

ROLE OF EGG ALBUMIN AS A BINDER AND DISSOLUTION RATE ENHANCER

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ABSTRACT: In present investigation, the effect of egg albumin on the rate of dissolution of analgesic tablets has been studied. Three sets of binder containing egg albumin in different ratios were used to prepare laboratory scale formulations and their dissolution behavior was studied.

The best result was achieved from formulation having all the three binders (egg albumin, gelatin and corn starch) in 1:1:1 ratio. The results were then compared to the commercially available tablets.

The results obtained show that egg albumin can be utilized as a binder in wet granulations of poorly water soluble drugs to improve their dissolution rate.

KEY WORDS: Analgesics, Binder, Dissolution rate, Egg albumin, Mefenamic acid.

INTRODUCTION

Analgesics are agents which relieve pain by acting centrally to elevate pain threshold without disturbing consciousness or altering other sensory modalities. Antipyretics are drugs which reduce elevated body temperature.

The analgesics and antipyretic drugs include a small, heterogeneous group of compounds which are without significant addiction liability, and therefore are not subject to regulation under the Controlled Substances Act. Most of these agents affect both pain and fever. Consequently, they are widely used for minor aches and pains, headaches, and the general feeling of malaise that accompanies febrile illnesses, and to alleviate symptoms of rheumatic fever, arthritis, gout and other musculoskeletal disturbances.

The number of non-steroidal anti-inflammatory drugs (NSAIDs) has increased to the point where they warrant a separate classification. All of these drugs inhibit the synthesis of prostaglandins. Mefenamic acid is included in this category of drugs (Swingard, 1985).

Mefenamic acid is absorbed from gastrointestinal tract and peak plasma concentrations occur about 2-4 hours after ingestion. The half-life is reported to be 3-4 hours. Mefenamic acid is extensively bound to plasma proteins. Approximately 50% of the dose may be recovered in the urine within 48 hours, mainly as conjugated metabolite (Laurence and Bennett, 1992). The drug is not recommended for use in children or pregnant women in United States (Flower et al, 1985).

It is used for the relief of mild to moderate pain including headache, dental pain, post-operative and post-pain, and dysmenorrhoea. It is also used in rheumatic disorders such as osteoarthritis and rheumatoid arthritis. Mefenamic acid may also be used in menorrhagia (Guillebaud, 1978; Laurence and Bennett, 1992).

In recent years, absorption enhancers have been actively investigated. Some absorption enhancers have also been found in folk medicines and health foods (Kai et al, 2002). Egg is included in the category of health foods. The protein of egg white is complete; it contains all of the essential amino acids in well-balanced proportions. The thick white is made up mainly of the proteins ovalbumin, conalbumin, ovomucin, ovoglobulins, ovomucoid and lysozyme (Encyclopedia of Food Science and Technology, 1991).

In present investigation egg albumin is investigated as a dissolution rate enhancer which ultimately results in the enhancement of absorption. Faster the drug is absorbed quicker it produces the therapeutic effect. Pain is a problem with which the sufferer wants to be relieved as quick as possible so analgesic drug was chosen for the present study. But egg albumin can be used as a dissolution rate enhancer in other classes of drugs also.

MATERIALS AND METHODS

Egg albumin was taken fresh. All other materials used were of analytical grade.

Wet granulation method was used to prepare tablets on laboratory scale. There were in total three types of formulations. Formulation no. 1 (A1) contained egg albumin, gelatin and com starch in 1: 1: 1 ratio, Formulation no. 2 (A2) contained egg albumin and com starch in 2:1 ratio and formulation no. 3 (A3) contained egg albumin and gelatin in 2: 1 ratio.

All formulations were compressed at same pressure. Each batch was tested for official and unofficial tests.

Paddle method at 100 rpm rpm was used for dissolution studies and the dissolution medium was 0.1 N Hcl. All other specification were according to the individual monograph stated in British Pharmacopoeia (1999).

RESULTS AND DISCUSSION

Pharmaceutical tablets are dosage forms which are evaluated on the basis of pharmacopoeial and non-pharmacopoeial tests. Pharmacopoeial tests are

uniformity of weight, hardness, % drug content, disintegration time and rate of release of drug from tablets. The unofficial tests are thickness, diameter and friability evaluation which are generally performed to minimize appearance problem, to assure that tablets can be accurately counted by filling equipment and to bear adequate packaging and shipping force.

These tests were performed on all the experimental batches and compared with commercially available tablets of same strength. The analytical data is provided in table 1 and table 2.

In our experimental tablets formulation no. 1 of mefenamic acid tablets 250 mg showed the best results as regard to the rate of release of drug.

From the results it was found that the tablets were of an average weight 600mg (\pm 5%) which is in agreement with the BP limits. The deviation in thickness and diameter is within \pm 5 %. This is tolerable for the normal manufacturing practices.

Table 1

FORM.	AV.WT.	AV.TH.	AV.DIA.	A V. HARD	FRIA	%DRUG CON.	D.T.
A1	599mg	3.27mm	12.32mm	10.05Kg	.27%	99.4%	0min.
A2	604mg	3.35mm	12.37mm	7.10Kg	1.3%	98.9%	10min.
A3	602mg	3.82mm	12.01mm	14.10Kg	0.22%	100.19%	15min.
A4	594mg	3.88mm	12.02mm	9.66Kg	0.57%	100.38%	10min.

A1 = Mefenamic acid tablets 250mg experimental formulation no. 1 A2 = Mefenamic acid tablets 250mg experimental formulation no. 2 A3 = Mefenamic acid tablets 250mg experimental formulation no. 3 A4 = Mefenamic acid tablets 250mg by Parke Davis (Ponstan 250mg)

Table 2
% Dissolution of different formulations

Formulations	% Drug dissolved in minutes						
	5	10	15	20	25	30	40
A1	45.0	-	70.2	72.0	82.2	93.6	-
A2	40.5	52.4	61.8	-	72.5	91.8	-
A3	30.4	40.5	-	59.6	-	65.1	76.5
A4	54.0	-	64.8	-	72.0	86.4	90.0

A1 = Mefenamic acid tablets 250mg experimental formulation no. 1 A2 = Mefenamic acid tablets 250mg experimental formulation no. 2 A3 = Mefenamic acid tablets 250mg experimental formulation no. 3 A4 = Mefenamic acid tablets 250mg by Parke Davis (Ponstan 250mg)

In all formulations values for active ingredient are within $\pm 2.5\%$ that is in confirmation with the limits given in BP (1999) i.e. $\pm 7.5\%$ for 250 mg tablets. When the tablets were evaluated for the uniformity of hardness, it was found that all tablets lie within $\pm 2\%$ limits. Table 1 shows that, the greater the hardness of the tablets, the lesser is the percentage friability. The possible reason for this result may be that at high compressional force the granules are packed strongly together and there is low degree of crumbling during friability test. Percentage friability of all the formulations prepared in laboratory lies within the limits i.e. within 1 % except formulation no. 2 which is 1.3%. The possible reason for this result may be low compressional force or less quantity of binder solution.

The disintegration time determines whether tablets or capsules disintegrate within prescribed time when placed in a liquid medium under the prescribed experimental conditions (King and Schwartz, 1985). The disintegration time of our experimental formulations lie between 10-15 minutes which is within BP limits.

Like the disintegration test, the dissolution test does provide a means of control in assuring that a given tablet formulation is the same as regards dissolution as the batch of tablets shown initially to be clinically effective. It also provides an invitro control procedure to eliminate variations among production batches (Banker and Anderson, 1986). It is clear from Table 2 that the dissolution rate of mefenamic acid tablets containing egg albumin as a binder is increased. This result is in concordant with the results obtained by Teruko Imai et. al that egg albumin is useful for the enhancement of the apparent absorption rate following the dissolution of some poorly water soluble acidic drugs in GI tract (Teruko et al, 1989).

Instead of egg albumin many other polymers were also used as dissolution rate enhancers.

Teruko et al enhanced dissolution rate of several acidic and basic drugs by preparing kneaded mixtures of drug with water soluble gelatin (Imai, T. 1989). Kenya et al 1989 used PVP and β -cyclodextrin to enhance the dissolution rate of tolbutamide (Kenya. et al 2000).

Zhijan. Xiaodong et al conjugated acetyl salicylic acid into polymers like poly hydroxyalkyl aspartamide which showed faster drug release (Zhijan, 1999).

CONCLUSION

Since the drug absorption and physiological availability depend on having the drug substance in dissolved state, different polymers are introduced into formulation to enhance the dissolution rate. Synthetic polymers like PVP, sodium CMC, HPMC, sodium lauryl sulfate, β -cyclodextrin etc. are used for this purpose. Beside these polymers egg albumin is a desirable as a carrier from the view point of safety and the fact that it is a naturally occurring polymer. The solubilities of poorly water soluble drugs are found to be increased by utilizing egg albumin as a water soluble carrier.

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Manuscript submitted on September 5, 2004

Accepted for publication on September 18,2004