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RELEASE OF A LOW DOSE WATER SOLUBLE MEDICINAL AGENT FROM INERT WAX MATRIX TABLETS

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ABSTRACT

Directly compressible wax matrix tablets have been developed for a low dose medicinal agent (Chloropheniramine maleate). A mixture of castor wax NF and Hydrogenated Vegetable Oil NF, was optimized in the ratio of 50:50 as matrix based on their bulk density and particle size distribution and compression properties The compression properties indicated that the increase in compression forces resulted in a tablet of higher hardness up to 8 Kp. However further increase in compression forces resulted in the decrease in hardness and capping was apparent.

The result of dissolution studies indicated no significant effect of hardness and tablet shape (Round and rectangular shaped) on the dissolution properties of wax matrix tablets. A plot of percent drug released various square root of time exhibited a linear relationship. The release rates of CPM from wax matrix tablets were found to be independent of the rotational speed of paddles between 50-75 RPM. From these results, the release mechanism of CPM from wax matrix tablets appears to be primarily diffusion controlled rather than matrix erosion.

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INTRODUCTION

Sustained release dosage forms have been known for more than two decades (1-4). The importance of such dosage forms came from the advantage of prolonged plasma-drug concentration resulted from the controlled release of the drug(5). Such dosage forms have been developed for many medicinal agents using different concepts (6-10). The primary objective of this investigation was to develop a directly compressible wax-matrix tablets using a low dose water soluble drug, chlorpheniramine maleate (CPM).

MATERIALS AND METHODS

Preparation of Wax-Matrix Tablets: The wax matrix tablets were prepared from a physical blend consisting of approximately 52% wax mixture, 42% diluent (Dipac, Amstar Inc., USA), 3% lubricant system (Talc, Cab-o-sil and magnesium stearate; Sigma Chemical Corp., USA) and 3% CPM (Sigma Chemical Corp., USA). Homogeneous mixing was accomplished by blending all ingredients into a Hobart mixer for 30 minutes. The wax ratio of 50:50 (Castor Wax: Luberitab) resulted in good flow and compression properties and was used throughout this investigation. The blends were compressed at several different pressures using a hydraulic press (Carver Press, Loomus Engineering and Manufacturing Company, USA) and Stokes B-2 Tablet Press was also used to compress 3/8 inch round and 9/16 x 3/16 inch rectangular tablets.

Dissolution Studies: CPM release studies were carried out using USP Dissolution Apparatus II equipped with paddles. Each tablet was placed in a 1000 ml dissolution vessel containing 900 ml of 0.1N hydrochloric acid. The amount of drug released was quantitatively measured spectrophotometrically (wavelength 262 nm and $E_1\%$ = 2200).

RESULTS AND DISCUSSION

Effect of Compression Pressure on Tablet Hardness: When tablets were compressed using Carver Press, fitted with a 3/8 inch round

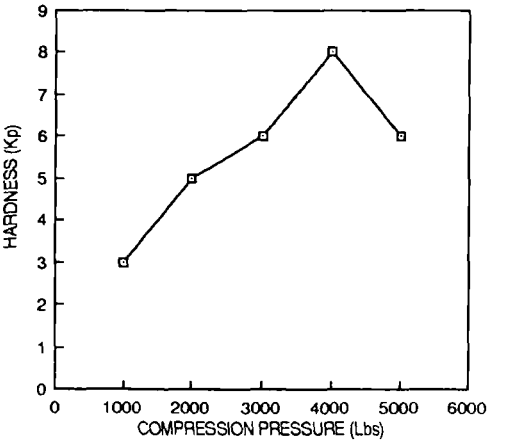

FIGURE 1

A Plot of Compression Pressure Versus Tablet Hardness, demonstrating the limit of Compression for the Wax Matrix Physical Blend.

punch and die set, at pressures between 1000-5000 lbs., the tablet hardness increases from 3 to 8 Kp. At applied pressures of 4000 lbs. and above, the tablet started to cap and at a pressure of 5000 lbs., tablets showed a lower hardness, 6Kp. (Figure 1). Results indicate that the compressibility limit of wax matrix physical blend is reached at a pressure of 4000 lbs. Further increase in applied pressure probably resulted into particle fracture leading to capping and lamination.

Effect of Tablet Hardness on Release Properties: The wax matrix tablets containing 12 mg of CPM were collected at three different hardness values (4,6 & 8 Kp). Results of dissolution studies (Figure 2) indicated no significant effect of hardness on CPM release from tablet matrix. These results may be explained based on the results reported by Foster et al (4) in terms of tortuosity. In addition, the dissolution rate of the wax matrix tablets (both round and rectangular shaped, tablet weight 385 mg) were found to be practically the same. Results of dissolution studies (Figure

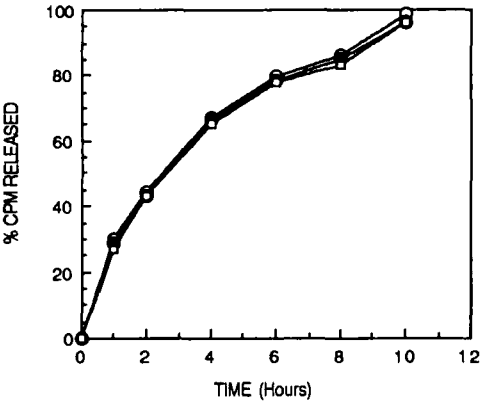

FIGURE 2

Dissolution Profile of CPM from Wax Matrix Tablets, prepared at Hardness --o-- 4Kp,--●-- 6Kp, --■-- 8Kp.

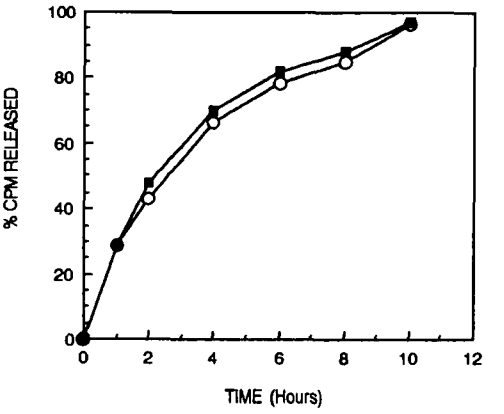

FIGURE 3

Comparative Dissolution Profiles of CPM from --O-- Round and --■-- Rectangular Wax Matrix Tablets.

3) show about 20% faster rate of dissolution for the rectangular tablets as compared to round tablets. This difference in dissolution rate is comparable to the difference in their surface area (calculated surface area of round tablets 0.33 sq. inches and rectangular tablets 0.40 sq. inches). These results further

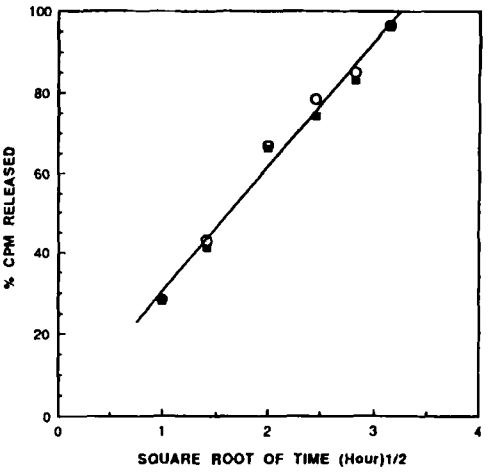

FIGURE 4

A Plot of Percent CPM Released from Wax Matrix Tablets versus Square Root of Time, --O-- Round Tablets, --■-- Rectangular Tablets.

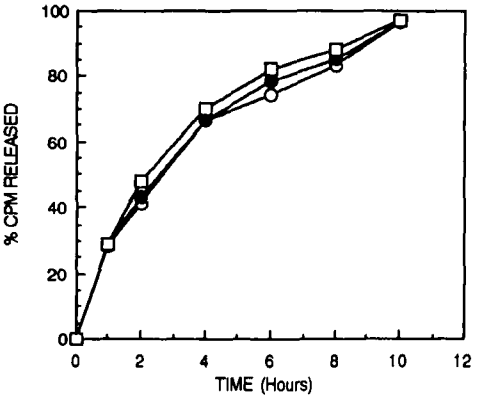

FIGURE 5

Comparative Dissolution Profiles of CPM from Wax Matrix Tablets at --O-- 50RPM, --●-- 60RPM and --□-- 75RPM.

suggest that the porosity and tortuosity of the wax matrix tablets regardless of the shape remained practically unaltered.

When the dissolution data of round tablets and rectangular tablets were plotted according to Higuchi equation (1) , a linear

plot was obtained in both cases (Figure 4). In addition, the line nearly passed through the origin. This may be fortuous or perhaps, the initial release from the tablet surface may have compensated for the absence of lag time. Results of this study indicate that the release of CPM from the wax matrix tablets is primarily via diffusion mechanism. In addition, the fact that the release profile of CPM from wax matrix tablets was practically unchanged at 50, 60 and 75 RPM (Figure 5), further support the diffusion controlled release of CPM from the wax matrix tablets.

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