Brand to brand variation in the disintegrant functionality of Polacrilin Potassium, NF.

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ABSTRACT

The current monograph for Polacrilin Potassium, NF does not specify tests that could assist in distinguishing between different brands of this disintegrant. The objective of this work was to examine the physical characteristics of four brands of Polacrilin Potassium, NF and relate the observed differences to differences in their functionality. Significant differences were observed in the particle size, true density, porosity, surface area and morphology of the samples. Functionality tests, such as settling volume, intrinsic swelling, rate and extent of water uptake were carried out. Significant differences were observed in intrinsic swelling and the initial rate of water uptake. The disintegration times of the tablets were found to be a function of the initial rate of water uptake. Since the disintegration times were shown to be significantly different despite negligible differences in settling volumes, wicking and water uptake, as opposed to the magnitude of swelling, appear to be the major mechanisms that distinguish disintegration performance between different brands of Polacrilin Potassium, NF when incorporated into insoluble tablet matrices. Thus, the measurement of the rate of water uptake may be a useful functionality test for Polacrilin Potassium in particular, and for ion exchange resin type disintegrants in general.

KEY WORDS: Polacrilin Potassium NF, functionality, physical characterization, disintegrants

INTRODUCTION

The advances in the field of biopharmaceutics and pharmacokinetics suggest that the factors affecting the performance of a dosage form must be controlled carefully in order to ensure bioavailability. Despite an increasing interest in controlled-release drug delivery systems, the most common dosage forms are tablets that are intended to be swallowed whole. They are expected to disintegrate and release the active pharmaceutical ingredient rapidly in the gastrointestinal tract. The appropriate choice of disintegrant and its consistency of performance are of critical importance to the rate of absorption of the drug from the tablets.

Ion-exchange resins are used as tablet disintegrants. Their disintegrant mechanism has been linked to the generation of swelling pressure because they hydrate in water. Polacrilin potassium is the partial potassium salt of a uni-functional low-cross-linked carboxylic

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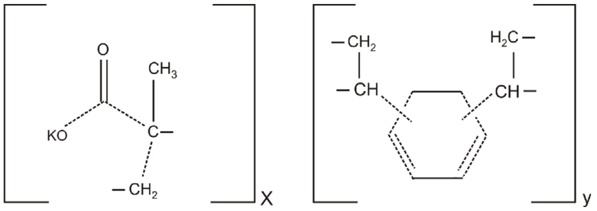

Figure 1 Chemical structure of Polacrilin Potassium NF

cation-exchange resin prepared from methacrylic acid and divinylbenzene (Figure 1) (1). Rohm and Haas specifically developed polacrilin potassium (Amberlite® IRP 88) as a tablet disintegrant (2).

This material is an effective disintegrant at low levels of incorporation in tablet formulations. It appears to be effective in hydrophobic tablet formulations, where standard disintegrants are less effective (3). The advantage of polacrilin potassium, compared to conventional disintegrants, is that it swells on hydration but does not dissolve and is not cohesive. The latter is commonly encountered with gums. Additionally, it is effective at lower levels than recommended for conventional disintegrants, such as starch. It works equally effectively with hydrophilic and insoluble formulations, especially with the latter, where conventional disintegrants are less effective (4, 5).

Ion exchange resins have also been used as disintegrants in orally disintegrating tablets. However, there are very few reports on their physical characteristics and evaluation of their functionality (6). Extensive literature is available for the physical characteristics and functionality of various brands of Crospovidone, NF (7) Crosscarrmellose Sodium, NF (8) and Sodium Starch Glycolate, NF (9). However, no such studies have been reported on the physical characteristics and functionality of Polacrilin Potassium, NF. Although there are multiple suppliers of Polacrilin Potassium, NF, no method to determine their functional equivalence has been published. Almost all testing in the compendial monographs relates to the identity and purity of the disintegrants. Differences in the source of raw material, solvents, reaction conditions, isolation and purification may result in differences in performance of the ion exchange resin disintegrants. Disintegrant characterization based on performance tests would make it easier to select excipients and provide a more meaningful system for quality control. Harmonization of excipient monographs is already being discussed and developments in this area will probably require some degree of functionality testing of excipients (10).

Table 1 lists the current monograph requirements for Polacrilin Potassium, NF and the values reported by the respective manufacturers in their Certificates of Analysis for the other four brands. The objective of this investigation was to examine the physical characteristics and functionality of brands of Polacrilin Potassium, NF and to identify tests which could be used to evaluate their *in vitro* performance.

Table 1 Current monograph requirements and corresponding values reported by the manufacturers of four brands of Polacrilin Potassium NF

TEST	MONOGRAPH REQUIREMENT USP30 NF 25	Amberlite® IRP 88	Doshion® P 544 DS	Indion® 294	Tulsion® 339
Description	White to off white free flowing powder	Complies	Complies	Complies	Complies
Identification	IR complies	Complies	Complies	Complies	Complies
Potassium content, dried basis	20.6-25.1%	24.8%	23.51%	22.2%	22.8%
Sodium content, dried basis	Max. 0.20%	0.04%	0.12%	0.08%	0.09%
Loss on drying	Max 10%	5.8%	6.4%	3.0%	4.2%
Particle size: % ≥ 0.15 mm 0.075 mm – 0.150 mm	Max 1% Max. 30.0%	0.5% 18.1%	- 7.5%	0.7% 6%	- 5.5%
Iron	Max. 0.01%	0.0005%	Complies	Complies	0.0012%
Heavy metals	Max. 0.002%	<0.001%	Complies	Complies	-l
Residual MAA	Max. 200 ppm	102 ppm	-	-	-
Total bacteria (col/g)	Less than 1000 col/g	2 col/ g	11 cfu/ gm	-	-
Total Molds (col/g)	Less than 100 col/g	2 col/ g	<10 cfu/ gm	-	-
Organic volatile impurities	Meets the requirements	Complies	Complies	-	-

EXPERIMENTAL

Materials

Four brands of polacrilin potassium were obtained for this study, Amberlite® IRP 88 (Rohm and Haas Ltd, Philadelphia, PA19106, USA), Doshion® P544 DS (Doshion Ltd., Ahmedabad, India), Indion® 294 (Ion Exchange Ltd, Mumbai, India) and Tulsion®

339 (Thermax Ltd, Pune, India). All the samples of polacrilin potassium were dried to a constant weight and kept in air tight containers prior to analysis. Samples of all four materials were gifts from their respective manufacturers. Lactose, Spray Dried, NF, Dicalcium Phosphate Dihydrate, USP and Magnesium Stearate, NF were gifts from Signet Chemicals, Mumbai, India. All other chemicals were of analytical reagent grade.

Methods

Particle size analysis

The particle size distribution of the four brands of polacrilin potassium was measured using laser diffraction (Mastersizer Micro, Malvern Instruments, Malvern, PA, USA). Since the dry powder feeder attachment was not available, the particle size was measured after dispersing the disintegrant powders in a non-swelling solvent, cyclohexane. The powders were dispersed in 500 ml of cyclohexane in the large volume dispersing unit of the Malvern Mastersizer which was connected to the circulating cell at a concentration sufficient to achieve an obscuration of 10% to 30%. The stirrer speed was set to 2200 rpm. The volume median diameters were recorded as the average of six measurements.

The lack of swelling of the disintegrants in this medium was validated by comparing the volume median diameters measured in cyclohexane and those measured using a dry powder dispersion method with a different instrument (Mastersizer 2000, Malvern Instruments, Malvern, PA, USA).

Density determination

True density

The true density was determined in triplicate by the helium displacement method using a helium densitometer (Ultrapycnometer 1000, Quantachrome Instruments, Boynton Beach, FL, 33426, USA). The true volume of the samples was calculated by determining the volume of the helium displaced by a known weight of sample under test.

Bulk density and tap density

The bulk densities of the disintegrants were determined using a Scott Volumeter (PEP-S-304, Prabha Engineering Ltd., Mumbai, India). The apparatus consisted of an upper brass funnel fitted with a 16-mesh screen. The powder flowed from the funnel through a baffle box containing four brass baffle plates, and through a lower brass funnel, into a 1.39±0.05 cm^3 capacity square cup which was filled to overflowing. The cup was then weighed and the bulk density determined.

The tapped density was determined using USP Method I. About 150 grams of powder was passed through a sieve to break the agglomerates. 100 grams of the sieved powder, accurately weighed, was introduced into a dry, 250 ml graduated, glass cylinder. The powder was carefully levelled without compressing it and the unsettled apparent volume V_0 was noted. The cylinder was placed on a USP tap density apparatus (ESTD 1020, Electrolab Ltd., Mumbai, India). The cylinder was initially tapped 500 times, and the tapped volume V_a was noted. The tapping was repeated for an additional 750 times and the tapped volume V_b was noted. The tapped density was determined from the tapped volume. Measurements were carried out in triplicate.

Specific surface area measurement

The specific surface area was determined using a BET adsorption apparatus (Autosorb 1C, Quantachrome Instruments, Boynton Beach, FL, 33426, USA). The technique provided a five point BET surface area analysis. All samples were preheated for 24 hours at 90°C and then degassed at a temperature of 100°C for 24 hours under vacuum to remove pre-adsorbed gases and vapors from the surface of the solid. Measurements were carried out in triplicate.

Determination of powder porosity and pore size distribution

Porosity and pore size distribution were determined using mercury intrusion porosimetry (Pore Master, model PM60-4, Quantachrome Instruments, Boynton Beach, FL, 33426, USA). A standard penetrometer sample cell with a 0.5 cm^3 stem volume and 2 mm internal diameter was used. A high pressure vacuum pump (Model DUO 5M, Pfeiffer) was used to evacuate the system prior to testing. Experiments were carried out using approximately 250-300 milligrams of powder up to a pressure of 60,000 psi. Samples were run in triplicate and the average pore volume and pore sizes were determined.

Scanning electron microscopy

The resin samples were photographed under a scanning electron microscope (Model S360, Cambridge Instruments). The samples were poured into an aluminum pan and transferred to aluminum mounts. The samples were dried overnight in a vacuum oven at 35°C and then sputter coated (E5000 sputtering system, Polaron Equipment Ltd.). The samples were observed at a working distance of 20 mm and an excitation voltage of 25 kV. Photomicrographs of random fields were recorded.

Viscosity

The viscosity of the disintegrant samples was studied over a one hour period. The disintegrant (5.4 grams) was added to 270 ml distilled water at 25°C in a 500 ml beaker whilst stirring. The disintegrant was added slowly over a period of one minute. The speed of the stirrer was adjusted to prevent the formation of vortex and incorporation of air. Stirring was continued for two minutes after which, the viscosity was measured immediately (0 minutes) using a Brookfield viscometer (Model DV III, Brookfield Engineering Lab, Stoughton, MA, USA) at 150 rpm using a UL adapter and ULA spindle. Measurements were made in triplicate. Viscosity was also measured at intervals of 1 minute, 10 minutes, 30 minutes and 60 minutes.

Settling volume determination

Settling volume studies were performed in distilled water at room temperature. Determinations were made in triplicate. The method used was adapted from the NF monograph for Croscarmellose sodium (11). 1.5 grams of polacrilin potassium was added to 75 ml water in a 100 ml graduated cylinder in 0.5 gram portions, shaking vigorously after each addition. After the powder had properly dispersed, the volume was made up to 100 ml. The mixture was further shaken until the powder was homogenously distributed, and was then allowed to stand. The volume (to the nearest 0.5 cm^3) of the settled mass was noted at the end of 4 hours and 24 hours.

Measurement of intrinsic swelling

The intrinsic swelling capacity of the samples of the four brands of Polacrilin Potassium, NF was assessed based on the increase in the volume median diameter (d_{50}) of the disintegrant powders after dispersion in an aqueous medium compared to their corresponding diameters in cyclohexane (8). The volume median diameters of polacrilin potassium particles after dispersion were determined in distilled water. 0.5 grams of the disintegrant powder was slowly added, over a period of 1 minute, to 100 ml distilled water in a beaker whilst stirring, taking care that vortex was not formed. The disintegrant was allowed to swell for 15 minutes. After 15 minutes, an aliquot of the suspension was introduced into the Malvern Mastersizer wet sampling unit in a quantity sufficient to achieve the obscuration of 10-30%. The stirrer speed was maintained at 2000 rpm. The volume median diameters were recorded as average of six measurements.

Water uptake determination

The water uptake properties of the samples of the four brands of polacrilin potassium were studied using a gravimetric liquid uptake rate

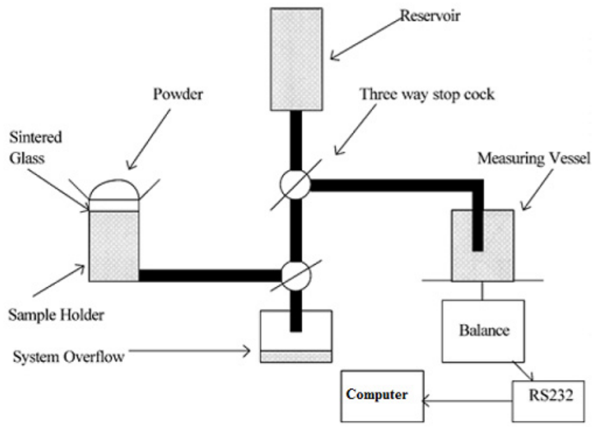

Figure 2 Water uptake rate measurement apparatus

measurement apparatus (7, 12). The apparatus consisted of a sample holder and a liquid holding beaker set on an electronic balance (Model AUW 220 D, Shimadzu Corporation, Kyoto, Japan) (See Figure 2). These two parts of the apparatus are connected by a glass tube. The two parts were adjusted so that the liquid was at the same level and could flow freely through the tubing from one side to the other. A fixed weight (400 milligrams) of the disintegrant powder was placed on the sintered glass platform of the sample holder. Liquid was passively withdrawn from the liquid holding vessel and taken up by the sample. The balance was connected to a computer via a RS-232 port. The loss of weight of the liquid was recorded by the computer at two-second-intervals using the Windows Direct$^{®}$ function of the balance. The data was recorded over a 15-minute period. The experiments were per-formed in triplicate using distilled water at room temperature.

Measurement of disintegration time

Directly compressible slow disintegrating tablets containing 1% disintegrant were prepared according to the formula given in Table 2. The batch size was 200 grams. Both the fillers were blended for 15 minutes in a drum blender. After addition of the disintegrant the blend was mixed for a further 5 minutes. Finally, magnesium stearate was added and the blend was mixed for an additional 5 minutes. Tablets were compressed at 600 kg force (5880 N), using a single station of a rotary tablet press fitted with flat-face punches of 7 mm in diameter (Remek Minipress, Karnavati Instruments, India).

Table 2 Formula of slow disintegrating directly compressed tablets containing 1% ion exchange resin disintegrant

INGREDIENT	QUANTITY (mg/TABLET)
Disintegrant	2
Magnesium stearate	2
PEG 6000	49
Dicalcium phosphate, dihydrate	147
Total weight	200

The thickness and hardness of the tablets was measured using a micrometer and a precision dial type hardness tester, respectively (Progressive Instruments Co. Ltd., Mumbai). Disintegration time was measured using 900 ml of distilled water at 37±2°C using USP disintegration test apparatus without discs (Model DTM, Veego Ltd, Mumbai, India). The disintegration time was taken as the time required for each of the six tablets to pass completely through the 10-mesh screen. The final value reported was the average of six tablets together with standard deviation.

Statistical treatment of data

One way analysis of variance was performed to determine the statistical significance of the data.

RESULTS AND DISCUSSION

Particle size analysis

A disintegrant's particle size can affect its performance (13). In addition, it has also been reported that for some disintegrants their larger particles perform better than the smaller ones (14). The particle size of the different resins was found to differ significantly ($p< 0.05$) (see Table 3). The following rank order was obtained for the volume median diameters: Amberlite$^{®}$ IRP88 > Doshion$^{®}$ P544 DS >

Indion® 294 > Tulsion® 339. The volume mean diameter was inversely correlated, $R^2>0.5$, with the disintegration time (see Table 3 below).

Table 3 Volume median diameters of four polacrilin potassium brands: mean (± SD), n=6

DISINTEGRANT	VOLUME MEDIAN DIAMETER D_{50} (µ)
Amberlite® IRP 88	64.60(3.48)
Doshion® P544 DS	51.46(1.89)
Indion® 294	20.44(2.19)
Tulsion® 339	14.22(0.29)

Density determination

There was no difference in the tapped volumes V_a and V_b, therefore V_a was used to calculate the tapped density of the powders. Table 4 shows the true, bulk and tapped bulk densities of the four brands of polacrilin potassium. No significant differences were observed in the true densities or bulk densities of the four disintegrants. However, the tapped densities differed significantly and were in the following rank order: Tulsion® 339 > Doshion® P544 DS > Amberlite® IRP 88 >Indion ® 294 ($p < 0.005$).

Table 4 Densities (g/cm^3) of different brands of Polacrilin Potassium NF: mean (± SD), n=3

DISINTEGRANT	TRUE DENSITY	BULK DENSITY	TAPPED DENSITY
Amberlite® IRP 88	1.55 (0.001)	0.58 (0.02)	0.75 (0.06)
Doshion® P 544 DS	1.56 (0.01)	0.55 (0.04)	0.83 (0.05)
Indion® 294	1.53 (0.007)	0.49 (0.02)	0.69 (0.08)
Tulsion® 339	1.55 (0.008)	0.51 (0.05)	0.87 (0.04)

Specific surface area

Table 5 shows the specific surface area of the four brands of polcrilin potassium. The difference between the surface areas of Amberlite® IRP 88 and Doshion® P544 DS was insignificant. However, the surface areas of the other two brands were significantly different from each other and also from the first two brands ($p<0.05$). As much as a threefold difference in the specific surface area was observed. Specific surface is an indirect measure of the particle size of non-porous materials. Generally, the smaller the particle size, the larger is the specific surface and the larger the surface area, the greater are the number of particles per unit weight in the formulation. The following rank order can be assigned to the specific surface of the polacrilin potassium particles: Indion® 294> Tulsion® 339 > Doshion® P544 DS ~ Amberlite® IRP 88.

Determination of powder porosity and pore size distribution

Liquid uptake is a phenomenon which largely depends on the availability of intra-particulate pores and inter-particulate voids. Therefore, intra- and inter-particulate porosity of the disintegrants was determined and the results are presented in Table 5 and Figure 3.

Table 5 Surface area, porosity and pore size distribution of Polacrilin Potassium NF: mean (± SD), n=3

DISINTEGRANT	SURFACE AREA (m^2/g)	TOTAL INTRUSION VOLUME (cc/g)	MEDIAN PORE DIAMETER (µm)	POROSITY (inter- and intra-particle) (%)
Amberlite® IRP 88	0.3786(0.005)	0.7647 (0.05)	13.04(0.49)	51.95 (1.34)
Doshion® 544DS	0.3846 (0.002)	0.6727 (0.02)	10.00 (0.24)	54.95 (2.60)
Indion® 294	1.0950 (0.016)	0.6426 (0.04)	6.42 (0.40)	46.59 (2.10)
Tulsion® 339	0.8791 (0.008)	0.6622(0.07)	8.31(0.65)	43.99 (1.33)

The porosities of Amberlite® IRP 88 and

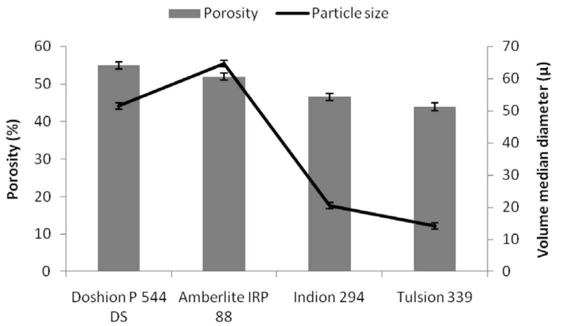

Figure 3 Effect of volume median diameters on porosities of four brands of Polacrilin Potassium NF

Doshion® P544 DS were significantly greater than the other two brands ($p < 0.05$). No significant difference was observed between Amberlite® IRP 88 and Doshion® P544 DS ($p>0.05$) or between Indion® 294 and Tulsion® 339 ($p > 0.05$). However, a significant difference was observed between the two pairs. The disintegrant comprising of finer particles had a lower porosity except in the case of Doshion® P544 DS. The volume median diameter of Doshion® P544 DS (51.46 μ) was significantly less than that of Amberlite® IRP 88 (64.66). However, its porosity is slightly more than Amberlite® IRP 88 ($p > 0.05$). It was not possible to distinguish between inter- and intra-particulate porosity data of the disintegrants. Thus, it can be assumed that, because Doshion® P544 DS has greater porosity than Amberlite® IRP 88 (despite its smaller particle size), it probably has a greater intra-particulate porosity. Greater porosity per particle is expected to lead to greater wicking.

Scanning Electron Microscopy

Polacrilin potassium particles appeared as flakes in the scanning electron photomicrographs, with varying degrees of porosity and surface roughness. The particle shapes and surface morphology differed greatly, as evident from the SEMs (see Figure 4). The surface area, porosity and particle size data supported this observation. Doshion® P544 DS and Amberlite® IRP 88 particles appeared to be more porous compared to the other two brands, which was consistent with the porosity data (see Figures 4(a) and 4(b)).

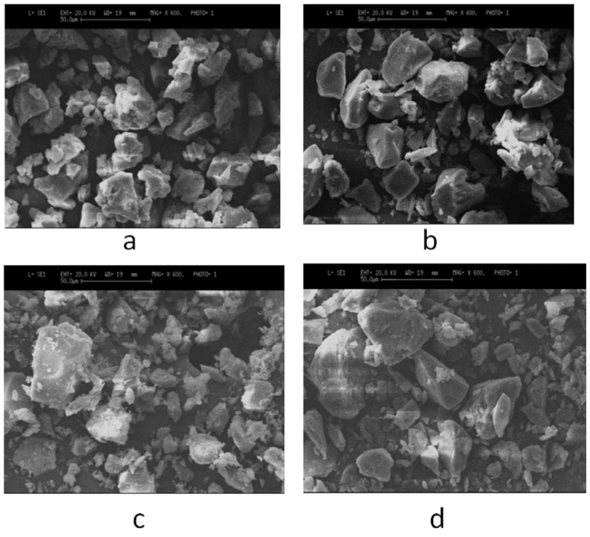

Figure 4 Scanning electron micrograph of (a) Amberlite IRP 88 (b) Doshion P544 DS (c) Indion (d) Tulsion 339 (magnification 600 X)

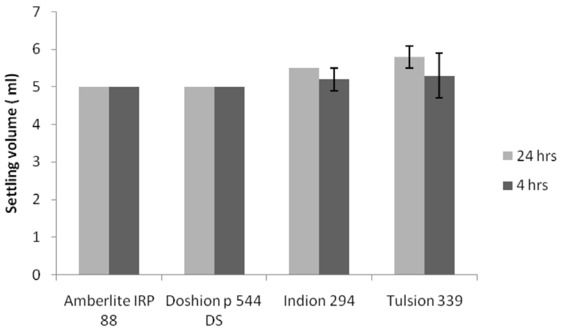

Figure 5 Settling volumes of four brands of polacrilin potassium NF in distilled water at room temperature after 4 hours and 24 hours

Viscosity

The measurement of viscosity that develops in a polymer slurry over a period of time can be considered as a measure of the degree of cross linking. The efficiency of several substituted and cross linked disintegrants have been evaluated as a function of the viscosity of their slurries. A method similar to the one employed to determine the viscosity of Explotab® (20), was used to determine the viscosity of the polacrilin potassium samples. None of the polacrilin potassium brands showed any increase in viscosity over time (Table 6).

Table 6 Viscosities in cps of Polacrilin potassium NF brands: mean (± SD), n=3

TIME (minutes)	AMBERLITE® IRP88	DOSHION® P544DS	INDION® 294	TULSION® 339
0	1.68 (0.04)	1.82 (0.18)	1.72 (0.32)	2.35 (0.07)
1	1.82 (0.20)	1.91 (0.23)	1.90 (0.63)	2.03 (0.48)
10	1.81 (0.12)	1.95 (0.43)	1.88 (0.36)	2.03(0.64)
30	1.82 (0.09)	1.97 (0.45)	1.92 (0.09)	2.05 (0.32)
60	1.82 (0.18)	1.94 (0.54)	1.95 (0.30)	2.04 (0.63)

This was expected since they are insoluble. This is considered an advantage over other disintegrants which do show increased viscosity since this increase in viscosity could slow down the rate of dissolution.

Settling volume determination

There were insignificant differences in the settling volumes of the four brands of polacrilin potassium. The swelling volumes of the disintegrants in distilled water are shown in Figure 5. The settling volume is a parameter that measures the extent of swelling of the disintegrants. The settling volumes were significantly less than those reported in the literature for some superdisintegrants.

Measurement of intrinsic swelling

The intrinsic swelling measured on individual disintegrant particles was significantly different ($p < 0.05$), although small (see Table 7). The greatest ratio of (water to powder) volume median diameter observed was 1.45 for Tulsion® 339. The following rank order was observed for intrinsic swelling of particles: Tulsion® 339 > Indion® 294 > Doshion® P544 DS > Amberlite® IRP 88.

The magnitude of the change in volume median diameters was not large enough to affect the settling volumes of the disintegrants. The swelling ratio (defined as the ratio of the diameter of the swelled particle to that of the non-swelled particle) was directly correlated (R^2>0.4) with the disintegration time (see Table 7 below).

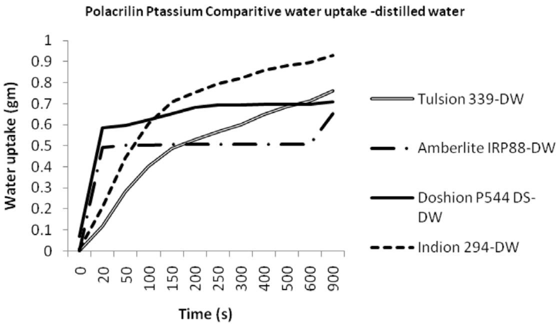

Figure 6 Water uptake rates of four brands of polacrilin potassium at room temperature

Table 7 Intrinsic swelling of four brands of Polacrilin Potassium NF in distilled water: mean (±SD), n=6

DISINTEGRANT	VOLUME MEDIAN DIAMETER D_{50}(μM)		WATER TO POWDER, VOLUME MEDIAN DIAMETER ΔD_{50} (μM), RATIO
	POWDER	WATER	
Amberlite® IRP 88	64 (3)	76 (0)	1.19
Doshion® P544DS	51 (2)	65 (1)	1.27
Indion® 294	14 (0)	19 (6)	1.36
Tulsion® 339	20 (2)	29 (2)	1.45

Water uptake determination

The water uptake of the four polacrilin potassium brands was studied to understand the relative hydrophilicities of these chemically equivalent materials and also to understand the differences in their wicking abilities. Figure 6 and Table 8 show the water uptake behavior of the four brands of polacrilin potassium.

Table 8 Water uptake properties of four brands of Polacrilin Potassium NF

DISINTEGRANT	LIQUID UPTAKE AFTER 20 SECONDS (g)	MEAN MAXIMUM LIQUID UPTAKE (g)	TIME TO 50% OF MAXIMUMLIQUID UPTAKE (s)
Amberlite® IRP 88	0.492	0.6519	4
Doshion® DS	0.586	0.7075	6
Indion® 294	0.207	0.928	52
Tulsion® 339	0.119	0.7613	88

It was found that the greater the porosity of the disintegrant, the greater was the rate of

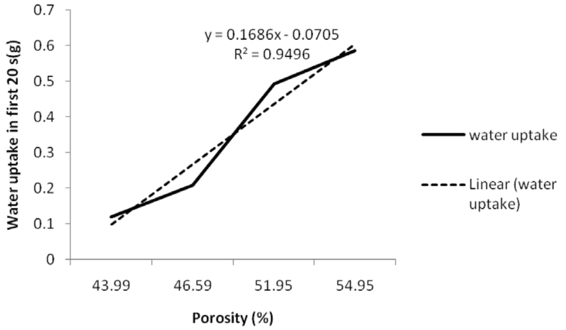

Figure 7 Co relation between porosity and water uptake rate in first 20 seconds of four brands of Polacrilin Potassium NF

liquid uptake. However, the extent of liquid uptake did not correlate with the porosity values. Figure 6 shows that the initial rate of water uptake was higher for Amberlite® IRP 88 and Doshion® P544 DS, represented by the initial larger slopes, which significantly decreased with time.

Although the overall uptake of water by Indion® 294 and Tulsion® 339 was greater than that for the other two brands, their water uptake profiles did not show a steep initial linear portion. Their liquid uptake rate profile showed a more gradual change over the whole profile. Amberlite® IRP 88 and Doshion® P544 DS showed a very high rate of water uptake which correlated with the shortest time of 50% of the total water uptake. The rate of water uptake correlated well with the porosity of the disintegrant powders ($R^2 > 0.94$, see Figure 7).

Measurement of disintegration time

Lactose and dicalcium phosphate have been used as fillers by many researchers representing soluble and insoluble tablet matrices respectively. Lactose tablets, however, dissolve rather than disintegrate even in the presence of disintegrants. Dicalcium phosphate tablets, on the other hand, show very long disintegration times, even when the disintegrant was used at a concentration of 0.5%. Therefore, in order to better distinguish between the functionalities of the different brands of polacrilin potassium, it was decided to use a slow disintegrating tablet matrix consisting of PEG 6000 (25%) and dicalcium phosphate (75%). Tablets prepared with all the four brands of disintegrants presented hardness of 5.3±0.4 kg and thickness of 4.04±0.56 mm. The tablets containing this slow disintegrating matrix without disintegrant gave mean disintegration times of 980 seconds. Table 9 shows the average disintegration times of tablets made containing the different brands of polacrilin potassium. The disintegration times were found to be in the following rank order: Doshion® P544 DS < Amberlite® IRP 88 < Indion® 294 < Tulsion® 339.

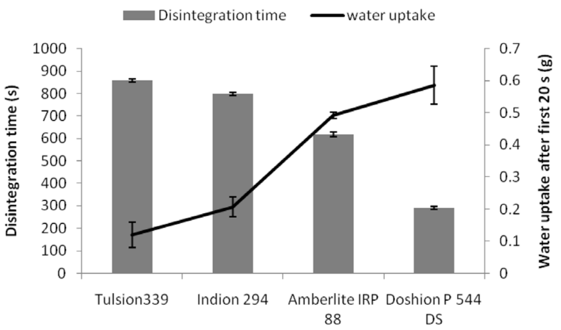

Figure 8 Effect of extent of water uptake in first 20 seconds on disintegration times of slow disintegrating tablet matrices containing 1% of Polacrilin Potassium NF

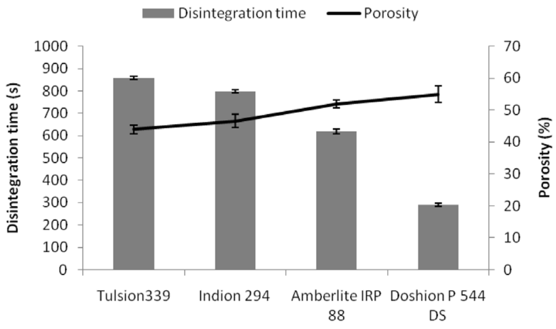

Figure 9 Effect of porosity on disintegration times of slow disintegrating tablet matrices containing 1% of Polacrilin Potassium NF

Table 9 Disintegration time of slow releasing matrices of PEG 6000 + DCP containing 1% disintegrant mean (± SD), n=6

DISINTEGRANT	DISINTEGRATION TIME (s)
Amberlite® IRP 88	618 (11)
Doshion® P 544 DS	291 (8)
Indion® 294	798 (6)
Tulsion® 339	858 (7)

The order of the disintegration times was consistent with the order of the resin water uptake rates in the first 20 seconds (see Figure 8), and in turn with the porosities (see Figure 9). The greater the water uptake rate of the disintegrant in the first 20 seconds, the shorter the disintegration time of the tablets.

SUMMARY AND CONCLUSIONS

The NF monograph for Polacrilin Potassium provides purity and identity tests. However, all the brands compliant with this monograph were found to differ in their performance as disintegrants. The particle size, porosity, swelling ratios and water uptake rates of all the four brands were significantly different which resulted in differences in their performance.

The particle sizes of the disintegrants were significantly different, as were the surface areas, and porosities. The tapped densities also differed significantly. The particle sizes of Amberlite® IRP 88 and Doshion® P544 DS were significantly larger than the other two brands. The difference in particle size did result in differences in intrinsic swelling of the particles with the larger particles exhibiting a lesser swelling ratio. This observation is contrary to the accepted norm that Amberlite® is an effective distintegrant due to its extremely large swelling capacity in aqueous solutions. However, when incorporated into insoluble tablet matrices, its swelling ability may actually impede the penetration of water into the tablet, a phenomenon that is less likely to occur when incorporated into hydrophilic tablet matrices.

The limiting rate for tablet disintegration in the former instance therefore may be the rate of water uptake, as opposed to the extent of swelling in the latter. Hence, the swelling capacity may influence disintegration time differently depending upon the tablet matrix composition. More work needs to be carried out in this area.

The differences in intrinsic swelling among the different brands did not result in significant differences in settling volumes. The differences in the intrinsic swelling of the particles were probably too small to have caused significant differences in their settling volumes. All the four brands probably settled to a very closely packed mass which did not differ in volume.

The brands that have a larger particle size had greater porosities as expected, and the greater porosity resulted in higher rates of water uptake. Higher water uptake rates in the early stages of disintegration, that is, within the first 20 seconds, correlated with shorter disintegration times. Figures 8 and 9 show the correlation of disintegration times with water uptake and porosity respectively. The data from the first 20 seconds was selected solely on the basis of correlation to disintegration time.

At first glance, there does not seem to be any dependence on thermodynamic first principles except for the fact that the ratio of the slopes (steep linear initial portion to the gradually rising later portion) of the curves could possibly be correlated to the disintegration times, with a larger ratio indicative of a lesser disintegration time when incorporated into insoluble tablet matrices.

If that were the case, it would imply a 'tighter' pore size distribution (lesser polydispersity in pore size, and hence broadly equal thermodynamic physisorption potential between pores) in Amberlite® IRP 88 and Doshion® P544 DS than the pore size distributions in Indion® 294 and Tulsion® 339. Future work should therefore also address the homogeneity of pore size distributions in disintegrant excipient powders perhaps by detailed analysis of the BET adsorption curve. It should further be recognized that any predictive model from disintegrant excipient characterization may not be capable of being translated to its behavior when incorporated into tablet matrices due to the changes in pore structure, distribution, homogeniety and, so on, upon compression, as well as, the ability of the disintegrant to modify the mean pore diameter and porosity of the tablet matrix itself (15).

The brands that have finer particle sizes, i.e. Indion® 294 and Tulsion® 339, showed greater water uptake, probably because of their larger surface area. However, this study shows that it was not the extent, but the rate, of water uptake in the early stage of disintegration that correlated with shorter disintegration times for polacrilin potassium.

As discussed earlier, the settling volumes of polacrilin potassium brands were significantly less than those reported for some other commonly used disintegrants. Moreover, the brand to brand variation in the settling volumes of polacrilin potassium was insignificant and does not explain the significant differences in the disintegration times of the tablets.

Thus, it may be concluded that swelling makes a negligible contribution to the mechanism of disintegrant action of polacrilin potassium when incorporated in insoluble tablet mat-rices. The major mechanism that contributes to their disintegration mechanism seems to be wicking and capillary action.

The data presented here indicates that settling volume may not be an appropriate parameter to evaluate the functionality of polacrilin potassium as a disintegrant when incorporated into insoluble tablet matrices. Measurement of the rate of water uptake is a more approp-riate test since it showed differences in the functionalities of the four brands of polacrilin potassium investigated.

It can be concluded that the primary mechanism responsible for the disintegrant action of polacrilin potassium is wicking and tests for measuring particle size, porosity and rate of water uptake can reliably be used to distinguish between the different brands of Polacrilin Potassium NF.

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