinetic modelling of *in vitro* dissolution (n = 6)

Code	Higuchi (r2)	Higuchi (kh)	Peppas (r2)	Release exponent (n)	Kkp (min-n)	Kinetic mechanism
F4	0.890	26.80	0.958	0.33	40.09	Fickian diffusion
F8	0.969	24.24	0.973	0.45	27.13	Anomalous transport
F12	0.963	24.64	0.970	0.44	28.50	Fickian -anomalous transport

F4 (CPV 8 %), F8 (SSG 8 %), F12 (CCS 8 %), CPV (crospovidone), CCS (croscarmellose), SSG (sodium starch glycolate)

DISCUSSION

The flow property of the formulations was acceptable which revealed that the types and concentration of superdisintegrants have no significant effect on flowability. Angle of repose (θ) for all batches was below 30 °, which is the upper limit generally regarded as indicating acceptable powder flowability [14]. The good to excellent flow properties of these batches are attributed to the binary diluent system, the synergistic effect of microcrystalline cellulose (Avicel PH-102), highly porous and granular shape, and spray-dried mannitol. All of these reduced the cohesive Van Der Waals forces related to superdisintegrant polymers. Spray-dried mannitol has a spherical, non-cohesive crystalline shape that reduces inter-particulate friction within the powder bed, alongside silicon dioxide which was the glidant. Uniform flow properties ensure consistent tablet die filling and minimum weight variation of tablets. This clearly limits the cause of variation in disintegration time due to polymer hydration mechanisms [15]. All batches exhibited uniform weight within acceptable SD variation (< 1.9 %), which was < ± 7.5 % USP tolerance. There was no significant variation in tablet hardness as well ($p > 0.05$) across all formulations, indicating consistent compression force. As a result, any differences observed in disintegration and dissolution are attributed to superdisintegrant type and concentration rather than variability in compaction [16]. Friability was below 1 % of the pharmacopoeial limit. Friability increased significantly (up to 0.85 %) with F8 (SSG 8 %) and F12 (CCS 8 %), although within 1 % of the pharmacopoeial limit. Both SSG and CCS cause structural defects and reduce interparticulate hydrogen bonding of microcrystalline cellulose during plastic deformation, while CPV particles undergo plastic deformation during tablet compression and do not affect tablet friability even at higher concentrations [17]. There was a non-linear relationship between superdisintegrant concentration and liquid penetration. Above 4 % w/w, further increase in concentration did not improve wetting performance. Wetting efficiency was reduced significantly at higher concentrations (6 – 8 % w/w) for SSG, and CCS. Formulation F8 (8 % SSG) exhibited the highest wetting volume (1.65 mL) and wetting time (45 sec). This paradoxical delay indicated structural saturation and gel-blocking. At high concentrations, hydrophilic particles swell upon hydration and coalesce to form a viscous gelatinous layer. This forms a coat surface layer, which prevents water penetration into the tablet core and reduces disintegration time [18]. The relatively small reduction in wetting time between F1 2 % (4.8 sec) and F2 4 % (4.2 sec) CPV suggests that efficient capillary action was already established at lower concentration, and further increase produced only minimal improvements due to an early saturation of the wicking network. Incorporating 6 – 8 % w/w of this highly deformable polymer likely causes excessive matrix densification during compression. This may have occluded the inter-capillary action, reduced hydraulic conductivity and increased the wetting time to 16.5 s for F4 [19].

The ANOVA revealed that the effect of concentration on disintegration time differed significantly among polymer types ($p < 0.05$), with CPV demonstrating continuous improvement across all concentrations. This confirmed that optimal superdisintegrant concentration depends on the underlying physicochemical mechanism. Because CPV forms a rigid, non-gelling porous network, increasing its concentration proportionally increases connectivity of capillary channels, allowing water to penetrate continuously without blocking the tablet structure. Comparing F7 with F8 and F11 with F12 showed no significant change in disintegration time as concentration of SSG and CCS increases above 6 %. Upon hydration, the swollen polymer undergoes fast fusion forming a viscous gel-like coat, which acts as a physical barrier and occludes capillary pores, resulting in higher disintegration time [20]. Selection of F4, F8, and F12 (8 %) formulations for dissolution profile and mathematical kinetic study was based on several criteria. They represented the highest concentration of polymers, so they had high values for the measured parameters. Formulation containing CPV achieved its minimum disintegration time

(22 sec) at 8 % through progressive capillary enhancement. Also, at 8 %, SSG and CCS exhibited maximum gel-blocking resulting in no further change in disintegration time. Formulations F2, F6 and F10 (4 % w/w) formulations were omitted from the dissolution profile study, although they had optimal wetting and disintegration characteristics. This would limit the ability to distinguish between wicking and swelling mechanisms. The 4 % formulations served as the recommended formulations based on disintegration and wetting criteria, while the 8 % formulations were selected to compare the mechanism of early drug release. The non-gelling CPV matrix ensured that following capillary-driven rupture, API-containing particles dispersed freely into the bulk fluid, maximising effective surface area and minimising boundary layer thickness. The gel layer formed by SSG increases diffusional path length and reduces effective diffusion coefficient, slowing mass transfer of dissolved drug molecules into the bulk medium [21]. Furthermore, this study investigated early-stage dissolution behaviour, as rapid drug release within the first few minutes is the key performance indicator for orodispersible tablets (ODTs). Differences among formulations were primarily observed during the first 5 min, which is the most critical phase for rapid-onset products. After this stage, all formulations showed similarly high release values, making later time points less discriminatory. The similarity factor (f2) calculation served as a model-independent index to evaluate the equivalence of dissolution profiles between the optimised wicking-driven matrix (F4) and maximal swelling-based formulation (F8). The similarity factor (f_2) was calculated using three early time points (1, 2, and 5 min), at which all formulations remained below 85 % dissolution, thereby satisfying FDA/EMA prerequisite conditions for f_2 applicability. This indicated that the two dissolution profiles (F4 and F8) were dissimilar in vitro, with CPV releasing significantly more drug during the first 5 min. In contrast, the f_2 value between F8 and F12 was 90.8, indicating that the dissolution profiles of the SSG and CCS formulations were highly similar. These findings demonstrated that swelling-based superdisintegrants at high concentrations significantly reduce early drug release compared to wicking agents. The observed gap was likely due to gel-layer formation in SSG and CCS formulations, which increased diffusional path length and slowed drug transfer during the first 5 min of dissolution [22]. The kinetic modelling results demonstrated distinct release mechanisms depending on the superdisintegrant type used at 8 % concentration. Within each formulation, the Korsmeyer–Peppas model showed a better fit compared to Higuchi model. Furthermore, F4 showed a release exponent (n) of 0.33, which is below 0.45 and therefore reflects Fickian diffusion. This suggests that drug release from CPV formulation is primarily controlled by simple diffusion through the porous tablet matrix.

Crospovidone acts mainly by wicking, creating rapid capillary channels without forming a viscous gel layer. This allows efficient water penetration and fast drug diffusion, which explains both the lower n value, relatively higher Higuchi release constant, and Korsmeyer-Peppas constant. Higher K values further confirm faster drug release for CPV compared to SSG and CCS formulations [23]. Formulation F12 showed n = 0.44, marginally below 0.45 threshold, indicating predominantly Fickian diffusion while F8 (n = 0.45) demonstrated Fickian / anomalous behaviour. This suggests that at 8 % w/w, swelling-based polymers shift drug transport toward the anomalous behaviour compared to CPV (n = 0.33), reflecting additional diffusional resistance imposed by gel-layer formation. The similar kinetic behaviour of SSG and CCS suggests that their swelling-dominated mechanism produces comparable release control even at high concentration (8 %) [24].

CONCLUSION

Crospovidone shows significantly superior early-phase dissolution at all concentrations compared with SSG and CCS, with drug release following Fickian diffusion.

DECLARATIONS

Acknowledgement/Funding

None.

Ethical approval

Not applicable.

Use of artificial intelligence / large language models

The authors confirm that AI-based tools were used solely for language editing and manuscript polishing purposes (e.g., grammar, phrasing, and clarity). No AI tool was used to generate content, interpret data, or influence study design, results, or conclusions. All intellectual contributions, study analyses, and interpretations reported in the manuscript were the original work of the authors.

Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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