J. Pharm. Pharmacol. 1992, 44: 79–83
Received May 23, 1991

Effect of Physical and Chemical Properties on Drug Release From Selected Thermosoftening Vehicles

MICHAEL KOPCHA AND *NICHOLAS G. LORDI

*Schering-Plough Research, Kenilworth, NJ 07033, USA, *Rutgers, The State University, College of Pharmacy, Piscataway, NJ 08854, USA*

Abstract—The release profile of several drugs, (chlorpheniramine maleate, salicylic acid, hydrochlorothiazide, *p*-hydroxy benzoic acid, sulphafurazole, anhydrous theophylline) and the marker (D&C yellow No. 10) was detailed to determine the effect of physical and chemical properties on release from selected thermosoftening matrices (Gelucire 50/02 and 50/13). At a concentration of drug or marker of 2·5% w/w, hydrochlorothiazide showed the slowest release from G50/02, due to its low aqueous solubility, while theophylline showed the highest release owing to its low mol. wt and moderate aqueous solubility. Release reflected two of the selection criteria, aqueous solubility and mol. wt, set forth for the drug/markers used in the study. The hydrophobic matrix, G50/02, offered no enhancement in drug release and functioned in a manner commensurate with other hydrophobic matrices. No hydrogen bonding was noted between any of the drugs or markers and the matrix. As drug or marker concentration increased from 2·5 to 15% w/w, potential hydrogen bonding was noted between *p*-hydroxy benzoic acid and the matrix. Theophylline no longer had the highest release being replaced by chlorpheniramine maleate and D&C yellow No. 10. With Gelucire excipient G50/13, chlorpheniramine maleate showed the highest release; it dissolved within the matrix at experimental temperature and lowered the matrix melting point. The matrix swelled upon exposure to the dissolution medium and it was from this swollen layer that release occurred. Sulphafurazole, hydrochlorothiazide, salicylic acid and *p*-hydroxy benzoic acid exerted a similar effect to chlorpheniramine maleate on the matrix. No hydrogen bonding was observed between the drugs and matrix. As drug or marker concentration was further increased, chlorpheniramine maleate and D&C yellow No. 10 demonstrated the highest release; all other drugs formed a cluster. Apparent diffusion coefficients for G50/02 and G50/13 matrices were in agreement with published data confirming the predictive ability of the experimental design and postulated mechanistic models of release from hydrophilic and lipophilic matrices.

Methodology has been reported for monitoring the release of drugs or markers from thermosoftening matrices, using a stationary disc/rotating fluid system (Kopcha et al 1990). Two compounds were initially used, with diverse physical and chemical properties, to determine the effect on release. The thermosoftening matrices employed were ethoxylated mixtures of partial glycerides of fatty acid esters with controlled hydrophilicity (i.e. Gelucire). Release profiles were found to be biphasic, with an initial or transiently rapid release for approximately the first hour.

This study investigates further how the physical and chemical properties of drugs and markers affect their release from hydrophilic and lipophilic thermosoftening matrices making use of diffusional and erosional release mechanisms.

Materials and Methods

Materials

All chemicals were stored over a desiccant of silica gel at a temperature of 22°C: Gelucire 50/02 (G50/02) and 50/13 (G50/13) (Gattefosse Corporation, NY, USA), D&C yellow No. 10 (Warner Jenkinson, MO, USA), anhydrous theophylline USP (Amend Drug and Chemical Company, NJ, USA), chlorpheniramine maleate USP (Amend Drug and Chemical Company, NJ, USA), salicylic acid (Fisher Scientific, PA, USA), hydrochlorothiazide (Sigma Chemical Company, MI, USA), *p*-hydroxy benzoic acid (Eastman Kodak Company, NY, USA) and sulphafurazole (Pfaltz & Bauer Inc., CT, USA). The physicochemical properties of the drugs employed for this study are detailed in Table 1. The dissolution medium was a simulated gastric fluid (pH 1·2) consisting of 0·034 M NaCl and 0·085 M HCl.

Correspondence: M. Kopcha, Schering-Plough Research, 2000 Galloping Hill Road K-11-2, Kenilworth, NJ 07033, USA.

Release methodology

The method and operating conditions used to monitor release from a stationary disc/rotating fluid system were as described previously (Kopcha et al 1990) for both continuous and discrete sampling.

Experiments were performed at a paddle speed of 50 rev min^{-1} with a paddle height of 1 cm and temperature maintained at 37 ± 1°C. Results are reported as the average of six replicates ± s.e.

Preparation of stationary discs

Ten g of the appropriate Gelucire was heated to 10°C above its melting point at which time the drug or marker (2·5, 7 or 15% w/w) was incorporated into the molten mass using a high speed, desk-top homogenizer (Tissumizer, Model SDT-1810, Tekmar, OH, USA). The molten material was poured into the female half of a 6·98 cm^2 Millipore filter holder. The luer-lock tip was sealed with a threaded screw to prevent leaking of the molten mass. The molten material was poured in three stages into the holder to prevent cracking on cooling. Each layer was allowed to cool and solidify at room temperature (21°C) undisturbed. Once the mass completely congealed, the surface was levelled with a hot spatula.

Prepared discs were stored in a desiccator at ambient temperature (21°C) for no longer than 24 h.

Table 1. Physical and chemical properties of drugs and marker.

Material	K[a]	Mol. wt	pK_a	Solubility (g L^{-1})/SGF[b]
D&C yellow No. 10[c]	—	>300	5	50·2
Anhydrous theophylline[d]	1·40	180·17	8·6	10·0
Chlorpheniramine maleate[c]	—	390·87	9·2	172
Salicylic acid[e]	11·0	138·12	3	2·17
Hydrochlorothiazide	1·94	297·73	7·9	1·12
p-Hydroxybenzoic acid	0·13	138·12	4·6	8·33
Sulphafurazole[f]	14·0	267·31	5·0	14·9

[a] Partition coefficient: $\frac{\text{concentration in n-octanol}}{\text{concentration in water}}$.

[b] SGF = simulated gastric fluid (pH = 1·2). [c] Particle size = 50–82 μm. [d] Particle size = 5–12 μm. [e] Particle size = 8–17 μm. [f] Particle size = 10–15 μm.

Differential scanning thermoanalysis

All differential scanning calorimetric (DSC) thermograms (Model DSC-7, Perkin-Elmer Corporation, CT, USA) were obtained on a sample (1 to 10 mg) of the prepared Gelucire. Each sample was heated to 100°C at a rate of 20°C min^{-1} to generate the first thermogram. The sample was then cooled to a final temperature of −10°C and maintained there for 5 min; thermograms were not recorded during the cooling cycle. Each sample was reheated to 100°C to provide a second thermogram. This cycling process was implemented to determine if cooling imposed any time dependent changes in the properties of the thermosoftening vehicles.

Solubility determinations

An amount of drug or marker in excess of its reported solubility was placed in a 30 mL screw-top test tube and 20 mL of simulated gastric fluid was added. The test tubes were immersed in a water bath maintained at 37°C for seven days. The sample was filtered through a preheated filtering apparatus and the filtrate analysed spectrophotometrically. A rapid filtering process was employed to prevent drug precipitation from the saturated solution during the filtering process.

Results and Discussion

The Gelucire-class of excipients have found widespread use as thermosoftening drug-delivery vehicles in the pharmaceutical industry. These excipients are relatively inert and are used in the filling of oily or pastey materials into hard gelatin capsules because of their varied hydrophilicity. This offers the Gelucire-class of excipients an advantage over the more traditional matrices such as polyethylene glycol and various fatty materials.

The two Gelucires chosen as representative thermosoftening matrices for this study were G50/02 and G50/13. This selection was based upon their similar melting point (i.e. 50°C) but divergent hydrophilicity. Thus, these two materials provide different milieu for drug release while keeping matrix melting temperature constant. Also, G50/13 swells when placed in an aqueous medium which makes it similar to another hydrophilic matrix, hydroxypropyl methylcellulose. Therefore, these materials demonstrate, to some degree, the properties of other commonly used materials so enabling comparison of release mechanisms with other, more conventional, matrices.

Chlorpheniramine maleate, salicylic acid, hydrochlorothiazide, *p*-hydroxy benzoic acid, sulphafurazole, D&C yellow No. 10 and anhydrous theophylline were chosen, as test compounds, based upon their different solubilities in the dissolution medium, divergent affinities for aqueous or organic media (i.e. partition coefficient) and varying pK_a values and mol. wt (Table 1). D&C yellow No. 10 and chlorpheniramine maleate were selected to represent salts which are highly water soluble compounds. Salicylic acid and sulphafurazole represented lipophilic materials which demonstrate affinity for a lipophilic matrix, such as G50/02, in contrast to a hydrophilic matrix (i.e. G50/13). Theophylline was used to exemplify the release of low mol. wt pharmaceutical compounds, with moderate aqueous solubility, from both hydrophilic and lipophilic matrices. Hydrochlorothiazide represents a class of poorly water-soluble compounds. Salicylic acid and *p*-hydroxy benzoic acid, identical in mol. wt, were used to explore the phenomenon of hydrogen bonding between drug and matrix. Salicylic acid is able to hydrogen bond intra-molecularly while *p*-hydroxy benzoic acid has two free hydroxy sites for potential intermolecular hydrogen bonding. Possible hydrogen bonding would take place between the drug and free hydroxy residues of G50/02 and G50/13.

Thermal stability of G50/02 preparations

The DSC scan for chlorpheniramine maleate in G50/02 is shown in Fig. 1 and is representative of thermograms for other drugs in G50/02; there were no noticeable interactions between drug and matrix. For all G50/02 preparations in this study, the second thermogram in the recycling technique was superimposable on the first. Thus, the preparation did not affect the melting point or other thermal transitions or induce polymorphism of the Gelucire.

In addition, thermal analysis was performed on these solid dispersions after three and six months of ageing and compared with their initial thermograms. No changes were noted.

We can conclude that G50/02 and G50/13 are robust matrices which do not depend on thermal history influencing their performance as drug-delivery vehicles. Also, it can be concluded that during the manufacture of these solid

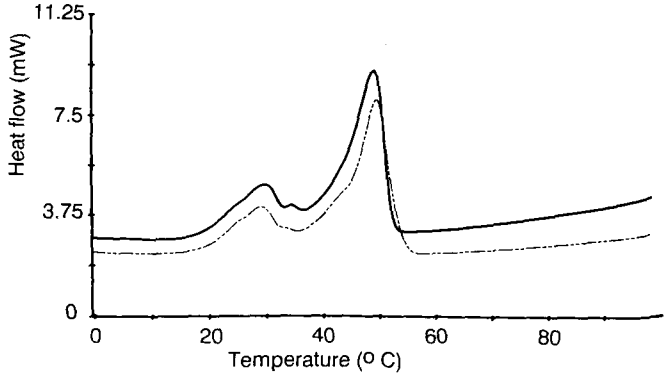

FIG. 1. Thermogram of G50/02 with and without chlorpheniramine maleate.

dispersions, a rapid cooling technique can be adopted without affecting the physical and thermal integrity of the finished product.

Effect of structure on release rate from G50/02 preparations

Salicylic acid and *p*-hydroxy benzoic acid showed identical release profiles ($P > 0.05$) with A/B ratios of 5·08 and 5·90, respectively; suggesting that *p*-hydroxy benzoic acid does not hydrogen bond with the matrix. This was confirmed by thermoanalysis.

The release rate of theophylline (the highest of the compounds tested) was predominately diffusion controlled due to its low mol. wt, moderate aqueous solubility and low partition coefficient.

Release of chlorpheniramine from Gelucire preparations

Table 2 numerically models the effect of concentration of chlorpheniramine maleate on the release of the drug from a G50/02 matrix according to the following equations:

$$M = At^{1/2} + C \quad (1)$$

$$M = At^{1/2} + Bt + C \quad (2)$$

where M is the amount of solute released, A is the diffusional coefficient, B is the erosional coefficient and C is a constant (Kopcha et al 1990). The model represented by equation 1 includes matrix diffusion, whether it is from a swollen matrix or not, whereas equation 2 includes matrix diffusion coupled with erosion as an additional process for drug release.

As drug concentration increased, the total amount released also increased. The A term of equation 1 is related to the square-root of the concentration of dispersed drug in the matrix and as concentration increased, A was also found to increase.

As the percentage of incorporated drug increased, the mechanism of release reflected both diffusion and erosion. For this mixed model, erosion became more pronounced as concentration increased, as there is less matrix available to maintain the integrity of the disc.

When the excipient was changed to G50/13 similar trends were noticed. For all concentrations of chlorpheniramine maleate tested, release was fitted by a combined model of erosion and diffusion. At 2·5% w/w the A/B ratio was 2·14 which increased to 4·90 when concentration was raised to 7% w/w. This demonstrates that diffusion outpaced erosion. However, when concentration was increased to 15% w/w, erosion dominated thereby decreasing the A/B ratio. Hence, matrix integrity decreased due to less points of contact as drug loading increased. Also, the A term was found to be approximately linear with respect to the percentage of drug or marker incorporated into the matrix reflecting drug release from a hydrated matrix (Touitou & Donbrow 1982).

Drug release for the same concentration of drug

The effect of different drugs on release from G50/02, when the concentration of all drugs was kept constant (2·5% w/w) is summarized in Table 3. Hydrochlorothiazide, with low aqueous solubility and high mol. wt, had the lowest release which was attributed to surface release.

Table 2. Model coefficients ± s.e. for Gelucire 50/02 and chlorpheniramine maleate (2·5, 7, 15%) in simulated gastric fluid at 37°C. Paddle speed, 50 rev min^{-1}; paddle ht, 1 cm.

Chlorpheniramine maleate (%)	Gelucire	A ($mg\ h^{-1/2}$)	B ($mg\ h^{-1}$)	C (mg)	A/B ($h^{1/2}$)
2·5	G50/13	5·020 ± 0·307	2·348 ± 0·122	1·279 ± 0·148	2·14
	G50/02	0·821 ± 0·072	—	−0·094 ± 0·092	—
7·0	G50/13	18·35 ± 1·14	3·746 ± 0·451	1·639 ± 0·547	4·90
	G50/02	3·427 ± 0·268	0·794 ± 0·106	1·007 ± 0·129	4·32
15	G50/13	33·71 ± 2·15	13·19 ± 0·852	2·881 ± 1·03	2·56
	G50/02	3·607 ± 0·565	3·048 ± 0·224	3·162 ± 0·272	1·18

Table 3. Model coefficients ± s.e. for Gelucire 50/02 with drug/marker (2·5, 15%) in simulated gastric fluid at 37°C. Paddle speed, 50 rev min^{-1}; paddle ht, 1 cm.

Material	A ($mg\ h^{-1/2}$)	B ($mg\ h^{-1}$)	C (mg)	A/B ($h^{1/2}$)
2·5% Drug/marker				
D&C yellow No. 10	0·668 ± 0·038	—	0·025 ± 0·049	—
Anhydrous theophylline	2·674 ± 0·077	—	0·081 ± 0·099	—
Chlorpheniramine maleate	0·821 ± 0·072	—	−0·940 ± 0·092	—
Salicylic acid	0·883 ± 0·036	0·174 ± 0·014	0·231 ± 0·017	5·08
Hydrochlorothiazide	0·070 ± 0·006	—	0·103 ± 0·008	—
p-Hydroxy benzoic acid	1·045 ± 0·026	0·177 ± 0·010	0·085 ± 0·013	5·90
Sulphafurazole	0·318 ± 0·019	—	0·457 ± 0·024	—
15% Drug/marker				
D&C yellow No. 10	14·61 ± 0·321	—	0·008 ± 0·411	—
Anhydrous theophylline	3·559 ± 0·116	—	0·973 ± 0·149	—
Chlorpheniramine maleate	3·607 ± 0·565	3·048 ± 0·224	3·162 ± 0·272	1·18
Salicylic acid	2·993 ± 0·209	1·229 ± 0·083	0·371 ± 0·100	2·44
Hydrochlorothiazide	0·641 ± 0·014	—	0·042 ± 0·018	—
p-Hydroxy benzoic acid	1·524 ± 0·076	0·289 ± 0·030	0·168 ± 0·037	5·32
Sulphafurazole	2·008 ± 0·034	—	−0·044 ± 0·043	—

Chlorpheniramine maleate, D&C yellow No. 10 and sulphafurazole exhibited similar release profiles but with release rates in the same rank order as their solubilities. All four compounds were incorporated into the base as dispersions which indicated low solubility of these drugs in the matrix.

Effect of increased drug concentration on release from G50/02 preparations

Table 3 numerically models the effect of increasing drug or marker concentration from 2·5 to 15% w/w on release rate from G50/02. Hydrochlorothiazide had the slowest release rate at both concentrations but the A or diffusional term increased reflecting diffusion concentration dependency.

D&C yellow No. 10 showed the highest release rate at the 15% concentration. Even though it has one of the highest mol. wts, the increased concentration offset this effect to allow for an increase in release rate. Also, its high aqueous solubility allowed for partitioning of the drug from the matrix but since its release is predominately diffusion controlled, this rate will decrease over time.

There was a larger difference in release profiles for salicylic acid and *p*-hydroxy benzoic acid at the 15% concentration. The higher A coefficient for *p*-hydroxy benzoic acid compared with that for salicylic acid may reflect hydrogen bonding, which would lower the overall release of *p*-hydroxy benzoic acid because of a decreased ability to diffuse through the matrix.

Theophylline remained predominantly diffusional with erosion making no contribution at the higher concentration. Theophylline demonstrated some organic solubility which indicates that it would partition into an aqueous environment less than that of a salt, such as D&C yellow No. 10 or chlorpheniramine maleate. It should also be noted that theophylline did demonstrate some solubility in molten G50/02. Upon cooling of the matrix, dispersed theophylline was found to have a 5–12 μm particle size as compared with that of D&C yellow No. 10 and chlorpheniramine maleate (50–82 μm). The larger particles of the latter compounds thus disrupted the matrix to a greater extent than the smaller particles of theophylline. Therefore, upon dissolution of the drug, the channels formed within the matrix were greater for those materials with larger particle sizes which, in-turn, would further enhance their release. For this type of system, the rate of drug release is controlled by the rate of drug diffusion and not by the rate of solid dissolution (Lee & Robinson 1978); particle size therefore is less of a factor.

Sulphafurazole showed an increase in its predominately diffusional profile which, again, is indicative of an increase in its A term. No erosion was noted for this system even though there was an increase in concentration. Its particle size was found to be 10–15 μm, which may account for the lack of an erosional effect.

Release from G50/13 preparations

The results of release from G50/13 preparations are summarized in Table 4. The highest release was seen with chlorpheniramine maleate; the low A/B ratio indicated that erosion was a significant component of release. From thermoanalysis, it was apparent that chlorpheniramine maleate altered the thermal behaviour of the G50/13 matrix, with a second endotherm at approximately 35°C indicating dissolution of drug in the matrix. Also, the main melting peak was shifted downward to approximately 45°C. Since the matrix softened at a lower temperature, erosion became a more significant component in release. When exposed to the dissolution medium, the G50/13 matrix swelled which allowed drug to dissolve within the swollen layer. Consequently, matrix density decreased which, in additiion to drug dissolution in the swollen layer, hastened release compared with its lipophilic counterpart, G50/02.

Release of sulphafurazole showed a slowing in release rate at 5 hours which was indicative of its diffusional mechanism of release. Theophylline, on the other hand, continued to increase as erosion was an additional process.

Sulphafurazole, like chlorpheniramine maleate, also affected the thermal behaviour of the matrix. It depressed the melting point of the matrix to approximately 42°C, thereby allowing drug to diffuse through the matrix more easily. At approximately 37°C, drug dissolved within the matrix, as confirmed by thermoanalysis.

The same phenomenon of drug dissolution in the matrix at 37°C and matrix softening at 42°C was observed with hydrochlorothiazide, salicylic acid and *p*-hydroxy benzoic

Table 4. Model coefficients ± s.e. for Gelucire 50/13 with drug/marker (2·5, 15%) in simulated gastric fluid at 37°C. Paddle speed, 50 rev min^{-1}; paddle ht, 1 cm.

Material	A (mg $h^{-1/2}$)	B (mg h^{-1})	C (mg)	A/B ($h^{1/2}$)
2·5% Drug/marker				
D&C yellow No. 10	4·183 ± 0·269	—	−0·892 ± 0·343	—
Anhydrous theophylline	5·847 ± 0·355	0·804 ± 0·141	0·517 ± 0·171	7·27
Chlorpheniramine maleate	5·020 ± 0·307	2·348 ± 0·122	1·279 ± 0·148	2·14
Salicylic acid	2·024 ± 0·538	0·749 ± 0·213	1·047 ± 0·259	2·70
Hydrochlorothiazide	3·656 ± 0·532	0·629 ± 0·211	0·077 ± 0·256	5·81
p-Hydroxy benzoic acid	4·494 ± 0·169	—	0·101 ± 0·215	—
Sulphafurazole	7·774 ± 0·198	—	−0·578 ± 0·252	—
15% Drug/marker				
D&C yellow No. 10	63·57 ± 2·333	—	−2·590 ± 0·854	—
Anhydrous theophylline	17·91 ± 1·326	3·826 ± 0·526	0·866 ± 0·638	4·68
Chlorpheniramine maleate	33·71 ± 2·15	13·19 ± 0·852	2·881 ± 1·03	2·56
Salicylic acid	24·93 ± 1·230	—	4·413 ± 1·079	—
Hydrochlorothiazide	15·84 ± 2·144	3·623 ± 0·851	0·926 ± 1·032	4·37
p-Hydroxy benzoic acid	22·87 ± 1·100	2·479 ± 0·437	−1·128 ± 0·530	9·23
Sulphafurazole	36·05 ± 0·843	—	−6·822 ± 1·06	—

Table 5. Apparent diffusion coefficient for selected drugs in Gelucire 50/02 and 50/13. Paddle speed, 50 rev min^{-1}; paddle ht, 1 cm.

%	Drug	Apparent diffusion coefficient (cm^{-2} s^{-1}) G50/02	G50/13
2·5	D&C yellow No. 10	$2{\cdot}66 \times 10^{-7}$	$8{\cdot}82 \times 10^{-6}$
15		$1{\cdot}95 \times 10^{-5}$	$5{\cdot}66 \times 10^{-5}$
2·5	Theophylline	$1{\cdot}98 \times 10^{-5}$	$1{\cdot}72 \times 10^{-5}$
15		$3{\cdot}50 \times 10^{-5}$	$4{\cdot}49 \times 10^{-6}$
2·5	Chlorpheniramine	$1{\cdot}62 \times 10^{-7}$	$1{\cdot}27 \times 10^{-5}$
15		$3{\cdot}63 \times 10^{-7}$	$1{\cdot}59 \times 10^{-5}$
2·5	Salicylic acid	$9{\cdot}77 \times 10^{-6}$	$1{\cdot}06 \times 10^{-6}$
15		$1{\cdot}86 \times 10^{-5}$	$8{\cdot}70 \times 10^{-6}$
2·5	Hydrochlorothiazide	$1{\cdot}19 \times 10^{-7}$	$6{\cdot}74 \times 10^{-6}$
15		$1{\cdot}66 \times 10^{-6}$	$3{\cdot}51 \times 10^{-6}$
2·5	*p*-Hydroxy benzoic acid	$3{\cdot}61 \times 10^{-6}$	$1{\cdot}02 \times 10^{-5}$
15		$1{\cdot}26 \times 10^{-6}$	$7{\cdot}32 \times 10^{-6}$
2·5	Sulphafurazole	$1{\cdot}89 \times 10^{-7}$	$3{\cdot}05 \times 10^{-5}$
15		$1{\cdot}23 \times 10^{-6}$	$1{\cdot}82 \times 10^{-5}$

acid. Both hydrochlorothiazide and salicylic acid fit a combined model of release while *p*-hydroxy benzoic acid fit a diffusional model. Salicylic acid and *p*-hydroxy benzoic acid had similar release profiles suggesting the absence of any significant hydrogen bonding with the matrix. The release of hydrochlorothiazide increased, as compared with release from G50/02, due to the hydrated layer allowing easier partitioning of drug from the matrix.

At a concentration of 15% w/w, both chlorpheniramine maleate and D&C yellow No. 10 showed the highest release rate (Table 4). This is similar to observations with the G50/02 matrix. Chlorpheniramine maleate probably had a higher release profile than D&C yellow No. 10 because of its higher solubility and its predominantly erosional mechanism of release.

Release of the other drugs were similar to each other and were not statistically different ($P > 0{\cdot}05$).

Predictive ability

To evaluate the predictive nature of the models generated elsewhere (Kopcha et al 1990), apparent diffusion coefficients for the drug or marker in G50/02 and G50/13 matrices, at 2·5 and 15% w/w concentration, were determined. For G50/02, the A term was evaluated for a rigid matrix as described by Paul & McSpadden (1976). Strict matrix diffusion was assumed for this calculation. No hydrodynamic diffusion boundary layer was considered, as a first approximation. The results (Table 5) support the hypothesis that the matrix controls release and not dissolution.

The apparent diffusion coefficients for drug or marker dispersed in G50/13 were calculated by the following equation derived by Lapidus & Lordi (1966, 1968):

$$\frac{M}{t^{1/2}} = 2Wo\left(\frac{S}{V}\right)\left(\frac{D'}{\pi}\right)^{1/2} \quad (3)$$

where M is the amount of solute released per unit area, D′ is the apparent diffusion coefficient of drug in the hydrated matrix, Wo is the initial drug loading per unit volume, S is the effective diffusional area, V is the effective volume of the hydrated matrix and t is time.

The calculated apparent diffusion coefficients in the G50/13 matrix are somewhat higher than those in the G50/02 matrix; the system swells which allows drug to diffuse more easily thereby increasing the apparent diffusion coefficient. The order of magnitude for these coefficients confirms the ability of the release schemes to predict release from thermosoftening matrices.

References

Kopcha, M., Tojo, K. J., Lordi, N. G. (1990) Evaluation of methodology for assessing release characteristics of thermosoftening vehicles. J. Pharm. Pharmacol. 42: 745–751

Lapidus, H., Lordi, N. G. (1966) Some factors affecting the release of a water-soluble drug from a compressed hydrophilic matrix. J. Pharm. Sci. 55: 840–843

Lapidus, H., Lordi, N. G. (1968) Drug release from compressed hydrophilic matrices. Ibid. 57: 1292–1301

Lee, V. H. L., Robinson, J. R. (1978) Methods to achieve sustained drug delivery—the physical approach: oral and parenteral dosage forms. In: Robinson, J.R. (ed.) Sustained and Controlled Release Drug Delivery Systems. Marcel Dekker Inc., New York, pp 123–209

Paul, D. R., McSpadden, S. K. (1976) Diffusional release of a solute from a polymer matrix. J. Membr. Sci. 1: 33–48

Touitou, E., Donbrow, M. (1982) Drug release from non-disintegrating hydrophilic matrices: sodium salicylate as a model drug. Int. J. Pharm. 11: 355–364