Investigation of Drug Release from Carnauba Wax Matrices: A Case Study of Propranolol Hydrochloride

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A study was carried out to assess the effect of carnauba wax particle size on sustained release characteristics, the effect of drug loading on release and the kinetics of propranolol hydrochloride release from carnauba wax matrices.

The results obtained showed that small particles (180 – 250 μm) of carnauba wax had superior release on sustaining characteristics than larger particles (> 250 μm). Drug release from small particles was best explained by either the Higuchi mechanism or first order kinetics. In general, as particle size increased, zero order kinetics seemed to contribute to the release mechanism. There was also an increase of drug release as the drug loading was increased. This increase in drug release was probably due to increased porosity.

Key Words: Carnauba wax, sustained release, particle size and kinetics.

INTRODUCTION

Carnauba wax is widely used as an additive in cosmetics, certain foods stuffs and pharmaceutical formulations. When carnauba wax is used alone or in combination with other ingredients it can form matrices that release drug by diffusion in a sustained release fashion [1-6]. The mechanism of drug release from carnauba wax-based matrices seems to be affected by additional ingredients added to the matrix system. Tableted microcapsules of carnauba wax and beeswax have been shown to release drug in a prolonged manner according to first order kinetics [5]. In another study, a matrix system made from carnauba wax and Eudragit L released drug by a combination of a diffusion – erosion mechanism [7].

Therefore this study was aimed at assessing the effect of carnauba wax particle size on sustaining release characteristics, determining the effect of drug loading on drug release and investigating the kinetics of drug release from carnauba wax matrices with respect to propranolol hydrochloride.

EXPERIMENTAL MATERIALS

Carnauba wax was the basic sustained release matrix material. It was supplied by Croda Chemical Company (Harare, Zimbabwe). Propranolol hydrochloride (Varichem Pharmaceutical Company, Harare, Zimbabwe) was used to evaluate the release characteristics of the matrices.

METHODS

Tablet Preparation

Carnauba wax flakes were pulverized using a mortar and a pestle. The resulting powder was sieved through a series of test sieves of varying mesh to yield the four particle size ranges namely: 710 – 500 μm, 500 – 355 μm, 355 – 250 μm, and 250 – 180 μm. Sieved wax powder was then dry mixed with the drug (propranolol hydrochloride). The carnauba wax – propranolol hydrochloride mixtures were directly compressed on a single punch manually operated Erweka tablet machine (Type EK 0, G.m.b.H, Germany) equipped with 9 mm flat faced punches. Tablets (200 mg) were prepared by manually compressing 200 mg of the one sample (carnauba wax – drug samples). The drug content ranged from 20 – 40 % w/w while tablet strength range was 6 – 6.5 kN.

Dissolution Studies

Dissolution evaluation was carried out using the rotating basket as specified in the USP [8]. The dissolution medium was distilled water. Analysis of the released drug was carried out

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using a UV-visible spectophotometer (Shimadzu, UV 1601, Japan) at 307 nm.

RESULTS AND DISCUSSION

Student t – tests were carried out on some of the data obtained. The results were evaluated at the 5 % significant level (p = 0.05). The calculated t values (t_{cal}) and the statistical table's t-value (t_{tab}) at the appropriate degrees of freedom were also considered.

The effect of particle size on drug release from carnauba wax is summarised in figure 1. For the first 1.5 h matrices made from three particle size ranges (250 – 355 μm, 355 – 500 μm and 500 – 710 μm) had comparable sustained release characteristics. After 1.5 h, matrices containing the 355-500 μm particle size range had inferior release relative to the other two matrices. These latter two matrices appear to have the same sustained release characteristics of approximately 4 h.

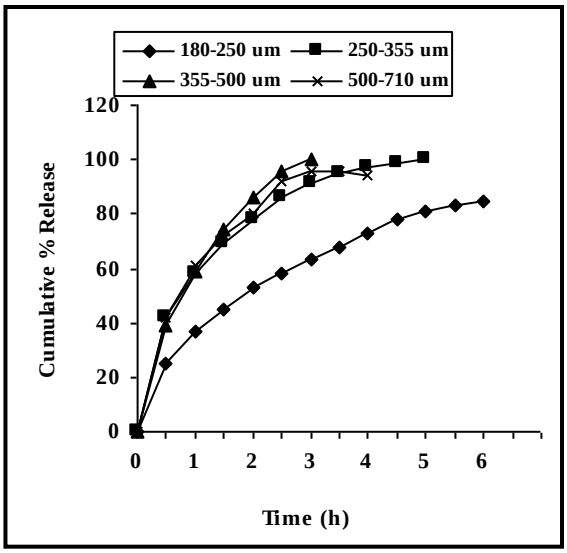

Figure 1 : Effect of Particle Size on Propranolol Hydrochloride (20%) Release from Carnauba Wax Matrices

However, the smaller particles (180 – 250 μm) produced compacts that had superior sustained release characteristics compared to compacts made from the rest of the larger particles.

The effect of drug loading on release is shown in figure 2. At high drug loading (40 % w/w) release was faster than at 20 % w/w. This was probably due to higher porosity of the matrix at high drug loading than at low drug loading.

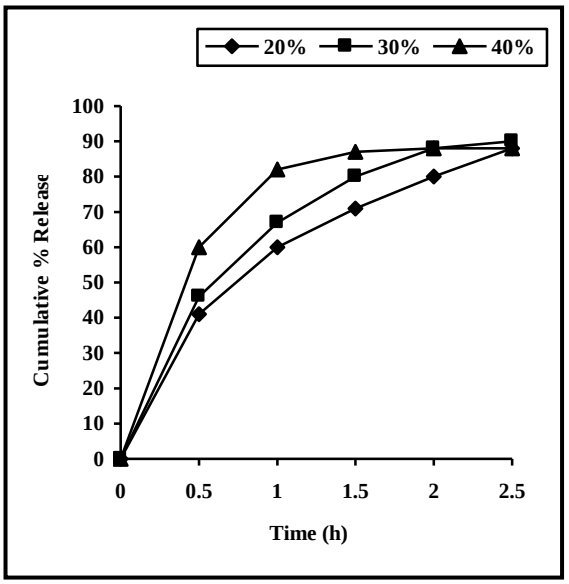

Figure 2 : Effect of Drug Loading on Release from Carnauba Wax Matrices (Particle Size = 500 – 710 microns)

The summary of the release kinetics from matrices made of the various particle size ranges is recorded in table 1. The correlation coefficient serves as a good indicator of the mechanism that best explains drug release from the various matrices. The Higuchi mechanism or first order kinetics could explain drug release from the 180 – 250 μm matrixes (t_{cal} = 0.413, t_{tab} = 2.776, p = 0.05). Zero order kinetics seemed to play no role in the release mechanism from this particular size range ($t_{cal} \geq 12.56$). However, zero order kinetics, the Higuchi mechanism or first order kinetics could explain drug release from the 250 – 355 μm and 500 – 710 μm matrices ($t_{cal} \leq 0.939$, $t_{cal} \leq 1.668$, respectively). The Higuchi mechanism best explained drug release from compacts made from the 355 – 500 μm particle size range ($t_{cal} \geq 3.948$).

CONCLUSION

Small particles (180 - 250 μm) of carnauba wax produced matrices that had the best drug release sustaining characteristics. The Higuchi mechanism or first order kinetics could be responsible for drug release from such matrices.

In general, as particle size increases, zero order kinetics seems to play a role in the drug release mechanism. Increasing drug loading in carnauba wax matrices increases release rate probably due to high porosity.

Table 1: Release Kinetics from Carnauba Wax Matrices Containing 20 % w/w Propranolol Hydrochloride

Particle Size (μm)	Correlation Coefficient (γ)		
	Zero Order Kinetics	**First Order Kinetics**	**Higuchi Mechanism**
180 – 250	0.97777 ± 0.00175	0.99705 ± 0.00200	0.99758 ± 0.00097
250 – 355	0.92666 ± 0.05187	0.96209 ± 0.03976	0.96882 ± 0.03358
355 – 500	0.98149 ± 0.00460	0.97947 ± 0.00081	0.99709 ± 0.00150
500 – 710	0.92683 ± 0.03513	0.97763 ± 0.01853	0.96712 ± 0.02272

n = 3

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