East and Central African Journal of Pharmaceutical Sciences
Vol. 7(2) 24-26

Investigation of Synthetic Spermaceti Wax as a Potential Oral Sustained Release Drug Delivery System

R.T.J. CHIGWANDA * AND A. KUUDZADOMBO

Department of Pharmacy, College of Health Sciences, University of Zimbabwe, Box MP 167, Mt Pleasant, Harare, Zimbabwe

The present study was aimed at investigating drug release from spermaceti wax matrices. Materials such as ethylcellulose and methylcellulose were incorporated into the spermaceti wax matrices and release was evaluated.

Spermaceti wax can form matrices that release drug in a sustained release fashion. Higuchi or first order release kinetics were found to explain drug release from spermaceti wax, spermaceti wax-ethylcellulose and spermaceti wax-methylcellulose matrices. However, ethylcellulose and methylcellulose enhanced release rate from spermaceti wax matrices. Spermaceti wax matrices can be used to provide drug delivery systems with prolonged action. Release rate from such systems can be regulated by incorporation of materials such as ethylcellulose and methylcellulose.

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

INTRODUCTION

Sustained release formulations slow down the release rate of a drug thus increasing its duration of action. They reduce the frequency of drug administration and this is a big advantage to the patient compliance. Drug release from oral sustained release matrices can be evaluated by zero order kinetics (equation 1), first order kinetics (equation 2), or the Higuchi mechanism (equation 3).

$$Q = kt \quad \ldots\ldots (1)$$
$$\text{Log}(100\% - Q) = kt \quad \ldots\ldots (2)$$
$$Q = kt^{0.5} \quad \ldots\ldots (3)$$

Where Q is the amount of drug released at time t and k is a constant.

Materials used to prepare oral sustained release devices can be either hydrophilic or hydrophobic substances. Hydrophilic substances include materials such as gum tragacanth and agar [1]. Hydrophobic materials can be substances such as hydrogenated vegetable oils [2] and glycerol monostearate [3]. Synthetic spermaceti wax (known also as cetyl esters wax) can be classified as a hydrophobic matrix material [4]. In one study [5], synthetic spermaceti wax has been proposed as a suitable component of ophthalmic gelatine – based, controlled release delivery matrix. In this study prolonged release of pilocarpine was achieved through pharmaceutical modification of the device by embedding cetyl esters wax retardant in the pores. The device released drug via zero order kinetics for up to 5 hours. Qiu *et al.* [6] prepared a patented tablet for controlled release, which might have contained spermaceti wax. The tablet had a matrix layer of active agent embedded in non–swelling, non–gelling hydrophobic matrix. This matrix could well have been spermaceti wax since it has such characteristics. The tablet also had a first barrier layer laminated to a single face of the matrix layer and an optional second barrier layer laminated to the opposite face of the matrix layer. This is rather a complicated device.

This study was aimed at preparing simple matrices of synthetic spermaceti wax and analysing their release kinetics. An attempt was also made to add other excipients to the spermaceti wax matrix and investigate the release effects.

MATERIALS

Spermaceti wax was the basic sustained release matrix material and it was obtained from Croda Chemical Company, Harare, Zimbabwe.

* Author to whom the correspondence may be addressed

Sodium salicylate used to evaluate the release characteristics of the various matrices was from Saarchem Private Limited Company, Krugersdorp, South Africa.

Ethylcellulose (a primarily hydrophobic material added to the spermaceti wax basic sustaining release matrix so as to evaluate release effects) and methylcellulose (a principally hydrophilic material that was also added to the spermaceti wax matrix so as to evaluate release effects) were both obtained from Sigma Chemical Company, St Louis, USA.

METHODS

Preparation of the Matrix Materials and the Tablets

The drug, sodium salicylate, was added to the molten spermaceti wax and stirred until cold. Where methylcellulose or ethylcellulose were incorporated, they were first mixed with the drug and then added to the molten spermaceti wax. The resulting mixtures were then weighed into samples so as to obtain tablets of 250 mg upon on compaction. The samples were then individually manually compressed into tablets using a single punch Erweka type EKO tableting machine (Heusenstamm, Western Germany) equipped with 9 mm flat faced punches. A compaction force of 7 units was used for all the tablets prepared. The drug constituted 30 % of the tablet weight. The ratio of ethylcellulose or methylcellulose to spermaceti wax was kept constant at 1:1.

Dissolution Studies

Evaluation of release characteristics was carried out using the BP (2001) rotating basket dissolution test apparatus (VanKel, model 10 – 1100, North Carolina, USA). Each 250 mg tablet (drug content approximately 75 mg) was placed in the dissolution vessel containing 1000 ml of distilled water maintained at 37 ± 0.5 °C and stirred at 50 rpm. Samples were collected at 15 min intervals and replaced into the dissolution vessel after drug concentration evaluation. The concentration was determined spectrophotometrically (Shimadzu, UV1601, Japan) at 296 nm.

RESULTS AND DISCUSSION

Spermaceti wax matrices were found to release drug in a sustained release fashion for over 3.5 hrs. The matrices produced were monolithic and remained intact post dissolution.

The effect of the type of matrix on drug release is shown in figure 1. Spermaceti wax on its own had the best sustained-release characteristics. Ethylcellulose although hydrophobic probably disrupted the spermaceti wax matrix, increasing porosity and hence release. Tablets made from spermaceti wax and methylcellulose tended to swell when placed in the dissolution medium. This was due to the fact that methylcellulose is hydrophilic and forms colloidal dispersions in aqueous environment. Hence it increased porosity and decreased the tortuosity of the matrix. The overall result was an increase in drug release rate.

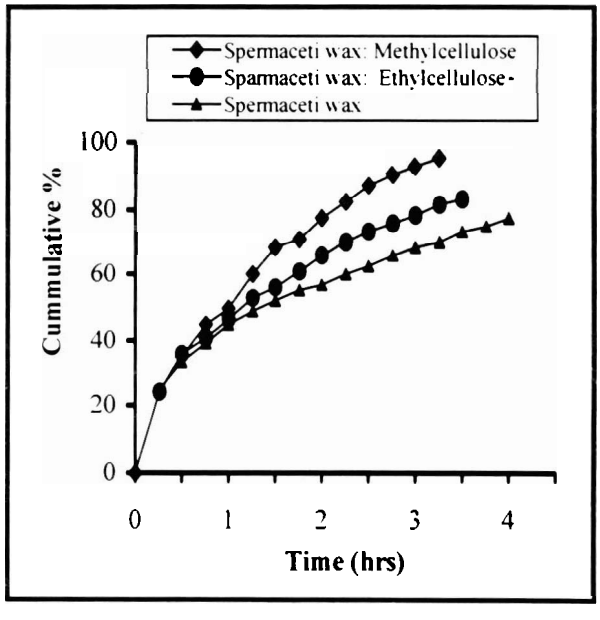

Figure 1: Effect of type of matrix on sodium salictlate release

The release data from the 3 different matrices (spermaceti wax, spermaceti wax-methylcellulose and spermaceti wax-ethylcellulose) were fitted into zero order, first order and Higuchi

Table 1: Release Kinetics of the arious Matrices Prepared (n = 3)

FIRST ORDER KINETICS	
Matrix Type	**Correlation Coefficient**
Spermaceti wax	0.99427 ± 0.00355
Spermaceti wax: Ethylcellulose	0.99251 ± 0.00132
Spermaceti wax: Methylcellulose	0.99521 ± 0.00338
ZERO ORDER KINETICS	
Matrix Type	**Correlation Coefficient**
Spermaceti wax	0.97880 ± 0.00163
Spermaceti wax: Ethylcellulose	0.96570 ± 0.00417
Spermaceti wax: Methylcellulose	0.99112 ± 0.00024
HIGUCHI KINETICS	
Matrix Type	**Correlation Coefficient**
Spermaceti wax	0.99750 ± 0.00184
Spermaceti wax: Ethylcellulose	0.99126 ± 0.00194
Spermaceti wax: Methylcellulose	0.99818 ± 0.00087

mechanism equations (equations 1–3) and the various correlation coefficients obtained are shown in table 1. Student t tests were carried out on the data and results were evaluated at the 5 % level. The calculated t values, t_{cal}, and the t values from the statistical table, t_{tab}, at the appropriate degrees of freedom are quoted in the text. The Higuchi or first order kinetics could be used to explain drug release from spermaceti wax, spermaceti wax-ethylcellulose and spermaceti wax-methylcellulose matrices (t_{cal} = 1.398, 0.922, and 1.473 respectively, t_{tab} = 2.776). Zero order kinetics appeared to have no significant role in drug release in all the matrices prepared

CONCLUSIONS

Spermaceti wax can form compacts with sustained release characteristics. Higuchi or first order kinetics can be used to explain drug release from such compacts. Adding materials such as ethylcellulose or methylcellulose to spermaceti wax matrices does not improve the release kinetics. However, such materials enhance the release rate from such matrices. Such spermaceti wax matrices can be used to prepare prolonged drug delivery formulations for patients. Release rate of such devices can be regulated by the incorporation of materials such as ethylcellulose and methylcellulose.

ACKNOWLEDGEMENTS

The researchers would like to thank the Research Board of the University of Zimbabwe for sponsoring this research.

REFERENCES

[1] R.T.J. Chigwanda and I. Pfaira, *East & Centr. Afr. J. Pharm. Sci.* 2 (1999) 16 – 19.

[2] R.T.J. Chigwanda and J.N. Staniforth, *East & Centr. Afr. J. Pharm. Sci.* 3 (2000) 49 – 51.

[3] R.T.J. Chigwanda and T. Zinyeka, *East & Centr. Afr. J. Pharm. Sci.* 4 (2001) 55 – 58.

[4] P.J. Weller, Cetyl esters wax in *Pharmaceutical Excipients*, 2002.

[5] S.R. Nodkarni and S.H. Yalkowsky, *Pharm. Res.*, 10 (1993) 109 – 112.

[6] Y. Qiu, J.S. Trivedi, S.L. Graham, K.M. Flood and S.L. Krill, Patent No. 6033685, 2000.