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Use of percolation theory to interpret water uptake, disintegration time and intrinsic dissolution rate of tablets consisting of binary mixtures

R. Luginbühl, H. Leuenberger *

School of Pharmacy, University of Basel, Totengaesslein 3, CH-4051 Basel, Switzerland

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Abstract

Percolation theory represents a novel powerful concept which covers a wide range of applications in pharmaceutical technology. In the present work the tablets used consist of StaRX1500® as a disintegrant and of caffeine as a model drug. The disintegrant content of the compacts is varied from 0 to 90% (w/w). The disintegration time t_D, the kinetic constant of water uptake K and the intrinsic dissolution rate J are determined using appropriate methods.

Plotting the results obtained as a function of the concentration of the disintegrant in percent (v/v), the resulting curves show an interesting section around 10% (v/v) StaRX1500 where the kinetic constant of water uptake K and the intrinsic dissolution rate J pass through maximum values and the disintegration time t_D goes through a minimum value. Based on these observations it is evident that the concentration p of StaRX1500 reaches a critical value $p^*(1)$ where the characteristics of the binary system change clearly. By plotting the whole curves in a log–log scale, three linear sections can be distinguished clearly. Therefore a second critical concentration $p^*(2)$ is obtained in addition to the one described before.

The critical concentration $p^*(1)$ corresponds to the first percolation threshold p_{c1}. For concentrations $p < p_{c1}$ only finite clusters of StaRX1500, causing a positive influence on the disintegration process, exist in the tablets. Thus the isolated clusters within the pore structure of the more lipophilic caffeine increase the wettability of the porous system. For concentrations $p > p_{c1}$ an infinite cluster of StaRX1500 percolates through the compact, causing now a slower disintegration. The reason for the reducing effect lies in the fact that the pores start to close by the swelling of StaRX1500. Thus the entrance of water into the compact will be hindered as a function of the amount of disintegrant in the tablet. It can be assumed that the critical concentration $p^*(2)$ corresponds to the upper percolation threshold p_{c2}. Thus for concentrations of StaRX1500 above p_{c2} the caffeine is present as isolated clusters.

Keywords: Binary mixtures; Disintegration time; Intrinsic dissolution rate; Percolation theory; Percolation threshold; Water uptake

1. Introduction

1.1. Theoretical aspects

Water uptake, disintegration time and intrinsic dissolution rate (IDR)

Water uptake, disintegration time and intrinsic dissolution rate are important properties for characterization of tablets. In many cases the fast disintegration of a tablet is the first step in the bioavailability process of drugs. The mechanisms which are responsible for breaking up the binding forces in a tablet and therefore for the disintegration are swelling, deformation, wicking and repulsion (Kanig and Rudnic, 1984):

Swelling: Particles swell and break up the matrix from within. Swelling sets up localized stresses that spread throughout the matrix.

Deformation: Particles swell to precompression size when exposed to moisture. This fact also leads to localized stresses followed by breaking up of the matrix.

* Corresponding author. Tel.: 061-2617940; Fax: 061-2617907.

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Wicking: Water is pulled into pores by the disintegrant and reduces the physical bonding forces between particles.

Repulsion: Water is drawn into pores and particles start to repulse each other because of the resulting electrical force.

By addition of tablet disintegrants which support the mechanism described above, disintegration time can be influenced in a powerful way.

In addition to the disintegration time it is useful to quantify the kinetic process of water uptake into the tablet until complete disintegration is reached. This effect depends on the porosity of the tablet and on the wettability of the pores and can be determined with an Enslin-type apparatus (Nogami et al., 1966, 1969; Van Kamp et al., 1986). Calculating volume change, weight increase and the kinetic constant of the resulting water uptake, the kinetic process of disintegration can be described in more detail.

Assuming that the drug is very soluble, one can expect that the disintegration time of the tablet is the limiting step for a fast dissolution. Thus for a more complete description of this complex process it is of interest to determine in addition the intrinsic dissolution rate of the drug as a function of the amount of disintegrant in the formulation.

Percolation theory

Percolation theory (Stauffer, 1985) allows new insights into the physics of tablet formation and the properties of compacts. Percolation theory is based on the formation of clusters and the existence of a site- and/or bond-percolation phenomenon. It can be applied if a system can be sufficiently well described by a lattice, where the sites are occupied at random, e.g. by particles (site-percolation), or in the case that all sites are already occupied, where bonds between neighbouring particles are formed at random (bond-percolation). Thus the formation of a tablet could be described by a site/bond-percolation phenomenon (Leuenberger and Leu, 1992).

In a three-dimensional system consisting of two different components A and B two percolation thresholds are expected. Below the first percolation threshold p_{c1}, component A completely surrounds the particles of component B so that component B exists only in finite clusters. Above the first percolation threshold p_{c1} and below the second percolation threshold p_{c2}, the two components percolate each other and both form infinite clusters. That means that none of the two components exists in isolated areas only. Above the second percolation threshold p_{c2}, component B completely surrounds component A, and therefore component A exists in finite clusters. Depending on the two percolation thresholds p_{c1} and p_{c2}, three different sections are formed where either one component predominates over the other (A below p_{c1} or B above p_{c2}) or both components influence each other (between p_{c1} and p_{c2}).

The tablet properties (e.g. the disintegration time) in a binary system A/B have to be discussed in relation to the three different sections as a function of the concentrations in percent (v/v) of the two components A and B. It is evident that the porosity of these tablets has to be kept constant for such an evaluation. In the case of a matrix type controlled release system A/B consisting of highly soluble drug particles A embedded in an inert non-swelling matrix substance B the effects of the site-percolation phenomenon were clearly observed (Bonny and Leuenberger, 1991).

The fundamental equation of percolation theory

According to percolation theory, a system property X follows at the percolation threshold p_c a power law:

$$X = \Phi * | p - p_c |^q \quad (1)$$

with Φ = scaling factor and q = critical exponent.

Eq. 1 is strictly valid only close to the percolation threshold. In practical cases (Ehrburger and Lahaye, 1989), Eq. 1 often showed a much larger range of validity than originally anticipated.

2. Materials and methods

2.1. Materials

Tablets (round, flat, diameter 11 mm, height 3.191 mm ± 0.007 mm) consisting of different binary mixtures A/B (component A: caffeine as model drug; component B: StaRX1500® as disintegrant; see Table 1) were compressed to a constant porosity of 12% ±

Table 1
Physical characterizatiion of the substances used

Substances	Densities					Mean particle size (μm)
	true (g/ml)	poured (g/ml)	ρ_p (rel)	tapped (g/ml)	ρ_t (rel)	
Caffeine Boehringer Ingelheim Nr. 921	1.42	0.55	0.39	0.57	0.40	727
StaRX1500® Sandoz Nr. 86823	1.50	0.61	0.41	0.74	0.49	76

0.2% using the Zwick 1478 (Zwick GmbH, Ulm, Germany) Universal Testing Instrument (Leuenberger and Leu, 1992).

2.2. Methods

Disintegration time t_D

A tablet disintegration test unit (Sotax DT-3; Sotax AG, Basel, Switzerland) was employed for the disintegration time tests. Six tablets selected from each binary composition were tested individually in a disintegration compartiment. The medium consisted of 750 ml distilled water maintained at 37 ± 0.5°C. The average disintegration time t_D of six tablets was calculated for each mixture (see Table 2).

Water uptake measurements, kinetic constant K

Liquid uptake measurements were performed using the apparatus previously described by Van Kamp et al. (1986) and were carried out with distilled water in controlled temperature conditions at 20 ± 1°C. The weight loss due to evaporation was taken into account. After determining the maximal amount of water uptake Q_{max}, a characteristic value K was calculated using a modified form of the Washburn equation (Eq. 2) taking into account that the water uptake process is following a $\sqrt{t}$ kinetics (Eq. 3) (Washburn, 1921; De Beukelaer and Van Doteghem, 1985).

Washburn equation:

$$L(t)^2 = \frac{d * \gamma * \cos \Theta}{4 * \eta} * t \qquad (2)$$

where L = distance of liquid penetration (length of parallel capillaries perpendicular to the surface exposed to the penetrating liquid); d = mean pore diameter (capillary diameter); Θ = solid/liquid contact angle; t = time; γ = surface tension of the penetrating liquid; η = viscosity of the liquid.

Eq. 3 is valid up to ca. 60% (w/w) of water uptake. Thus only the initial part of the kinetics, i.e. up to 40% (w/w), was evaluated. The average K value of six tablets was calculated for each mixture according to following equation (Eq. 3; see Table 2).

Modified equation:

$$M(t) = K * \sqrt{t} \qquad (3)$$

where $M(t)$ = amount of water uptake; t = time; K = water-uptake constant.

Intrinsic dissolution rate J

The rotating disk method described in detail by Bonny and Leuenberger (1991) was used to measure the intrinsic dissolution rate J in distilled water at a temperature of 37 ± 0.5°C and with a rotating velocity of 100 rpm. The average value J of the intrinsic dissolution rate was determined based on the test of six tablets for each binary mixture (see Table 2).

In order to compare the obtained results with the results received from the water uptake experiments only the initial part of the intrinsic dissolution rate kinetics (up to 40% (w/w) of the total amount of the caffeine liberated) was evaluated.

Table 2
Experimentally determined values for the water-uptake constant K, the intrinsic dissolution rate J and the disintegration time according to Eq. 3, Eq. 4 and the disintegration test method

StaRX1500® (% (w/w))	(% (v/v))	Water-uptake constant K (mg $H_2O/s^{1/2}$)	IDR J (% caffeine/(min * cm^2))	Disintegration time t_D (s)
0.0	0.0	4.16 ± 0.29	1.01 ± 0.09	361 ± 19
2.5	2.37	7.49 ± 0.46	1.37 ± 0.10	207 ± 17
5.0	4.75	11.14 ± 0.93	1.99 ± 0.16	156 ± 11
7.5	7.13	15.09 ± 1.57	3.27 ± 0.49	112 ± 14
10.0	9.51	17.25 ± 2.06	3.86 ± 0.44	148 ± 17
12.5	11.92	16.00 ± 0.74	3.78 ± 0.41	196 ± 18
15.0	14.32	13.65 ± 0.99	3.38 ± 0.53	260 ± 39
20.0	19.12	11.26 ± 0.91	2.83 ± 0.30	364 ± 41
30.0	28.85	8.84 ± 0.75	2.33 ± 0.33	734 ± 67
40.0	38.67	6.63 ± 0.44	1.84 ± 0.20	1144 ± 61
50.0	48.61	4.93 ± 0.31	1.33 ± 0.13	1514 ± 61
60.0	58.66	4.42 ± 0.18	0.96 ± 0.12	2220 ± 135
70.0	68.82	4.19 ± 0.42	0.52 ± 0.19	2844 ± 99
80.0	79.10	4.07 ± 0.44	0.28 ± 0.07	3692 ± 220
90.0	89.49	4.02 ± 0.33	0.06 ± 0.01	5400 ± 659

Intrinsic dissolution rate:

$$J = \frac{dm}{dt} * \frac{1}{F_s} \quad (4)$$

where J = intrinsic dissolution rate; m = amount of caffeine liberated; t = time; F_s = exposed surface of the tablet (= 0.950 cm^2).

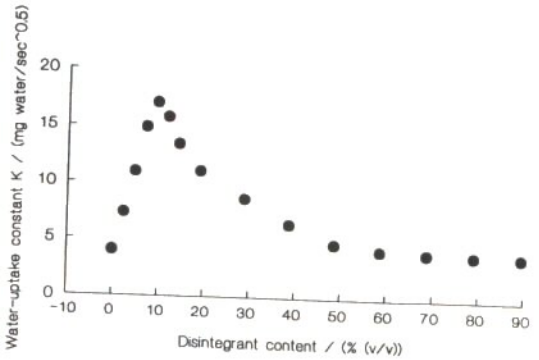

Fig. 1. Water-uptake constant K of the binary system caffeine/StaRX1500®.

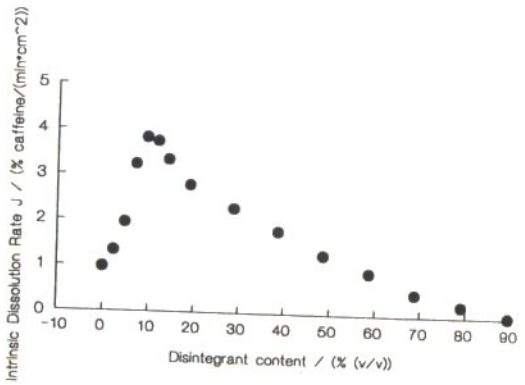

Fig. 2. Intrinsic dissolution rate J of the binary system caffeine/StaRX1500®.

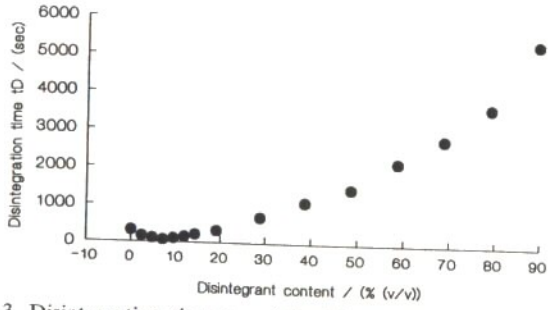

Fig. 3. Disintegration time t_D of the binary system caffeine/StaRX1500®.

3. Results and discussion

3.1. Water uptake, disintegration time and intrinsic dissolution rate

According to Eqs. 3 and 4, the water uptake constant K and the intrinsic dissolution rate J were determined and plotted as a function of the concentration p of StaRX1500 in percent (v/v) (Figs. 1 and 2). In both cases the resulting curves show an interesting section around 10% (v/v) StaRX1500 where the water uptake constant K and the intrinsic dissolution rate J pass through a maximum value. On the other hand the disintegration time t_D goes through a minimum value around the same concentration (Fig. 3). Based on these observations it seems quite certain that the concentration p of StaRX1500 in this part reaches a critical value $p^*(1)$ where the characteristics of the binary system change clearly.

In a next step the whole curves were plotted in a log–log scale and then three linear sections can be distinguished. Therefore a second critical concentration $p^*(2)$ between 60–70% (v/v) StaRX1500 is obtained in addition to the one described above (see Table 3, Figs. 4, 5 and 6).

3.2. Use of percolation theory

The lower percolation threshold p_{c1} seems to be reached around 10% StaRX1500 (v/v) for every parameter tested and this corresponds to the critical concentration $p^*(1)$. The characteristic parameter K of the water-uptake kinetics, the intrinsic dissolution rate J and the disintegration time parameter t_D^{-1} (t_D = disintegration time) increase until the percolation threshold p_{c1} is reached. Thus it seems that disintegration of the tablet is mainly influenced by the number n_s of isolated finite clusters of an optimal size s formed by particles of the disintegrant. At this time, the optimal size s and the number n_s of isolated finite clusters

Table 3
Experimentally determined values for the critical concentrations $p^*(1)$ and $p^*(2)$ (% (v/v) StaRX1500®)

	$p^*(1) \pm s$	$p^*(2) \pm s$
Water uptake K	9.9 ± 0.8	66.1 ± 4.3
Intrinsic dissolution rate J	10.6 ± 2.5	64.0 ± 7.8
Disintegration time t_D	8.0 ± 0.5	65.7 ± 3.1
Mean values	9.5 ± 2.7	65.3 ± 9.4

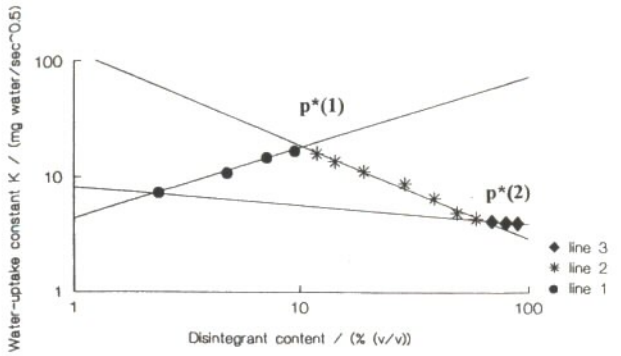

Fig. 4. Log–log plot of water-uptake constant K vs disintegrant content percent (v/v) StaRX1500®. Expected percolation thresholds: $p^*(1) \pm s = 9.9 \pm 0.8\%$ (v/v) StaRX1500®; $p^*(2) \pm s = 66.1 \pm 4.3\%$ (v/v) StaRX1500®.

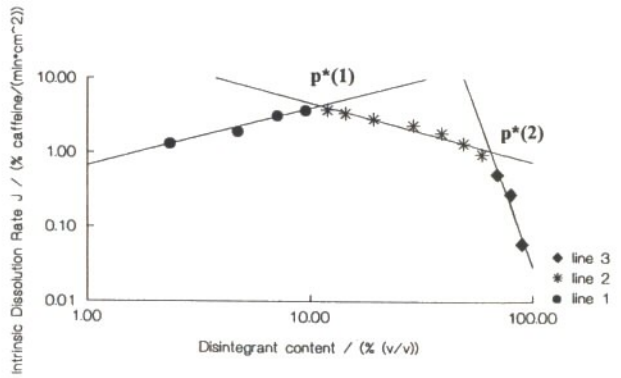

Fig. 5. Log–log plot of intrinsic dissolution rate J vs disintegrant content percent (v/v) StaRX1500®. Expected percolation thresholds: $p^*(1) \pm s = 10.6 \pm 2.5\%$ (v/v) StaRX1500®; $p^*(2) \pm s = 64.0 \pm 7.8\%$ (v/v) StaRX1500®.

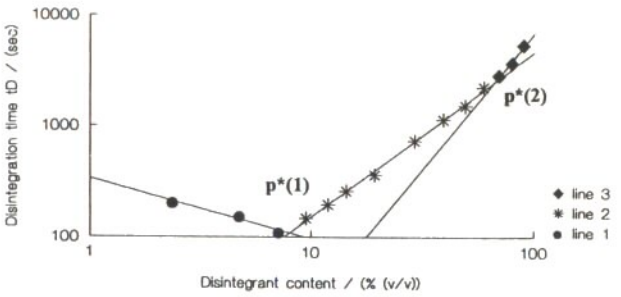

Fig. 6. Log–log plot of disintegration time t_D vs disintegrant content percent (v/v) StaRX1500®. Expected percolation thresholds: $p^*(1) \pm s = 8.0 \pm 0.5\%$ (v/v) StaRX1500®; $p^*(2) \pm s = 65.7 \pm 3.1\%$ (v/v) StaRX1500®.

of this optimal size s are unknown. However, the following two hypotheses can be made:

A As a rough approximation the number $n_s(p)$ of finite isolated clusters may be related to the mean cluster size $S(p)$ of the disintegrant.

B The results $K(p)$, $J(p)$ and $t_D^{-1}(p)$ are assumed to be proportional to the number of isolated clusters $n_s(p)$ of the disintegrant. For the practical evaluation the properties K, J, t_D^{-1} and the number n_s are normalized as follows:
$K(p)/K(p_c)$, $J(p)/J(p_c)$, $t_D^{-1}(p)/t_D^{-1}(p_c)$ and $v_s = n_s(p)/n_s(p_c)$.
The value v_s decreases exponentially according to the Fisher droplet model (Fisher, 1967).

Case A:
According to Stauffer (1985) the mean cluster size $S(p)$ can be calculated as follows:

$$S(p) = A * |p_{c1} - p|^{-\gamma} \quad (5)$$

where A is a proportionality constant (scaling factor) and γ is the critical exponent for the mean cluster size $S(p)$ and depends on the dimensionality of the lattice. In case of a three-dimensional lattice γ is equal to 1.8, and for a Bethe-lattice γ is equal to 1. Depending on the physical process, however, γ may assume other values, e.g. 1/2 for thermal processes. According to Eq. 5 one can see that the mean cluster size $S(p)$ diverges at the threshold p_{c1} where $|p_{c1} - p|$ goes to zero (Stauffer, 1985). Assuming the results $K(p)$, $J(p)$ and $t_D^{-1}(p)$ are proportional to the mean cluster size $S(p)$ of the disintegrant at least in the range $p < p_{c1}$, the following equation should hold:

$$X_i = \Gamma_i * |p_{c1} - p|^{-q_{1_i}} \quad (6)$$

where X_i represents the respective tablet property (K, J or t_D^{-1}), Γ_i a proportionality constant (scaling factor) and q_{1_i} a critical exponent. For $p < p_{c1}$ the disintegrant particles of the isolated clusters swell and consequently facilitate the disintegration process. However, with no infinite cluster spreading the whole tablet size, the number of pores closed up by the swelling process is negligible.

As the concentration $p = p_{c1}$ (percolation threshold p_{c1}), an infinite cluster of StaRX1500 starts to percolate through the tablet. This infinite cluster has an important influence. Due to the swelling of the disintegrant particles within the infinite cluster an important percentage of pores are closed up. Therefore the entrance of water into the tablet will be hindered with an increasing concentration p of StaRX1500 in the tablet ($p > p_{c1}$) as more and more pores are closed up. As a consequence the disintegration time t_D increases and the water-uptake constant K and the intrinsic dissolution rate J decrease as a function of the amount of StaRX1500. The slow down of the disintegration process and therefore the increase of the disintegration

time t_D for concentrations $p > p_{c1}$ is possibly correlated with the fraction $P(p)$ of sites belonging to the infinite network of StaRX1500 and can be calculated by

$$P(p) = B * | p - p_{c1} |^{\beta} \quad (7)$$

where B is a proportionality constant (scaling factor) and β is the critical exponent for the fraction $P(p)$ of sites belonging to the infinite cluster (Stauffer, 1985). At the percolation threshold the infinite network goes to zero with an exponent $\beta = 0.41$ for a three-dimensional lattice and with an exponent $\beta = 1$ for a Bethe-lattice.

Taking into account the superposition of the above two processes (i.e. the rise of the infinite network and the decrease of the finite clusters) in the range $p > p_{c1}$ the decrease of the properties K, J and t_D^{-1} may be still described by the following equation:

$$X_i = \Gamma_i * | p_{c1} - p |^{-q_{ri}} \quad (8)$$

where X_i represents the respective tablet property (K, J or t_D^{-1}), Γ_i a proportionality constant (scaling factor) and q_{r_i} a critical exponent.

Assuming that the critical concentration $p^*(1)$ corresponds fairly well to the lower percolation threshold p_{c1}, Eqs. 6 and 8 were used to determine by iteration the best values of the critical exponent q_{l_i} and q_{r_i} and the scaling factor Γ_i with a non-linear regression analysis program (SYSTAT, Version 5) (see Table 4).

For concentrations p below p_{c1} the following critical exponents

$q_l(K) = 0.15 \pm 0.06$,
$q_l(J) = 0.34 \pm 0.09$,
$q_l(t_D^{-1}) = 0.30 \pm 0.05$

are determined. A critical analysis yields, however, that q_{l_i} and Γ_i are correlated. In case of a higher value estimated for q_{l_i} a smaller value of Γ_i results. Thus in a first approximation it is meaningful to calculate a mean value $\bar{q}_l(K,J,t_D^{-1}) = 0.26 \pm 0.12$.

For concentrations p above p_{c1} the following critical exponents could be determined:
$q_r(K) = 0.21 \pm 0.06$,
$q_r(J) = 0.17 \pm 0.08$,
$q_r(t_D^{-1}) = 0.42 \pm 0.05$.

As a mean value $\bar{q}_r(K,J,t_D^{-1}) = 0.27 \pm 0.11$ is found for the different properties. Comparing the mean values of the critical exponents $\bar{q}_l$ and $\bar{q}_r$, it can be assumed in this first approximation that $\bar{q}_l = \bar{q}_r$. Therefore in the vincinity of the percolation threshold p_{c1} the progress of the tablet properties K, J or t_D^{-1} seems to be characterized by a common critical exponent q, which is valid both below and above the optimal concentration of the disintegrant.

Case B:
The properties K, J and t_D^{-1} are assumed to be proportional to the normalized value v_s (Fisher, 1967) of isolated finite clusters of optimal size s.

Fisher droplet model:

$$v_s = \exp[-\text{const} * | p - p_c | s^{\sigma}] \quad (9)$$

assuming an optimal value s, i.e. $s = \text{const}$. Eq. 9 can be modified as follows

$$v_s = \exp[-f * | p - p_c |] \quad (10)$$

$$\ln v_s = -f * | p - p_c | \quad (11)$$

where f = a constant and equal to $[\text{const} * s^{\sigma}]$.

In case of a proportionality between v_s and the property X the following equation should hold:

$$\ln X_i = \ln C_i - f_i * | p - p_c | \quad (12)$$

where f_i = a constant representing a slope factor and is equal to $[\text{const} * s^{\sigma}]$; $\ln C_i$ = a constant representing an intercept value.

Table 4
Experimentally determined values for the scaling factor Γ, the critical exponent q_l and the critical exponent q_r according to Eqs. 6 and 8 based on a nonlinear regression analysis (r^2 = correlation coeffient)

	Constant K	IDR J	t_D^{-1}
p_{c1} in [% (v/v) StaRX1500®]	9.9	10.6	8.0
$q_l \pm s$	0.15 ± 0.06	0.34 ± 0.09	0.30 ± 0.05
$q_r \pm s$	0.21 ± 0.06	0.17 ± 0.08	0.42 ± 0.05
Γ	15.86 (mg H_2O/ $s^{1/2}$)	4.11 (% caffeine/ (min * cm^2))	0.00852 (s^{-1})
r^2	0.999	0.993	> 0.999

Table 5
Experimentally determined values for the lower percolation threshold p_{c1}, the slope factor f_l, the slope factor f_r and the intercept value C according to Eq. 12 based on a nonlinear regression analysis (r^2 = correlation coefficient)

	Constant K	IDR J	t_D^{-1}
p_{c1} in [% (v/v) StaRX1500®]	7.4 ±0.4	8.7 ±0.3	5.0 ±0.7
$q_l \pm s$	0.179 ± 0.016	0.164 ± 0.009	0.160 ± 0.036
$f_r \pm s$	0.028 ± 0.002	0.028 ± 0.001	0.054 ± 0.004
C	16.98 (mg H_2O/ $sec^{1/2}$)	4.00 (% caffeine/ (min * cm^2))	0.00661 (s^{-1})
r^2	0.999	0.998	0.999

Using a non-linear regression program (SYSTAT, Version 5) the parameters C_i, f_i and p_{c1} are determined by iteration (Table 5). Assuming that the intercept value of the parameter C_i is equal as well for concentrations p below and as for concentrations p above p_{c1}, two critical slope factors f_{l_i} and f_{r_i} exist in the vicinity of the percolation threshold p_{c1}.

For concentrations p below p_{c1} the following slope factors f_{l_i} could be determined:

$f_l(K) = 0.179 \pm 0.016$;
$f_l(J) = 0.164 \pm 0.009$;
$f_l(t_D^{-1}) = 0.160 \pm 0.036$.

As all three values do not differ significantly a mean value $(K, J, t_D^{-1}) = 0.168 \pm 0.040$ can be determined.

For concentrations p above p_{c1} the following slope factors f_{r_i} are found:

$f_r(K) = 0.028 \pm 0.002$;
$f_r(J) = 0.028 \pm 0.001$;
$f_r(t_D^{-1}) = 0.054 \pm 0.004$.

Although the value $f_r(t_D^{-1})$ seems to be different from the other values $f_r(K)$ and $f_r(J)$ a mean value $\bar{f}_r(K,J,t_D^{-1}) = 0.037 \pm 0.004$ is calculated for the different properties K, J and t_D^{-1} in addition to the mean value (K,J,t_D^{-1}).

It can be noticed that the values of the slope factors f_{l_i} and f_{r_i} (below and above the percolation threshold p_{c1}) are significantly different. Thus the disintegration process, the intrinsic dissolution rate and the water uptake process are strongly influenced by the formation of the infinite cluster above the percolation threshold p_{c1}.

Concerning the practical determination of critical exponents q_i and the percolation threshold p_c some additional general remarks of caution have to be made. As already mentioned it is important to realize that both parameters q_i and p_c are correlated (Leuenberger and Leu, 1992).

At the percolation threshold fractal structures are expected (Stauffer, 1985) which may influence the value of the critical exponent (Ehrburger and Lahaye, 1989). The fractal structure is related to the particle size distribution and the relationship between the grain size of StaRX1500 and caffeine. If the much finer particles of the disintegrant are not distributed randomly within the tablet but adhere preferentially at the coarser grains of the caffeine particles, it has to be expected that effects due to a correlated percolation phenomenon may occur. In addition due to the rather small size of the tablets (diameter = 11.0 mm, thickness = 3.2 mm) compared to the grain size of the particles (mean particle size for caffeine = 727 μm and for StaRX1500 = 76 μm) finite size effects have to be taken into account. Both effects (type of percolation, finite size) can strongly influence the location of the percolation threshold. In principle one cannot a priori expect to find identical percolation thresholds for different properties of the compact. In case of the process studied (water uptake kinetics, intrinsic dissolution rate and disintegration time) no significant differences concerning the values of the percolation thresholds could be obtained. As the goal of this study was to get a better insight into the process of fast tablet disintegration process the evaluation of this process was limited to the lower percolation threshold. For scientific curiosity and additional information the upper percolation threshold was determined as well. This upper percolation threshold may be specially important for controlled release matrix type systems (Bonny and Leuenberger, 1991) based on the swelling effect of the matrix.

4. Conclusion

The application of the concepts of percolation theory allowed the following new insights:

It was possible to determine a first percolation threshold p_{c1} where the disintregation time t_D passes through a minimum value and the water-uptake constant K and the intrinsic dissolution rate J pass through maximum values.

For concentrations $p < p_{c1}$ (% (v/v) StaRX1500®) only finite clusters are present. These isolated clusters of StaRX1500 have a positive influence on the disintegration process. Thus the isolated clusters within the pore structure of the more lipophilic caffeine increase the wettability of the porous system which results in an increase of the water-uptake constant K and the intrinsic dissolution rate J.

For concentrations p of StaRX1500 above the percolation threshold p_{c1}, an infinite cluster of StaRX1500 percolates through the compact causing now a slower disintegration. The reason for the reducing effect can be explained by the fact that the pores start to close by the swelling of StaRX1500. Thus the entrance of water into the compact will be hindered as a function of the amount of disintegrant in the tablet.

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