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COMMUNICATION

Effect of Polysorbates on Drug Release from Wax Matrices

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ABSTRACT

The purpose of this study was to investigate the effect of various types and amounts of polysorbates on potassium chloride release. Potassium chloride, which is a highly water-soluble model drug, was embedded into wax (containing surfactants) to produce a sustained-release dosage form. Various kinds of polysorbates were chosen as surfactants to control the dissolution profile. The release of the model drug was tested by rotating paddle method of USP 23 and the dissolution process was characterized by the Weibull distribution. The surface tension of the aqueous solutions of polysorbates was determined by a computer-controlled Sigma 70 tensiometer.

The application of polysorbates in more than 2% concentration did not alter either the release rate of the embedded potassium chloride, or the surface tension values of the aqueous solutions. The results of this study allow the determination of the optimal concentration of polysorbates in the case of the potassium chloride release.

INTRODUCTION

Several pharmaceutical investigations were carried out to develop new types of sustained-release solid oral dosage forms and controlled-release drug delivery systems (1). The embedding of a drug into lipophilic coating material is often applied to ensure sustained or slow release for a formulation containing a highly/freely water-soluble drug. The release mechanism of the embedded drug is diffusion- and/or erosion-controlled type (2). The wax or other waxy-type materials are commonly used for melt coating (3-5).

The addition of polysorbates is often applied to modify the release rate of potassium chloride from wax

matrix (6). Hemolytic effect of non-ionic surfactants may occur (7), therefore it is essential to avoid their application over a certain concentration range.

MATERIALS

Potassium chloride of USP 23 grade was selected as a highly water-soluble model drug. White beeswax, USP 23 grade, the base material of the matrix purchased from the Fluka Chemie AG (Buchs, Switzerland), and polysorbate 20, 40, 60, and 80, USP 23 grade, were chosen as non-ionic surfactants.

METHODS

Sample Preparation

The thermosoftening matrix material was filled into Erweka equipment (type SG 3/W, Erweka GmbH, Germany). The temperature-regulated container was heated to 70°C (±1°C). Constant stirring was applied (30 rpm) until the wax was completely molten. The crystals of the model drug together with the various amounts of polysorbates were mixed into the molten mass. After 10 min of homogenization, the mixture was filled into hard gelatin capsules before it congealed to form a skeletal sustained-release dosage form.

Surface Tension Determination

Aqueous solutions of varying concentrations of each polysorbate polymer were prepared by dissolving an aqueous quantity of polymers, accurately weighed into 100 ml of distilled water. The surface tension of varying concentrations of each polysorbate was determined after equilibrium at 20°C for 1 hr, and applying the Du Nouy ring method of a computer-controlled tensiometer (KSV Sigma 70, R. Braumann GmbH, Munich, Germany).

Dissolution Study

The release of the model drug was studied using rotating paddle method of USP 23 in a Pharmatest PTW2 dissolution tester (Pharmatest Apparatebau GmbH, Hainburg). The amount of the released potassium chloride was continuously followed by a digital pH meter (Radelkis OP 211/1, Budapest), using a chloride-selective electrode (Radelkis OP-CI 7111P type).

Surface Morphology Study

The surface morphology of the specimens was studied by scanning electron microscope (JSM-25, Jeol, Japan) after gold vacuum coating.

RESULTS AND DISCUSSION

For the characterization of the dissolution profile of various matrix samples, the Weibull distribution was applied (8,9) in the following form:

$$M_t/M_\infty = 1 - \exp\{-[(t - t_0)/\tau_d]^\beta\}$$

where M_t = the dissolution (%) at time t (min), M_∞ = the dissolution (%) at infinite time, t_0 = the lag time (min) of the dissolution, β = shape parameter of the curve, τ_d = the time when 63.2% of M_∞ has been dissolved.

The computer software package TableCurve 3D (Jandel Scientific, Belgium) was applied for the nonlin-

Table 1

Dissolution Kinetic Parameters of Potassium Chloride Calculated by the Weibull Distribution (Coating Level of the Samples 25%)

Surfactant	Concentration (%)	β Shape Parameter	τ_d Value (min)	t_{lag} (min)	Coefficient Correlation
	0	0.8099	84.1	0.3	0.9911
Tween 20	1	0.7662	31.6	1.3	0.9979
	2	0.8250	30.4	0.1	0.9963
	10	1.2597	27.4	0.0	0.9968
Tween 40	1	0.8264	46.7	0.2	0.9945
	2	0.8780	38.9	0.0	0.9937
	5	0.8948	35.9	0.0	0.9903
	10	0.9251	35.2	0.1	0.9948

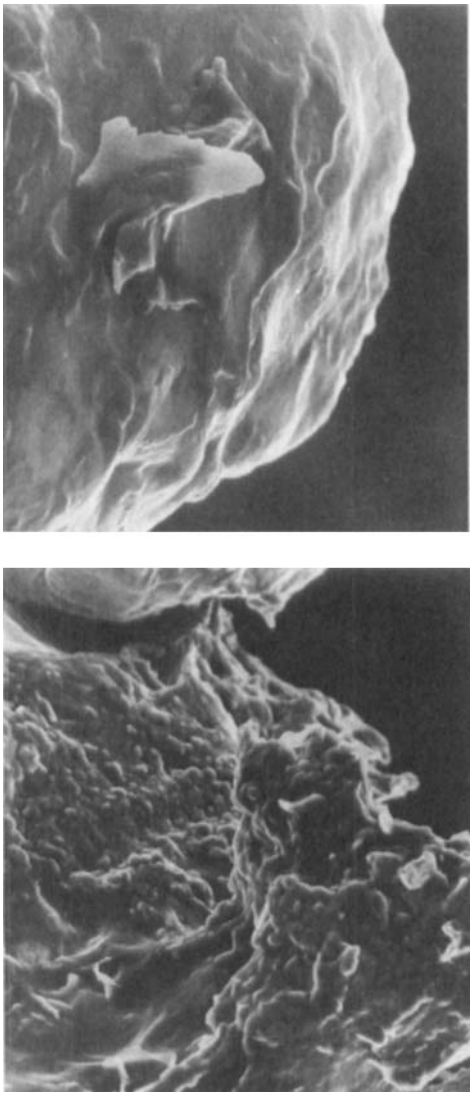

Figure 1. SEM (×1500) photos of matrices (a) without polysorbate and (b) with 1% polysorbate 20.

ear parameter estimation and for the surface fitting. Table 1 summarizes the estimated dissolution kinetic parameters of potassium chloride matrix samples containing various types and amounts of polysorbates. The different β values refer to the different porosities of the samples caused by pore-forming effect of polysorbates.

Figure 1 also demonstrates the changes in the surface morphology according to the polysorbate content of the examined samples.

The results indicate that the presence of each of the examined polysorbates in the wax matrix increased the

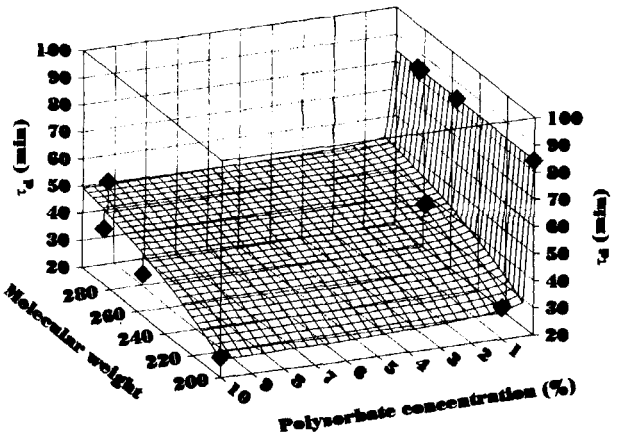

Figure 2. Effect of the concentration of various polysorbates on the time when 63.2% of potassium chloride has been dissolved (τ_d).

wettability of the system, and consequently decreased the τ_d values of the embedded potassium chloride (Fig. 2).

From the surface tension results it can be seen that at low concentration, the presence of polysorbate polymers caused a decrease in the surface tension of the solution. As the concentration increased, the surface tension leveled out to approximately constant values (Fig. 3).

The τ_d values of potassium chloride matrix samples, containing various types and amounts of polysorbate polymer, decreased in a similar manner to the surface

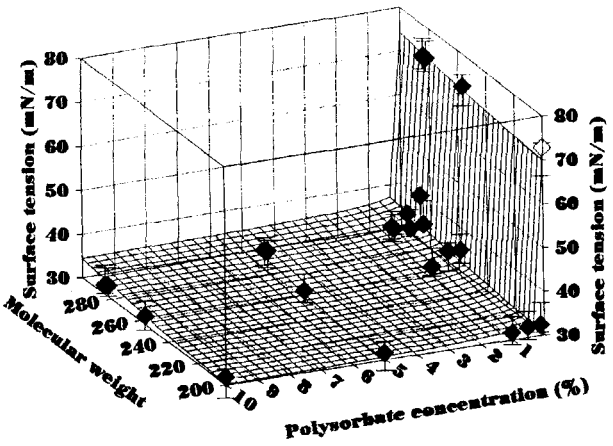

Figure 3. Effect of the concentration of various polysorbates on the surface tension values of aqueous solutions

tension values of the aqueuos solutions of the same polymer.

CONCLUSIONS

It can be concluded that there is a close connection between the physical and interfacial properties of macromolecules and their effect on drug release. Neither the surface tension of the aqueous polysorbate solutions nor the τ_d of potassium chloride have changed over a certain polysorbate concentration (2%). On the basis of the surface tension measurement of aqueous polysorbate solutions, it is possible to determine and apply optimum polysorbate concentration concerning drug release in wax matrix systems.

REFERENCES

1. I. Rácz, *Drug Formulation*, Wiley, New York, 1989, pp. 353–375.
2. M. Z. I. Khan, Drug Dev. Ind. Pharm., 21(9), 1037 (1995).
3. J. Z. Y. Wang and R. H. Bogner, Int. J. Pharm., 11, 81 (1995).
4. H.-P. Huang, S. C. Mehta, G. W. Radebaugh, and M. B. Fawzi, J. Pharm. Sci., 83, 795 (1994).
5. M. Kopcha and N. G. Lordi, J. Pharm. Pharmacol., 44, 79 (1992).
6. A. T. M. Serrajuddin, P.-C. Sheen, and M. A. Augustine, J. Pharm. Sci., 79, 463 (1990).
7. G. P. Martin, M. Linda, E. L.-Hariri, and C. Marriott, J. Pharm. Pharmacol., 44, 646 (1992).
8. F. Langenbucher, Pharm. Ind., 38, 472 (1976).
9. W. Weibull, J. Appl. Mech., 18, 293 (1951).