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THE EFFECT OF PINHOLES ON THE DISSOLUTION BEHAVIOUR OF ENTERIC-COATED ACETYLSALICYLIC ACID TABLETS

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ABSTRACT

A statistically significant number of enteric-coated acetylsalicylic acid tablets were found to fail the USP Drug Release test. It was demonstrated that failure was caused by pinhole defects in the enteric coating. Fluid would enter the tablets through these defects during the acid resistance stage of testing. Poor performance during the buffer stage of testing was attributed to a failure of the core tablets to disintegrate and undergo dissolution because all disintegration mechanisms had already been exhausted. Pinhole defects were observed to exist primarily in the engraved logos on the tablet faces. A switch to plain-faced tablets resulted in a dramatic reduction in dissolution failures.

INTRODUCTION

Enteric coatings are applied to tablets, capsules or pellets to prevent drug release in the highly acidic environment of the stomach and yet release drug under the mildly acidic or neutral conditions found in the intestine. This formulation approach is used to either prevent degradation of drugs unstable at low pH (e.g. omeprazole) or protect the stomach from the irritant effect of the drug (e.g. acetylsalicylic acid).

The enteric-coated acetylsalicylic acid tablet under investigation consisted of a direct-compression core tablet coated with a coloured subcoat and a cellulose acetate phthalate/polyvinyl acetate phthalate enteric coat applied from an acetone/methanol solvent system.

During analytical testing of some production batches of tablets, a statistically significant number of tablets (>2%) were found to swell (Fig. 1) during the acid resistance stage (0.1 N hydrochloric acid, 2 hours) of the USP Drug Release test and to exhibit poor disintegration/dissolution behaviour during the buffer stage (pH 6.8 phosphate buffer, 90 minutes) of testing.

A high incidence of pinhole and bubble coating defects were also observed within the engraved logos on the faces of these tablets (Fig. 2). In an earlier publication (1), it was proposed that these defects create weak points in the film through which fluid can penetrate relatively easily. It was postulated that fluid entering a tablet through such defects during the acid stage of testing would retard dissolution during the buffer stage of testing.

EXPERIMENTAL

In order to study the impact of pinhole coating defects on the dissolution behaviour of tablets, 100 to 150 micron diameter holes were punctured through the enteric coating on tablets from a "good" lot (<2% of tablets swelling during the acid resistance stage of testing) prior to performing the USP Drug Release test. The test was performed using Method B (2) with Apparatus 1 (3) operated at 100 rpm. Drug release was determined by uv spectrophotometry at a wavelength of 265 nm.

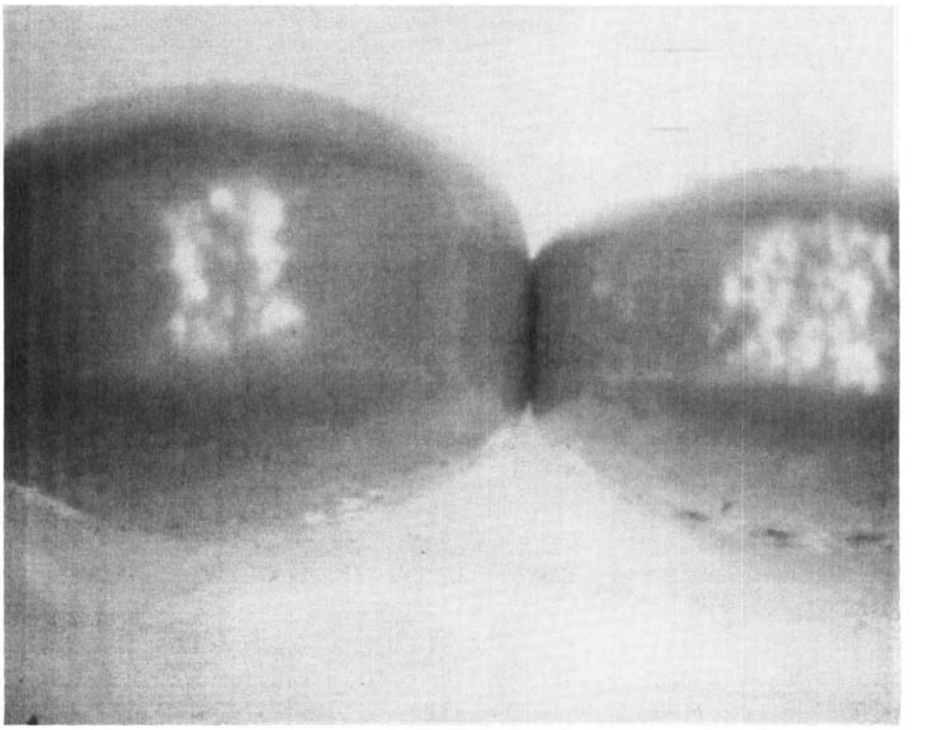

FIGURE 1
Enteric-coated acetylsalicylic acid tablets after the acid resistance stage of testing. Fluid entered the tablet on the left through defects in the enteric coat causing it to swell.

To confirm the role of the engraved logo in producing coating defects, a mixed bed of plain-faced tablets and market-image tablets (containing a logo on each face) was enteric coated in a Wurster-type coater using bottom-spray application. Samples were taken periodically during application and subjected to the acid resistance stage of the USP Drug Release test and the number of tablets showing fluid penetration was determined.

RESULTS & DISCUSSION

When tablets from a "good" lot were tested, they exhibited no swelling during the acid resistance stage of the USP Drug Release test and dissolved readily

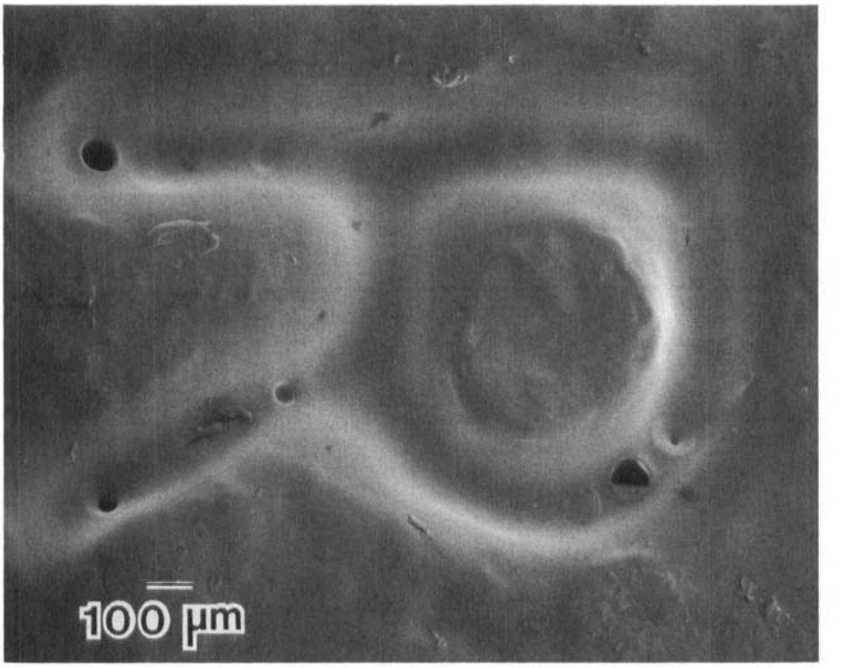

FIGURE 2
Natural pinhole defects in the enteric coating on a typical enteric-coated acetylsalicylic acid tablet.

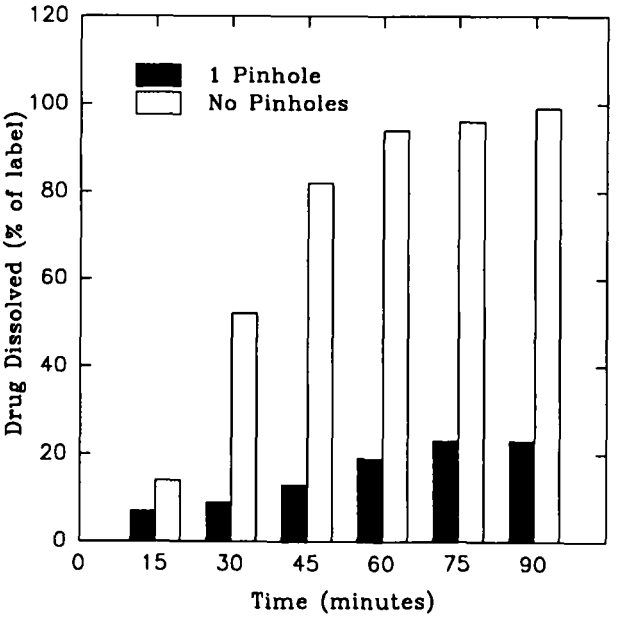

FIGURE 3
Graph showing dissolution values as a function of time, comparing tablets with a single pinhole punctured in the enteric coat and control tablets containing only natural defects in the enteric coat.

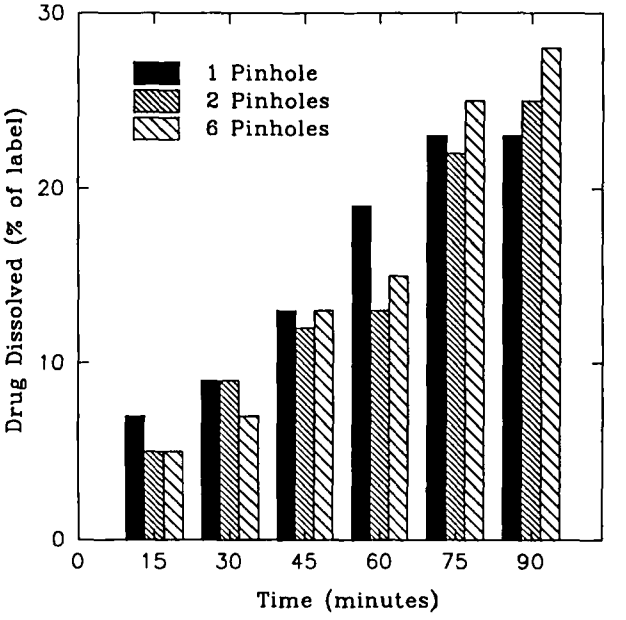

FIGURE 4
Graph showing dissolution values as a function of time, comparing tablets with various numbers of pinholes punctured in the enteric coating.

during the buffer (pH 6.8) stage of the test. Conversely, when pinholes were pierced through the enteric coat, all the tablets swelled in acid and disintegrated poorly in pH 6.8 buffer. Swelling of the tablets during the acid resistance test indicated that disintegrant swelling had taken place. The failure of further disintegration action once the enteric coating was allowed to dissolve in buffer indicated that the disintegration mechanisms had probably been exhausted. Figure 3 illustrates that with a single pinhole, the dissolution result (Q=75%, 90 minutes) was reduced dramatically. Multiple pinholes (Fig. 4) resulted in the same depressed dissolution profile. On the other hand, when the acid resistance stage of testing was bypassed, tablets with pinholes were found to demonstrate good disintegration/ dissolution in buffer possibly due to the simultaneous dissolving of the enteric coat and the swelling of the disintegrant.

Figure 5 illustrates the striking difference in performance in the acid resistance test between tablets with a logo and those without. The amount of film coating

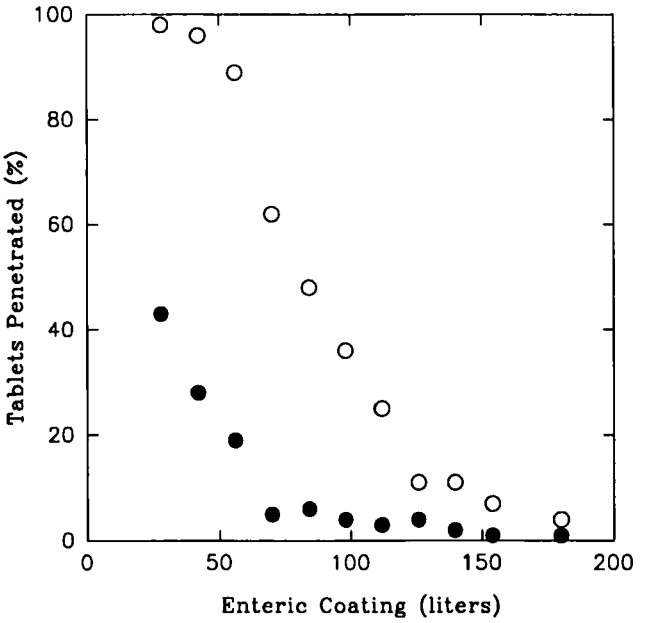

FIGURE 5
Graph illustrating the percentage of tablets in a test sample showing fluid penetration during the acid resistance test as a function of the quantity of enteric coating applied. Compared are tablets with an engraved logo on both faces (O) and plain-faced tablets (●).

solution required to cover defects in the enteric coating was found to be considerably less for tablets without logos. This clearly demonstrates the role of the logo as a source of enteric coating defects. As discussed by Down (1), logos act as protected areas, free from tablet-to-tablet abrasion, and allow the accumulation of bubbles formed during spray application of coating solution. These bubbles can set within the film or partially collapse to form pinholes.

CONCLUSIONS

It is concluded that pinhole defects are created in the enteric coating on acetylsalicylic acid tablets during the film coating operation, particularly in the engraved logos. Fluid penetrates through these defects into the tablet core

during the acid resistance stage of the USP Drug Release test, exhausting the disintegration mechanisms and causing the tablets to swell. As a result, tablets fail to disintegrate during the buffer stage of testing, resulting in poor dissolution. Removal of the engraved logo (with off-set ink printing for branding) results in a dramatic reduction in dissolution failures with the possibility of reducing the amount of enteric coating applied to the tablets.

ACKNOWLEDGEMENTS

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