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THE SWELLING OF CORE TABLETS DURING AQUEOUS COATING II: AN APPLICATION OF THE MODEL DESCRIBING EXTENT OF SWELLING AND WATER PENETRATION FOR INSOLUBLE TABLETS.

Damrongsak Faroongsarng and Garnet E. Peck*
Department of Industrial and Physical Pharmacy
School of Pharmacy and Pharmacal Sciences
Purdue University, W. Lafayette, IN., 47907.

ABSTRACT

A mathematical model successfully describing the extent of swelling and water penetration for dicalcium phosphate dihydrate(Ditab) tablets is able to be applied to the anhydrous form. The extent of swelling/water penetration behavior exhibited by anhydrous dicalcium phosphate(ATAB) is quite different from that of dihydrate form, which exhibits non-swelling. More water tends to penetrate into ATAB tablets than those tablets prepared from Ditab. The water uptake is coincident to the very large surface tablet porosity.

* To whom correspondence should be addressed.

INTRODUCTION

The simple mathematical model describing extent of swelling and water penetration during thermodynamically quasi-static coating process was developed(1). It is expressed as a linear equation;

$$D = -[\alpha/(1+\varepsilon)]\, l_1 + [\alpha/(1+\varepsilon)]\, l_0 \qquad (1)$$

where D, l_0, l_1, α and ε are the depth of water penetrating into tablets, initial tablet thickness, the remaining dried tablet thickness, swelling and porosity parameters, respectively. The equation was successfully applied for the tablets containing dicalcium phosphate dihydrate as an insoluble filler. The model is then to be expanded to describe other insoluble excipients, particularly an anhydrous form of dicalcium phosphate.

EXPERIMENTAL

Anhydrous dicalcium phosphate is commercially available under the trade name of ATAB. Used as a direct compression excipient, ATAB has typical properties in tableting very similar to those of Ditab(2). The experiment was set up as previously described(1). Ditab(Phone-Poulenc) was replaced by ATAB (Stauffer Chemicals) in such formulations. Five disintegrants, which included corn starch, cross-linked carboxymethyl starch(Primojel, Generi Chem), microcrystalline cellulose(Avicel PH102, FMC Corp.), cross-linked carboxymethyl cellulose(Ac-di-sol, FMC corp.), and cross-linked polyvinyl pyrrolidone(Polyplasdone XL, GAF corp.), were also employed at a 15% w/w concentration level. The t-statistical comparisons were performed among fitted slopes of D-l_1 lines to determine the significance of them.

Ditab and ATAB powders were separately compressed by a Carver press to form 20 mg. flat-faced pellets with a 1/8-inch tooling set. The compression force was controlled at 500 pounds level. Six pellets for each material were

Table 1: Fitted parameters of D vs l_1 plots.

Tablets	Slope(β_1)	Inter-cept(β_0)	r[1]	p-value[2] ($H0:\beta_1=1$)
Ditab, only	1.082	2.419	0.993	0.21
ATAB, only	0.736	1.786	0.947	0.05
ATAB with 15%				
Ac-di-sol	0.943	2.377	0.922	0.78
Corn starch	0.789	1.968	0.976	0.06
Primojel	0.935	2.316	0.956	0.67
Polyplasdone XL	1.060	2.761	0.980	0.60
Avicel PH102	0.904	2.245	0.951	0.54

1 r is correlation coefficient,
2 p-value is based on t-statistic test with null hypothesis of $\beta_1=1$.

employed to determine surface area and total pore volume by Nitrogen adsorption method(Autosorb-1, Quantachrome).

RESULTS AND DISCUSSION

Statistically, the depth of water penetrating into a tablet(D) is linearly correlated with the remaining dried tablet thickness(l_1) for all cases(table 1). It is seen from table 1 that the value of slope of D vs L_1 plot for the tablets made from ATAB only is somewhat less than unity (with significant p-value). The value implies that $1+\varepsilon$ is greater than α, thus, they undergo water penetration as a dominate condition. Figure 1 compares plots of D vs l_1 between Ditab which exhibits non-swelling condition(unity slope) and ATAB tablets.

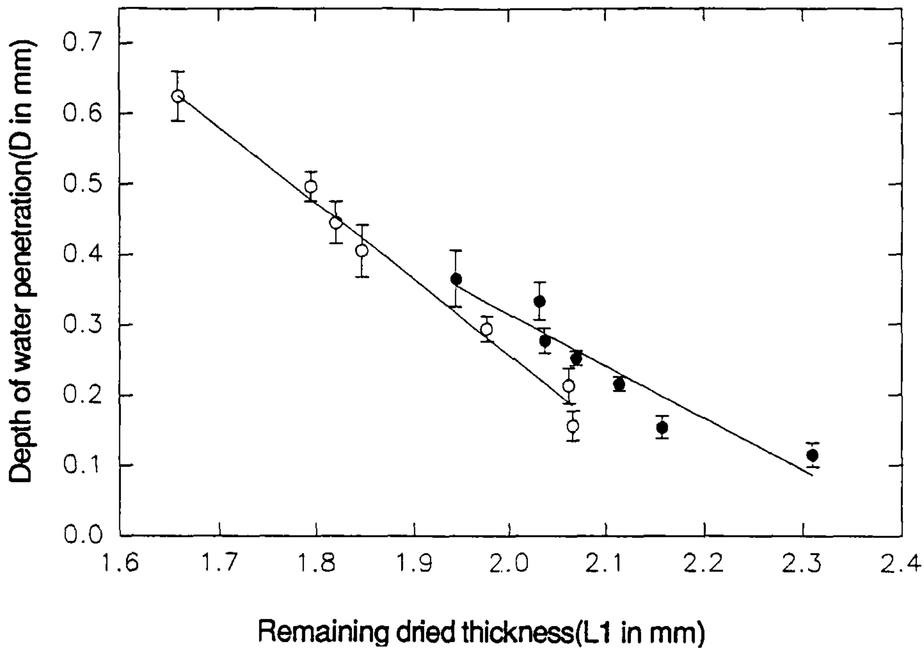

Figure 1: Depth of water penetration-Remaining dried thickness plots compared between dicalcium phosphates tablets of dihydrate form(open circles) and of anhydrous form(filled circles).

The performance of a disintegrant, i.e. the swelling, in ATAB tablets cannot be seen as clearly as that in Ditab tablets(1). For the tests of slopes, no such a case exhibits a significant p-value even in case of tablets containing 15% Ac-di-sol, which shows the most swelling when presence in Ditab tablets(1). It is doubtful that the pore volume of ATAB tablet may be too large for disintegrant volume expansion to macroscopically show the swelling.

To clarify the above discrepancy, pore volumes of Ditab and ATAB tablets were determined. Figure 2 and 3 illustrate the Nitrogen adsorption isotherms of Ditab and ATAB pellets, respectively. Both exhibit Type II isotherms where their pore diameters are larger than micropores(3). Table 2 shows the results of surface area determinations.

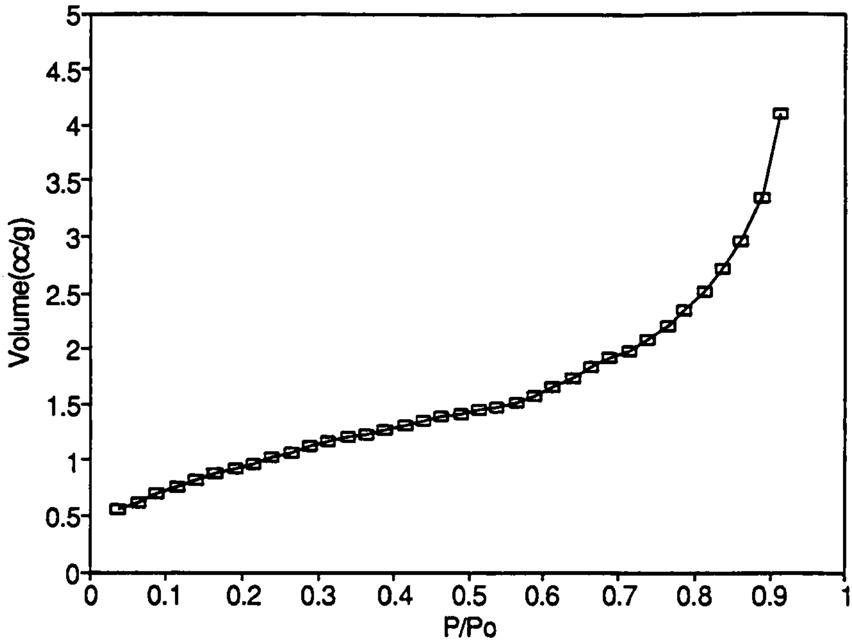

Figure 2: Nitrogen adsorption isotherm of dicalcium phosphate dihydrate(Ditab) pellets (1/8 inches in diameter).

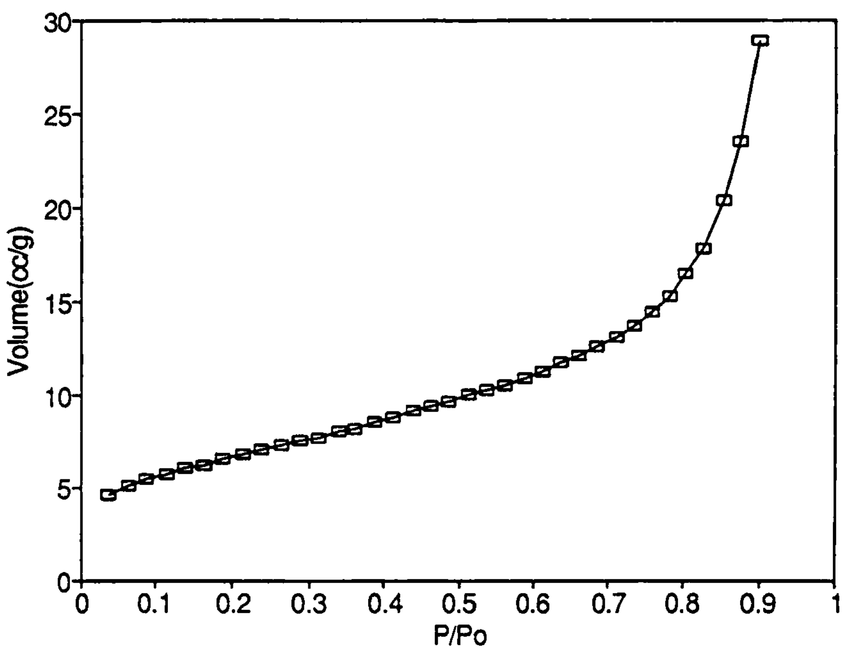

Figure 3: Nitrogen adsorption isotherm of anhydrous dicalcium phosphate(ATAB) pellets (1/8 inches in diameter).

Table 2: Surface area and porosity determinations based on the BET equation.

Material	Ditab	ATAB
Surface area(m^2/g)	3.764	23.410
Total pore volume(cc/g)	0.038[1]	0.168[2]
Porosity(%)[3]	6.44	27.66
Average pore radius(Angstroms)	202.5	143.3

1 Total pore volume for pores less than 1088.7 Angstroms,
2 Total pore volume for pores less than 1033.4 Angstroms,
3 porosity = (pore volume/pellet volume) 100.

It is seen from Table 2 that pellets made from ATAB have considerably greater porosity compared with that of pellets made from Ditab. As seen in Figures 4 and 5, the adsorption and desorption volumes obtained from ATAB pellets are also very much greater than those obtained from Ditab pellets. The average pore radius of Ditab pellets seems to be bigger than that of ATAB. The calculation of pore radii, in these cases, is based on Kelvin equation(4, 5) in which the calculated pore radius is dependent on pressure over a curved surface, i.e., the less radius, the greater pressure is. When it comes to coating, the pressure developed over surface helps pooling the water into the pores. Thus, smaller pore size of ATAB tablets supports the previous evidence. In summary, the results are consistent with the previous discussion.

CONCLUSION

The mathematical model describing the extent of swelling and water penetration is able to be applied to anhydrous dicalcium phosphate tablets showing significant statistical correlations. The swelling performance of a disintegrant such as Ac-di-sol at 15% w/w level cannot be clearly seen for ATAB

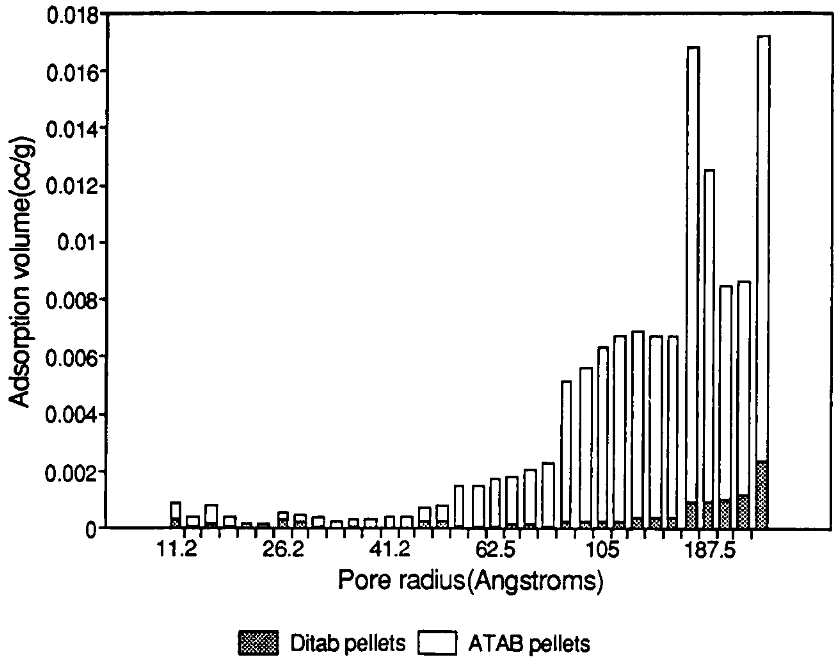

Figure 4: Pore size distributions compared between dibasic calcium phosphate pellets of dihydrate form(Ditab) and of anhydrous form(ATAB) in adsorption range.

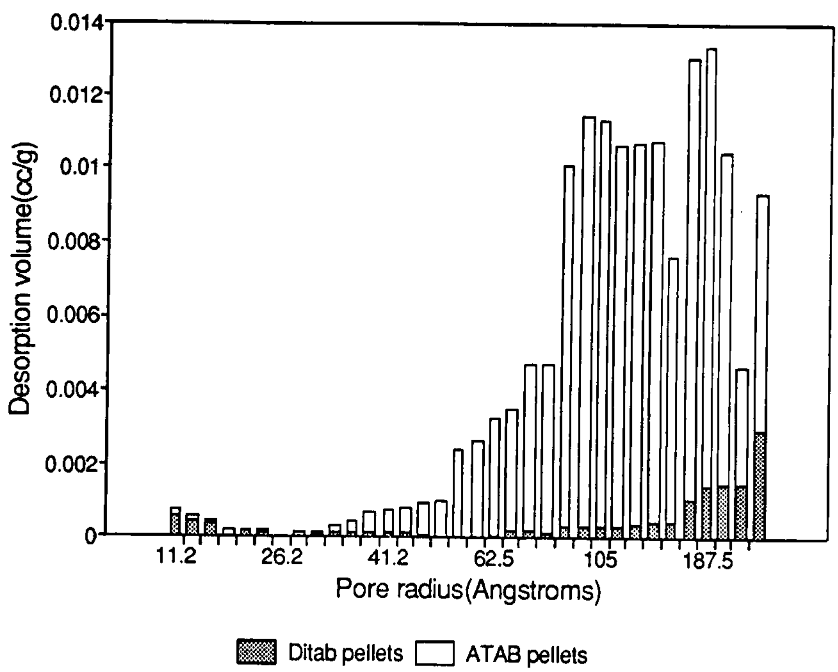

Figure 5: Pore size distributions compared between dibasic calcium phosphate pellets of dihydrate form(Ditab) and of anhydrous form(ATAB) in desorption range.

tablets. The large ATAB tablet porosity may play a significant role in water penetration and disintegrant swelling suppression. This would be important for the preparation of a tablet of satisfactory dissolution or for consideration in aqueous film coating of such a system.

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