Original Research Article

In vitro evaluation of *Moringa oleifera* gum for colon-specific drug delivery

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Abstract

Background: Moringa gum obtained from stem of the plant *Moringa oleifera* Lam. belonging to family Moringaceae. Number of naturally occurring polysaccharides obtained from plant (guar gum, inulin), animal (chitosan, chondrotin sulphate), algal (alginates) or microbial (dextran) origin. **Objective:** The present study was evaluated *Moringa oleifera* gum as a carrier for colon specific drug delivery using *in vitro* drug release studies. **Materials and Methods:** Six formulations of curcumin were prepared using varying concentration of *Moringa oleifera* gum containing 50 mg curcumin by wet granulation method. Tablets were subjected for evaluation by studying the parameter like hardness, friability, drug content uniformity and *in vitro* drug release study. Hardness was found to be in the range of 5.5 to 7.3 kg/cm^2, the percentage friability was in the range of 0.60 to 0.89%, and tablet showed 98.99% to 99.89% of the labeled amount of curcumin indicating uniformity in drug content. **Results and Discussion:** *In vitro* drug release study was performed using simulated stomach, intestinal and colonic fluid. The susceptibility of Moringa gum to colonic bacteria was also assessed using drug release study with rat caecal contents. 30% Moringa gum containing formulation (F-3) was shown better drug released that is 90.46%, at the end of 24 h of dissolution study in the presence of rat caecal contents in comparison to 40% Moringa gum containing formulation (F-4) that was 78.03%. **Conclusion:** The results illustrate the usefulness of *Moringa olefera* gum as a potential carrier for colon-specific drug delivery.

Key words: Cancer, curcumin, rat caecal content

INTRODUCTION

Targeting pharmaceutical drugs to the colon makes it possible to guarantee local or systemic drug delivery to this site. To deliver the drugs in non-degraded form to the last part of gastrointestinal tract, they must first of all pass through the stomach, the upper part of the intestine and must use the characteristic of the colon specifically released drugs in this part of the digestive tract. In recent times, colon-targeted drug delivery systems have gained importance for the systemic delivery of protein and peptide drugs.[1] Drug delivery to the colon is desired not only for oral delivery of peptide and proteins but also to treat different diseases associated with the colon such as irritable bowel syndrome, colon cancer, colitis, and ulcerative colon.[1] Drug targeting to colon is also useful when a delay in drug absorption is desired from therapeutic point of view, such as treatment of diseases that have peak symptoms in the early morning like nocturnal asthma, angina, or arthritis.[1-3] By definition, an oral colonic delivery system should retard drug release in the stomach and small intestine but allow complete release in the colon. The fact that such a system will be exposed to a diverse range of gastrointestinal conditions on passage through the gut makes colonic delivery via the oral route a challenging proposition. Targeted drug delivery to the colon would therefore ensure direct treatment at the disease site, lower dosing, and fewer systemic side effects.[4]

Moringa oleifera Lam (syn. M. ptreygosperma Gaertn.) is one of the best known and most widely distributed and naturalized species of a monogeneric family Moringaceae. Different parts of this plant contain a profile of important minerals, and are a good source of protein, vitamins, β-carotene, amino acids and various phenolics.[5,6] Moringa gum obtained from stem of the plant *Moringa oleifera* Lam. Belonging to family Moringaceae. Number of naturally occurring polysaccharides obtained from plant (guar gum, inulin), animal (chitosan, chondrotin sulphate),

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algal (alginates) or microbial (dextran) origin. These natural polysaccharide using for colon-targeted drug delivery system. A novel matrix tablet formulation for oral administration using Moringa gum as a carrier and curcumin as a model drug has been investigated for colon-specific drug delivery using *in vitro* methods.

Curcumin is the principal curcuminoid of the popular Indian curry spice turmeric. The curcuminoids are polyphenols and are responsible for the yellow color of turmeric. Curcumin is known for its antitumor, antioxidant, antiarthritic, anti-amyloid, anti-ischemic, and anti- inflammatory properties. Its anticancer effects stem from its ability to induce apoptosis in cancer cells without cytotoxic effects on healthy cells. Curcumin can interfere with the activity of the transcription factor NF-κB, which has been linked to a number of inflammatory diseases such as cancer. Indeed, when 0.2% curcumin is added to diet given to rats or mice previously given a carcinogen, it significantly reduces colon carcinogenesis.[7]

The inability of GIT enzyme to digest certain plant polysaccharide is taken advantage to develop colon-specific drug delivery system. Biodegradable polymer matrix core embedded the drug by compressing the blend of active drug, a biodegradable polymer and additives. Various polysaccharides are being evaluated for colon targeting like pectin, guar gum, gum ghatti, dextran, chitosan, and xylan. *Moringa oleifera* gum, obtained by the deep incision in stem of *Moringa oleifera* Lam. tree, shows degradation in the large intestine due to the presence of microbial enzymes. [8,9] The bacterial enzymes of colon degrade the carrier polymer in a well defined way and release the contents for localized colonic delivery or systemic absorption through colon.[10,11] In this regard our aim was directed to identify *Moringa oleifera* Lam. gum as a polymer to deliver the drug (curcumin) in colon.

MATERIALS AND METHODS

Chemical

Curcumin were purchased from National Chemical, Vadodara, and Gujarat. Moringa gum was collected manually from *Moringa oleifera* Lam. tree, in Mandsaur region (M.P.), India.

Characterization of Moringa gum

The Moringa gum was identified and characterized [Table 1] using following parameters: Particle characters, Angle of repose, Bulk density, Tape density, Hausner ratio, loss on drying were included in Characterization.[12,13]

Tablet formulation of curcumin using Moringa gum

Matrix tablets using Moringa gum were prepared by the wet granulation method. Lactose was used as diluent and a mixture of talc-magnesium stearate (2:1) was used as lubricant. Moringa gum was included in the formulations in various proportions [Table 2]. In all the formulations, *Moringa oleifera* gum was sieved (<250 μm) separately and mixed with drug (<150 μm) and lactose (<250 μ m). The powders were blended and granulated with 8% starch paste. The wet mass was passed through sieve no. 18 and the granules were dried at 50°C for 2 h. The dried granules were passed through sieve no. 22 and these granules were lubricated with a mixture of talc-magnesium stearate (2:1). The lubricated granules were added on an eight station tableting machine for formulation of matrix tablet.

Evaluation of tablet

Evaluations of tablet included parameters such as weight variation, hardness, friability, and content uniformity.[14]

In vitro drug release studies in 0.1N HCL, pH. 7.4 Sorensen's phosphate buffer and pH. 6.8 Sorensen's phosphate buffer

The ability of matrix tablets of curcumin to remain intact in the physiological environment of stomach and small intestine was assessed by conducting drug release studies under conditions mimicking mouth to colon transit. Drug release studies were carried out using USP dissolution rate test apparatus (Apparatus 1, 100 rpm, 37°C) for 2 hr in 0.1N HCl (900 ml). Then the dissolution medium was replaced with pH. 7.4 phosphate buffer (900 ml) and tested for drug release for 3 hr. After that the dissolution medium was replaced with pH. 6.8 phosphate buffer (900 ml) and experiment was continued up to 24 hr. At different time intervals, 5 ml of the sample was withdrawn without a pre-filter and replaced with 5 ml of fresh phosphate buffer. About 1 ml of the liquid was suitably diluted, filtered and analyzed for percentage drug release at 421 nm for curcumin by UV method using double beam UV-spectrophotometer. The % drug release was calculated using the standard curve of curcumin in different dissolution media.[1,15-17]

Drug release studies in presence of rat caecal contents

To assess the susceptibility of *Moringa oleifera* gum being acted upon by colonic bacteria, drug release studies were carried out in the presence of rat caecal contents because of the similarity with human intestinal microflora. In order to induce enzymes specifically acts on Moringa oleifera gum in the caecum, male albino rats maintained on normal diet were administered with 4 ml, 1% dispersion of guar gum in water for 7 days. Thirty minutes before the commencement of drug release studies, three rats were killed by spinal traction. The abdomen was opened, isolated, ligated at both ends, cut loose, and transferred into pH. 6.8 phosphate buffer, previously bubbled with CO_2. The

Table 1: Characterization of *Moringa oleifera* gum

Parameter	Obtained value	Result
Bulk density	0.76 g/ml	-
Tapped density	0.86 g/ml	-
Carr's index	11.6%	Good flow property
Hausner's ratio	1.13	Good flow property
LOD	10%w/w	-
Total ash value	2%w/w	-
Acid insoluble ash	0.65%w/w	-
Angle of repose	22.50	Good flow

LOD - Limit of detection

Table 2: Quantity of different ingredients of tablet F_1 to F_6

Ingredient	Quantity of different ingredients					
	F-1 (%)	F-2 (%)	F-3 (%)	F-4 (%)	F-5 (%)	F-6 (%)
Curcumin	10	10	10	10	10	10
MOG	10	20	30	40	50	60
Lactose	75	65	55	45	35	25
Starch paste (8%)	Qs	Qs	Qs	Qs	Qs	Qs
Magnesium stearate	2	2	2	2	2	2
Talc	1	1	1	1	1	1
SLS	2	2	2	2	2	2

MOG - *Moringa oleifera*

rat caecal bags were opened, their contents were weighed and 4% w/v solution of rat caecal contents was prepared in pH. 6.8 phosphate buffer.

RESULTS AND DISCUSSION

Six formulations of curcumin were prepared using Moringa gum as a polymer. The evaluation of formulation was done and the results obtained were presented in Table 3. 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).

From the *in vitro* dissolution studies it was found to be that formulation F1 with 10% moringa gum, F2 with 20% moringa gum, were unable to retard drug release in the stomach and small intestine effectively, because F1 and F2 shown 34.19% and 18.51% drug release at the end of 5 h means up to small intestine. However, formulation F5 with 50% mog and F6 with 60% mog released non significant amount of drug in environment of colon. Formulation containing 30% (F3) and 40% formulation (F4) moringa gum released 45.89% and 34.79% curcumin from matrix tablet at the end of 24 h in dissolution study [Table 4, Figure 1].

From the *in vitro* drug release studies with 4% w/v rat caecal content it was found to be that formulation F3 with 30% mog and F4 with 40% moringa gum, gave 90.46% and 78.03% drug release at the end of 24 h, respectively [Table 5].

The result of *in vitro* drug release studies in pH. 6.8 phosphate buffer saline (PBS) with 4% rate caceal content demonstrated that mog is susceptible to enzymatic action of caecal contents that caused better drug release (90.46%) (F3) in the presence of rat caecal contents than that of without rat caecal contents (45.89%) (F3). Hence, data reveals that mog may be used as a potential carrier for colon-specific drug delivery [Table 6, Figure 2].

Moringa gum in the form of directly compressed tablet has the capability to protect the release of active drug curcumin in the physiological environment of stomach and small intestine as established the *in vitro* drug release studies under the condition mimicking mouth to colon transit. The susceptibility of *Moringa oleifera* gum to colonic bacteria and drug release in colon was also

Table 3: Evaluation of tablets

Formulation code	Weight (mg)	Hardness (kg/cm²)	Friability (%)	Content uniformity (%)
F-1	501	5.5	0.89	99.10
F-2	510	5.8	0.82	99.54
F-3	508	6.4	0.64	98.99
F-4	507	7.2	0.61	99.54
F-5	501	7.3	0.62	99.01
F-6	511	7.3	0.60	99.79

All values are the average of three determinations

Table 4: Cumulative % drug release of different formulations

Time (hr)	Cumulative % drug release					
	F-1	F-2	F-3	F-4	F-5	F-6
2	27.61	14.67	9.49	5.05	4.43	3.20
5	34.19	18.51	12.13	7.43	6.63	5.40
7	43.30	25.26	17.34	10.19	8.94	7.07
9	46.37	30.29	20.55	16.56	13.94	11.01
12	49.16	33.68	24.98	21.15	15.49	12.56
18	56.66	41.33	33.22	27.12	20.08	15.92
24	79.61	59.61	45.89	34.79	28.93	25.21

Table 5: Cumulative % drug release of different formulations with rat caecal contents

Time (hr)	Cumulative % drug release	
	F-3	F-4
2	9.49	5.05
5	12.13	7.43
7	28.84	21.38
9	42.24	31.29
12	54.36	42.16
18	70.93	58.84

Table 6: Cumulative percentage of curcumin released from matrix tablet containing 30% (F3) of MOG in drug release studies without and with rat caecal contents

Time (hr)	Cumulative % drug release	
	Without RCC	With RCC
2	9.49	9.49
5	12.13	12.13
7	17.34	28.84
9	20.55	42.24
12	24.98	54.36
18	33.22	70.93
24	45.89	90.46

MOG - *Moringa oleifera*, RCC - Rat caecal contents

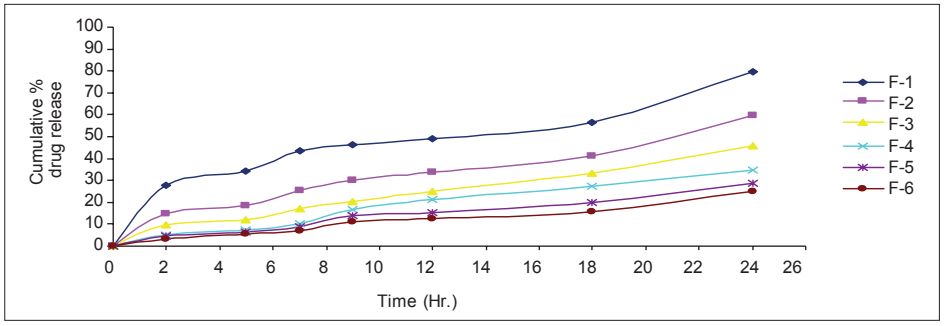

Figure 1: Cumulative percentage of curcumin released from matrix tablet containing 10% (F1), 20% (F2), 30% (F3), 40% (F4), 50% (F5), and 60% (F6) of MOG in drug release studies without rat caecal contents

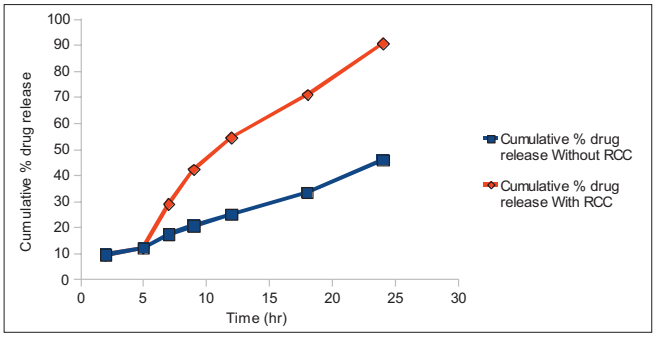

Figure 2: Cumulative percentage of curcumin released from matrix tablet containing 30% (F3) of MOG in drug release studies without and with rat caecal contents

assessed using *in vitro* drug release study with rat caecal contents. By using this approach curcumin could be used more effectively in treatment of colon cancer and oral dose of curcumin may be decreased but still the bioavailability can be increased.

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