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Research Papers

THE ROLE OF PORES IN DISSOLUTION PROCESSES

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SUMMARY

The influence of pores on the dissolution rate of non-disintegrating sodium chloride tablets was investigated. Artificial pores of different diameters were created by drilling in highly compressed tablets. The dissolution rate increase appeared to be dependent on the pore diameter, and was supposed to be caused by an enlarged dissolution surface. By comparison of the – geometry based – predicted dissolution rate increase and the experimental results, the contribution of the pores to the dissolution under experimental conditions could be calculated. The diameter below which the inside of the pores take no part in dissolution, has been estimated by extrapolation at approximately 200 μm.

INTRODUCTION

Irrespective of the fact if one wishes to adhere to a specific theory describing the dissolution of solids, one has to include a proportionality of dissolution rate with the surface available for dissolution. In order to obtain a true estimate of this parameter an estimate of the contribution of pores, present in the dissolving surface, is required. In measuring intrinsic dissolution rates, pores are avoided as much as possible by using high compaction forces. However, in regular tablets porosities up to 20% may be encountered, involving pores of diameters at least up to 50 μm. Little is known how dissolution proceeds from such surfaces.

Although the film theory may well be an oversimplification it is useful in approaching this question. For the dissolution model we thus assume a diffusion layer at the surface having a linear concentration gradient towards the homogeneous bulk. Considering pores of different diameters this leads to the following cases.

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(a) Small pores will be filled up rapidly with a saturated solution, as long as the diffusional pathlength is small in comparison with that in the diffusion layer. This equalizes the dissolving surface with the macroscopic surface as calculated from the tablet dimensions. In this case the dissolution rate should be independent of porosity. Parrott et al. (1955) described this type of behaviour for benzoic acid spheres. Also, dissolution rates for sodium chloride discs complied to this model, with the restriction that the porosity did not exceed 10–15% (de Blaey and van der Graaff, 1977). No data on the pore dimensions were available from these studies, leaving the question of their actual size open.

(b) Larger pores might behave differently, as soon as the diffusional pathlength within the pore becomes comparable or larger than the pathlength in the diffusion layer. In that case a situation might arise in which the diffusion layer might be visualized as being curved within the pores. This would increase the area available for dissolution, and thus the dissolution rate (Armand et al., 1975). Thus the rate would become dependent on the porosity. Our results with sodium chloride discs of 20 and 28% porosity showed such a behaviour (de Blaey and van der Graaff, 1977). Also Wurster and Seitz (1960) showed that the dissolution rate of benzoic acid increased when the 1 mm pores were evacuated prior to dissolution.

The present paper describes the findings of investigations exploring the size of pores taking part according to case (a) and (b), respectively.

MATERIALS AND METHODS

Sodium chloride tablets (9 mm diameter) were used, having porosities between 1.2 and 13.7%. Mean pore diameters, as measured by mercury penetration, ranged from approximately 3 to 35 μm. The highest number is a rough estimate only since with the mercury penetration it is not possible to detect larger ones. The tablets having the lowest porosity were used to create larger pores by using a 15,000 rpm drill. Thus pores were obtained from 500 to 3000 μm wide and 2.0 mm deep. By varying their number, the artificial porosity at each diameter was varied between 0 and 12%. In order to avoid wetting and/or penetration problems the pores were filled with a saturated sodium chloride solution prior to dissolution. For this purpose the tablets were mounted at the bottom of a beaker with one face exposed to the solution. A centrifugal stirrer, as described earlier (de Blaey and van der Graaff, 1977), was used at 80 rpm. This speed was in a range where the plot according to Levich's equation, i.e. the diffusion layer, h, versus the rotation speed, $W^{-1/2}$, provided a straight line, parallel to the theoretical Levich plot for these conditions, which means that in this rotation speed range the dissolution process can be considered as diffusion controlled (Levich, 1962). The dissolution was recorded conductometrically and the rate of dissolution calculated from the initial part of the curves, where there were good straight lines. From electron microscopic observations the tablet surface appeared smooth, i.e. wrinkles and holes with a maximum size of about 2 μm, that are small enough to permit the use of the macroscopic dimensions in calculating the dissolving surface, especially when the existence of a diffusion layer of about 40 μm, as calculated from the Noyes Whitney dissolution rate equation, is assumed.

RESULTS AND DISCUSSION

The dissolution rate is plotted versus the porosity in Fig. 1, showing a linear relation between them. This implies that for the drilled pores the porosity influences the dissolution rate through an increased surface, represented in the slope of the respective lines. *Pores smaller than 30 μm show very little influence of the porosity, if any, indicating that* these pores fill up rapidly with a saturated solution, and behave as solid material during the dissolution process. As can be seen from the plot all lines intersect the Y-axis at the same point, from which the true intrinsic dissolution rate for this compound can be calculated as about 90 mg · cm^{-2} · min^{-1}, by accounting for the surface area exposed.

In Fig. 2 the measured slopes from Fig. 1 have been compared with the maximum value for this slope if the complete surface of the pore would take part in the dissolution exactly as the outside surface of the tablet does. As this would imply that the diffusion layer everywhere has the same thickness, this visualization is hardly realistic from the fluid dynamics point of view, but merely serves as an aid to obtaining an estimate of the extent to which the drilled pores take part in the dissolution process. The theoretical value decreases rapidly with the diameter, showing that the extra contribution of cylindrical pores decreases with their size because of the lower surface/volume ratio. The experimental values cover the theoretical ones in case of large pores, where the fraction F of the pore surface, that contributes to the dissolution process, is equal to 1. Since this fraction decreases with decreasing pore size, the experimental curve shows a maximum. The ratio of both curves represents the F value, from which the actual portion of the pore surface involved in the dissolution may be estimated. This is plotted in Fig. 3.

This plot shows that large pores contribute nearly completely, taking into account the very schematic way of calculating the available surface. These assumptions become less

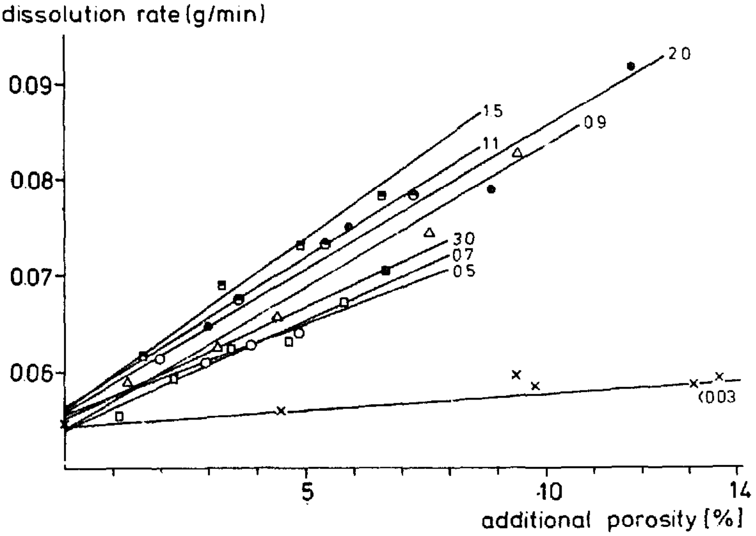

Fig. 1. Dissolution rate of sodium chloride discs, with one face exposed, as a function of the porosity due to drilled pores of varying diameter. Pore diameter from <0.03 mm up to 3.0 mm.

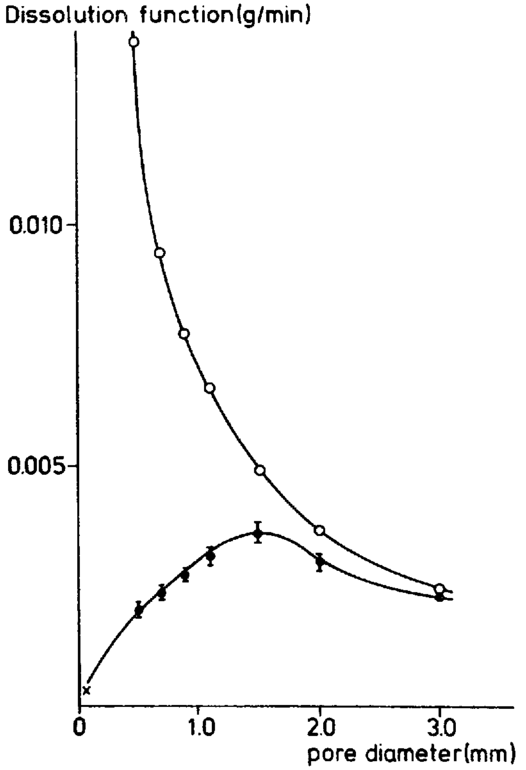

Fig. 2. Dissolution function, (dm/dt) × tablet porosity, of sodium chloride discs with one face exposed, measured for a series of discs having different pore diameters. ○——○, predicted line for the case in which the complete surface of the pores would contribute to the dissolution process; ●——●, experimental data obtained with discs containing artificial, drilled, pores; ×, data point for discs containing pores formed during compression only.

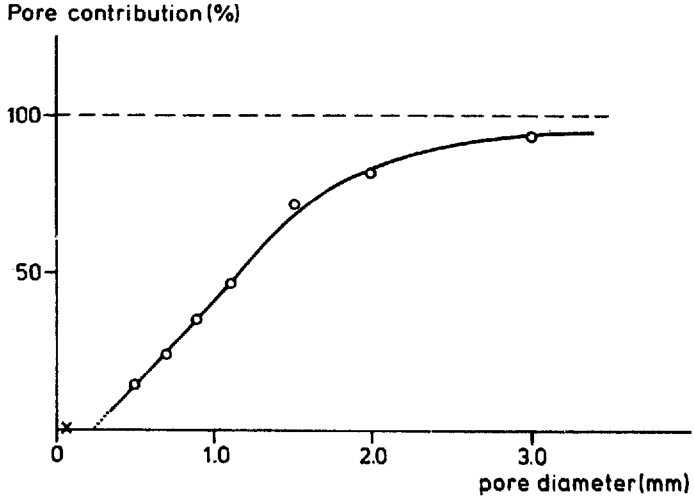

Fig. 3. Percentage of the pore surface, of sodium chloride discs with one face exposed, contributing to the dissolution of a series of discs having different pore diameters. ○——○, data points for discs containing drilled pores; ×, data point for discs containing pores formed during compression only.

and less serious with a decreasing F value; thus by extrapolating the lower branch of the curve to F = 0 a value of around 225 μm is obtained, suggesting that these pores do contribute to the dissolution rate only through their surface lying in the surface of the tablet. This diameter is approximately 5 times the thickness of the diffusion layer, as calculated from the Noyes Whitney dissolution rate equation.

The pores of normally compressed tablets (dimensions 0–30 μm) show F values not quite equal to zero, which may be caused either by the presence of some large pores or by a contribution of the pores between 0 and 30 μm. The latter possibility would indicate that the lower branch of the curve will probably be S-shaped. Nevertheless, it seems that, considering the normal pore distribution in tablets, even large pores will usually be saturated with material, at least for sodium chloride under the stirring conditions studied. This would mean that in measuring intrinsic dissolution rates tablets will not necessarily have to be produced at as high compression forces as obtainable.

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