Drug Development and Industrial Pharmacy, 24(11), 1095–1099 (1998)

COMMUNICATION

Evaluation of Guar Gum in the Preparation of Sustained-Release Matrix Tablets

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ABSTRACT

Polymeric hydrophilic matrices are widely used for controlled-release preparations. The process of drug release is controlled by matrix swelling or polymer dissolution. It has been shown that the swelling of guar gum is affected by concentration of drug and viscosity grade of the polymer. This study examines the mechanism of behavior of guar gum in a polymer-drug matrix. The swelling action of guar gum, in turn, is controlled by the rate of water uptake into the matrices. An inverse relationship exists between the drug concentration in the gel and matrix swelling. This implies that guar gum swelling is one of the factors affecting drug release. The swelling behavior of guar gum is therefore useful in predicting drug release.

INTRODUCTION

The study of the controlled release of drugs for their extended and safe use has recently become an important field of research. Polymeric hydrogels are being increasingly studied for controlled-release applications because of their good biocompatibility (1). In addition, the ability of hydrogels to release an entrapped drug in aqueous medium and to regulate the release of such drug by control of swelling and cross-linking makes them particularly suitable for controlled-release applications (2–4). Hydrogels can be applied for the release of both hydrophilic and hydrophobic drugs. However, hydrophilic drugs show greater permeability through hydrogel membranes.

In the present investigation, guar gum hydrogel matrices were used as carriers for the controlled release of theophylline, a water-soluble drug. The process of drug release from a guar gum drug matrix involves water penetration into the dry matrix, hydration and swelling of the polymer, and diffusion of the dissolved drug in the matrix. Investigations of the hydration and gelation of guar gum may give an insight into the various stages of the release process. The aim of this study was to examine the manner by which guar gum exerts its effect on the

swelling process and the correlation of guar gum swelling behavior with the drug-release profile of these matrices (5).

MATERIALS

Vidogum GHK-250 (a grade of high-viscosity [4000 cps] guar gum) manufactured by Dabur, India, was used. Theophylline anhydrous (Bakul Chem, India), starch, lactose, talc, and magnesium stearate used were of USP grade. All other chemicals were of reagent grade.

METHODS

Theophylline, starch, and guar gum were weighed and sifted through 60 mesh. The three ingredients were mixed using a laboratory model planetary mixer. The blend was granulated with guar gum paste (5%). The granules were dried in a fluid bed dryer (FBD) at 50°C–60°C for 20–25 min. The semidry granules were passed through 16 mesh using an oscillating granulator. These granules were dried to have the loss on drying in the range 4–5% (w/w). The dried granules were sifted through 20 mesh. Talc (2%) and magnesium stearate (1%) were sifted through 60 mesh and mixed with dried granules. The lubricated granules were then compressed to 13-mm flat-faced tablets using a hydraulic press (Allied Engg, India) by applying different compression pressures and times.

Matrix-Tablet Erosion Study

The matrix-tablet erosion studies were conducted in triplicate, and the results were averaged. Tablets were placed in the basket of the dissolution apparatus, and the basket was dipped 2.0 cm below the upper layer of the dissolution medium (100 rpm). After the specified time, tablets were taken out, dried, and weighed, and the medium was analyzed for the amount of drug released from the tablets.

Drug Release from the Gel

Theophylline was dispersed with the help of an electric stirrer (1400 rpm) in a measured volume of water. Varying concentrations of theophylline solutions were made (2%, 4%, 6%, 8%, and 10% w/w) separately. In the same solution with continued stirring, the weighed amount of guar gum was added to disperse uniformly without the formation of lumps (concentration of guar gum in the solution was 5%).

After the gum was added and dispersed evenly, the dispersion was heated in an oven at 80°C for 1 hr to set the gel. The hot gel was used to fill the stainless steel die with an internal diameter of 2.5 cm and thickness of 10 mm; one end was sealed with aluminum foil, and the dispersion was left to gel in the refrigerator overnight. The die was then kept in constant humidity (95%) at 37°C for 1 hr. The whole assemblage was placed into a trough containing water maintained at 37 ± 0.5°C. The cell was filled with 45 ml distilled water and stirred with the help of a magnetic stirrer. Every 10 min, a 250-µl sample was withdrawn for the first 100 min, and then a sample was withdrawn every 30 min until 310 min had passed. The sample was analyzed by high-performance liquid chromatography (HPLC) for the amount of theophylline diffused into water.

The diffusion apparatus used in this study is shown in Fig. 1. The stainless steel cylindrical die (2.5 cm internal diameter, 10 mm thickness) was filled with guar gum gel; one side of the die was sealed with aluminum foil. It was connected to an L-shaped horizontal glass cell (2.7 cm internal diameter, 6.25 cm length) with a vertical sampling tube (1.95 cm internal diameter, 10.2 cm length). Flexible rubber O-rings were inserted between the die and cell to prevent liquid leakage from the diffusion apparatus (6).

Study of Tablet Volume as a Function of Time

The dimensions of each tablet were measured using vernier calipers prior to swelling determination. The method used includes dipping the tablet in water; after the specified time, the tablet was collected on a glass slide, and the linear increase in the tablet diameter and thickness was monitored. The volume of the tablet was then calculated. The results from at least three matrices were averaged.

RESULTS AND DISCUSSION

Matrix Erosion Study

The matrix erosion studies measured the weight loss from matrix tablets immersed in dissolution media as a function of time (Table 1). Weight loss and drug release from the tablets containing guar gum was in constant progression until the end of the study. Total matrix eroded remained unchanged until the end of 120 min.

A plot of weight loss (mg) versus theophylline released (mg) from the tablet was created and was very

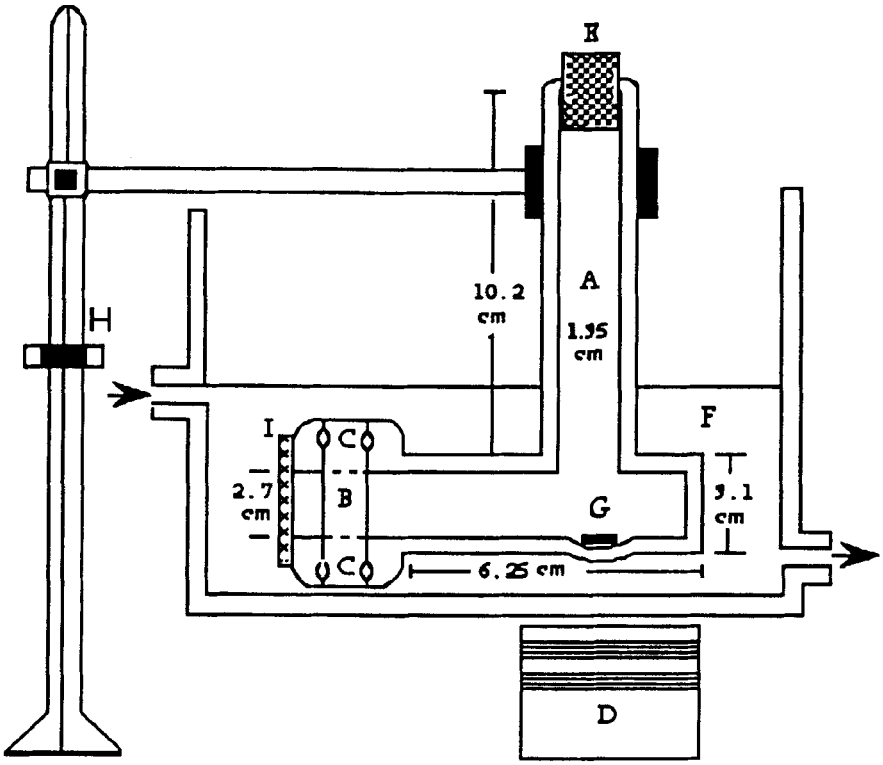

Figure 1. Apparatus for drug-release test: A, sampling tube; B, stainless steel die; C, O-ring; D, magnetic stirrer; E, sampling space; F, water bath; G, stirrer bar; H, holding stand; I, sealed end of the die.

close to linearity. The near linearity of the plot suggests that the drug release followed the erosion mechanism (Fig. 2). Moreover, the constant matrix erosion until the end of the study indicates that guar gum achieves the steady diffusion state after initial swelling.

Drug Release from the Gel

Drug release data in initial stages suggest a slow release of the drug; after a short induction time, the drug release obtained was linear. The amount of drug release

Table 1

Theophylline Release from Matrix Tablets

Sr. No.	Time (min) (t)	Table weight (mg) Initial	After Time (t)	Weight Loss (mg)	Drug Dissolved (mg)	Total Matrix Eroded (mg)	Average Percentage of Matrix Eroded
1	10	500.06	451.83	48.23	22.78	25.45	5.09
2	20	500.30	432.67	67.63	39.20	28.43	5.68
3	30	499.47	428.01	71.46	41.76	29.70	5.95
4	45	500.08	422.71	77.37	48.16	29.21	5.84
5	60	500.10	420.34	79.76	52.25	27.51	5.50
6	120	500.72	412.72	88.34	60.54	27.80	5.55

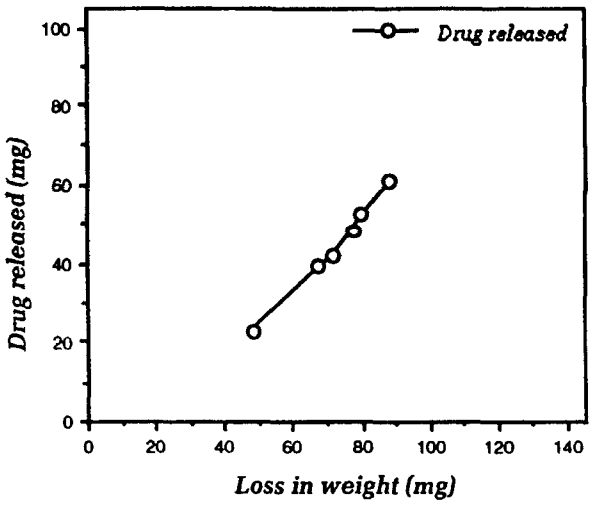

Figure 2. Matrix erosion study of weight loss versus drug released in water.

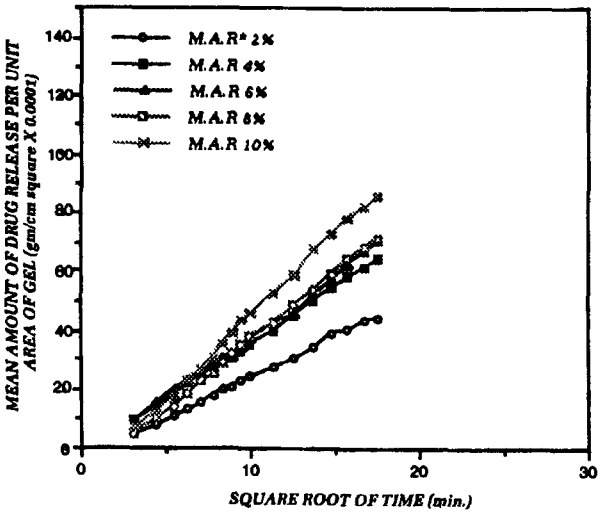

Figure 4. Relationship between amount released per unit area of gel and square root of time.

when plotted against time (Fig. 3) exhibits that all the plots are linear after a short lag period. The linearity of the straight line increases with an increase in the initial loading of the drug (2%, 4%, 6%, 8%, and 10%) in the gel. The amount of drug permeated through unit area of the gel was also plotted against the square root of time (Fig. 4), and the plot obtained was also linear. The above findings imply that diffusion of theophylline from gel appears to be concentration dependent because the interaction between theophylline and gel is probably not responsible for the above concentration dependency; moreover, no effect of guar gum on the solubility of theophylline in water was found.

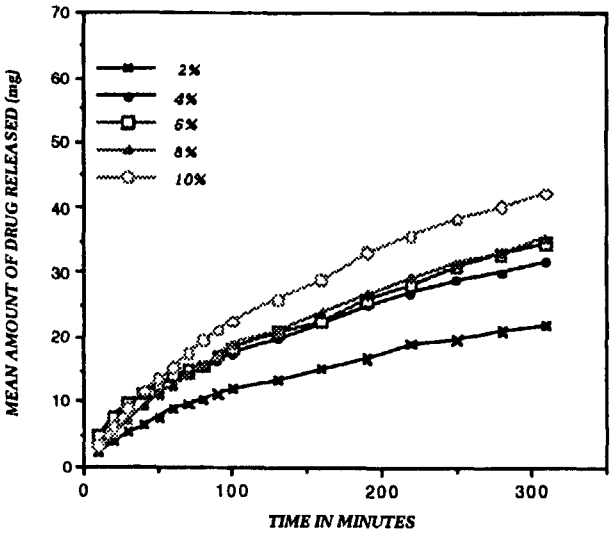

Figure 3. Amount of drug released from gel versus time as a function of drug loading.

Study of Tablet Volume as a Function of Time

The process of drug release from a matrix of guar gum and drug is a complex. The overall drug release is affected by the rate of water uptake and the diffusion rate of the drug through the swollen gel. The water uptake rate into the matrix is enhanced in the presence of guar gum because of its high hydrophilicity. However, like all swellable polymers, guar gum swells as it absorbs water. The thickness of the gel layer formed varies with the function of time. This gel increases the diffusional path length of the drug. The plot between the square root of time and volume of the tablet was linear (Fig. 5). This linear relationship suggests that the swelling process is dependent on the surface area exposed to the aqueous medium. Statistical data expressing the regression analysis were calculated for the above plot, and correlation coefficients (r) 0.986 and r^2 0.974 were obtained.

CONCLUSION

Guar gum was studied as a matrix former for sustained-release tablets. It was found to be effective in pro-

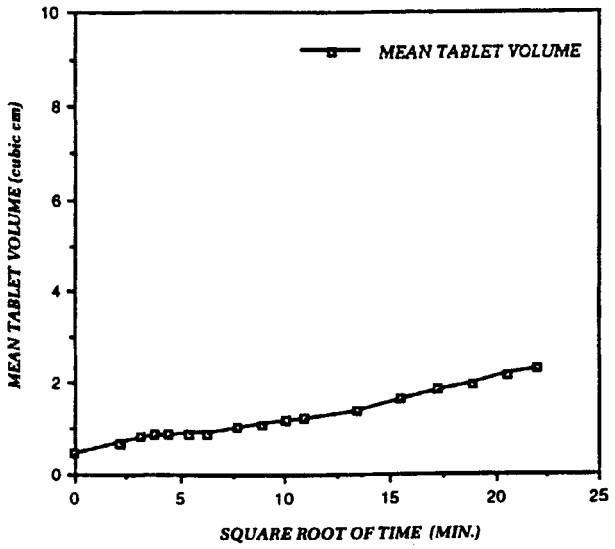

Figure 5. Effect of time on matrix swelling.

longing drug release. After hydration of the gum, the drug release was essentially through a diffusion process. The drug release from the matrix depends on the releasing area produced. Increasing the drug concentration in the gel and keeping the amount of gum constant in the formulation increases the amount of drug released as the diffusional path length of the drug remains constant. Swelling of the gum attains a steady state after initial hydration, and the drug is released in a sustained fashion over a long period of time.

ACKNOWLEDGMENT

The authors are grateful to Dr. Anand C. Burman, Director, Dabur Research Foundation, for helpful discussions, guidance, and generosity in providing research facilities.

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