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Influence of storage on in-vitro release of ibuprofen from sugar coated tablets

Dorothy J. Saville *

School of Pharmacy, University of Otago, PO Box 913 Dunedin, New Zealand

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Abstract

Studies performed on ibuprofen tablets (one brand of 400 mg, two brands of 200 mg sugar coated and one brand of film coated tablets) are reported. Tablets were subjected to conditions of 23 °C, 30 °C and 40 °C; at 75% RH and 96% RH for periods of up to 4 weeks. Tablets were stored in different ways—unpacked, packed in air-tight/moisture proof containers, packed in tablet vials and packed in two unit dose packs. Dissolution was carried out in pH 7.2 phosphate buffer using USP or FDA conditions for ibuprofen (Basket-150 rpm or Paddle-50 rpm) with sampling and UV analysis up to 90 or 120 min. Serious reduction in dissolution was noted for the 400 mg sugar coated tablets exposed to moisture. Mean % released at 30 mm (USP conditions) was as low as 1% and, for these tablets, dissolution continued to proceed extremely slowly for the full dissolution period. The film coated tablets were not affected. The tablet vials and unit dose packs showed some protection. Investigation showed not only a change in the subcoat properties (which did not break down easily) but also in the tablet core, which became hard and non-disintegrating.

Keywords: Ibuprofen; Sugar coated tablets; Dissolution; Storage; Unit dose Dispensing packs

1. Introduction

Ibuprofen, a non-steroidal anti-inflammatory drug (NSAID), is available in many different tablet formulations throughout the world. Many of these are coated, either with film coating or sugar coating. Published research has indicated that commercially available ibuprofen tablets may show considerable variability, both in dissolution in vitro and in rate of bioavailability in vivo. (Gillespie et al., 1982; Stead et al., 1983; Dash et al., 1988; Källström et al., 1988; Romero et al., 1988; Bosanquet and Betteridge, 1993) Sometimes the release characteristics are much reduced. This may have been inherent in the products at manufacture or may have resulted from storage conditions, wherein the tablets were exposed to stressed conditions of temperature and/or humidity. Romero et al. (1988) have shown commercial sugar coated ibuprofen tablets to be adversely effected by storage in humid conditions (37 °C/

* Corresponding author. Tel.: 64-3-479-7255; fax: 64-3-479-7034.

E-mail address: dorothy.saville@stonebow.otago.ac.nz (D.J. Saville).

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75% RH for 4 weeks) and Pandit et al. (1989) showed the release from experimental batches of ibuprofen tablets to be influenced by temperature. We were therefore interested in determining whether commercially available ibuprofen tablets in New Zealand would be influenced by stressed storage conditions of temperature and humidity. In particular, we were interested in the protection offered to ibuprofen tablets from the effects of the environment by tablet vials or unit dose dispensing packs as tablets of many drugs are often repacked from the manufacturer's original pack (blister pack or bottle) by the pharmacist (to assist with patient medication) (Ware et al., 1991, 1994) or repacked in small containers by the patients themselves. Since patients may also leave containers uncapped, the effect of temperature/humidity may be even more important. The aim of this research (carried out in three stages—Study One; Study Two and Study Three) was to investigate the effect of temperature (23 °C; 30 °C; 40 °C) and humidity (stressed conditions: 75% RH; 96% RH) on the in vitro release from selected ibuprofen tablets (200 mg sugar coated; 400 mg sugar coated; 400 mg film coated) when stored in different ways—original packs; repackaged into plastic tablet vials (vial P), air-tight/moisture-proof plastic containers (container Q) or unit-dose dispensing packs (Pack X and Pack Y) or left open to the test environment. (Full study design is outlined later and shown in Table 1, Table 2 and Table 3). Some subsequent investigation into the mechanism of dissolution retardation was carried out.

2. Materials and methods

2.1. Materials

2.1.1. Ibuprofen

Ibuprofen (free acid) (Alphapharm B601049) was used as reference for XRD studies; sodium ibuprofen (lot 124H0843; Sigma Chemical Co) was used for the preparation of the UV standard curve.

Table 1
Study One: % ibuprofen dissolved at 30 min from 400 mg sugar coated tablets [Product A], two 200 mg sugar coated tablets [products B and C] and 400 mg film coated tablets [product D] ($n = 6$; mean ± S.D.)

	Control	75% RH		96% RH	
		(i) Unpacked	(ii) Packed [P]	(iii) Unpacked	(iv) Packed [P]
	% dissolved	% dissolved	% dissolved	% dissolved	% dissolved
A	87 ± 5.1				
B	98.5 ± 8.9				
C	103.1 ± 2.9				
D	91.3 ± 5.9				
1 week					
A				1.7 ± 1.38[a]	61.3 ± 12.0[a]
2 weeks					
A				0.6 ± 0/13[a]	19/5 ± 4.0[a]
4 weeks					
A		6.0 ± 3.5[a]	45.9 ± 9.0[a]	2.8 ± 1.1[a]	3.4 ± 0.38[a]
B		91.8 ± 11.1	96.4 ± 4.4	1.9 ± 0.96[a]	98.1 ± 11.3
C		102.4 ± 5.1	100.5 ± 2.9	2.0 ± 0.9[a]	104.4 ± 8.8
D		not tested	not tested	65.6 ± 13.9[a]	85.4 ± 3.8

Controls before storage; storage conditions (40 °C) were (i) unpacked—75% RH; (ii) amber plastic dispensing vial [P]—75% RH; (iii) unpacked—96% RH; (iv) amber plastic dispensing vial [P]—96% RH. Storage periods of 1 week, 2 weeks and 4 weeks were used. [pH 7.2 phosphate buffer; Paddle; 50 rpm].

[a] $P < 0.05$; % dissolved significantly different to control.

Table 2
Study Two: % ibuprofen dissolved at 30 min from 400 mg sugar coated tablets [Product A] ($n = 6$; mean ± S.D.)

		23 °C		30 °C		40 °C	
		(i) Unpacked	(ii) Packed [Q]	(iii) Unpacked	(iv) Packed [Q]	(v) Unpacked	(vi) Packed [Q]
	% dissolved	% dissolved	% dissolved	% dissolved	% dissolved	% dissolved	% dissolved
Control	90.1 ± 1.6						
3 days		87.3 ± 4.1	89.3 ± 6.1	68.8 ± 3.6	86.68 ± 3.8	11.3 ± 7.5	89.8 ± 3.7
2 weeks		6.0 ± 0.9	92.4 ± 2.4	4.1 ± 2.4	87.0 ± 4.9	5.8 ± 1.3	58.8 ± 9.5
4 weeks		5.1 ± 1.4	89.5 ± 4.3	2.3 ± 1.6	84.9 ± 5.0	6.9 ± 1.4	56.7 ± 6.6

Controls before storage; storage conditions (96% RH) were (i) unpacked—23 °C; (ii) packed in plastic container [Q]—23 °C; (iii) unpacked—30 °C; (iv) packed [Q]—30 °C; (v) unpacked—40 °C; (vi) packed [Q]—40 °C. Storage periods of 3 days, 2 weeks and 4 weeks were used. [pH 7.2 phosphate buffer; Basket; 150 rpm]. $P < 0.05$; % dissolved significantly different to control.

2.1.2. Ibuprofen tablets

Four hundred milligram sugar coated ibuprofen tablets (Study One: lot 16YY6, exp 05/97; Study Two: lot 3N2, exp 07/00; Study Three: lot 3S5 exp 02/0l)[Product A], 200 mg sugar coated tablets (Study One: lot 1A6, exp 10/97; lot 6A2, exp 10/97) [Products B and C] and 400 mg film coated ibuprofen tablets (Study One: AMLO63, exp 11/97; Study Three: lot TG089 exp 07/01) [Product D] available in NZ were used in this study. All products were tested before their expiry dates.

2.1.3. Tablet vials

Study One used amber plastic tablet vials (vial P) in common use in New Zealand pharmacies.

2.1.4. Unit dose dispensing packs

Two brands of unit dose dispensing packs, available in New Zealand, were used [designated Pack-X and Pack-Y]. These were obtained from local pharmacies just prior to use. Each consisted of 4 × 7 blisters with a foil sealing layer.

2.2. Dissolution testing and ibuprofen analysis

Dissolution testing was carried out in 900 ml pH 7.2 phosphate buffer, 37 °C either using paddle (USP Apparatus II) at 50 rpm [Study One] or basket (Apparatus I) at 150 rpm. [Studies Two and Three]. (Hanson 6 vessel Dissolution Test Unit, model 72-RL, series 2023-13 fitted with a Hanson Speed Control, model 48.300–202 and Soft Flo Control Solid State Temperature Control, model 64.700–006; Hanson Research, Northridge, USA). Five milliliter samples were removed (via a 10 μ filter) at 15 min intervals up to 90 min (basket method) and up to 120 min (paddle method). Samples were analysed using UV spectroscopy at 264 nm. (Shimadzu Corp Spectrophotometer UV-1601 (PC) S or 8452A Diode Array Spectrometer). Each dissolution run involved testing of tablet samples of either two products with the same storage history, or one product with two or three different storage histories. As at least 6 tablets of each product/storage history were tested, this meant a minimum of two (or three) runs were carried out, thus ensuring any possible run differences were experienced by all groups of tablets being tested.

2.3. Storage of tablets

2.3.1. Humidity conditions

Humidities of 75% RH and 96% RH were maintained using the appropriate saturated salt solutions within large air-tight plastic containers.

2.3.2. Temperature conditions

Temperatures of 30 °C (± 1) and 40 °C (± 1) were obtained using incubators. Room temperature was 23 °C (average).

2.3.3. Study One

Four products were tested. 400 mg sugar coated tablets [Product A], two brands of 200 mg sugar coated tablets [B and C], and 400 mg film coated tablets [D] were stored unpacked in open petri dishes or in closed tablet vials [P]. More than one type of product were stored in each humidity chamber, thus ensuring the same moisture exposure. Storage conditions were 40 °C; 75% RH and 96% RH; 1 week, 2 weeks and 4 weeks (as indicated in Table 1).

2.3.4. Study Two

Four hundred milligram sugar coated tablets [A] and 400 mg film coated tablets [D] were stored unpacked or in air-tight/moisture proof plastic containers [Q]. Both types of tablets were stored in each humidity chamber. Storage conditions were 96% RH; 23 °C, 30 °C and 40 °C; 3 days, 2 weeks and 4 weeks (as indicated in Table 2).

2.3.5. Study Three

Four hundred milligram sugar coated tablets [A] and 400 mg film coated tablets [D] were used in this study. Storage was unpacked, in air-tight/moisture proof plastic containers [Q] and in the two unit dose dispensing packs [X and Y]. Sugar coated and film coated tablets were placed into alternate blisters of each unit dose dispensing pack and the sealing film was firmly applied. This sealed all blisters independently and, to ensure there was no accidental failure of seal around the perimeter of the packs during storage, a layer of autoclave tape was applied around the edges. Storage conditions were 96% RH; 23 °C, 30 °C and 40 °C; 2 weeks (as indicated in Table 3).

2.4. Investigation of the mechanism resulting in non-dissolving tablets

Some non-dissolving tablets were investigated further after exposure to the dissolution testing procedure. The subcoat was stripped off and the exposed core was re-subjected to dissolution testing. Alternatively, the non-disintegrating core was broken up or crushed and returned to the dissolution medium.

Other stored tablets (anticipated to show reduced release) were tested for dissolution in 0.1 N HCL, reflecting the acidic environment of the stomach.

Fresh (non-stored) tablets were also exposed to different pretreatments. For some tablets, the sugar coating was carefully removed before storage (leaving subcoat intact). For other tablets, both the sugar coating and subcoating were removed and the tablets quartered before storage while some tablets (both sugar and subcoating remaining) were quartered before storage. Storage conditions used in this study were 40 °C/96% RH for 1 week.

Table 3
Study Three: % ibuprofen dissolved at 30 min from 400 mg sugar coated tablets [Product A] ($n = 6$ usually; mean ± S.D.)

		(i) 23 °C	(ii) 30 °C	(iii) 40 °C
	% dissolved	% dissolved	% dissolved	% dissolved
Control	90.3 ± 4 ($n = 12$)			
Unpacked		11.1 ± 5.9[a]	4.1 ± 2.0[a]	6.0 ± 0.87[a]
Container Q		87.0 ± 10.1	91.2 ± 3.4	66.8 ± 8.8[a]
Pack X		not tested	65.2 ± 19.6[a]	56.3 ± 8.3[a]
Pack Y		not tested	78.0 ± 12.2[a]	$11/4 \pm 8.6$[a]

Controls before storage; storage conditions (96% RH) were (i) 23 °C: unpacked; plastic container [Q]; Pack X; Pack Y; (ii) 30 °C: unpacked; plastic container; Pack X; Pack Y; (iii) 40 °C: unpacked; plastic container [Q]; Pack X; Pack Y. Storage period of 2 weeks was used. [pH 7.2 phosphate buffer; Basket; 150 rpm].

[a] $P < 0.05$;% dissolved significantly different to control.

2.5. X-ray diffraction (XRD)

For X-ray diffraction measurements, reference ibuprofen powder was packed into an aluminium holder with a circular cavity. Tablets were also placed into these holders using adhesive tape to keep them in place. In order to ensure a flat surface was exposed to the Xray beam, the top surface of the tablet was carefully sanded (with very fine sand paper) to expose the tablet core. The cavity was sufficiently deep, such that a minimum of core was removed in the sanding process. To obtain the diffractograms, a wide-angle powder X-ray diffractometer composed of an X-ray diffraction generator (Philips PW 1130/00, Philips, Almelo, The Netherlands), equipped with a goniometer (Philips PW 1050, Philips, Almelo, The Netherlands) was used. A copper tube coupled with a graphite monochromator was used as the anode material ($\lambda = 1.541$ Å CuKα), and operated at 40 kV and 30 mA. The monochromator removed secondary fluorescence radiation from the samples, to improve the peak to background signal. The automatic divergence slit was 1° and the receiving slit was set at 0.1°. The take-off angle was fixed at 3° 2θ. The diffraction signals were recorded digitally at a scanning rate of 50 steps/° 2θ and a count time of 1 second/step from 3°–45° 2θ scattering angle. They were then graphed by the software package MacDiff (free software by R. Petschick).

2.6. Scanning electron microscopy

Tablets, after halving or quartering to expose the inner core, were subjected to sputter-coating under argon vacuum (Bio-Rad ES 100, Bio-Rad Micro science Division, Watford, England) resulting in a thin gold/palladium layer (80 nm). A Cambridge S360 scanning electron microscope (Cambridge Instrument, Cambridge, England) which was operated with an acceleration voltage of 5 kV was used. SEM of coating surface; coat cross-section and core cross section were recorded.

2.7. Statistical analysis

Dissolution data (% released at selected times) were compared statistically using one way analysis of variance with two-way comparison using Tukey's test (95%) (Mimtab® software).

3. Results

3.1. Study One

Table 1 shows the % dissolved at 30 min for the different products under different humidity conditions (both at 40 °C) and storage periods (1 week, 2 weeks, 4 weeks). The 400 mg sugar coated tablets [A] show significant retardation ($P < 0.05$) in dissolution when stored unpacked or packed in the dispensing vials [P] at both humidity levels. Significant reduction can be seen even after only 1 week of storage. The two 200 mg sugar coated tablets are not significantly affected by 4 weeks storage at 75% RH ($P > 0.05$) but are affected by 96% RH ($P < 0.05$), while the film coated tablets are only slightly affected by the higher (96% RH) humidity ($P < 0.05$). Interestingly, the dispensing vials offered some, but not complete protection from moisture. The full dissolution profiles were obtained over 120 min. Tablets with extremely low release at 30 min, continued to release drug only very slowly, with usually less than 10% in solution after 120 min.

3.2. Study Two

Table 2 shows the % dissolved at 30 min for the 400 mg sugar coated tablets stored unpacked or packed in air-tight plastic containers [Q]under conditions of 96% RH and temperatures 23 °C, 30 °C and 40 °C. With increasing temperature, the reduction in dissolution rate occurs more quickly, such that the stressed storage at 40 °C results in significant reduction within 3 days. There was no significant change between 2 weeks and 4 weeks. The reduction in dissolution does however occur even at the very moderate temperature of 23 °C. Fig. 1 shows the average dissolution profiles for 23 °C storage. Considerable between-tablet variability was found with the tablets stored unpacked for 2 weeks.

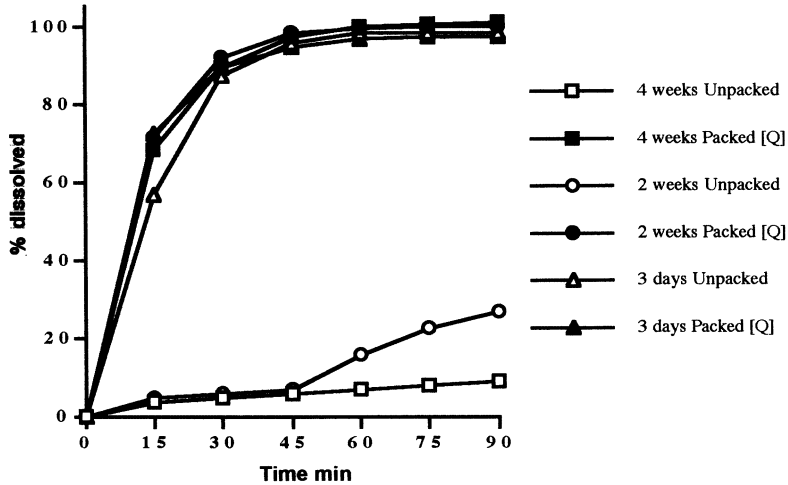

Fig. 1. Mean % ibuprofen dissolved ($n = 6$) from 400 mg sugar coated tablets, stored packed [container Q] or unpacked at 3 days, 2 weeks and 4 weeks at 23 °C. [Study Two].

The non-disintegrating/non-dissolving tablets also failed to disintegrate in 0.1 N HCl and, when the subcoat layer (still intact) was peeled off a hard core remained. This too, failed to disintegrate but did dissolve extremely slowly. When crushed, all ibuprofen was released into solution.

Special pretreatment/storage of tablets showed that the presence of the sugar coating was required for the process of core hardening. Fig. 2 shows SEM of the sugar coated cores of fresh tablets and those pretreated/stored unpacked. The core of the tablet stored with all coating intact (Fig. 2 (iv)) contains large crystalline components.

3.3. Study Three

Table 3 shows% dissolved at 30 min for 400 mg sugar coated tablets stored for 2 weeks at three different temperatures, but this time, also stored in unit dose dispensing packs. Both packs offer a reasonable protection from the effects of humidity at 30 °C but the protection in Pack Y is not very good when 40 °C is reached. Fig. 3 and Fig. 4 show the full dissolution profiles (each the mean of 6 tablets) obtained at 30 °C and 40 °C. Fig. 5 shows the XRD of the 400 mg sugar coated tablets [A] and 400 mg film coated tablets [D]. XRD of stored sugar coated tablets were only slightly different to the controls; XRD of stored film coated tablets were not significantly different to the controls.

4. Discussion

The initial dissolution studies (Study One) were carried out using Paddle (USP Apparatus II) at 50 rpm while subsequent studies (Studies Two and Three) used Basket (USP Apparatus I) at 150 rpm. The agitation conditions for the first study were selected as Romero et al. (1988) had reported these FDA conditions to be most discriminatory for release from ibuprofen products. The later studies utilised the same agitation conditions as the USP dissolution test for ibuprofen tablets, thus allowing some comparison of % released at 30 min with that required (not less than 70% in 30 min) by the official test and possibly providing a better indication of potential bioavailability problems. Dash et al. (1988) showed better correlation between bioavailability and the USP dissolution conditions.

The 400 mg sugar coated tablets showed significant reduction in dissolution when openly exposed to moisture, even at room temperature. When storage was not moisture-proof many indi-

vidual 400 mg sugar coated tablets failed to meet the USP requirements of 70% dissolved in 30 min. The 200 mg sugar coated tablets were less affected by humidity/temperature but some did not meet USP release requirements. The 400 mg film coated tablets were however remarkably resistant to the stressed storage conditions and continued to release ibuprofen in a relatively consistent manner.

When in moisture-proof containers [Q], little change in dissolution was found with most of the tablets while storage of the 400 mg sugar coated tablets (those most susceptible to dissolution reduction) in the unit dose dispensing packs [X and Y] offered some but not complete protection from moisture effects. It is thought the moisture exposure of tablets in the amber vials [P] (Study One) was related to an inadequate seal created by the soft cap, while with the unit dose dispensing packs [X and Y] (Study Three), moisture permeation through the blisters or tiny imperfections in the foil backing may have occurred. Permeation of moisture through the blister material is enhanced as temperature increases. The possibility of seal failure at the edges of the packs had been minimised by applying autoclave tape around the edges. This precautionary step was taken as earlier studies had shown there was considerable risk of seal failure at the edges.

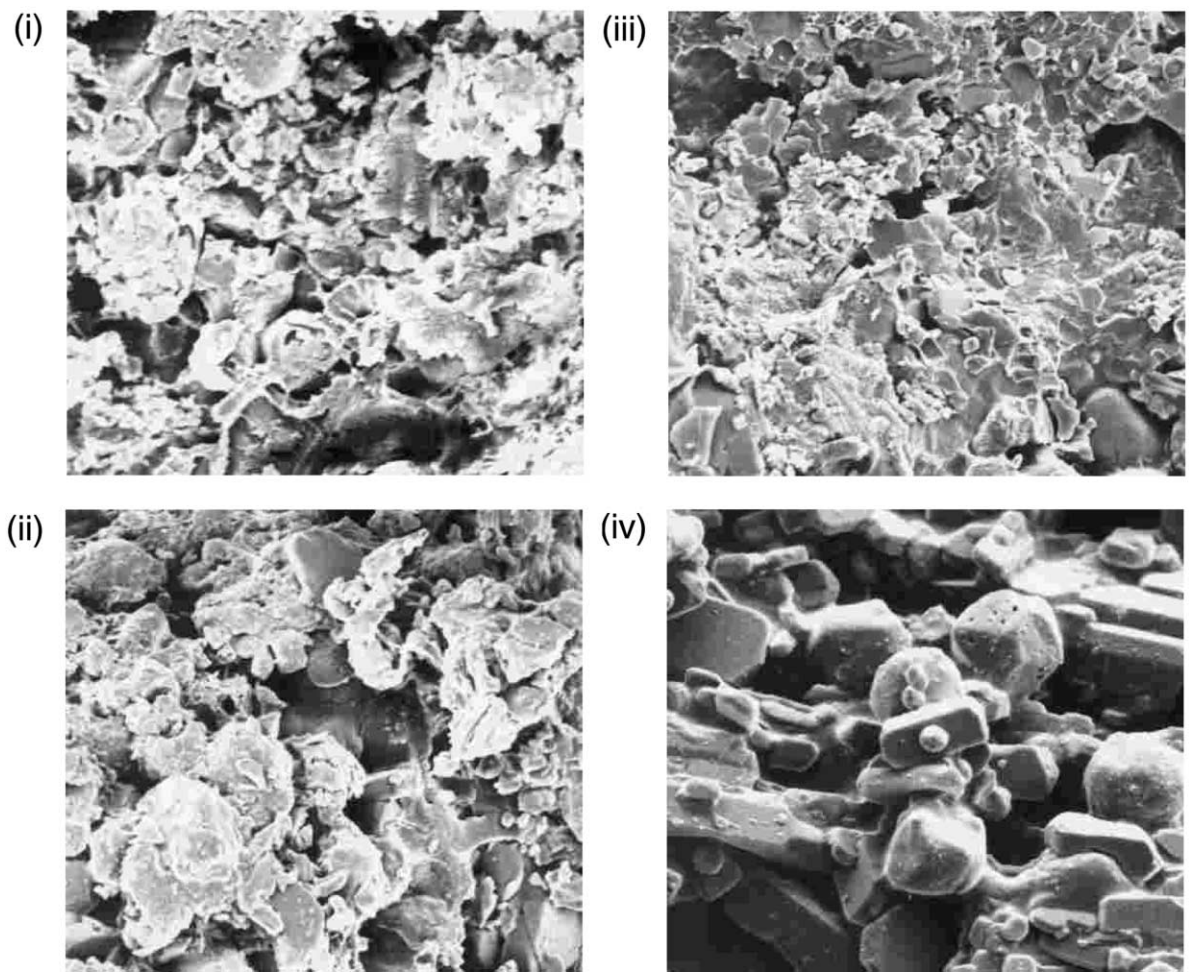

Fig. 2. SEM of 400 mg sugar coated cores, fresh and stored exposed to humidity (96% RH; 40 °C) for 1 week. (i) fresh tablet; (ii) stripped core (no subcoat) stored; (iii) core with intact subcoat stored; (iv) intact tablet stored. (magnification × 1000).

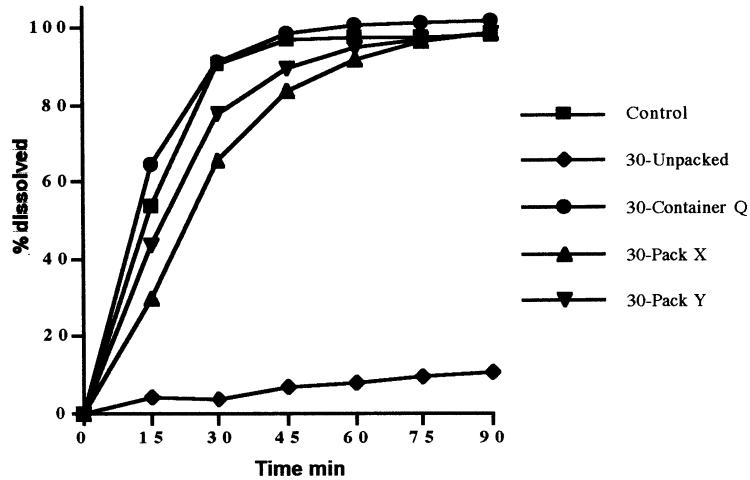

Fig. 3. Mean% ibuprofen dissolved ($n = 6$) from 400 mg sugar coated tablets stored at 30 °C; 96% RH for 2 weeks in different states of packing; control release profile (no storage) included. [Study Three].

Some stored tablets (unpacked or in unit dose packs) showed very large between tablet variability with one or more of the tablets having little reduction in dissolution while others had very large reduction in dissolution. The potential for a large deleterious effect of moisture is evident, although not all tablets showed this effect. The possibility of an even larger, but more consistent, reduction in dissolution with a longer storage period is considered likely.

4.1. Mechanism of dissolution retardation

The various investigations involving storage of stripped cores, quartered tablets with sugar coating intact and intact cores with subcoat intact, led to the conclusion that the presence of the components of the sugar coating were necessary to induce large decrease in disintegration and dissolution. The serious dissolution retardation, found for the 400 mg sugar coated tablets, was not seen with the two 200 mg sugar coated tablets (although some retardation did occur). Whether this is a function of different excipients present within the core or a different proportion of ibuprofen to excipient (large dose *v* small dose) is not known. Other workers have commented that storage of sugar coated tablets exposed to moisture may result in failure of the subcoat to rupture but not influence the disintegration or dissolution of the core (Ondari et al., 1984). This was clearly not the case in our study; both subcoat and core failed to disintegrate. Romero et al. (1991) have also shown that low concentrations of disintegrant may lead to slowed release from ibuprofen tablet cores and that the active/diluent ratio may also influence drug release. Pandit et al. (1989) found ibuprofen release from experimental tablet batches could be reduced by storage at moderately high temperatures (45 °C), within well sealed containers. They commented that ibuprofen was not known to exist in more than one polymorphic form and postulated that ibuprofen-excipient interaction may be occurring.

The XRD difiractograms after storage (all conditions) were very similar to the controls but those of the sugar coated tablets differed from those of the film coated tablets, particularly in the 12 2θ region, which has been noted by Romero et al. (1993), to be influenced by manufacturing processes. Other minor differences in XRD were noted. The XRD of a number of crystal modifications of ibuprofen have been reported (Labhasetwar et al., 1993; Romero et al., 1993; Khan and Jiabi, 1998). The crystal modifications show different dissolution characteristics, yet the XRD difiractograms do not appear to be significantly different. Thus we cannot exclude the possibility

that some crystal modification is occurring, induced in some way by the presence of moisture and other excipients of the core or coat. Romero et al. (1993) showed via SEM that a hydrophobic ibuprofen network could be built up within the granulate and the tablet via a sintering process. A change in this hydrophobic network could also be involved in the dissolution changes we have found. Our SEM of the cores of the tablets before and after storage showed an increase in crystal-like structures within the sugar coated cores (tablets exposed to moisture) but little change in the sugar coated tablets stored, protected from moisture. No significant changes in the cores of the film coated tablets were observed. The larger crystal structures may indicate a recrystallisation of ibuprofen, either to form a different habit or different particle size. However, since the cores failed to disintegrate, even when stripped of the subcoat, some interaction between the ibuprofen and core excipient, an excipient-excipient interaction or a loss of disintegrant capacity cannot be excluded. The 400 mg sugar coated tablets contain maize starch, colloidal silicon dioxide and stearic acid in the core. It is possible the maize starch, on contact with moisture, is acting as a super-binder alone or facilitating the formation of some form of ibuprofen-starch network which does not disintegrate. This could lead to small changes in XRD. The subcoat of the 400 mg sugar coated tablets is thought to contain sodium carboxymethylcellulose, acacia and calcium sulphate dihydrate. Hardening of the subcoat may occur by mechanisms reported by other authors or involve interaction with ibuprofen, as ibuprofen has been detected (via infra-red studies) in the subcoat after storage. Further investigation of the hardening mechanisms of both core and subcoat are required.

4.2. Implications of reduced release rates

Although in vivo studies were not carried out, it would be anticipated that in vivo bioavailability would be affected. However, Stead et al. (1983) have reported the difficulties of establishing an in vitro test which discriminates between products of different bioavailability, yet does not artificially discriminate between products of equivalent bio availability. Thus, although we have found significant differences in in vitro release rate induced by storage, the effect in vivo is difficult to predict.

4.3. Implications for product storage

For the sugar coated tablets it is important to observe not just the manufacturer's recommendation for storage temperatures less than 25 °C, but

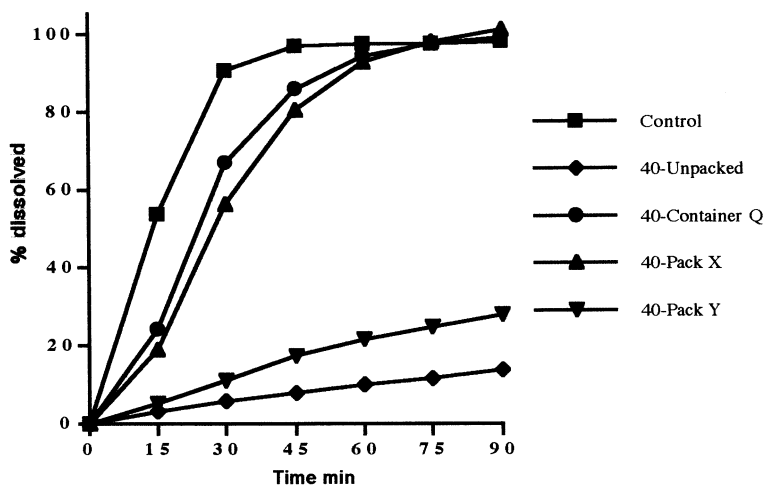

Fig. 4. Mean% ibuprofen dissolved ($n = 6$) from 400 mg sugar coated tablets stored at 40 °C; 96% RH for 2 weeks in different states of packing; control releaseprofile (no storage) included. [Study Three].

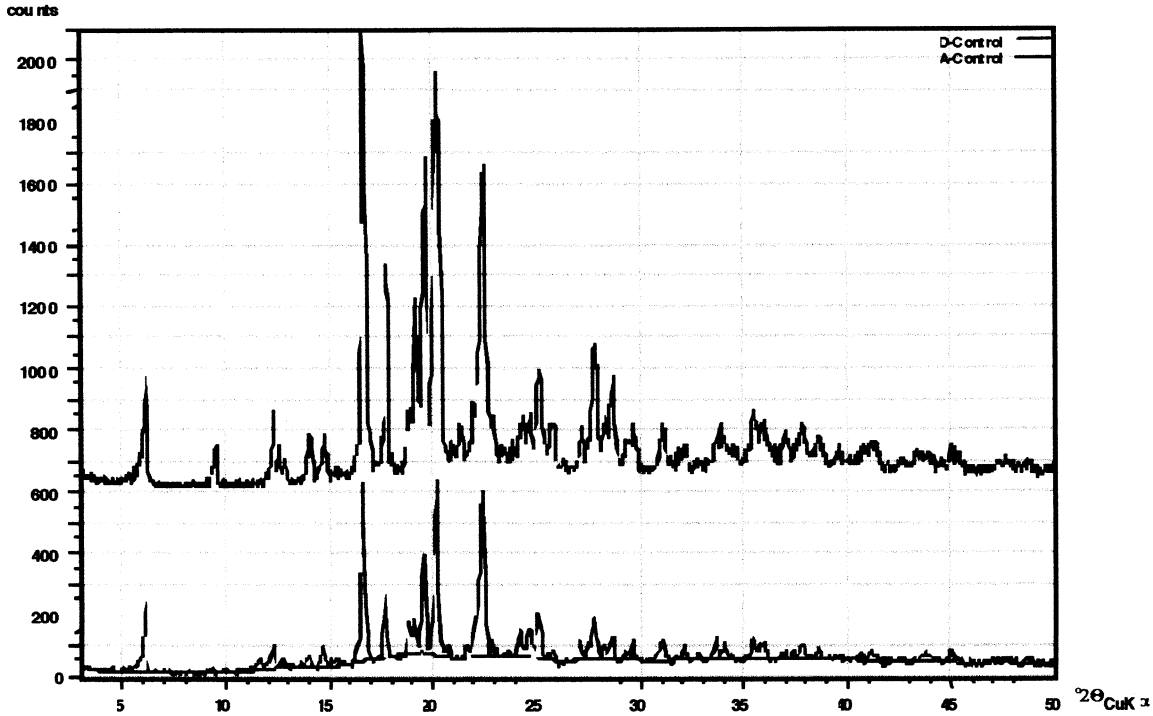

Fig. 5. XRD diffractograms of 400 mg sugar coated tablet (A—lower) and 400 mg film coated tablet (D—upper).

also to protect from moisture, particularly in hot climates. In use, the unit dose dispensing packs may be subjected to a reasonable degree of handling, during which accidental rupturing of nearby blister seal may occur. Exposure of individual tablets, in this manner, may lead to an even greater exposure to humidity, with deleterious effects on release. However, the risks of moisture exposure in using unit dose packs must be weighed against the considerable value of these packs in aiding patient medication (Ware et al., 1991, 1994), and the dissolution-stability of tablets within these packs is certainly greater than that of tablets left unpacked, such as when the patient leaves the lid off the bottle for ease of access each day.

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