EFFECT OF CERTAIN TABLET FORMULATION FACTORS ON DISSOLUTION OF ASPIRIN TABLETS

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Abstract

Formulation of drugs into various dosage forms may modify profoundly the onset, intensity and duration of physiological response, the correct dosage for the patient, the incidence and intensity of side effects and the stability of the drugs. These effects are illustrated by examples from the clinical and scientific literature. It is the purpose of this paper to show that the physiological response to the administration of a given drug products is frequently a function of both the pharmaceutical formulation of the particular dosage form as well as of the active ingredient (JPMA 29:91,1979).

Introduction

In recent years much attention has been focussed on the problem of drug availability. The drug availability is determined by the rate of release from the physical system commonly referred to as the dosage form.

The clinical effectiveness of tablets and other pharmaceutical dosage forms of drugs depends on at least two factors: the medication must not only be present in the labelled amount, but also must be available to the body. Considerable evidence exists which indicates that during production of various dosage forms, the absorbability of the active ingredient of drug preparations may be modified markedly, either intentionally or unintentionally. As a result, the amount of drugs available to the body may be considerably less than the total amount of drug in the dosage form. It is apparent, therefore that in addition to exami-

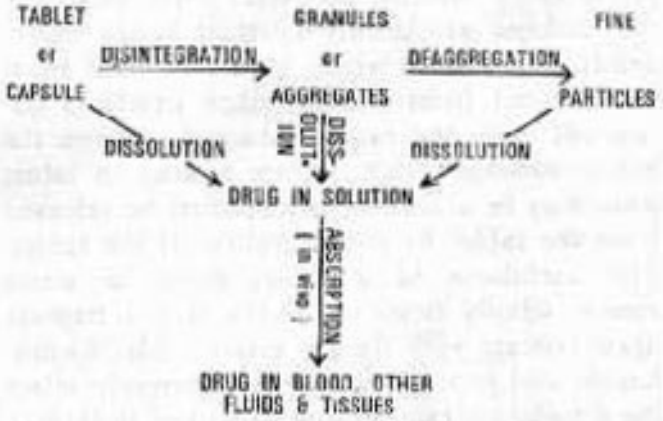

Table I: Formulation of Aspirin Tablets 0.3 G.

Excipients	Formulation Nos. 1 mg	2 mg	3 mg	4 mg	5 mg	6 mg	7 mg	8 mg
Lactose	25	25	25	—	—	25	—	25
Starch dried	25	30	30	25	45	20	35	27
Starch for Paste	9	10	—	—	—	—	—	—
Acacia	—	—	—	7	3	—	—	—
Gelatin	—	—	—	—	—	2	—	—
X. 1 S. C. M. C.	—	—	—	—	—	—	5	—
X. 2 P. V. P.	—	—	—	—	—	—	—	8
Sod. Lauryl Sulphate	—	—	3	—	3	—	3	—
Talcum	3	2	2	3	2	2	2	2
Magnesium Stearate	—	3	3	—	3	4	4	3

X. 1 Sodium Carboxymethyl Cellulose.

X. 2 Polyvinyl Pyrrolidone.

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Table II: Dissolution Characteristics of Aspirin Tablets

Formula	Hardness (Kg)	Contents/ tablet (mg)	Amount in solution in 10 min (mg)	Disintegration Time (sec)	Dissolution Half Time (min)
1	4	295.5	42.47	5	More than 30 min
2	4.5	296.2	158.69	30	Less than 10 min
3	4.5	298	135.72	15	More than 10 min
4	4	296.58	31.73	25	More than 30 min
5	5	297	200	8	Less than 10 min
6	5	298	99.11	30	More than 30 min
7	5.5	297.7	250	15	Less than 10 min
8	5	298.5	270	15	Less than 10 min

nation of oral dosage forms for amount, identity and purity, there must be some evaluation of the physiological availability of the active ingredients thereof. Such information is absolutely necessary to ensure clinical effectiveness.

The following scheme indicates the processes involved when a tablet or capsule is exposed to a fluid under suitable conditions *in vitro* or in the gastro-intestinal contents *in vivo* after oral administration.

Compressed tablets which are the most widely used dosage forms, also present some of the most difficult problems with respect to the biologic availability of their active ingredients. The rate at which a physiological effect is produced from a drug taken orally is dependent upon the rate of absorption from the gastro-intestinal tract. Before a drug in tablet form may be absorbed, it must first be released from the tablet by disintegration of the tablet. The usefulness of a tablet therefore arises almost wholly from its ability to disintegrate upon contact with fluid. Certain tablet formulations and processing factors apparently affect the dissolution rate of drug contained in tablets. Since it has been found that generically identical tablet products made by different manufacturers exhibit significant differences in dissolution rate of the active ingredient (Levy and Hayes, 1960) in a number of instances, poor tablet formulation has been shown to cause a significant reduction of physiologic availability of the active ingredient and impairment of clinical response (Campagna et al., 1963).

Experimental

In the present study the different disintegrants i.e. starch, gum acacia, gelatin, sodium carboxymethyl cellulose and polyvinylpyrrolidone, either alone or in combination with magnesium stearate (lubricant) and/or sodium lauryl sulphate (surfactants) were used. The tablets were compressed on a single punch machine operating at about 60 tablets/minutes. All the dissolution tests were at 37°C in 0.1N HCl. The samples were taken at five, fifteen and thirty minutes and were appropriately diluted with 0.1N HCl and analysed spectrometrically at 280 and 308 mm for acetylsalicylic acid and salicylic acid respectively using a Unicam Spectrophotometer Model SP 500 (Table I and II).

Results and Discussion

The most rapid disintegration was achieved with polyvinylpyrrolidones and sodium carboxymethyl cellulose. The addition of a lubricant delayed the disintegration of the tablets. The effect of lubricant on disintegration may be attributed to their water repellant nature (Bergaman and Bandelin, 1965). However good results were observed by the addition of sodium lauryl sulphate which is water-soluble and a surface active agent that actually promotes contact between drug solids and aqueous medium and furthers penetration of solvent into agglumerates of solid particles. Tablets formulated with gum acacia and gelatin gave delayed disintegration time and formed a layer of viscous solution around the dissolving drugs solids. Rapid disintegration was also achieved with corn starch at a concentration of 10 and 15%.

References

Bergaman, L.A. and Bandelin, F.J. (1965) Effects of concentration, aging, and temperature on tablet disintegrants in a soluble direct-compression system. J. Pharm. Sci., 54:445.

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