Research Article

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Formulation and Evaluation of Sustained Release Matrix Tablets of Propranolol Hydrochloride Using Sodium Carboxymethyl Guar as Rate Sustaining Polymer

Khan Arshad Bashir*, N.G.Nanjundaswamy

#52, 5-A Cross, 34th Main, TMCS Layout, J.P. Nagar 1st Phase, BANGALORE – 560 078, INDIA

Sodium carboxy methyl guar (SCMG), which is a guar gum derivative, was investigated as a sustaining material to formulate sustained release tablets of the model drug, Propranolol hydrochloride. Tablets, based on SCMG polymer were made keeping the hardness constant. *In vitro* release rate study was carried out for all the formulations and curve-fitting analysis was done on the selected formulation.

A swelling index study was also carried out. The selected tablets were kept for accelerated stability study. The study indicated that the guar derivative, SCMG, could be utilized for formulation of sustained release tablets of Propranolol hydrochloride. All the selected formulations were found to be physically and chemically stable at different storage conditions at the end of the eight week.

Keywords: Sodium carboxymethyl guar, propranolol hydrochloride, sustained release tablets.

INTRODUCTION

Guar gum is a galactomannan polysaccharide, which is inexpensive and freely available in India. It has already been investigated as an adjuvant in the pharmaceutical industry as a suspending agent, sustaining agent[1] and a granulating agent. But still, its pharmaceutical use is limited due to its susceptibility to microbial contamination, uncontrolled swelling characteristics, and fall in viscosity when exposed to higher temperatures[2].

Many derivatives of guar gum have synthesized to overcome the drawbacks of guar gum; one of those derivatives is sodium carboxymethyl guar (SCMG) [3, 4] which is being investigated for its pharmaceutical applications.

Sodium carboxymethyl guar (SCMG) has also been investigated as film- forming agent, sustaining agent and a suspending agent[6]. The present study sought to investigate the use of guar gum derivative- sodium carboxymethyl guar (SCMG), as sustaining agent in the formulation of sustained release tablets of the model drug Propranolol hydrochloride.

Propranolol hydrochloride was chosen as the model drug due to its short $t_{1/2}$ (3.5 hours) and water solubility[7].

Corresponding Author

Khan Arshad Bashir

E-Mail: arbakh@gmail.com

MATERIALS AND METHODS

Propranolol hydrochloride was a generous gift from M/s Micro labs Pvt Ltd., Hosur. Guar gum (Dealca 150, viscosity of 2% w/v dispersion in water- 3600 cps) was procured from Madhuri Agencies, Bangalore. Sodium carboxymethyl guar (viscosity of 2% w/v dispersion in water - 500 cps was synthesized and characterized in the Pharmaceutics laboratory of Govt. College of Pharmacy, Bangalore. All the chemicals used were of analytical grade. All the materials were used as received.

Formulation of sustained release tablets:

All the formulations were prepared according to Table- 1. Tablets based on SCMG were coded M. The weighed amounts of drug, polymer and the diluents were mixed uniformly. 25% w/v of polyvinyl pyrrolidone (PVP) in water was used as a binding agent. The coherent mass thus obtained was passed through sieve no.16 and the dried granules were regranulated by passing through sieve no. 20 and blended with magnesium stearate and talc. These granules were punched into tablets weighing 400 mg (I.P. 1996 limit: 380 mg to 420mg) on a 'Rimek' RSB- 4 Minipress, 10-station tablet punching machine. The hardness of each tablet was maintained at around 4 kg/ cm^2.

Compatibility study:

In order to check for any chemical interaction between the drug and the polymer, a compatibility study was carried out for a period of eight weeks at 60^0C. At the end of

the eighth week, the contents were analyzed for any possible degradative products by thin layer chromatography using Benzene: Methanol: Ammonia in the ratio of 72: 25: 0.25 as the mobile phase and silica gel GF as the stationary phase[8].

TABLE-I: FORMULATION CHART

Ingredients	All the quantities in mg per tablet						
Drug: polymer	1:1	1:2	1:3	1:4	1:5	1:6	1:7
Propranolol HCl	32	32	32	32	32	32	32
SCMG	32	64	96	128	160	190	224
PVP	50	50	50	50	50	50	50
Talc	8	8	8	8	8	8	8
Magnesium stearate	4	4	4	4	4	4	4
Dicalcium phosphate	274	242	210	178	146	114	74

Pre-compression and post compression parameters of the formulated tablets

Bulk density and tapped bulk density was found out using measuring cylinder tap method. Angle of repose was found out using the funnel method. The dimensional specifications were measured using vernier calipers. Hardness test was performed by using Monsanto hardness tester. The friability test was performed using Roche friabilator. The assay was performed for the tablets by taking the average weight of five tablets and triturating the tablets and taking triturate equivalent to the average weight. The triturate was transferred to a 100 ml volumetric flask and shaken with warm phosphate buffer pH 7.4 and kept in the oven at 50^0C for two hours. At the end of two hours, the volume was made up with phosphate buffer pH 7.4 and vigorously shaken and filtered. Out of this filtrate, 1 ml was pippeted out and transferred to another 100 ml volumetric flask and the volume made up with phosphate buffer pH 7.4. The absorbance of this solution was noted at λ_{max} 289 nm in Elico SL 154 uv-vis spectrophotometer against phosphate buffer pH 7.4 as blank.

***In vitro* dissolution profile[9]:**

The dissolution profiles of all the tablets were determined by using the USP XXII apparatus -1 taking pH buffer 1.2 for the first two hours and pH buffer 7.4 for the subsequent hours as dissolution media. The volume of the media was maintained at 500 ml at a temperature of 37^0C ± 1^0C and 75 rpm. At every hour, 5 ml of the medium was pippeted out and transferred to 25 ml volumetric flask and the absorbance was recorded at 289 nm in Elico SL 154 uv-vis spectrophotometer.

Swelling index study[10]:

The tablets from the selected M4 weighing 400 mg (W_2) were taken and soaked in a Petri dish filled with water. At the end of each hour, the swollen tablet was re- weighed (W_1). The gain in weight for the tablet at every hour was recorded and the time v/s swelling index [(W_1-W_2)/W_2] graph was plotted. This study was carried out to observe the swelling behavior of the tablet.

Curve- fitting analysis for the selected formulation M4:

The curve fitting analyses was carried out for the selected tablet formulation, M4. The following were the results tabulated using the software, Graphpad, Prism 3.0.

It can be inferred from the above table that the selected formulation M4 fits both Krosmeyer- Peppas model and Higuchi model as the R^2 values for all the tablet formulations is more than 0.9, whereas, the formulation does not fit the zero order model as the R^2 value the tablet formulation is below 0.9.

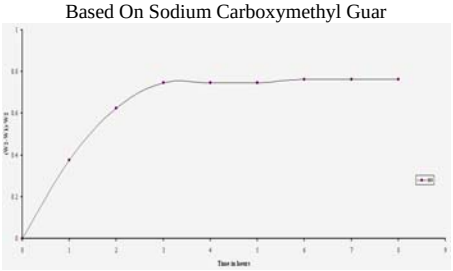
Stability study

Tablets from the selected batch, M4, were kept for accelerated stability study in screw capped bottles at different storage conditions of 40^0C and 75% RH, 50^0C and 60^0C for eight weeks. The tablets were analyzed every week for any possible chemical or physical degradation.

TABLE II: Curve fitting analysis data

Zero order Model	
K	9.63
R^2	0.7735
Krosmeyer- Peppas Model	
K	24.03
n	0.5779
R^2	0.9981
$t_{0.5}$	3.554
Higuchi Model	
K	28.16
R^2	0.9905
$t_{0.5}$	3.152

Graph- I: Swelling Index Profile of Tablet Formulation M4 Based On Sodium Carboxymethyl Guar



RESULTS & DISCUSSION

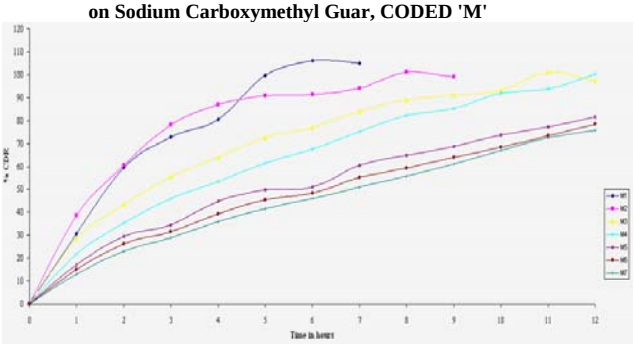
The present investigation was undertaken to investigate guar derivative SCMG, as sustaining agent in the formulation of sustained release tablets of the model drug, Propranolol hydrochloride. It was found that there was no interaction between the drug and the polymer at the end of the eighth week in the present study. The bulk density was in the range of 0.426 g/cc to 0.622 g/cc for the granules from lower to higher ratio of drug: polymer. The tapped bulk density was found to be in the range of 0.530 g/cc to 0.800 g/cc from lower to higher ratio of drug: polymer. The Carr's Index was found to be between 14.9% and 26% from lower to higher ratio of drug: polymer. The angles of repose were found to be between $29^0$3' to $38^0$22' from lower to higher ratio of drug: polymer. The hardness was maintained at 4 kg/cm^2 for all the tablet formulations. The weight variation was found to be within the specification of I. P. 1996 and was between 386 mg to 415 mg (I.P. limit: 380 mg to 420 mg). The thicknesses of all the tablet formulations were found in the range of 4.9 mm to 5.6 mm. The diameter of all the tablets was found to be 8 mm. The friability was found to be within the acceptable limits of 0.1% to 0.5%. The assay of all the tablet formulation was found to be between 90.53% w/w to 113.5% w/w of Propranolol hydrochloride.

The results for *in- vitro* dissolution study showed a sustaining effect for all the batches. Percentage cumulative drug release (%CDR) of 104.8% was recorded at the end of the seventh hour for batch M1, whereas, for batchM2, the % CDR was 98.93% at the end of the ninth hour. For the batches M3, M4, M5, M6, and M7 the % CDR was 97.34%, 100.12%, 81.6%, 78.3%, and 75.7% respectively at the end of the twelfth hour (fig. 2). The batch M4 was selected as the % CDR was about 100% at the end of the twelfth hour. The selected formulation M4 was subjected to curve- fitting analysis using the software, 'Prism', version 3.0. The results are given in table-2. It can be interpreted from the analysis that the probable mechanism for drug release from these tablets followed 'Non-Fickian diffusion' which is characterized by diffusion of the drug accompanied by chain relaxation of the polymer[11].

The swelling index profile, fig.5, of tablets from batch M4 showed initial rise in swelling followed by latter constant swelling.

Tablets from selected formulation M4 were found to chemically and physically stable at all the storage conditions mentioned earlier at the end of the eight week, though at temperatures 50^0C and 60^0C, all the tablets showed a slight increase in their hardness.

Graph- II: Comparative Dissolution Profiles of Tablets Based on Sodium Carboxymethyl Guar, CODED 'M'



CONCLUSION

Guar gum has an uncontrolled and almost instantaneous swelling behavior[1, 2]. Sodium carboxymethyl guar swells over a period of about three hours. The matrix tablets formulated with Sodium carboxymethyl guar showed good sustaining effect over a period of twelve hours. Further studies can be carried out with other drugs. Different dosage forms can be tried using the polymer. Hence, it can be concluded that Sodium carboxymethyl guar is a promising candidate for use as an adjuvant in the formulation of sustained release tablets.

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