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DRUG DEVELOPMENT RESEARCH 65:76–83 (2005)

Research Article

Development of Colon-Targeted Albendazole-β-Cyclodextrin-Complex Drug Delivery Systems

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Strategy, Management and Health Policy				
Enabling Technology, Genomics, Proteomics	Preclinical Research	Preclinical Development Toxicology, Formulation Drug Delivery, Pharmacokinetics	Clinical Development Phases I-III Regulatory, Quality, Manufacturing	Postmarketing Phase IV

ABSTRACT Albendazole, a drug for the treatment of gastrointestinal nematode infection, is variably and erratically absorbed from the gastrointestinal tract after oral administration. The present study was aimed at developing matrix tablets of albendazole using guar gum as carrier for colon targeting in order to provide an effective and safe therapy for helminthiasis. To improve its bioavailability, the formation of inclusion complexes of albendazole with β-cyclodextrins was investigated. Matrix tablets of albendazole–β-cyclodextrin complex were prepared by the wet granulation method using guar gum as matrix carrier in various proportions: 20% (SAC-20), 30% (SAC-30), and 40% (SAC-40). A high-performance liquid chromatography–ultraviolet method was developed to quantitate albendazole using mebendazole as internal standard at 254 nm. The granules were compressed using 12-mm round, flat, and plain punches. Tablets were evaluated for various physical characteristics such as thickness, hardness, and drug content uniformity. The matrix tablets were subjected to in vitro drug release studies in 0.1 N HCl (2 h), pH 7.4 Sorensen's phosphate buffer (3 h) and simulated colonic fluids. The SAC-30 released $67.7 \pm 1.9\%$ of albendazole in the presence of rat caecal contents, whereas in the control study the formulation released only $29.7 \pm 0.2\%$ of albendazole. A significant difference ($P < 0.001$) was observed at 24 h in the amount of albendazole released from SAC-30 when compared to the dissolution study without rat caecal contents. The study shows that the release of albendazole in the physiological environment of colon is due to the microbial degradation of guar gum compression-coated tablets in the presence of rat caecal contents. Stability studies were carried out at 40°C/75% relative humidity for 6 months to assess their long-term (2 years) stability. No change either in their physical appearance or in drug content was observed. Drug Dev. Res. 65:76–83, 2005.

Key words: colon targeting; matrix tablet; albendazole–β-cyclodextrin; guar gum

INTRODUCTION

Anthelmintics are used in the treatment of worm infections caused in humans by cestodes, trematodes, and nematodes. Albendazole (methyl 5-propylthio-1H-benzimidazol-2-yl-carbamate) is active against infections with gastrointestinal nematodes including mixed infections of *Ascaris*, *Trichuris*, and hookworms, and is the drug of choice for treating helminthiasis including trichuriasis (whipworm infections), ancylostomiasis

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Received 5 May 2005; Accepted 11 September 2005

Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/ddr.20010

(hookworm infections), and ascariasis (roundworm infections) [James and Leslie, 1996]. Conventional albendazole tablets release the drug along the gastrointestinal tract (GIT) and may cause the unwanted systemic effects. The targeting of albendazole for local action only in the colon may be beneficial in avoiding the systemic side effects, and even a lower dose of albendazole may be sufficient to treat helminthiasis.

Oral colon-targeted drug delivery systems are necessary for effective and safe therapy for colonic diseases such as ulcerative colitis, irritable bowel syndrome, colonic infections including amoebiasis and helminthiasis, colon cancer, and so on. Several approaches [Van den Mooter and Kinget, 1995; Rama Prasad et al., 1996] are available for colon-specific drug delivery, which include i) coating with pH-dependent systems, ii) design of timed-release dosage forms, and iii) the use of carriers that are degraded exclusively by colonic bacteria. The poor site specificity of pH-dependent systems and timed-release systems is well established [Touitou and Rubinstein, 1986; Peters and Kinget, 1993]. Timed-release systems [Gazzaniga et al., 1994; Pozzi et al., 1994] release their load after a predetermined period of administration. The site specificity of these systems is considered poor because of large variations in gastric emptying time [Davis et al., 1984] and passage across the ileocaecal junction [Marvola et al., 1987]. The best alternate approach for colon-specific drug delivery is the use of carriers that are degraded exclusively by colonic bacteria. The microflora of colon is in the range of 10^{11}–10^{12} CFU/mL [Moore and Holdeman, 1975], consisting mainly of anaerobic bacteria, e.g., *Bacteroides, Bifidobacteria, Eubacteria, Clostridia, Enterococci, Enterobacteria,* and *Ruminococcus,* and so on. This vast microflora fulfills its energy needs by fermenting various types of substrates that have been left undigested in the small intestine, e.g., disaccharides and trisaccharides, polysaccharides, and so on [Rubinstein, 1990; Cummings and Englyst, 1987]. For this fermentation, the microflora produce a large number of enzymes such as β-glucoronidase, β-xylosidase, α-arabinosidase, β-galactosidase, nitroreductase, azareductase, deaminase, and urea dehydroxylase [Scheline, 1973]. Because of the presence of the biodegradable enzymes only in the colon, the use of biodegradable polymers for colon-specific drug delivery seems to be a more site-specific approach as compared to other approaches. These polymers shield the drug from the environments of stomach and small intestine and are able to deliver the drug to the colon. On reaching the colon, they undergo assimilation by microorganism [Potts et al., 1973] or degradation by enzyme [Huang et al., 1979; Swift, 1992] or breakdown of the polymer backbone [Ratner et al., 1988; Hergenrother et al., 1992], leading to a subsequent reduction in their molecular weight and thereby loss of mechanical strength. They are then unable to contain the drug entity [Park et al., 1993].

Polysaccharides that have been investigated for colon-specific drug delivery include pectin and its salts [Ashford et al., 1993, 1994; Rubinstein et al., 1993; Wakerly et al., 1996a,b; Munjeri et al., 1997], chondroitin sulfate [Rubinstein et al., 1992a,b] amylose [Milojevic et al., 1995], and inulinHP [Vervoort and Kinget, 1996]. Guar gum is a natural nonionic polysaccharide derived from the seeds of *Cyamopsis tetragonolobus* (Leguminaciae) that is not affected by the physiological environment of the stomach and small intestine, but is degraded in the colon by the resident bacteria of the large intestine. It consists of linear chains of (1→4)-β-D-mannopyranosyl units with α-D-galactopyranosyl units attached by (1→6) linkages. In pharmaceutical formulations, guar gum is used as a binder, disintegrant, suspending agent, thickening agent, and stabilizing agent. It forms viscous colloidal dispersions when hydrated in cold water. The optimum rate of hydration is between pH 7.5 and 9.0 [Goldstein et al., 1973]. Cyclodextrins are cyclic oligosaccharides having a hydrophilic outer surface and a lipophilic central cavity. Cyclodextrins and some of their derivatives, through their ability to include various kinds of molecule in their hydrophobic cavity, can appreciably change not only the water solubility of the guest molecule, but also many of its other unsatisfactory pharmacotechnical characteristics. [Duchene and Wouessidjewe, 1990].

The present study was aimed at developing matrix tablets of albendazole using guar gum as carrier for colon targeting so as to provide an effective and safe therapy for helminthiasis. Albendazole is variably and erratically absorbed from the GIT after oral administration. To improve its bioavailability, in this work we planned to investigate formation of inclusion complexes of albendazole with β-cyclodextrins.

MATERIALS AND METHODS

Materials

Albendazole (98.5–102% purity) and mebendazole (98.6–101.4% purity) were gift samples from M/s. Indechemie Laboratories Ltd., India and M/s. CIPLA Ltd., Bangalore, India, respectively. Guar gum (viscosity of 1% aqueous dispersion is 125 cps; particle size <75 μm;) was obtained from Dabur Research Foundation, India and was of pharmacopoeial grade (USNF). Acetonitrile [high-performance liquid chromatography (HPLC) grade] and glacial acetic acid were obtained from M/s. Qualigens Fine Chemicals, Mumbai, India.

Other materials used in the study such as microcrystalline cellulose (Avicel, FMC Type pH-105), starch, magnesium stearate, and talc were of pharmacopoeial quality (USNF). The care of the rats was in accordance with institutional guidelines.

Methods

Preparation of albendazole-β-cyclodextrins inclusion complex

Initially, albendazole was complexed with several proportions of β-cyclodextrin, 1:2;1:1;1:0.5; and 1:0.25, to study the improvement of solubility of albendazole in distilled water. Accurately weighed quantities of albendazole–β-cyclodextrin were taken in a glass mortar and triturated well with a few milliliters of 0.5 M methanolic HCl continuously until a smooth paste was obtained. It was then dried at 70°C in a tray drier. The powder was then collected and triturated well and passed through sieve 100.

The dried complexes of the drug were added in excess to 100 mL distilled water taken separately. The beakers were maintained at 37°C for 24 h with intermittent sonication. One milliliter of the supernatant liquid was pipetted out and filtered through a 0.45-μm membrane filter. After suitable dilutions were made, the drug content was noted using UV HPLC (Table 1).

Preparation of albendazole matrix tablets

Matrix tablets of albendazole-β-cyclodextrin complex in the ratio of 1:0.25 (equivalent to albendazole 200 mg) were prepared by wet granulation method. Microcrystalline cellulose (MCC) was used as diluent, and a mixture of talc and magnesium stearate (2:1 ratio) was used as lubricant. Guar gum was included in the formulations in various proportions: 20% (SAC-20), 30% (SAC-30), and 40% (SAC-40). In all the formulations, guar gum was sieved (<250 μm) separately and mixed with albendazole (<150 μm) and MCC (<250 μm). The powders were blended and granulated with 10% starch paste. The wet mass was passed through a mesh (1,680 μm), and the granules were dried at 50°C for 2 h. The dried granules were passed through a mesh (1,190 μm), and these granules were lubricated with a mixture of talc and magnesium stearate (2:1). The lubricated granules were compressed at a compression force of 5,000–5,500 kg using 12-mm round, flat, and plain punches on a single-station tableting machine (M/s Cadmach Machinery Pvt. Ltd., India). Matrix tablets of each composition were compressed (100 No.) and evaluated for their hardness, drug content, and drug release characteristics with a suitable number of tablets for each test. The hardness of the matrix tablets was determined using a Monsanto Hardness Tester.

TABLE 1. Solubility of Albendazole From Albendazole–β-Cyclodextrin Inclusion Complex in Distilled Water

Sl no.	Albendazole–β-CD	μg/mL
1	1:0.0	17.9
2	1:0.25	125.4
3	1:0.5	152.2
4	1:1	340.5
5	1:2	862.9

HPLC analysis of albendazole in matrix tablets and dissolution fluids

A gradient HPLC (Shimadzu HPLC Class VP series) with two LC-10AT VP pumps, variable wavelength programmable UV/VIS Detector SPD-10A VP, CTO-10AS VP Column oven (Shimadzu), SCL-10A VP system controller (Shimadzu), a disposable guard column LC-18 (Pelliguard, LC-18, 2 cm, Supelco, Inc., Bellefonte, PA), and RP C-18 column (150 mm × 4.6 mm I.D., particle size 5 μm; YMC Inc., USA) was used. The HPLC system was equipped with the software Class-VP series version 5.03 (Shimadzu).

The mobile phase used was acetonitrile and triple distilled water (TD water) containing 0.4% of triethylamine (pH adjusted to 3.6 with 5% orthophosphoric acid) in the ratio of 46:54. The filtered mobile phase was pumped at a flow rate of 1.2 mL/min. The column temperature was maintained at 40°C. The eluent was detected by UV detector at 254 nm and the data were acquired, stored, and analyzed with the software Class-VP series version 5.03 (Shimadzu). A standard curve was constructed for albendazole, in the range of 1 to 30 μg/mL using mebendazole as internal standard. A good linear relationship was observed between the concentration of albendazole and the ratio of the peak area of albendazole to that of mebendazole (internal standard) with a high correlation coefficient ($r = 0.9999$). The required studies were carried out to estimate the precision and accuracy of this HPLC method of analysis of albendazole. The standard curve constructed as described above was used for estimating albendazole either in the matrix tablets or in dissolution fluids.

Determination of drug content

The albendazole–β-cyclodextrin complex (equivalent to albendazole 200 mg) matrix tablets were tested for their drug content. Ten tablets were finely powdered, and 100 mg of the powder was accurately weighed and transferred to a 100-mL volumetric flask. Initially about 50 mL of glacial acetic acid was added to the volumetric flask and allowed to stand for 6 h

with intermittent sonication to ensure complete solubility of the drug. Then the volume was made up to 100 mL with glacial acetic acid, the mixture was centrifuged, and 1 mL of the supernatant liquid was suitably diluted, filtered, and analysed for albendazole content by reverse-phase HPLC method as described above.

In Vitro Drug Release Studies

The ability of guar gum matrix tablets of albendazole–β-cyclodextrin complex to remain intact in the physiological environment of stomach and small intestine was assessed by conducting drug release studies simulating the conditions prevailing in the GIT. Drug release studies were carried out using USP dissolution rate test apparatus (Apparatus 1,100 rpm, 37°C) for 2 h in 0.1N HCl (900 mL). Then the dissolution medium was replaced with pH 7.4 Sorensen's phosphate buffer (900 mL) and tested for drug release for 3 h. At the end of the time periods, 1 mL of the samples were taken without a prefilter. The dissolution samples were taken without a prefilter to include drug particles that might erode from the outer layer of the swollen guar gum matrix tablets. One milliliter of glacial acetic acid was added to the dissolution sample along with 20 µg of mebendazole (internal standard), the volume made up to 10 mL with TD water, filtered through a 0.2-µm membrane filter, and analysed for albendazole by HPLC as described previously.

The susceptibility of the matrix tablets to the enzymatic action of colonic bacteria was assessed by continuing the drug release studies in rat caecal content medium (4% rat caecal contents after 7 days of enzyme induction) in view of our earlier report on the utility of guar gum as a carrier for colon-specific drug delivery. The rat caecal content medium was prepared as described previously [Rama Prasad et al., 1998].

Drug release studies were carried out using USP dissolution rate test apparatus (Apparatus 1,100 rpm, 37°C) with slight modifications. A beaker (capacity 150-mL) containing 100 mL of rat caecal content medium was immersed in the water maintained in the 1,000-mL vessel, which, in turn, was in the water bath of the apparatus. The tablets were placed in the baskets of the apparatus and immersed in the rat caecal content medium. Because the caecum is naturally anaerobic, the experiment was carried out with continuous CO_2 supply into the beakers.

At different time intervals, 1 mL of the sample was withdrawn without a prefilter and replaced with 1 mL of fresh phosphate-buffered saline bubbled with CO_2. The experiment was continued for another 19 h because the usual colonic transit time is 20–30 h. One milliliter of glacial acetic acid was added to the dissolution sample along with 20 µg of mebendazole (internal standard), the volume made up to 10 mL with TD water, centrifuged, the supernatant liquid was filtered through a 0.2-µm membrane filter and analysed for albendazole by HPLC as described previously. Glacial acetic acid was added to the dissolution samples to ensure the complete dissolution of the water-insoluble albendazole particles that may be eroded out of the guar gum matrix tablets.

To assess the long-term stability (2 years), drug release studies in simulated gastric and intestinal fluids and in rat caecal content medium were also carried out on albendazole matrix tablets SAC-30 and SAC-40 after storage at 40°C/75% relative humidity (RH) for 6 months [Mathews, 1999]. At the end of the study period, the formulations were observed for change in physical appearance, color, and drug content and drug release characteristics.

Statistical analysis

The cumulative percent of albendazole released from guar gum matrix tablets (n = 3) in the dissolution medium at 24 h with and without rat caecal contents (control study) was compared, and the statistical significance was tested by using Student's t-test. A value of $P < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

The present study was aimed at developing oral colon-targeted formulations for albendazole from albendazole–β-cyclodextrin complex (1:0.25) using guar gum as a matrix carrier of tablet. It was reported earlier that guar gum could be used as a carrier for colon-specific drug delivery in the form of either a matrix tablet or as a compression coat over a drug core tablet [Rama Prasad et al., 1998; Krishnaiah et al., 1998]. Matrix tablets, though, release a minimal percent of the drug in stomach and small intestine, are the choice for colon-targeting of drugs as their preparation involves less processing variables and are manufactured by compression with conventional tableting facilities.

Initially, albendazole–β-cyclodextrin complexes in various proportions, 1:2, 1:1, 1:0.5, and 1:0.25 were studied. The bulk powder mix was evaluated for its solubility at the end of 24 h at 37°C. The results (Table 1) indicate that the solubility of albendazole increases with increasing proportions of β-cyclodextrin and show that the solubility of albendazole alone is 17.92 µg/mL in distilled water. By incorporating β-cyclodextrin at the 1:0.25 ratio solubility was increased to 125.4 µg/mL in distilled water. To increase the release of albendazole from colon-targeted guar gum matrix tablets, a ratio of 1:0.25 (albendazole:β-

TABLE 2. Characteristics of Albendazole Matrix Tablets ($n = 3$) Containing 20% (SAC-20), 30% (SAC-30), and 40% (SAC-40) of Guar Gum

Matrix formulation	Thickness ±SD (mm)	Hardness (kg/cm^2) ±SD	% Drug content ±SD
SAC-20	5.225±0.13	4.5±0.11	99.8±0.91
SAC-30	5.303±0.17	4.8±0.08	100.3±1.10
SAC-40	5.414±0.15	5.0±0.92	101.6±0.92

Y = 0.01486+0.19913 X ($r = 0.9999$).
SAC-20 = matrix tablets of albendazole containing 20% w/w of guar gum; SAC-30 = matrix tablets of albendazole containing 30% w/w of guar gum; SAC-40 = matrix tablets of albendazole containing 40% w/w of guar gum; SD = standard deviation.

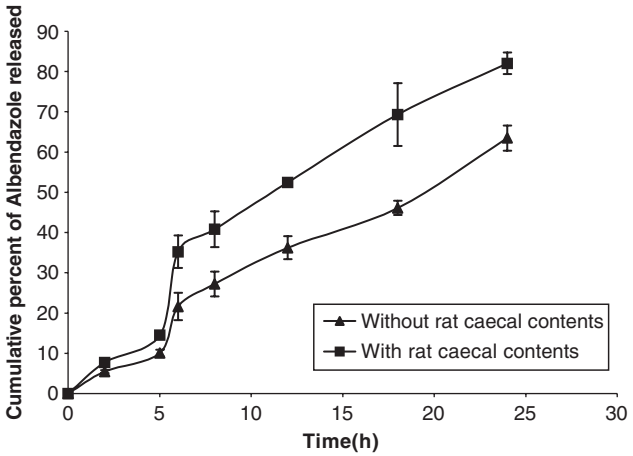

Fig. 1. In vitro release of albendazole from matrix tablets containing 20% w/w of guar gum (SAC-20).

cyclodextrin) was determined as useful because at this ratio there was an approximate 700% increase in the solubility of albendazole from the complex.

Because guar gum has poor flow properties and was to be incorporated in the matrix tablets in a larger proportion, albendazole tablets were prepared by a wet granulation technique using starch paste as binder. Assaying three samples of the powder mix drawn randomly from the lot assessed the uniformity of mixing of albendazole, guar gum, and MCC. The matrix tablets were prepared by applying maximum force of compression, and the hardness of the tablets was found to be in the range of 4.5 to 5.0 kg/cm^2 (Table 2). The HPLC method used in the study was precise and accurate as indicated by less than 1.5% CV (intra- and interday) and high recovery (99.5–100.2%) of albendazole, respectively. Albendazole tablets containing various proportions of guar gum ranging from 20% to 40% of guar gum were prepared, and were subjected to drug content uniformity and in vitro drug release studies. The matrix tablets were found to contain 99.8% to 101.6% of the labeled amount, indicating uniformity of drug content (Table 2).

In vitro release studies

Matrix tablets were subjected to in vitro drug release studies in 0.1 N HCl (2 h), pH 7.4 Sorensen's phosphate buffer (3 h) and simulated colonic fluids (rat caecal content medium at 4% w/v level after 7 days of enzyme induction). Earlier reports from our laboratory indicated that rat caecal content medium at 4% w/v level after 7 days of enzyme induction provides the best conditions for assessing the susceptibility of guar gum to colonic bacterial degradation [Rama Prasad et al., 1998].

During control studies (without rat caecal contents), the albendazole–β-cyclodextrin-complex matrix tablets containing 20%, 30%, or 40% of guar gum as matrix carrier retained their physical integrity up to 24 h of dissolution study conducted. SAC-20 matrix tablets were susceptible to the simulated colonic fluid (rat caecal medium). The percent of albendazole released from SAC-20 tablets at the end of 24 h was 82.0±2.7%, whereas in the control study (without rat caecal medium) only 63.5±3.1% of albendazole was released. A difference ($P < 0.001$) was observed in the amount of albendazole released at the end of the dissolution study (24 h) with rat caecal medium when compared to the dissolution study without rat caecal contents. The cumulative percent of albendazole released from SAC 20 is shown in Figure 1.

When the drug content that remained either in the tablet mass or in the swollen form was determined and summed up with the total drug released in the dissolution study, it was equal to the total amount of albendazole present in the formulation. This ensured the estimation of all the drug particles that might have eroded during the in vitro dissolution study.

On increasing the amount of guar gum in the matrix tablets, the release of albendazole decreased at the end of 24 h of the dissolution study. The SAC-30 released 67.6±1.9% of albendazole in the presence of rat caecal contents, whereas in the control study the formulation released only 29.7±0.2% of albendazole. A difference ($P < 0.001$) was observed at 24 h in the amount of albendazole released from SAC-30 when compared to the dissolution study without rat caecal contents. The cumulative percent of albendazole released from SAC 30 is shown in Figure 2.

Similarly, SAC-40 released 43.4±0.7% of albendazole in the presence of rat caecal contents, whereas in the control study the formulation released only 19.6±1.4% of albendazole. A difference ($P < 0.001$) was observed at 24 h in the amount of albendazole released from SAC-40 when compared to dis-

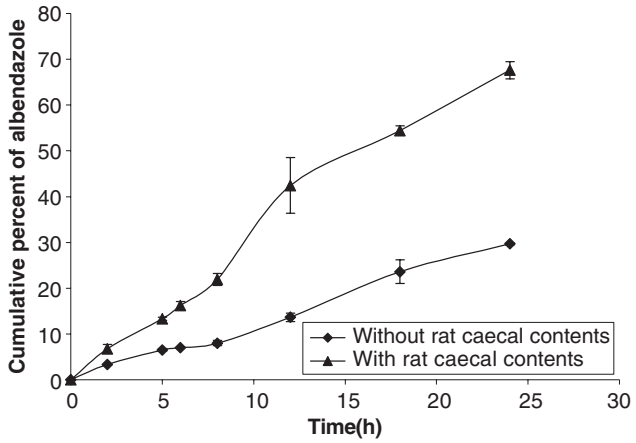

Fig. 2. In vitro release of albendazole from matrix tablets containing 30% w/w of guar gum (SAC-30).

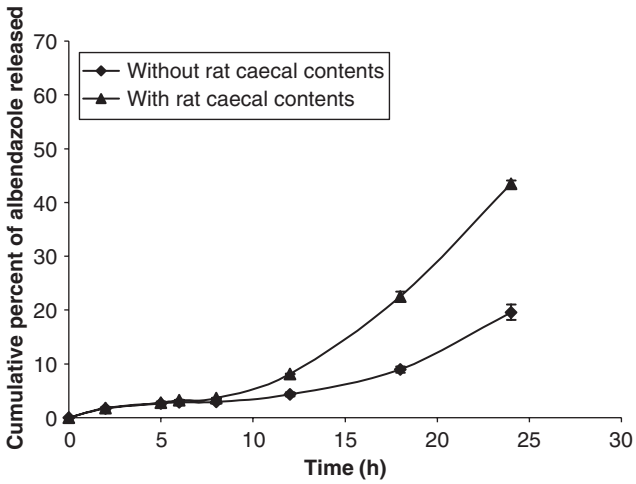

Fig. 3. In vitro release of albendazole from matrix tablets containing 40% w/w of guar gum (SAC-40).

solution without rat caecal contents. The cumulative percent of albendazole released from SAC 40 is shown in Figure 3.

The present study shows that the release of albendazole in the physiological environment of colon is due to the microbial degradation of guar gum compression-coated tablets in the presence of rat caecal contents. On exposure to the dissolution fluids, the guar gum becomes hydrated and forms a viscous gel layer that slows down further seeping-in of dissolution fluids towards matrix tablets. On coming in contact with biological fluids, guar gum swells up and the drug release takes place by diffusion. The mechanical erosion of the swollen guar gum layer would follow this. Unless the swollen guar gum layer erodes, further hydration and swelling of the guar gum does not take place. On reaching the colonic environment, the colonic bacterial enzymes act upon the swollen guar gum layer and release the drug contained in the swollen guar gum layer.

At the end of the 24-h dissolution study, matrix formulations SAC-30 and SAC-40 released more than 40% of their drug content in the physiological environment of stomach, small intestine, and colon. It is clear from these results that SAC-30 and SAC-40 could target albendazole to colon and may be considered as potential formulations for targeting of albendazole to colon, especially because human caecal contents would be greater than that used in the present study. However, the relative potential of the formulations SAC-30 and SAC-40 in providing colonic drug delivery needs evaluation in humans.

In view of the potential utility of SAC-30 and SAC-40 formulation for targeting of albendazole to colon, stability studies were carried out at 40°C/75% RH for 6 months to assess long-term (2 years) stability. The protocol of the stability studies was in conforma-

TABLE 3. Percent of Albendazole Released From Guar-Gum Matrix Tablets, SAC30 and SAC40 Before and After Storage at 40°C/75% RH for 6 Months

	Percent of albendazole released from SAC 30±SD		Percent of albendazole released from SAC 40±SD	
Time (h)	Before storage	After storage	Before storage	After storage
2	0±0	0.0±0.45	0±0	0±0
5	6.74±0.93	6.72±0.37	5.72±0.79	5.54±0.33
6	13.35±0.35	13.12±0.44	10.77±0.93	10.54±0.24
8	16.25±0.81	16.21±0.90	14.41±0.96	14.24±0.77
12	21.91±1.33	21.7±1.77	18.9±0.90	18.63±0.34
18	42.44±6.07	42.34±0.57	39.45±0.89	39.22±0.33
24	54.44±1.00	54.34±1.64	50.15±0.97	50.09±0.63

SAC-30 = matrix tablets of albendazole containing 30% w/w of guar gum; SAC-40 = matrix tablets of albendazole containing 40% w/w of guar gum; SD = standard deviation; RH = relative humidity.

tion with the recommendation in a World Health Organization document for stability testing of products intended for global market [Mathews, 1999]. After storage, the formulations were subjected to assay of the drug and in vitro drug release studies. When the matrix tablets SAC-30 and SAC-40 were stored at 40°C/75% RH for 6 months, there appeared to be no change either in their physical appearance or in drug content. When the dissolution study was conducted in the simulated physiological environment of stomach, small intestine, and colon as described above, no significant difference ($P < 0.05$) was observed in the percent of albendazole released from SAC-30 and SAC-40 stored at 40°C/75% RH for 6 months when compared to that released from the same formulations before storage (Table 3). The insignificant change in the physical appearance, drug content, or dissolution profile of SAC-30 and SAC-40 formulation after storage at 40°C/75% RH for 6 months indicates that the formulations could provide a minimum shelf life of 2 years.

CONCLUSIONS

The present study was carried out to develop colon-targeted delivery systems for albendazole from albendazole–β-cyclodextrin inclusion complex (1:0.25) using guar gum as a matrix carrier. Guar gum matrix tablets containing various proportions of guar gum were prepared and subjected to in vitro drug release studies. Albendazole matrix tablets containing 20% of guar gum are not suitable for colon targeting because they release another 18.5% of the drug in simulated colonic fluid. The matrix formulations containing 30% and 40% guar gum are most likely to target albendazole in improved concentrations to colon without being released significantly in stomach and small intestine. The matrix formulations SAC-30 and SAC-40, after storing at 40°C/75% RH for 6 months, showed no change in physical appearance, drug content, or dissolution pattern. Bioavailability studies in healthy human volunteers and clinical studies in patients are ongoing to assess the relative usefulness of the SAC-30 formulation in comparison with conventional albendazole tablets.

ACKNOWLEDGMENTS

The authors acknowledge the financial support received from Government of India, Department of Science and Technology (DST), All India Council for Technical Education (under MODROBS and TAPTEC research schemes) and University Grants Commission, New Delhi. The authors greatly acknowledge M/s. Brown and Burk Pharmaceuticals Ltd., Mumbai, India, M/s. IPCA Laboratories, India and M/s. Dabur Research Foundation, New Delhi, India for the gift samples of albendazole, mebendazole, and β-cyclodextrin and guar gum, respectively. One of the authors, Mr. Somashekar Shyale, is thankful to Dr. S.M. Shantakumar, Principal, V.L. College of Pharmacy, Raichur, and also to the Management of V.L. College of Pharmacy, Raichur, in their encouragement to pursue the Ph.D. program.

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