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PHARMACEUTICAL TECHNOLOGY

DISSOLUTION PROPERTIES AND KINETIC STUDY OF SULFADIMIDINE AND TRIMETHOPRIM TABLETS CONTAINING FOUR DIFFERENT SUPERDISINTEGRANTS

ŁUKASZ ZIMMER*, REGINA KASPEREK and EWA POLESZAK

Department of Applied Pharmacy, Medical University of Lublin, 1 Chodźki St., 20-093 Lublin, Poland

Abstract: The objective of this study was to evaluate and compare the effect of four superdisintegrants such as croscarmellose sodium (Ac-Di-Sol), crospovidone (Kollidon CL and with smaller particle sizes Kollidon CL-F), sodium starch glycolate (Explotab) in combination with β-lactose and microcrystalline cellulose (Avicel PH-102) as base excipients exhibiting properties of directly compressed tablets and increasing the disintegration and the dissolution rate of sulfadimidine sodium (SDD-Na) and trimethoprim (TMP). All tablets were prepared by direct compression method and superdisintegrants were used at 2% for all formulations. The tablets were evaluated with regard to uniformity of weight, hardness, friability, drug content, disintegration time and dissolution properties. Dissolution properties such as $t_{50\%}$ and $t_{80\%}$ (time to release 50 and 80% of drug), $DP_{30,45}$ (percent of drug dissolved in 30 and 45 min) and the dissolution rate constant value (K) were considered in comparing the dissolution results. The results showed that crospovidone (Kollidon CL) provides the shortest disintegration time and the fastest rate of dissolution for both TMP and SDD-Na. The kinetic study of the dissolution data reveals that *in vitro* release profiles of TMP and SDD-Na can be best explained by first order model or by Higuchi model. The obtained data were plotted into Korsmeyer-Peppas equation to find out the confirmed diffusion mechanism. For TMP release, the values of the release exponent are beyond the limits of Korsmeyer model, so-called, power law. For SDD-Na release, exponent values are characteristic for anomalous transport (non-Fickian) or the value of the release exponent is beyond the limits of Korsmeyer model.

Keywords: dissolution, tablet excipients, sulfadimidine, trimethoprim, superdisintegrant, kinetic analysis

Solid dosage forms like tablets are the most popular and most preferred drug delivery systems. They have high patient compliance and they are relatively easy to produce and market in accurate dosing. Such a form presents good physical and chemical stability (1).

Despite the increasing interest in controlled-release drug delivery systems, the most common tablets are intended to be swallowed as a whole and to disintegrate and release their medicines rapidly in the gastrointestinal tract (2). Conventional tablet formulations generally require rapid disintegration to aid drug dissolution. The choice of formulation ingredients can have a significant effect on the rate and extent of drug dissolution (1). The simplest way to achieve quick disintegration is to use the superdisintegrant combined with suitable diluents.

The term superdisintegrant refers to a substance which achieves disintegration faster than the substances conventionally used. A tablet or a capsule content breaks up, or disintegrates, into smaller particles that dissolve more rapidly than in the case of the absence of such disintegrants (3). Superdisintegrants are generally used at a low level in a solid dosage form, typically from 2 to 5% of the weight of the total weight of a given dosage unit (4, 5).

A number of agents were formerly used as tablet disintegrants, but only a few acceptable disintegrants are currently available for pharmaceutical purposes (6). Superdisintegrants such as croscarmellose sodium, crospovidone and sodium starch glycolate are frequently used in tablet formulations to improve the rate and extent of tablet disintegration and thereby increase the rate of drug dissolution (7, 8).

Mechanism of disintegration

Despite all theories proposed, the mechanism of disintegration is still not completely understood.

* Corresponding author: e-mail address: lukasz.zimmer@umlub.pl

The rate of water uptake is of critical importance for a number of tablet disintegrants (9, 10).

However, no single mechanism is applicable to all disintegrating agents. It is likely that in most cases a combination of mechanisms take place simultaneously. The three major mechanisms affecting tablet disintegration include water uptake. The combination of swelling, wicking and deformation were found to be the primary action mechanisms for tablets disintegrants (5).

The most widely used veterinary antimicrobials in the European Union include tetracyclines, macrolides, penicillins, aminoglycosides and sulfonamides. In veterinary, sulfonamides are widely used to treat animals as well as to enhance feed efficiency, promote animal growth and improve productivity. They cover infectious diseases of the digestive and respiratory tracts, secondary infections, mastitis, metritis and foot rot (11–13). They are used in the treatment of otitis, bronchitis, sinusitis and pneumoystis pneumonia as well as in urinary tract infections in combination with trimethoprim (TMP) (14).

After the β-lactam class of compounds (among others containing penicillin), sulfonamides are the most commonly used antibiotics in most countries due to their ability to inhibit Gram-positive and Gram-negative bacteria as well as protozoa (15, 16). The objective of this study was to evaluate and compare the effect of four superdisintegrants such as croscarmellose sodium (Ac-Di-Sol), crospovidone (Kollidon CL and with smaller particle sizes Kollidon CL-F), sodium starch glycolate (Explotab) in combination with β-lactose and microcrystalline cellulose (Avicel PH-102) as base excipients exhibiting properties of directly compressed tablets and increasing the disintegration and the dissolution rate of sulfadimidine sodium (SDD-Na) and TMP.

EXPERIMENTAL

Materials

All chemicals were of analytical reagent grade. SDD-Na and TMP were purchased from P.O.Ch. S.A. (Gliwice, Poland). β-lactose (lactose) was purchased from Sigma, Germany. Microcrystalline cellulose (Avicel PH-102) and superdisintegrant – croscarmellose sodium (Ac-Di-Sol) were gift samples from IMCD (FMC Biopolymer, USA). Crospovidones (Kollidon CL and CL-F) were gift samples from BASF (Ludwigshafen, Germany) and sodium starch glycolate (Explotab) was a gift sample from JRS Pharma GmbH (Rosenberg, Germany). Magnesium stearate used as the internal lubricant was obtained from P.O.Ch. S.A. (Gliwice, Poland) and ethanol was from P.P.H.”STANLAB”. All the reagents and chemicals used were of AR analytical grade.

Water was purified by Cobrabid-Aqua CA-ROD 3 ECO system.

Methods

Blending and tableting

All tablets were prepared by direct compression method and the formulae used in the study are

Table 1. Formulation details of kinetic model for investigated tablets.

Formulation ingredients (mg/tablet)	Formula no.				
	F1	F2	F3	F4	F5
SDD-Na	89.9	89.9	89.9	89.9	89.9
TMP	16.7	16.7	16.7	16.7	16.7
Avicel PH-102	141.7	141.7	141.7	141.7	141.7
Lactose	141.7	141.7	141.7	141.7	141.7
Ac-Di-Sol	8	-	-	-	-
Explotab	-	8	-	-	-
Kollidon Cl-F	-	-	8	-	-
Kollidon Cl	-	-	-	8	-
Magnesium stearate (lubricant)	2	2	2	2	2
Total tablet weight (mg)	400	400	400	400	400

Table 2. Physical properties of SDD-Na and TMP formulations prepared.

Test	Results				
	F1	F2	F3	F4	F5
Mean weight (mg) (± %)	402 (1.5)	407 (2.5)	405 (2.7)	398 (1.8)	397 (1.3)
Thickness (mm) ± SD	5.0 ± 0.03	5.2 ± 0.02	5.2 ± 0.03	5.0 ± 0.04	4.9 ± 0.02
Hardness (kg/mm^2) ± SD	0.258 ± 0.04	0.266 ± 0.03	0.251 ± 0.03	0.255 ± 0.04	0.248 ± 0.05
Friability (%)	0.8	0.3	0.6	0.28	0.58
Disintegration time (min) H_2O ± SD	9.4 ± 0.75	10.5 ± 0.6	5.2 ± 1.2	4.2 ± 0.5	17.5 ± 1.7
Disintegration time (min) 0.1 M HCl ± SD	15.2 ± 1.7	17.5 ± 0.8	7.5 ± 1.1	4.4 ± 1.2	21.4 ± 1.4
Drug content (%) SDD-Na (%) TMP	100.74 99.32	98.44 97.62	100.85 98.75	98.44 98.15	99.52 101.35

shown in Table 1. Different types of super disintegrants such as Ac-Di-Sol, Kollidon CL and CL-F and Explotab were used.

Avicel PH-102 and β-lactose were used as diluents. SDD-Na and TMP were premixed with diluents and superdisitnegrant for 15 min in a cube mixer and then lubricated with magnesium stearate for another 5 min. The magnesium stearate level was fixed at 0.5% for all the formulations. Superdisintegrants were used at 2% for all the formulations.

The round flat-faced tablets were prepared using a single-punch tablet press (Erweka, EK-O, GmbH, Hausenstamm, Germany) with 9.0 mm punches.

Tablets properties

The tablets were evaluated as per standard procedure according to European Pharmacopoeia 7th edition (Ph. Eur.) for uniformity of weight, hardness, friability, drug content, disintegration time and dissolution properties (Table 2) (17).

Thickness and weight

Tablets were tested for thickness and weight variation to determine any variability associated with the tablet press or the method of preparation. Thickness was determined using digimatic caliper. Uniformity of mass was determined by weighing 20 tablets on an analytical balance (OHAUS Adventurer Pro).

Measurement of friability

Friability was evaluated from the percentage weight loss of 20 tablets tumbled in an Erweka TAR 120 friabilator (Erweka) at 25 rpm for 4 min. The tablets were dedusted and the loss in weight caused by fracture or abrasion was recorded as the percentage weight loss. Friability below 1% was considered acceptable.

Hardness test

The hardness of six tablets was determined using an Erweka TBH 30 hardness tester (Erweka). The hardness coefficient was calculated from equation:

$$T = \frac{P_{max}}{h \cdot d} \qquad \text{(Eq. 1)}$$

where: T – tablet hardness coefficient (kG/mm^2), P_{max} – tablet breaking force (kG), d – tablet diameter (mm), h – tablet thickness (mm).

All results are presented as the mean value ± SD (n = 6). A hardness coefficient above 0.1 kG/mm^2 was considered acceptable.

Disintegration time

Respective disintegration times of the prepared tablets were measured in 900 mL of purified water or 0.1 M HCl with disks at 37^{o}C using an ERWEKA ZT 222 tester.

The disintegration time (n = 6) was recorded till all the fragments of the disintegrated tablet passed through the screen of the basket.

In vitro dissolution test

The dissolution profiles of SDD-Na and TMP were determined in an Erweka DT 600 HH dissolution tester following the paddle method. All tests were conducted in 900 mL of purified water. The dissolution medium was maintained at a temperature of 37 ± 0.5^{o}C at a paddle rotation speed of 100 rpm. At specified time intervals (5, 10, 15, 30, 45 and 60

Table 3. Linear regression calibration formulae used for first derivative bivariate algorithm.

Component	Calibration equations and determination coefficients	
	λ = 249 nm	λ = 268 nm
SDD-Na	$^1D = –0.001761[SDD-Na] – 0.002453$ ($r^2 = 0.960$)	$^1D = – 0.161052[SDD-Na] – 0.010271$ ($r^2 = 0.999$)
TMP	$^1D = –0.164800[TMP] + 0.026986$ ($r^2 = 0.999$)	$^1D = 0.059386[TMP] + 0.021784$ ($r^2 = 0.999$)

Table 4. Recovery results for SDD-Na and TMP in the binary mixture applying the first derivative bivariate method.

TMP		SDD-Na	
Added (µg/mL)	Bivariate method (% found)	Added (µg/mL)	Bivariate method (% found)
2.0	102.7	2.0	99.9
4.0	100.1	4.0	98.8
8.0	96.7	8.0	100.1
12.0	99.5	12.0	100.6
16.0	98.1	16.0	99.6
20.0	97.2	20.0	98.9
% Mean recovery	99.1	% Mean recovery	99.6
%RSD (n = 6)	2.22	%RSD (n = 6)	0.71

Table 5. Wetting time and modified method disintegration time of prepared tablets.

Formula no.	Disintegration time H_2O (min) ± SD	Disintegration time HCl (min) ± SD	Wetting time H_2O (min) ± SD
F1	15.8 ± 0.6	18.4 ± 1.17	12.6 ± 3.5
F2	17.5 ± 0.9	21.3 ± 2.5	14.1 ± 2.2
F3	11.8 ± 1.5	12.7 ± 2.2	10.1 ± 2.7
F4	10.7 ± 1.1	11.1 ± 3.5	8.3 ± 1.7
F5	> 20	> 20	> 20

min), 2 mL of dissolution medium was withdrawn and replaced with an equal volume of purified water to maintain a constant total volume. The samples withdrawn were filtered through Whatman filter paper and SDD-Na and TMP content in each sample was analyzed after a suitable dilution by first derivative spectrophotometric method at λ = 249 nm and λ = 268 nm. Linear regression calibration formulae used for first derivative bivariate algorithm and recovery results for SDD-Na, and TMP in the binary mixture applying the first derivative bivariate method are shown in Tables 3 and 4 (18).

A Thermo Scientific Helios Omega UV-VIS spectrophotometer connected to PC fitted with VISION pro software was used for all the measurement and treatment of the data. The drug content in each sample was calculated using calibration equations. The dissolution rate was studied for the prepared formulations.

Drug content estimation

The powder content of 10 tablets from each formulation was mixed well and a powder sample equivalent to 89.9 mg of SDD-Na and 16.7 mg of TMP was placed in individual 100 mL volumetric flasks. Each drug was dissolved in 25 mL of ethanol. The resulting mixture was vortexed for 5 min and the volume was raised to 100 mL with ethanol. The solution was filtered and then the suitable dilution

was analyzed for the drug content by first derivative spectrophotometric method (18).

Wetting time and disintegration time

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers with a 10 cm diameter were placed in a Petri dish with a 10 cm diameter. Ten milliliters of water containing eosin, a water-soluble dye, was added to the Petri dish. A tablet was carefully placed on the surface of the tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time.

The disintegration time was measured using a modified disintegration method (n = 5). For this purpose, a Petri dish (10 cm diameter) was filled with 10 mL of water or 0.1 M HCl. The tablet was carefully put in the center of the Petri dish and the time of the tablet necessary to completely disintegrate into fine particles was noted (19). The wetting time and modified method disintegration time of the prepared tablets are shown in Table 5.

Drug release kinetics

To study the release kinetics of the drugs release profiles, data obtained from *in vitro* drug release studies were plotted in various kinetic models: zero order (Eq. 2) as the cumulative percentage of drug release *vs*. time, first order (Eq. 3) as the log of percent drug remaining to be released *vs*. time, and Higuchi model (Eq. 4) as cumulative percentage drug release *Vs* the square root of time.

The zero order rate describes the systems where the drug release is independent of its concentration.

$$Q = K_0 \times t \qquad \text{(Eq. 2)}$$

where Q is the amount of drug released in time t, K_0 is the zero order rate constant expressed in units of concentration (20).

The first order describes the release where the release rate is concentration dependent.

$$Log\ Q = Log\ Q_0 - Kt/\ 2.303 \qquad \text{(Eq. 3)}$$

where Q is the amount of the drug released in time t, Q_0 is the initial amount of the drug and K is the first order rate constant (21).

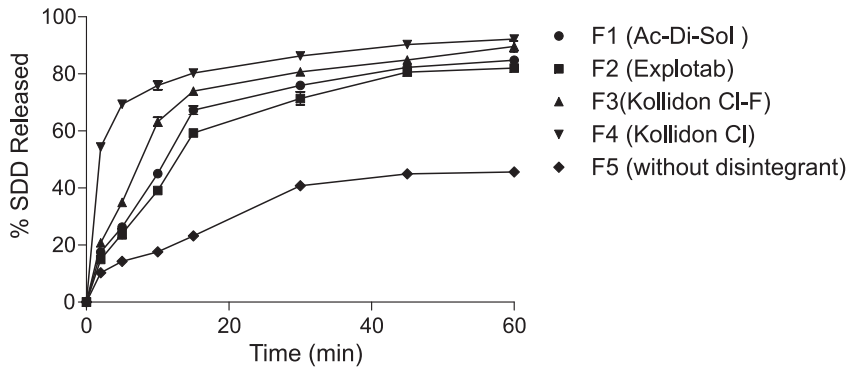

Figure 1. *In vitro* release profiles of sulfadimidine sodium from formulations: F1, F2, F3, F4, F5

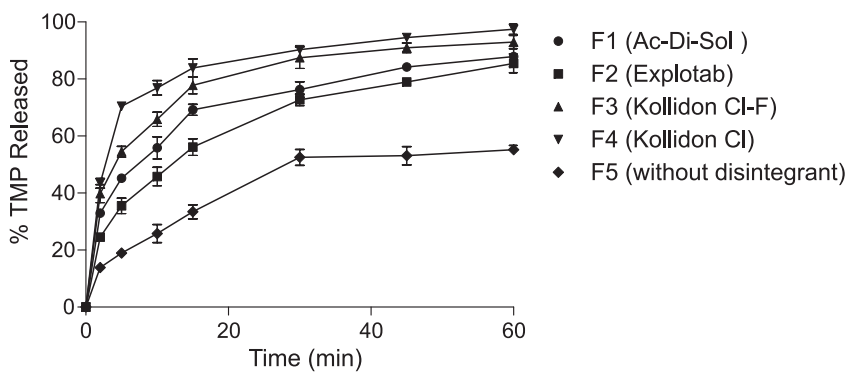

Figure 2. *In vitro* release profiles of trimethoprim from formulations: F1, F2, F3, F4, F5

Higuchi's model describes the release of drugs from insoluble matrices as a square root of time dependent process based on Fickian diffusion. The model, which is representative for the release of the soluble substances from the pharmaceutical formulas based on hydrophilic polymers, bases on the principle that the drug substance release profile decreases in time due to the increase in the length of the diffusion pathway followed by the drug substance.

$$Q = K\, t^{1/2} \qquad \text{(Eq. 4)}$$

where Q is the amount of the drug released in time t, K is the constant reflecting the design variables of the system (22).

Mechanism of drug release

To evaluate the mechanism of the drug release from tablets, the data of drug release were plotted in Korsmeyer-Peppas equation (Eq. 5) as the log of cumulative % of the drug released *vs.* log time, and the exponent n value was calculated through the slope of the straight line (23, 24) (Figs. 1, 2).

$$M_t / M_\infty = Kt^n \qquad \text{(Eq. 5)}$$

where Mt/M_∞ is the fraction of the drug released at time t, k is a constant incorporating the properties of the macromolecular polymeric system and the drug and n is an exponent used to characterize the transport mechanism. For cylindrical matrix tablets, if the exponent n = 0.45, then the drug release mechanism is Fickian diffusion, 0.45 < n < 0.89 for anomalous behavior or non-Fickian transport, n = 0.89 for Case II transport (relaxational), and n > 0.89 for Super Case II transport. Fickian diffusional release occurs by the usual molecular diffusion of the drug due to a chemical potential gradient. Case II relaxational release is the drug transport mechanism associated with stresses and state-transition in hydrophilic glassy polymers which swell in water or biological

Table 6. Drug transport mechanisms and diffusional exponents for cylindrical tablets.

Diffusional exponent, *n*	Type of transport	Time dependence
0.45	Fickian diffusion	$t^{1/2}$
0.45 < *n* < 0.89	Anomalous transport	t^{n-1}
0.89	Case II transport	time independent
n > 0.89	Super case II transport	t^{n-1}

Table 7. Time to release 50 and 80% of TMP ($t_{50\%}$ and $t_{80\%}$) and percent of drug dissolved at 30 and 45 min ($DP_{30,45}$).

Formula no.	$t_{50\%}$ (min) (mean ± SD)	$t_{80\%}$ (min) (mean ± SD)	DP_{30}(%) (mean ± SD)	DP_{45}(%) (mean ± SD)
F1	6.02 ± 0.4	38.38 ± 0.66	76.30 ± 2.78	84.2 ± 1.12
F2	13.09 ± 0.46	45.48 ± 0.28	72.67 ± 2.03	78.96 ± 1.26
F3	5.21 ± 0.22	25 ± 0.62	87.47 ± 3.80	90.93 ± 1.7
F4	4.11 ± 0.03	14 ± 0.33	90.32 ± 1.27	94.56 ± 0.15
F5	42.88 ± 0.77	-	52.51 ± 2.77	53.09 ± 3.23

Table 8. Time to release 50 and 80% of SDD-Na ($t_{50\%}$ and $t_{80\%}$) and percent of drug dissolved at 30 and 45 min ($DP_{30,}$ DP_{45}).

Formula no.	$t_{50\%}$ (min) (mean ± SD)	$t_{80\%}$ (min) (mean ± SD)	DP_{30}(%) (mean ± SD)	DP_{45}(%) (mean ± SD)
F1	15.11 ± 0.51	41.22 ± 0.67	75.93 ± 1.08	82.28 ± 2.11
F2	16.92 ± 0.61	44.89 ± 0.34	71.41 ± 4.00	80.61 ± 1.51
F3	11.09 ± 0.58	33.92 ± 0.88	80.70 ± 0.52	84.83 ± 1.32
F4	4.26 ± 0.09	22.21 ± 0.62	90.32 ± 1.27	94.56 ± 0.15
F5	-	-	40.77 ± 0.27	44.95 ± 2.41

fluids. Case II generally refers to the erosion of polymeric chain and anomalous transport (non-Fickian) refers to a combination of both the diffusion and erosion controlled drug release**.** To find out the mechanism of the drug release, the first 60% of the drug release data were fitted in Korsmeyer-Peppas model (23, 25).

Drug transport mechanisms and diffusional exponents for cylindrical tablets are presented in Table 6.

RESULTS AND DISCUSSION

Physical properties of tablets

The drug content of tablets was within the 100 ± 5% of the label claim and the results were satisfactory (Table 2). A good degree of uniformity of weight was achieved for all the batches of the tablet formulations prepared. The percent deviation did not exceed 5% indicating excellent uniformity of weight in all the batches of the tablet formulations prepared.

The tablet batches exhibited good mechanical properties with regard to both hardness and friability. The hardness values were above 0.1 kg/mm^2 and within the batches of tablet formulations they varied from 0.248 (kg/mm^2) for formulation F5 to 0.266 (kg/mm^2) for formulation F2. The fact that the strength of the tablets containing all the superdisintegrants was similar showed that the tablet hardness did not influence the dissolution. In the friability studies weight loss values of all the batches of tablet formulations were smaller than 1%.

The disintegration time was measured using a Ph. Eur. method and a modified disintegration method described above. The tablet formulations: F1, F2, F3 and F4 fulfilled the Ph. Eur. requirement for disintegration time for compressed tablets: less than 15 min. The order of disintegration times for the formulations of the tablets was: F4 < F3 < F1 < F2 < F5 (Tables 2, 5). The results of the Ph. Eur. disintegration time method correlated with both the modified disintegration time method and the wetting time. Significant prolongations of the disintegration time were observed for both sodium starch glycolate and croscarmellose sodium but not for crospovidone, a nonionic polymer. An acid medium significantly reduces the liquid uptake rate and capacity of ionic polymers.

In vitro dissolution studies

All tablet formulations were subjected to *in vitro* dissolution rate studies using purified water as the dissolution medium. Dissolution properties such as $t_{50\%}$ and $t_{80\%}$ (time to release 50 and 80% of drug), DP_{30}, DP_{45} (percent of drug dissolved at 30 and 45 min) and dissolution rate constant value (K) were considered in comparing the dissolution results. The corresponding values for SDD-Na and TMP tablet formulations are given in Tables 7, 8 and 9, 10. The dissolution profiles are shown in Figures 1 and 2. The results of the dissolution studies indicate that the dissolution rate of SDD-Na is increased in the following order: F5 < F2 < F1 < F3 < F4 and dissolution rate of TMP is increased in the same order: F5 < F2 < F1 < F3 < F4.

The dissolution rate of the model drugs correlated with the tablet disintegration time. Non-water-soluble crospovidones (Kollidon Cl and Kollidon Cl-F) provided the fastest dissolution in purified water for SDD-Na and TMP. Crospovidone is more effective than other superdisintegrants in enhancing the dissolution rate of poorly soluble TMP and water soluble SDD-Na. Crospovidone has solvent-like chemistry and high surface area resulting in high interfacial activity that enhances both the drug dissolution and release (4). The crospovidones act as disintegrants by absorbing water and subsequently swelling. This gain in volume is responsible for the disintegration of the tablet.

Water wicking and swelling are the two most important mechanisms of disintegrant action for croscarmellose sodium (Ac-Di-Sol). The cross-linked chemical structure of Ac-Di-Sol creates an insoluble, hydrophilic and highly absorbent excipient.

Derived from potato starch by cross linking, sodium starch glycolate (Explotab) demonstrates strong swelling properties in contact with water.

Despite their high hydration capacities, Ac-Di-Sol and Explotab were less effective in the tablet disintegration, probably their swelling formed a gel, which blocked tablet pores and prevented further penetration of water into the inner layers of the tablet (26). Crospovidone particles with their porous particle morphology quickly wick water into their capillaries to generate the rapid volume expansion and hydrostatic pressures that caused the tablet disintegration (27).

Kinetic analysis of dissolution data

The obtained drug release data were analyzed by zero order, first order, Higuchi and Korsmeyer-Peppas to know the mechanism of the drug release from the formulations. The release rate constants were calculated from the slope of the appropriate plot and determination coefficient (r^2) was determined (Tables 9 and 10).

Table 9. Dissolution kinetics of trimethoprim.

Formulation	Zero order		First order		Higuchi		Korsmeyer-Peppas	
	K_0	r^2	K_1	r^2	K_H	r^2	n	r^2
F1	0.8488	0.8296	0.02833	0.9563	8.4462	0.9388	0.3213	0.9994
F2	0.9909	0.8934	0.02787	0.9823	9.6923	0.9859	0.4032	0.9978
F3	0.6874	0.6594	0.004271	0.962	7.0926	0.8024	0.2123	0.8729
F4	0.8011	0.76	0.3639	0.9305	8.132	0.8949	0.3147	0.996
F5	0.7915	0.8052	0.01082	0.8808	6.6244	0.9448	0.4223	0.9782

Table 10. Dissolution kinetics of sulfadimidine sodium.

Formulation	Zero order		First order		Higuchi		Korsmeyer-Peppas	
	K_0	r^2	K_1	r^2	K_H	r^2	n	r^2
F1	1.0954	0.7687	0.00295	0.8982	11.712	0.9283	0.5799	0.9741
F2	1.1265	0.8227	0.02727	0.9275	11.52	0.9543	0.6694	0.9798
F3	0.5217	0.7427	0.0276	0.9267	5.2986	0.8757	0.1468	0.9533
F4	0.996	0.6874	0.03201	0.8847	11.728	0.8826	0.6838	0.9863
F5	0.7159	0.8609	0.00921	0.8951	6.1522	0.9468	0.471	0.9721

In this study, the *in vitro* release profiles of TMP from obtained tablet batches containing superdisintegrant were best explained by first order model as the plots showed the highest linearity and determination coefficient (r^2) was in the range from 0.9305 to 0.9823, followed by Higuchi model (r^2 equals from 0.8024 to 0.9859). The release of SDD-Na was best explained by Higuchi equation (r^2 equals from 0.8826 to 0.9543) followed by first order (r^2 equals from 0.8847 to 0.9275). This indicates that the release of the drug from matrix is a square root of time dependent process describing the drug release rate relationship with the concentration of the drug. The TMP and SDD-Na release profiles of the tablet batches without superdisintegrants showed best fit to Higuchi model (r^2 equals 0.9448 and 0.9468 for TMP and SDD-Na, respectively).

The obtained data were plotted according to Korsmeyer-Peppas equation to find out the diffusion mechanism.

For TMP release, the release profiles of tablet batches F1, F2, F4 and F5 showed good linearity (r^2) equals in the range from 0.9782 to 0.9994 and 0.8729 for F3 with exponent (n) values between 0.2123 and 0.4223. The value of the release exponent is beyond the limits of Korsmeyer-Peppas model, so-called, power law. Fickian diffusional release and a case-II relaxational release are the limits of this phenomenon.

For SDD-Na release, the release profiles of all the tablet batches showed good linearity (r^2) in the range from 0.9533 to 0.9833 with the release exponent (n) values in the range from 0.471 to 0.6838 and 0.1468 for tablet batch F3. This is characteristic for anomalous transport (non-Fickian), which appears to indicate a coupling of the diffusion and erosion mechanism or the value of the release exponent is beyond the limits of Korsmeyer-Peppas model.

CONCLUSION

The key is to choose superdisintegrant that would result in the maximum drug dissolution. The results of the present study conducted to evaluate the effect of crospovidone (Kollidon CL and CL-F), croscarmellose sodium (Ac-Di-Sol) and sodium starch glycolate (Explotab) on the dissolution rates of the model drugs: poorly soluble TMP and good soluble SDD-Na showed that Kollidon CL provides the shortest disintegration time and the fastest rate of dissolution for both TMP and SDD-Na.

The kinetic study of the dissolution data reveals that *in vitro* release profiles of TMP were

best explained by the first order model followed by Higuchi model. The release of SDD-Na was best explained by Higuchi's equation followed by first order. The data obtained were plotted into Korsmeyer-Peppas equation to find out the diffusion mechanism.

For TMP release, the values of the release exponent are beyond the limits of Korsmeyer model, so-called, power law. For SDD-Na release, the exponent values are characteristic for anomalous transport (non-Fickian) or the value of the release exponent is beyond the limits of Korsmeyer-Peppas model.

REFERENCES

1. Late S.G., Tu Y., Banga A.K.: Int. J. Pharm. 365, 4 (2009).
2. Sungthongjeen S. et al.: J. Control. Release 95, 147 (2004).
3. Madgulkar A.R., Bhalekar M.R., Padalkar R.R.: AAPS Pharm. Sci. Tech. 10, 574 (2009).
4. Balasubramaniam J., Bee T.: Pharm. Tech. 21, 9 (2009).
5. Mohanachandran P.S., Sindhumol P.G., Kiran T.S.: Int. J. Pharm. Sci. Rev. Res. 6, 105 (2011).
6. Bhalekar M.R., Desale S.S., Magdulkar A.R.: AAPS Pharm. Sci. Tech. 11, 3 (2010).
7. Gohel M.C., Parikh R.K., Brahmbhatt B.K., Shah A.R.: AAPS Pharm. Sci. Tech. 8, 9 (2007).
8. Nalluri B.N., Chowdary K.P., Murthy K.V., Becket G., Crooks P.A.: AAPS Pharm. Sci. Tech. 8, 36 (2007).
9. Zhao N., Augsburger L.L.: AAPS Pharm. Sci. Tech. 6, E634 (2005).
10. Zhao N., Augsburger L.L.: AAPS Pharm. Sci. Tech. 6, E120 (2005).
11. Papapanagiotou E.P., Fletouris D.J., Psomas I.E.: Anal. Chim. Acta 529, 325 (2005).
12. Accinelli C., Hashim M., Epifani R., Schneider R., Vicari A.: Chemosphere 63, 1539 (2006).
13. Yuqi L., Xin L., Dong Y., Cunku J., Jingyao Q.: Biomaterials 30, 3205 (2009).
14. Guneysel O., Onur O., Erdede M., Denizbasi A.: J. Emerg. Med. 36, 338 (2009).
15. Kümmerer K.: Chemosphere 75, 417 (2009).
16. Zhang Y., Marrs C.F., Simon C., Xi C.: Sci. Total Environ. 407, 3702 (2009).
17. European Pharmacopoeia 7th edn., Vol. 1, Council of Europe, Strasbourg 2010.
18. Zimmer Ł., Czarnecki W.: Ann. UMCS Sect. DDD 23, 27 (2010).
19. Gohel M., Patel M., Amin A. , Agrawal R., Dave R., Bariya N.: AAPS Pharm. Sci. Tech. 5, e36 (2004).
20. Hadjiioannou T.P., Christian, G.D., Koupparis, M.A.: Quantitative Calculations in Pharmaceutical Practice and Research, p. 345, VCH Publishers Inc., New York 1993.
21. Bourne D.W., Banker G.S., Rhodes C.T.: Modern Pharmaceutics, 4th edn., p. 67, Marcel Dekker Inc., New York 2002.
22. Higuchi, T.: J. Pharm. Sci. 52, 1149 (1963).
23. Korsmeyer R.W., Gurny R., Doelker E., Buri P., Peppas N.A.: Int. J. Pharm. 15, 25 (1983).
24. Siepmann J., Peppas N.A.: Adv. Drug Deliv. Rev. 48, 139 (2001).
25. Costa P., Sousa Lobo J.M.: Eur. J. Pharm. Sci. 13, 123 (2001).
26. Zhao N., Augsburger L.L.: Pharm. Dev. Technol. 11, 179 (2006).
27. Gonnissen Y., Remon J.P., Vervaet C.: Eur. J. Pharm. Biopharm. 68, 277 (2008).

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