International Journal of Pharmaceutics, 52 (1989) 83–86
Elsevier

IJP 01797

In vitro release of chlorpheniramine maleate from ointment bases

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(Received 28 October 1988)
(Modified version received 29 December 1988)
(Accepted 13 January 1989)

Key words: In vitro release; Ointment base composition; Chlorpheniramine maleate concentration; Diffusion cell; Release rate

Summary

The in vitro release of chlorpheniramine maleate from ointments was studied using the Sartorius Absorption Simulator and its artificial epidermis barrier. The amount of drug released depended on the composition of the vehicle and the concentration of drug incorporated in it. The rate of release increased in the following order: ointment < o/w emulsion < w/o emulsion.

Chlorpheniramine maleate is an alkylamine derivative with antihistaminic properties. It is one of the most potent of the antihistamines and it is used to cure several allergies and skin irritations (Martindale, 1982).

Chlorpheniramine maleate has the known side effects of all antihistamines, when given orally. The most common are sedation, varying from slight drowsiness to deep sleep, dizziness, muscular weakness, gastrointestinal disturbances. In order to bypass these side effects the topical application of chlorpheniramine maleate as an ointment has been proposed and its in vitro release from various ointment bases is described in this paper.

For this study we used the Sartorius Absorption Simulator technique, and described the ointment bases formulated, the concentration of drug in each base, the rate release of chlorpheniramine maleate, the influence of surfactants, the effect of the composition of the ointment bases and drug concentration on the release rate.

The semi-solid bases formulated were emulsions of the o/w and w/o type and anhydrous ointments. Chlorpheniramine maleate was incorporated in concentrations of 3% and 5%. Also modified o/w emulsions were prepared by adding Tween-80, Span-80 and o/w emulsions by adding propylene glycol or glycerine. The composition of the bases are presented in Table I.

For the in-vitro release of chlorpheniramine maleate from ointment bases the Sartorius Absorption Simulator (Fig. 1) was used in this study (Stricker, 1971). This apparatus consists of two main parts: the peristaltic pump with the containers I and II and the diffusion cell. The peristaltic pump is used to circulate the aqueous phases in the containers. With the aid of a magnetic stirring bar the solutions in each container are

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TABLE 1

Composition and type of ointment bases used

Chlorphen-iramine maleate %	Type of base	Composition	
3%	o/w emulsion	Cetostearyl alcohol	8 g
5%		Mineral oil	6 g
		White hard paraffin	25 g
		Sodium lauryl sulphate	1 g
		Purified water q.s.	100
3%	w/o emulsion	Stearyl alcohol	7 g
5%		Cholesterol	5 g
		White wax	12 g
		Petrolatum	20 g
		Purified water q.s.	100
3%	ointment	Cetostearyl alcohol	27 g
5%		Petrolatum	50 g
		Mineral oil	23 g
5%	o/w emulsion	Celostearyl alcohol	8 g
		Mineral oil	6 g
		White hard paraffin	25 g
		Glycerine or propylene glycol	10 g
		Sodium lauryl sulphate	1 g
		Purified water q.s.	100
5%	o/w emulsion *	Celostearyl alcohol	8,5 g
		White hard paraffin	15 g
		Mineral oil	6,5 g
		Tween-80	3,7 g
		Span-80	1,4 g
		Purified water q.s.	100

* The quantities of each component were calculated according to the HLB-values.

kept homogenous. Containers I and II are maintained at a constant temperature with the aid of thermostated holders. Container I is filled with distilled water. Container II is filled with a buffer solution of pH 7.2. The volume of each container is 100 ml and they are not connected to each other. The diffusion cell (Fig. 2) (donor chamber) consists of two plates. The back plate has an opening where 1 g of the ointment is applied. The ointment is then covered with a Sartorius artificial epidermis barrier, consisting of a barrier foil soaked in water and a membrane filter, liquid-impregnated, which are pressed together. Afterwards the front plate is screwed to the back plate so that a sealed compartment is formed above the membrane. The diffusion cell is connected with

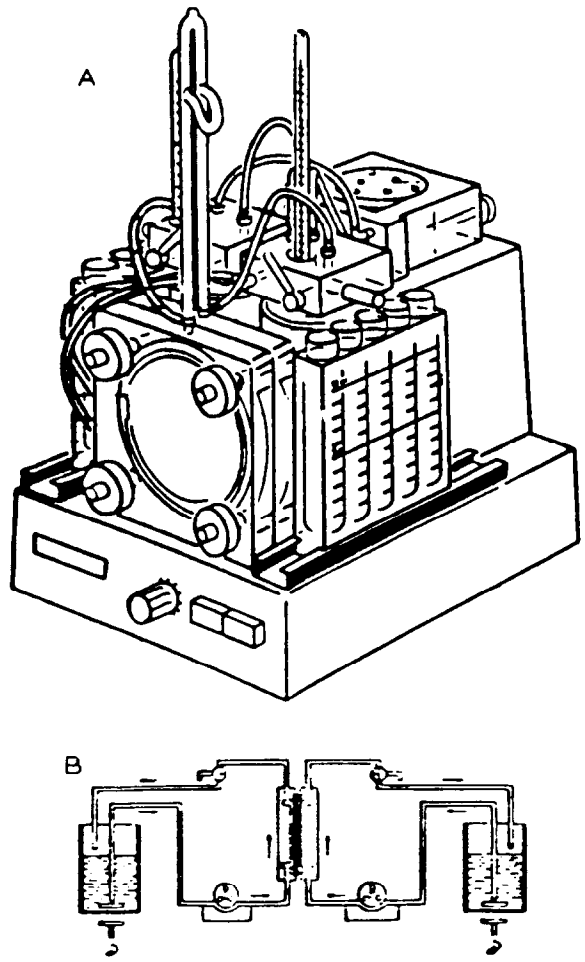

Fig. 1. A: the Sartorius Absorption Stimulator. B: the Sartorius Absorption Stimulator assembly.

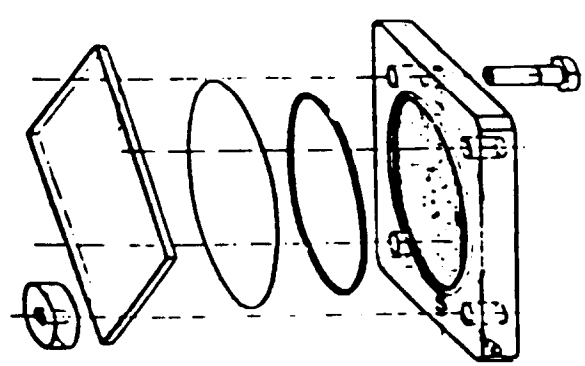

Fig. 2. Diffusion cell.

tubes to container II (receptor chamber). The buffer solution circulates through the artificial barrier, so that the drug diffuses through it, and then returns to container II (Delonca et al., 1977). Above the front plate another thin plate is screwed, which is connected to container I and through which warm water is passed so that the whole system is maintained at a constant temperature (35° ± 1°C). To avoid the formation of air bubbles between the artificial barrier and the buffer solution the diffusion cell is placed vertically (Flynn and Smith, 1971). Samples of 5 ml were withdrawn from container II at 30 min intervals for 3 h and replaced with an equal volume of buffer solution. The samples were analyzed spectrophotometrically at a wavelength of 260.8 nm (Merck Index, 1983) and the concentration of chlorpheniramine maleate in each sample was determined from a previously calculated, standard curve.

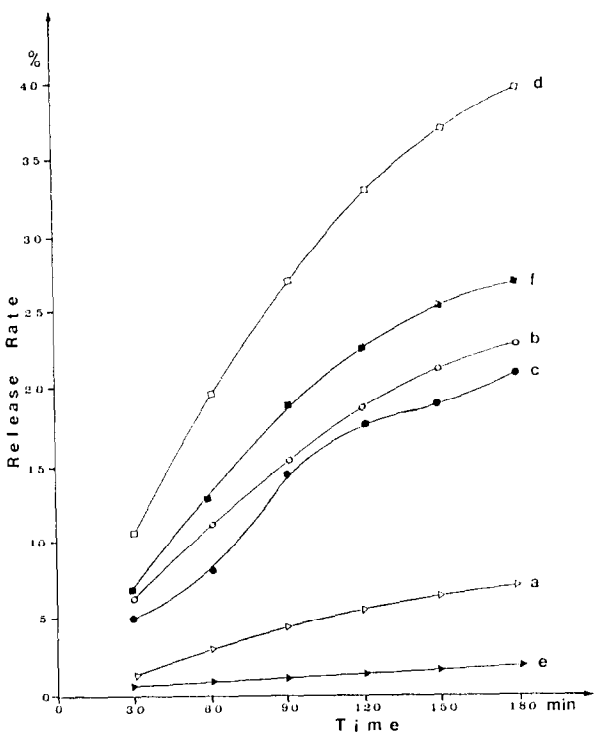

Fig. 3. Effect of ointment base composition and drug concentration on the release rate of chlorpheniramine maleate from ointment bases. a: o/w cream with 3% drug concentration; b: o/w cream 5% and o/w cream 5% with 10% propyleneglycol or with 10% glycerine; c: w/o cream 3%; d: w/o cream 5%; e: ointment 3% and ointment 5%; f: o/w cream 5% with 5% Tween-80, Span-80.

The release of chlorpheniramine from ointment bases is given in Fig. 3.

Chlorpheniramine maleate is dissolved in the o/w and w/o emulsion type ointments while it is suspended in the ointments. Fig. 3e shows that the release rate of chlorpheniramine maleate from ointment bases is very slow (release rate 1.75% after 3 h of experiment).

The release rate of chlorpheniramine maleate from the ointment bases increased in the following order: ointments < o/w creams < w/o creams as Fig. 3e, b, d shows.

The release rate from the w/o emulsion ointment is almost twice that of the o/w type (40% and 23% respectively, Fig. 3d, b). This may be due to phase inversion occurring in the w/o emulsion (Takamura et al., 1984) and because of the higher drug concentration in the water-soluble phase of the w/o emulsion to that of the water soluble phase of the o/w emulsion.

Fig. 3b, f shows the effect of the modified ointment bases on the release rate. When an o/w emulsion base is formulated with a mixture of 5% Tween-80–Span-80 the release rate is higher than from the o/w emulsion ointment (release rates 27% and 23% respectively).

When propyleneglycol or glycerine are used to modify the composition of the vehicle the release rate is not altered (release rates 22.9% and 22.8%, respectively, and 23% for the o/w emulsion). (Barry, 1983).

Drug concentration also plays a role in the drug release from vehicles. When the o/w emulsion base contains 3% chlorpheniramine maleate the release rate is 7.33% (Fig. 3a) and when the drug concentration is 5% (same vehicle) the release rate increases significantly and is 23% (Fig. 3b).

The same conclusions are drawn for the w/o type emulsion. When the drug is incorporated in the base at a concentration of 3% the release rate is 21% (Fig. 3c) and when chlorpheniramine maleate is incorporated in the same vehicle at a 5% concentration the release rate is 40% (Fig. 3d).

As for the ointment the release rate increases as the drug concentration increases, but in both cases the release rate is very slow (Fig. 3e).

The results obtained from this study may be useful for the formulation of topical preparations of chlorpheniramine maleate. The release of chlorpheniramine maleate from ointment bases depends on the composition of the base and the concentration of drug incorporated in it. The highest rate of release is obtained from the w/o emulsion ointments.

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