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COMMUNICATION

EFFECT OF STORAGE CONDITIONS ON THE PHYSICAL PROPERTIES AND IN VITRO DISSOLUTION OF DIRECTLY COMPRESSED TABLETS

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A B S T R A C T

Tablets of aspirin, ascorbic acid and pyridoxine hydrochloride were prepared by direct compression, using bone powder or Emcompress, respectively as direct compression fillers. Tablet properties such as mean weight, thickness, breaking strength and friability were monitored before and after storage for 30 days under specified temperature and relative humidity conditions. The tablet properties were apparently unaffected by the conditions of storage, while release parameters were, however, modified. In vitro dissolution rate constant, was found to exhibit good correlation with the dissolution efficiency.

INTRODUCTION

In vitro dissolution data have been used as close estimates of the bioavailability of drugs. Thus good correlations have been established between in vitro dissolution and in vivo absorp-

tion rates, using amounts of salicylate in plasma or urine as an index (1-3). Conditions which might modify the in vitro dissolution of drugs have been studied by Levy et. al. (4-5).

Since these studies pertain to tablets produced by wet granulation processes, it seems desirable to ascertain the conditions that might induce changes in the same physical properties of tablets produced by direct compression. To this end, the effect of ageing on the in vitro dissolution of aspirin, ascorbic acid and pyridoxine hydrochloride tablets prepared by direct compression were examined. The tablets were manufactured using bone powder and then Emcompress to which it is chemically related.

MATERIALS AND METHODS

Aspirin, stearic acid (Merck), ascorbic acid (Halewood), vitamin B_6 (Roche) and alginic acid (Fluka) were all used as procured from the suppliers. Bone powder and Emcompress were used as direct compression fillers.

The tablets were formulated to contain 60.5 %, 43.0 % and 42.5 % respectively of the direct compression filler. All formulations were compressed into tablets using an F 3 single punch tablet machine (Manesty). The same pressure adjustment was used for all tablets produced.

Dissolution rate tests were carried out in the USP dissolution apparatus, model DTD, (Erweka) using 0.1N HCl maintained at $37 \pm 0.5^{\circ}$ as dissolution medium. Three replicate tests were done for each tablet batch, and the mean results taken. All samples were analysed in an SP-8 UV spectrophotometer (PYE Unicam) at 229 nm, 245 nm and 291 nm for aspirin, ascorbic acid and pyridoxine respectively.

TABLE 1

Physical and Dissolution Data of Vitamin C Tablets

		Storage Conditions			
		Control	4°/80%RH	29°/50%RH	60°/92%RH
Mean Weight(mg.)	A	278.75	280.50	277.15	278.75
	B	278.25	275.23	274.98	274.71
Mean Breaking Strength (N)	A	3.92	3.24	2.43	4.02
	B	3.65	4.03	3.37	3.83
Friability (%)	A	1.30	1.60	1.60	1.70
	B	1.26	1.62	1.16	1.02
Disintegration Time (min.)	A	0.76	0.58	0.92	12.10
	B	4.43	4.93	3.75	6.15
Dissolution Rate constant (K)	A	15.75	13.29	15.75	12.97
	B	11.88	9.99	10.98	8.75
t_{50} (min.)	A	1.10	2.20	0.90	2.50
	B	2.60	4.90	2.90	4.70

A - Bone powder; B - Emcompress.

RESULTS AND DISCUSSION

The physical properties of the tablets were re-evaluated after 30 days of ageing. Table 1 shows the data obtained for vitamin C tablets. The mean weights, breaking strength and friability of the aged tablets revealed no significant changes from those of the control tablets.

Since bone powder and Emcompress are water insoluble and non-hygroscopic, the effect of high relative humidity on these excipients would not be expected to cause large changes in the physical properties of the tablets. Data in table 1. are

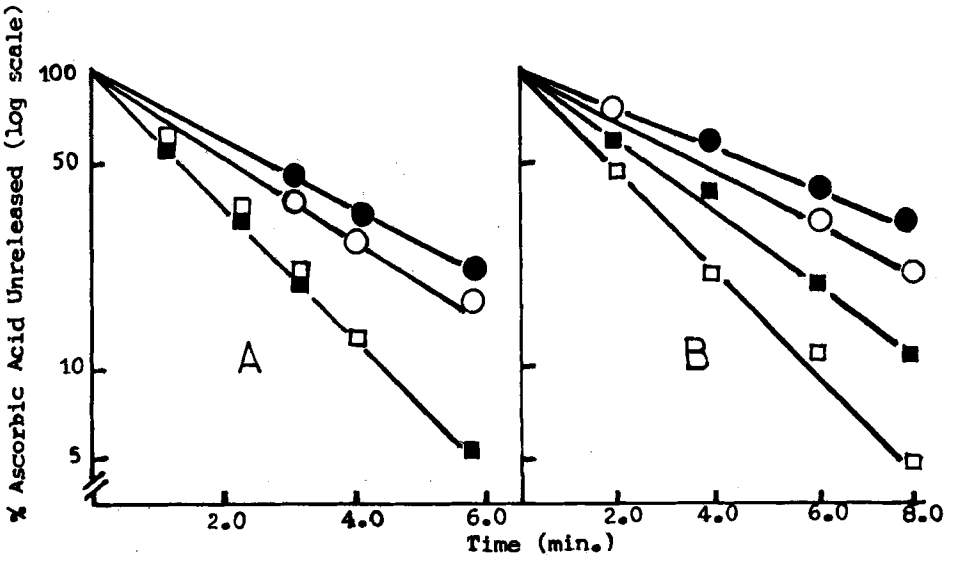

FIGURE 1

Apparent first order dissolution plots for ascorbic acid tablets. □ Control; ○ 4°/80% RH; ■ 29°/50% RH; ● 60°/92% RH. A - Bone powder; B - Emcompress.

consistent with the idea that changes in tablet hardness and disintegration time are not always related (6).

Kinetic data obtained from *in vitro* dissolution studies are usually applied to predict *in vivo* bioavailability of drugs. On the basis of the good correlations between *in vivo* and *in vitro* data already established (1-3), a modified form of the Wagner-Nelson Plot (7) was adopted in the present study to obtain the *in vitro* release rate constants of the various tablets. Representative plots using the data obtained for ascorbic acid tablets are shown in fig. 1. It is obvious

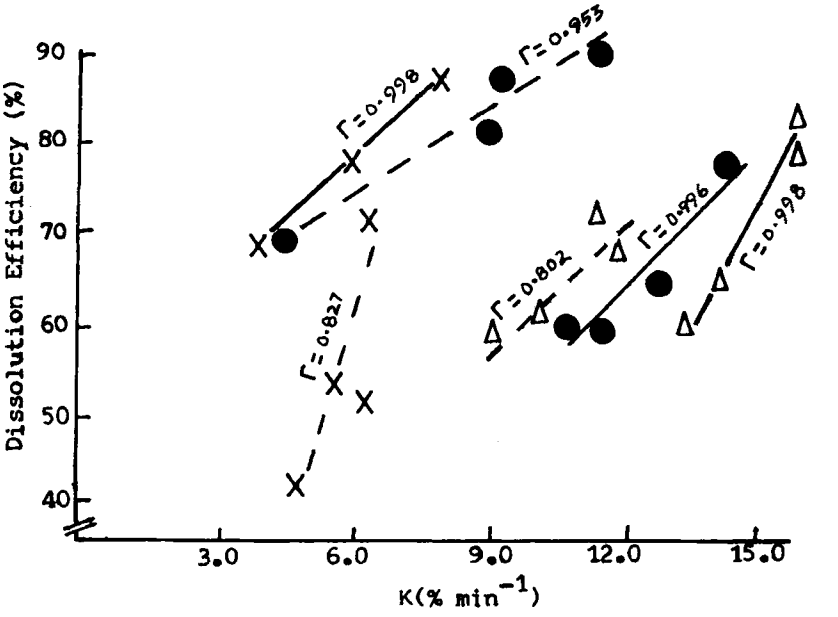

FIGURE 2

Dissolution efficiency as a function of Dissolution rate constants of tablets. X Aspirin, Δ Ascorbic acid, ● Pyridoxine hydrochloride. —— Bone powder, _ _ _ _ Emcompress.

that the tablets exhibited a first order release pattern which can be represented as:

$$\ln C_t = \ln Co - Kt$$

where C_t is the per cent drug yet unreleased at each sampling time, t; Co, the per cent of stated drug content at t = o and K, the first order release rate constant.

In order to present the data in a manner that would clearly bring out the effect of the storage conditions, t_{50}

and t_{90} of the tablets were determined. However, t_{90} was not always obtainable, probably because of instability of the drugs during ageing. The values for t_{50} are shown in table 1.

Dissolution efficiency is reported to be a more realistic parameter for evaluating the dissolution pattern of tablets (8). This parameter takes into account the dissolution profile as a whole, as against t_{50} or t_{90} which are single points on the curve. The dissolution efficiency was calculated using the method of Khan and Rhodes (9). Fig. 2 shows that dissolution efficiency is positively correlated with dissolution rate constant, presenting high values of correlation coefficient, r.

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