EFFECT OF BINDER AND DISINTEGRANT CONCENTRATION ON THE DISSOLUTION RATE OF MEDICAMENTS FROM TABLET FORMULATIONS.

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ABSTRACT

The separate effects of varying the concentrations of sorghum and maize starch when used as tablet binder and a disintegrant on the dissolution rate of acetylslicylic acid tablets have been investigated.

The dissolution rate of tablets decreased with increasing binder concentration and a direct correlation was observed between disintegrant concentration and dissolution rate.

Acetylsalicylic acid tablets formulated from sorghum starch had shorter disintegration times and higher dissolution rates than those formulated from maize starch under the same experimental conditions.

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INTRODUCTION

It is well known that there is a significant difference between chemical equivalence and bioavailability of drugs from their delivering systems. This difference has been commonly demonstrated in conventional tablets and its magnitude depends among other things on the formulation factors and the empiricism of tablet manufacture.

Tablet should contain the labelled amount of medicament which must be readily available to the body in order to achieve therapeutic response.

The absorption of medicament from solid dosage forms often depends on the dissolution rate of the drug from formulated system. Several workers have studied the effects of various formulation factors on dissolution rates of medicaments from compressed tablets, Levy et al 1963 reported the effects of granule size, starch concentration and compression pressures on the dissolution rate of salicylic acid from granules prepared by doubled compression.

Yen 1964 studies various factors affecting the dissolution of triamterence. Morrison and Coworkers 1965 studied tablet disintegration and physiologic availability of drugs.

While Jacob et al 1968 studied the effects of binder concentration, tablet hardness and storage conditions on the dissolution rate of phenobarbital from tablets.

Khalil et al 1984 investigated the dissolution rate profiles of commercial phenylbutazone tablets considering inter and intra-brand effects.

One or more formulation factors could contribute to the slow dissolution rate of medicament from tablets. The present communication deals with the effect of various concentrations of maize and sorghum starchbinder and disintegrant on the dissolution rate of acetylsalicylic acid for tablets compressed at a fixed compression pressure setting.

EXPERIMENTAL

MATERIALS - Acetylsalicylic acid and Talc used in this study were from BDH Chemical Ltd, Poole, England.

Maize starch used was obtained from May and Baker Ltd, Dagenham, England. The sorghum starch was prepared in our Laboratory by the following procedures.

METHODS

PREPARATION OF SORGHUM STARCH

The sorghum grains (white seeded, variety L 1500) were cleaned by sieving to remove the impurities, broken grains and foreign seeds.

The cleaned grains were conveyed in known weight into steep acid, prepared as described by Knight 1969. The steep acid softened the corn kernel and broke the protein structure within the endosperm thus loosening the starch granules and facilitating efficient separation.

The steep liquor was then removed, the wet sorghum grains were dropped in purified water and subjected to coarse grinding, to partially macerate the grain, and remove the pericarp free the germ from the endosperm.

Germ separation was achieved by flotation method. The underflow consisted of fibres starch and protein. This mixture was finely ground, the fibres which were not reduced by this process were removed by sieving.

The starch was allowed to settle and washed several times with 0.1N sodium hydroxide to neutralize the acidity and dissolve the gluten.

Excess alkali was removed by washing the starch several times with purified water.

The starch was collected on a buchner funnel and dried at 70oC for 6 hours and the size reduced to fine powder.

GRANULATION

The compositions of the tablet

formulations are given in Table 1a and b.

The wet granulation method was used, all in-gredients except the binder were dry mixed using pestle and mortar for 10 minutes.

In the first batches, the binder concentration was kept constant while the disintegrant concentrations were varied.

In the second batches, the disintegrant concentration was kept constant, while the binder concentrations were varied.

In both batches, the disintegrants were added as endo and exo-disintegrant.

The massing time of 8 minutes was kept constant for all the batches, using sufficient quantity of binder mucilage at 40 + 1°C.

The wet masses were passed through a mesh sieze of 1.6mm size in an oscillating granulator (Erweka apparatebau Type FGS made in Western Germany). The granules were dried immediately at 40°C for four hours in a hot air oven (Gallenkamp Oven BS size three) and reseived through 1.60mm size sieve.

Over wetting of granules was avoided and granules were dried immediatelyto minimize possible hydrolysis of acetylsalicylic acid. The exo-disintegrant and 0.25% w/w of 1:1 Talc and Magnesium stearate mixture used as lubricant were, added thoroughly mixed by rotating in a plastic bottle at different angles for 10 minutes.

Table 1: Tablet Composition For Determining Effects of Disintegrant Concentrations.

Active Ingredient - Acetylsalicylic acid as 300mg tablet. Starch as disintegrant - 2.50, 5.00, 7.50, 01.00% w/w of active ingredients.

Starch as binder	-	10.00% w/w
Talc	-	0.125% w/w) of dry granules
Magnesium Stearate	-	0.125% w/w

Note:- The starch concentration used as binder was kept constant

Table 2: Tablet Composition for Determining Effect of Binder Concentrations.

Active Ingredient - Acetylsalicylic acid 300mg tablets Starch as disintegrant - 2.50% w/w of active Ingredient.

Strach as binder	-	5.00, 10.00, 15.00% w/w
Talc	-	0.125% w/w)
Magnesium stearate	-	0.125% w/w) of dry granules

Note:- The percentage of starch used as disintegrant was kept constant.

Note: Sorghum and Maize starches were employed seperately as binder and disintegrant.

COMPRESSION

300mg tablets were prepared by compressing granules (250 um - 1.00 mm size fractions) in a single punch tableting mahcine (Manesty) fitted with 10.00mm die and flat faced punches at the rate of 30 tablets/minute and a fixed compression pressure setting at 6.00 units.

EVALUATION OF TABLETS

The tablets were evaluated on the basis of hardness, friability, disintegration time and dissolution rate.

DISSOLUTION STUDIES

Erweka dissolution rate tester, Type DT with a rotating basket type assembly, was used for determining the dissolution rate of active medicaments in the tablets

The dissolution medium used was 1 litre of 0.1N HC1. One tablet was placed in the basket and rotated at a speed of 120 r.p.m. All dissolution rate studies were carried out at 37 $\pm$ 0.5°C, 24 hours after compression..

At appropriate intervals, A 1.0ml sample was diluted with 0.1 NHC 1 and the solution was read on a SP8-100 Ultraviolet spectrophotometer (Pye Unicam) at a wavelength of 229nm; subsequent replacement of fresh medium was made.

The spectrophotometer readings were compared to a Beer-Lambert standard curve and the milligrams of acetylsalicylic acid dissolved were determined.

Three replicates were made and averaged. Any possible interference from the starchin solution was solution was ascertained by the following method: A mixture was prepared by adding 25mg of both sorghum and maize starch respectively to 100ml of distilled water and gently agitated for 1 hour on a flask shaker. A 3ml sample was filtered through a millipore filter and scanned on a spectrophotometer in the range of 200-400nm.

There was no absorption by any of the starches at the wavelength used in this assay for acetylsalicylic acid.

To determine the possible effect of wet-granulation on hydrolysis of acetylsalicylic acid formula-

ı, A 1.0ml sample from the solution medium after an hour diluted with fresh medium and d on a spectrophotometer at a velength of 297nm for salicylic d.

RESULTS AND DISCUSSION

able 3: Effect of Disintegrant Concentrations on Dissolution Rate of Acetylsalicylic acid from tablets.

ype of isintegrant	Disintegrant Conc. % w/w	Dissolution Times (mins) T50%	T90%
orghum arch	2.50	7.75	15.25
	5.00	4.75	13.38
	7.50	4.50	12.25
	10.00	4.25	9.50
laize Starch	2.50	13.00	22.50
	5.00	10.25	19.45
	7.50	6.50	14.25
	10.00	4.75	13.00

able 4: Effect of Binder Concentrations on Dissolution Rate of Acetylsalicylic Acid from Tablets.

ype of inder	Binder % w/w	Dissolution Times (Mins) T50%	T90%
orghum Starch	5.00	5.50	13.25
	10.00	8.00	15.00
	15.00	13.50	19.00
laize Starch	5.00	7.75	18.25
	10.00	10.25	19.50
	15.00	15.25	23.55

There was a direct correlation ween the concentrations of ntegrant and dissolution rate of ve ingredient. Dissolution rates ame faster with increasing ntegrant concentrations (Fig. 1).

Similar observations have been orted by Schroeter and others 2 and by Esezobo and Pilpel 6, it was noted that the numeri- terms in these relations depend siderably upon the drug and on the excipient involved.

On coming into contact with water a tablet disintegrates into granules and deaggregates into fine particles.

Considering that dissolution rate is proportional to the surface area available, the amount dissolved from the intact tablet will be negligible compared with that dissolved from the granules and fine particles (Pilpel et al 1978).

It follows therefore that disintegration is the rate determining step in dissolution.

From the data on tables 3 and 4 it can be seen that the type of starch used as a disintegrant did significantly affect the rate of dissolution of tablet formulation. The dissolution of drug was considerably faster from tablets formulated with sorghum starch as disintegrant than maize starch.

This is in accordance with observed shorter disintegration times of the starch compared to maize starch (Garr and Bangudu 1987).

An inverse relationship was observed between binder concentrations of both starches and dissolution rates: Fig. 3 & 4.

This is expected and it agrees with the relationship between binder concentration and tablet hardness.

The harder the tablet the higher it takes to disintegrate into granules and deaggregate into fine particles from where higher proportion of dissolution of active ingredients takes place.

No significant absorption was observed when 1.0ml sample from the dissolution medium affter an hour was diluted with fresh medium and read on a spectrophotometer at a wavelength of 297nm (for possible hydrolysis of the drug to salicylic acid).

This implies that hydrolysis must be minimal if any, and is attributed to avoidance of over wetting during granulation and rapid drying of granules.

CONCLUSION

The effect of various concentrations of sorghum and maize starch binder and disintegrant respectively on the dissolution rate of acetylsalicylic acid from tablet formulation was determined.

A direct relationship was observed between the disintegrant concentration and dissolution rate of tablets.

Different types of starch did have an effect on the dissolution rate of acetylsalicylic acid from tablets, sorghum starch exhibit faster drug release than maize starch.

The hydrolysis of acetylsalicylic acid during wet granulation could be reduced by avoidance of over wetting during graulation and rapid drying of granules.

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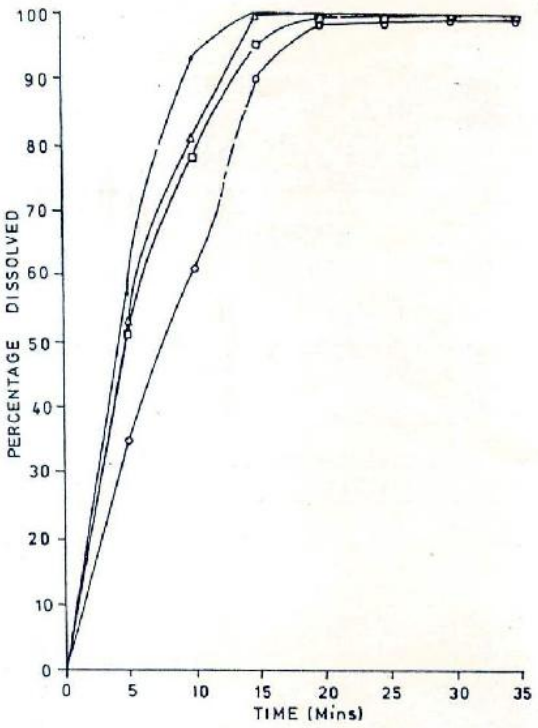
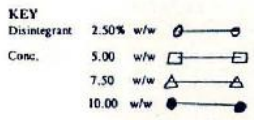


Fig. 1: Effect of Sorghum Starch Disintegrant on Dissolution Rates of Acetylsalicylic Acid Tablets.



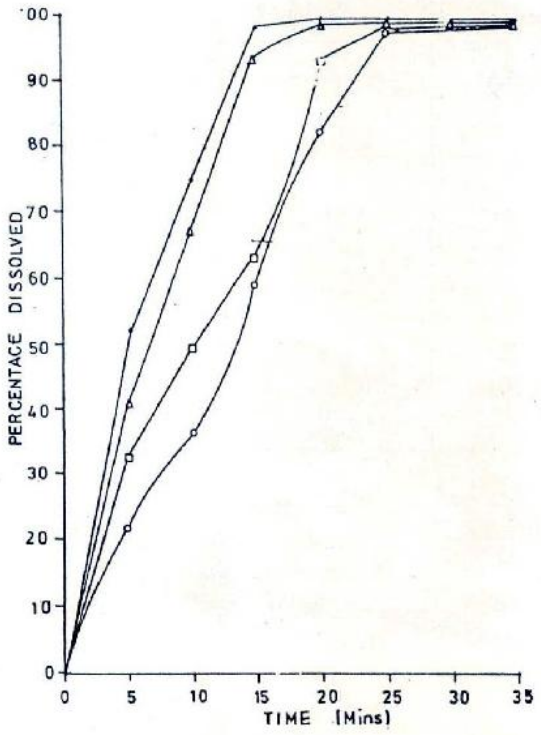


Fig. 2: Effect of Maize Starch Disintegrant on Dissolution Rates of Acetylsalicylic Acid Tablets.