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Original Article

In-Vitro Release Study of Paracetamol Using Carboxy Methyl Guar Gum as Binder

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ABSTRACT

The objective of the study was to develop the sustained release tablets of paracetamol, using carboxymethyl guar gum as a drug binder. Experimental approach: Tablets were prepared by wet granulation method. Granules were evaluated for loose bulk density (LBD), tapped bulk density (TBD) and compressibility index. Prepared tablet were evaluated for friability, hardness, uniformity of drug content and *In-vitro* release study. *In-vitro* release study was carried out by using USP type II apparatus in phosphate buffer (pH 6.8). Conclusion: Three different types of formulation were formulated (F1, F2, F3). F1 shows best result of 93.43% drug release over a time period of 12hrs amongst all the formulations.

Keywords: Paracetamol, carboxymethyl guar gum, controlled release, *In-Vitro* release study.

1. INTRODUCTION

In recent years controlled drug delivery system has gained increased importance. It is also necessary to improve the system absorption of the drugs and patient compliance. Controlled drug delivery systems maintain uniform drug levels, reduce dose, side effect and increased the safety margin. [1] Now a day, main aim is designing of drug products to reduce the frequency of dosing by modifying the rate of drug absorption. [2] Continuous researches is being carried out in this field for use of naturally occurring biocompatible polymeric

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materials and its derivatives in designing of dosage form for oral controlled release administration. [3-7] Natural polysaccharides are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media. [8-9]

Guar gum is natural polysaccharide with glycoside linkage. Guar gum is used to deliver drug to colon due to its drug release retarding property and susceptibility to microbial degradation in the large intestine. The gelling property retards release of the drug from the dosage form as well as it is susceptible to degradation in the colonic environment. [10-12]

Guar gum and its derivatives are used as a binder and disintegrate in tablets to add cohesiveness to drug powder. Guar gum is also used as a controlled release agent for the drug due to high hydration rate (swelling in aqueous media). [13-14]

But due to the uncontrollable viscosity of the guar gum solution, uncontrollable rate of hydration, instability of its solutions for longer time and susceptibility to microbial contamination restricts its use in pharmaceutical industries. To overcome these draw back guar gum should be chemically modified. [15-16] In present study we used carboxymethyl derivative of guar gum in tablet formulation. For the study paracetamol (Acetamenophen) is used as model drug, an antipyretic drug. The tablets were prepared by wet granulation method. Prepared tablets were evaluated for weight variation, friability test and hardness. The aim of the study is to formulate the controlled release matrix tablet of paracetamol with different concentration of carboxymethyl guar gum (CMGG), using no other varying parameter.

2. MATERIALS AND METHODS

Paracetamol was obtained from Farmson Pharmaceuticals Pvt. Ltd. Gujarat. Guar gum was purchased from S.D.Fine Chemicals, Mumbai. Starch and lactose was purchased from S.D. Fine Chemicals, Mumbai. Magnesium stearate was purchased from Loba Chemicals, Mumbai. All other ingredients and solvents used were of analytical grade.

Preparation of carboxymethylated guar gum

CMGG was synthesized by standard method as reported by N. K. Patel et al. [17] Purified guar gum was dispersed in 150 ml of iso propyl alcohol, in 250 ml round bottom flask equipped with a magnetic stirrer. After the gum was well dispersed, catalyst $AlCl_3$ and the phase transfer catalyst tetraethyl ammonium bromide were added. After that acetylating agent (acetyl chloride, 5 ml) was added and the reaction is continued at room temperature with constant stirring for 5 hrs. After completion of reaction carboxymethyl guar gum was precipitated with the help of methanol and the precipitated product was purified.

Preparation of tablets

Tablets were prepared by wet granulation method. All the ingredients were mixed in mortar & pestle. Then pass all the material through mesh (No.60). Then granulation was done using the solution of starch in sufficient amount of water. Then wet granules were dried in oven at 60^0C. The dry granules were then sized by mesh No.22 and mesh No.44 and mixed with magnesium stearate and talc. Tablets were compressed at 250mg weight on a 10-station mini rotary tableting machine. Three different formulas, having different concentration of carboxymethyl guar gum (1%, 2% and 3%), where developed to evaluate the drug release. The composition of different formulations was tabulated in table: 1.

Evaluation of granules

The angle of repose was measured by using funnel method. Angle of repose indicates the flowability of the granules. The physical properties of the granules were shown in table 2.

Loose bulk density (LBD) and tapped bulk density (TBD) were measured using the following formula:

$$LBD = \frac{\text{weight of the powder}}{\text{volume of the packing}}$$

$$TBD = \frac{\text{weight of the powder}}{\text{tapped volume of the packing}}$$

Compressibility index of the granules was determined by using the following formula:

$$CI(\%) - \frac{(TBD - LBD)}{TBD} * 100$$

Table 1: Composition of different formulation

Ingredients	Formulation		
	F1	F2	F3
Paracetamol	50mg	50mg	50mg
CMGG	1%	2%	3%
Starch	5%	5%	5%
Diluents	200mg	200mg	200mg
Lubricants(Magnesium stearate + Talc)	2%	2%	2%

Table: 2 Physical properties of the granules

Formulation code	Parameters			
	Angle of repose	LBD (gm/ml)	TBD (gm/ml)	Compressibility Index (%)
F1	30.74	0.7571	0.8412	9.997
F2	32.61	0.8130	0.9033	9.996
F3	33.91	0.8587	0.9541	9.998

Evaluation of tablets

All prepared tablets were evaluated for their uniformity of weight, hardness, friability.

Friability

Tablets were evaluated for friability. For this weight of 10 tablets were measured. After that tablets were placed in friabilator. The motor is activated and chamber is allowed to tumble for 4 minutes or 100 revolutions. After 4 minutes or 100 revolutions the tablets were removed and weighed again. The results were tabulated in table: 3.

Hardness

The hardness of tablets was measured by Monsanto hardness tester. The results were tabulated in table: 3.

Uniformity of weight

To determine uniformity of weight 10 tablets were randomly selected and weighed. The results were tabulated in table: 3.

Drug content

Five tablets were powdered in a mortar. An accurately weighed quantity of powdered tablets was extracted with pH 6.8 buffer and the solution was filtered. The absorbance was measured at 249nm after suitable dilution. The results were tabulated in table 3.

Table 3: Tablet properties of different formulation

Formulation code	Parameters			
	Friability (%)	Hardness (Kg/cm^2)	Uniformity of weight	Drug content (%)
F1	0.39	5.8 ± 0.2	250 ± 0.13	99.92 ± 0.21
F2	0.30	4.6 ± 0.1	250 ± 0.09	99.62 ± 0.12
F3	0.52	4.3 ± 0.2	250 ± 0.18	98.43 ± 0.27

***In-vitro* drug release studies**

In-vitro drug release studies were carried out using USP XXII dissolution apparatus type II at 50 rpm. The dissolution medium consisted of 900ml of pH 6.8 phosphate buffer, which is maintained at 37 ± 0.5^0C. The drug release at different time intervals was measured using an UV-visible spectrophotometer at 249nm.

3. RESULTS AND DISCUSSION

In the production of dosage form granulation is the key process. To avoid problems like, good content uniformity and weight variation problems, wet granulation method generally used. So the wet granulation method use in present study. The granules of the different formulations were evaluated for angle of repose, loose bulk density, tapped bulk density and compressibility index.

The results of angle of repose and compressibility index ranged from 30.74 ± 1.23 and 9.99 ± 1.0 respectively. The results of loose bulk density and tapped bulk density ranged from 0.81 ± 0.2 and 0.90 ±

0.3 respectively. The result of angle of repose indicates the good flow properties. The various physical properties of tablets are tabulated in table 3. It shows the tablets passed the test of friability and uniformity of weight as per requirements of Indian Pharmacopoeia, 1996. Drug content was found to be uniform for all the formulations.

The cumulative percentage of drug release for F1, F2 and F3 was 93.43%, 90.60% and 86.30% respectively. It can be concluded that % release of drug decreases with increase in CMGG concentration. *In-Vitro* drug release profile of F1-F3 formulations were shown in figure.

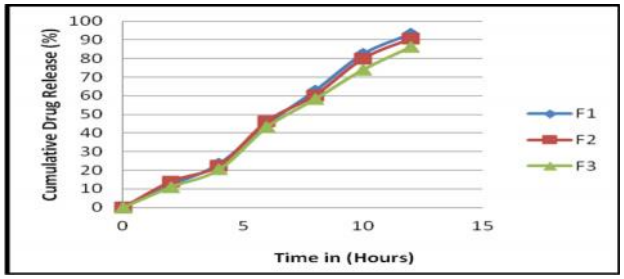

Figure 1: *In-Vitro* release profile of F1 to F3 formulations

4. CONCLUSION

In conclusion, we may asses that good quality tablets may be prepared by using ingredients suggested in formulation. Good results are obtained from controlled-release matrix tablets prepared with CMGG. This derivative of guar gum finds its suitability as a controlled-release agent. The formulation shows controlled release of paracetamol over a period of 12hrs. Among all the formulation F1 shows the 93.43% of drug release at the end of 12hrs.

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