International Journal of Pharmaceutical Sciences and Nanotechnology

*Volume* 2 ● *Issue* 4 ● *January – March* 2010

*Research Paper*

# Evaluation of *Cassia roxburghii* Seed Gum as Binder in Tablet Formulations of Selected Drugs

**Arul Kumaran KSG*, Palanisamy S, Rajasekaran A, Ahil hari**

KMCH College of Pharmacy, Coimbatore, India.

**ABSTRACT:** The purpose of the study was to evaluate *cassia roxburghii* seed gum powder as binder for paracetamol and diclofenac sodium. Granules of both drugs were prepared by wet granulation method. Two different laboratory developed methods were tried for the isolation of seed mucilage from seed powder. The phytochemical, physico-chemical and microbiological properties were performed on the seed gum and the pre-compression parameters like bulk density, tapped density, angle of repose, carr's index and hausner's ratio have shown that paracetamol and diclofenac granules prepared using *Cassia roxburghii* gum were well within the limits and comparable to those prepared using standard starch paste as binder. The *in vitro* dissolution study was performed for paracetamol formulations with sodium starch glycolate and the dissolution profile shows all the three formulations met with official specifications. The *in vitro* dissolution profile shows that drug release decreased in the order, tablets prepared by starch>*c.roxburghii* defatted>*c.roxburghii* filtered in both paracetamol and diclofenac formulations. The drug release from tablets prepared by *C.roxburghii* seed gum was more than 85% in 2 hours and filtered *C.roxburghii gum* has excellent mechanical, binding and release properties in paracetamol tablet formulations with the addition of sodium starch glycolate as an external disintegrant.

**KEYWORDS:** *Cassia roxburghii,* Isolation, Paracetamol, Diclofenac sodium, Gelatin, Guar gum.

## Introduction

Tablets are the most successful form of administrating medicines. Tablets also offer an efficient means of reducing powders and granules into a compact product. The tablet is versatile, compact, robust, and accurate and can be mass produced consistently at high speeds. It is an incredibly versatile drug delivery device whose limitations being defined only by the imagination of the tablet designer (Keith Marshall, 1986). A tablet can be formulated to deliver an accurate dosage to a specific site. Tablet formation represents the last stage in down-stream processing within the pharmaceutical industry. It consists of an active pharmaceutical ingredient (API) with biologically inert excipients in a compressed, solid form (Bhogi B Sheth et al., 1979; Loyd V Allen et al., 2005).

Binding agents are used to impart the structural strength required during the processing, handling and packaging of tablets (Mehta RM, 2008). In simpler words, binders or adhesives are the substances that promote cohesiveness. It is utilized for converting powder into granules through a process known as Granulation (Pharmpedia). Plenty of plant gums have been used as a binding agent in tablet formulations, besides semi synthetic and synthetic binders (Parikh DM, 1997). They have been found useful in producing tablets with different mechanical strength and drug release properties. Since they are nontoxic and widely available, has made them of continuing interest (Ashok Katdare, and Mahesh V Chaubal, 2007).

Seed galactomannans are vegetable, heterogeneous polysaccharides widely distributed in nature. Generally, they possess (1 4)-linked D-mannopyranose (Man) main chains to which are attached (1 6)-linked D-galactopyranosyl (Gal) units. The Man/Gal ratios differ from gum to gum, resulting in a change in structure, which, in turn, determines the various industrial applications of seed galactomannans (Mathur NK, and Mathur GM, 2006). In the legumes, endosperm galactomannans are the reserve seed polysaccharides, which are used up during the germination and growth of the plant embryo, till it starts photosynthesis. Germinating legume seeds produce β-mannase and α-galactase enzymes, which can cleave mannan backbone and galactose grafts respectively to degrade galactomannan polysaccharides. All galactomannan gums have a strong, but variable tendency to bind and hold water and these are important raw materials for food and other industries (Bradley Morris J, 1999). Out of the hundreds of legume plant seeds, bearing galactomannan, only a few are recognized as source of

* *For correspondence:* Arul Kumaran KSG,

E-mail: yesmiarul@yahoo.com

industrial gums. This has resulted in restricting industrial choice of gums to more abundant and cheap, generally annual crop products, rather than those originating from perennial trees (Patent Storm / US Patent 5847109).

In view of importance of binders in pharmaceuticals for the manufacture of tablet formulations, *Cassia roxburghii* seed gum was taken to evaluate its binding properties through assessment of various parameters essential for pharmaceutical formulations. Since *C.roxburghii* seed gum was found as a strong binder, the effect of different starch disintegrants including superdisintegrant were also studied through assessment of various parameters. The main objectives of this study were: 1. to provide reliable method for isolation of mucilage from *Cassia roxburghii* seeds, 2. to study physicochemical and microbiological characteristics of *Cassia roxburghii* gum, 3. to evaluate the granulating, binding and release properties of the seed gum in tablet formulations using paracetamol and diclofenac as model drugs and 4. to study the effects of different starch disintegrants and their mode of addition on mechanical and release properties of *Cassia roxburghii* gum in paracetamol formulations.

## Materials and Methodology

The *cassia roxburghii* seeds were collected from Tamil University Thanjavur and the same was authenticated by G.V.S Moorthy, Botanical Survey of India (BSI), Southern circle, Coimbatore, Tamilnadu. Paracetamol was obtained as a gift sample from Macleods Pharmaceuticals Pvt.Ltd. Mumbai India and Diclofenac was from Universal Medicament Pvt. Ltd. Nagpur. All other ingredients used were of analytical grade. The other ingredients used were petroleum ether, distilled water, acetone, potato starch, wheat starch, pre-gelatinised starch (starch1500), sodium starch glycolate, lactose, talc, magnesium stearate, methyl paraben sodium and propyl paraben sodium.

## Collection and Isolation of Seed Gum

The collected seeds were dried at room temperature (25°C), powdered into coarse powder using an elite grinder. The seeds of *Cassia roxburghii* contain the mucilage around the outer layer. Since it is difficult to separate from seeds different procedures were tried to separate the seed gum (Ghule BN et al., 2006).

## Method A (Defatted Seed Gum)

100 grams of seed powder was defatted by Soxhlet extraction using petroleum ether as a solvent at temperature 60-70°C. This was repeatedly extracted using hot water till the complete mucilage was extracted. The mucilaginous solution was then filtered through eight folds of muslin cloth. The mucilage was then precipitated by adding sufficient acetone. The extracted mucilage was then dried in microwave oven till it was completely dried. The obtained powder was then sieved to get fine gum powder. Yield -10%

## Method B (Filtered Seed Gum)

100 grams of seed powder was soaked in sufficient water, kept over boiling water bath for 30 minutes, with occasional stirring. It was left overnight and then filtered using eight folds of fine muslin cloth. The mucilage was then precipitated by adding sufficient acetone. The extracted mucilage was then dried in microwave oven till it was completely dried. The obtained powder was then sieved to get fine gum powder (Yield -24%) (Avachat A, 2007).

## Phytochemical Study of Extracted Seed Gum

Preliminary tests were performed to confirm the nature of mucilage obtained. The chemical tests that were conducted are molisch's test, ferric chloride test, ninhydrin test, Wagner's test, Fehling's test, ruthenium test, Shinoda test and Keller-Kilani test.

## Physicochemical Characterisation of Seed Gum

The separated gum was evaluated for solubility, swelling index, loss on drying, ash value, microbial load, density, angle of repose, compressibility index, porosity, Hausner's ratio (Kunle A, 2006; Odeku AO, 2003).

## Solubility

Solubility of separated mucilage powder was studied in warm and cool distilled water and various organic solvents like acetone, methanol, and chloroform (Ghule BN et al., 2006; Patel DM et al., 2007).

## Swelling Index

Swelling characteristics of the separated mucilage powder was studied in distilled water. One gram of powder was moistened with 0.5 ml ethanol (95%) and volume was made up to 10 ml with distilled water. The cylinder was shaken vigorously every 10 min for 1 h and allowed to stand for 3 h. The volume occupied by mucilage powder was measured. The test was carried out in triplicate and the average value of swelling index was recorded.

As the inherent moisture in disintegrant may influence the stability of the tablet dosage form containing moisture sensitive drugs, moisture content of the separated mucilage was detected by loss on drying method. The sample (1 g) was heated at $105^{o}$ until constant weight in a hot air oven and percentage loss of moisture on drying was calculated using the formula, LOD (%)= (weight of water in sample/weight of dry sample)× 100 (Kohli DPS, and Shah DH, 2005).

## Microbial Load

Microbial content determination: 1gram of sample powder was dissolved in 9ml of sterile distilled water. Serial dilutions were made and viability assessed using pour plate method. For detection of fungal growth in the sample, sadouraud dextrose agar medium was used. The plates were incubated at 27°c for 72 hours (Ghule BN et al., 2006). Casein digest medium was used. The plates were incubated at 37°c for 24 hours (British Pharmacopoeia, 1993).

***Bulk Density (Db)*:** 10 grams of gum powder of each batch were introduced into a clean, dry 100 ml measuring cylinder and the volume was recorded. It is expressed in gm/ml and is given by,

$$Db = M/Vo$$

Where, M is mass of the gum powder.

Vo is the bulk volume of the gum powder.

***Tapped Density (Dt)*:** 10 grams of gum powder of each batch were introduced into a clean, dry 100 ml measuring cylinder. The measuring cylinder was then tapped 2500 times from a fixed height and the tapped volume was read. It is expressed in gm/ml and is given by,

$$Dt = M/Vt$$

Where, M is mass of the gum powder.

Vt is the tapped volume of the gum powder.

***Angle of Repose (AOR*):** The fixed funnel method was employed for determining the angle of repose. The gum powder was poured carefully until the apex of the conical pile touched the tip pf the stem of the funnel. The angle of repose was calculated using the equation,

$$\theta = \tan (h/r)$$

Where, θ is the angle of repose.

h is the height of pile.

r is the radius of the base of the pile.

***Carr's Index (I)***: It indicates the ease with which a material can be induced into powder flow properties. It is expressed in % and is given by

$$I = (Dt - Db)/Dt \times 100$$

Where, Dt is the tapped density.

Db is the bulk density.

***Hausner's Ratio***: It previews the degree of densification which would occur during tabletting. It is the ratio of tapped density to bulk density.

$$H = Dt/Db$$

Where, Dt is the tapped density of the gum powder.

Db is the bulk density of the gum powder.

## *In-Vitro* Dissolution Studies of Paractamol and Diclofenac Formulations with *Cassia roxburghii* Seed Gum as Binder

***Parameters***

| | | |
|---|---|---|
| Instrument | : | USP DISSOLUTION RATE TEST APPARATUS |
| Type | : | paddle |
| Medium | : | 900 ml phosphate buffer pH 7.4 |
| Temperature | : | 37±0.5°c |
| RPM | : | 50 |
| Testing time | : | 2 hours |
| Amount withdrawn | : | 1ml |
| λmax for paracetamol | : | 257 nm. |
| λmax for diclofenac | : | 275nm |

The samples were withdrawn at predetermined time intervals and the same volume was replaced immediately to maintain sink condition. The study was run for 2 hours with the above fixed parameters. The withdrawn samples were suitably diluted and absorbance of the solution was determined at respective λ max.

## Formulation of Paracetamol and Diclofenac Tablets

Each batch of granules was compressed using twelfth station rotary tablet punching machine. Six batches of size 200 tablets were prepared. Batches of Paracetamol tablets were punched using 12.5mm flat faced beveled edge punches and batches of Diclofenac tablets were punched using 8mm concave faced punches. The prepared tablets of each batch were evaluated for weight variation, crushing strength, friability, tensile strength, disintegration time and *In-vitro* dissolution profile using methods specified in Indian Pharmacopoeia.

## Results and Discussion

### Phytochemical Study of *C.roxburghii* Seed Gum

The phytochemical study of mucilage of *C.roxburghii* seed gum shows the absence of alkaloids, anthraquinones and tannins (Tables 1 and 2). On treatment of mucilage with ruthenium red, it showed red colour conforming the

presence of mucilage. A violet ring was formed at the junction of two liquids on reaction with Molischs reagent confirming the product as carbohydrate. Post formulation parameters show that the effect of starch disintegrants on the mechanical and release properties of *Cassia roxburghii* seed gum in paracetamol tablets were excellent (Tables 3 and 4). Dissolution data for Paracetamol formulations containing sodium starch glycolate (ssg) show good and sustained solubility (Figure 1).

**Table 1.** Physicochemical characterisation of mucilage of *C.roxburghii.*

| **PARAMETERS** | | **RESULTS** | |
|---|---|---|---|
| Solubility | | Swells in cold water, dissolves in warm water forming colloidal solution. Insoluble in organic solvents | |
| Loss on drying | | 9.6% | |
| pH | | 6.5 | |
| Swelling ratio | In distilled water | 6.2 | |
| Microbial load | Bacteria (CFUs/g) | 172 | |
| | Fungi (CFUs/g) | 107 | |
| Density of powder | | DEFATTED GUM | FILTERED GUM |
| | Bulk density (g/cc) | 0.69 | 0.69 |
| | Tapped density (g/cc) | 0.82 | 0.81 |
| Compressibility index (%) | | 15.85 | 14.81 |
| Angle of repose | | 36.53° | 37.56° |
| Hausner's ratio | | 1.18 | 1.17 |

**Table 2.** Phytochemical screening of mucilage of *C.roxburghii.*

| **S.No** | **Tests** | **Observation** |
|---|---|---|
| 1 | Test for carbohydrates (molisch's test) | **+** |
| 2 | Test for tannins (ferric chloride test) | **-** |
| 3 | Test for proteins (ninhydrin test) | **-** |
| 4 | Test for alkaloids (wagner's test) | **-** |
| 5 | Test for reducing sugars (fehling's test) | **-** |
| 6 | Test for mucilage (ruthenium test) | **+** |
| 7 | Test for flavonoids (shinoda test) | **-** |
| 8 | Test for glycosides (keller-kilani test) | **-** |

**Table 3.** Preformulation parameters of paracetamol and diclofenac granules.

| **PARAMETERS** | **Fp1** | **Fp2** | **Fp3** | **Fd1** | **Fd2** | **Fd3** |
|---|---|---|---|---|---|---|
| Angle of repose | 31.6° | 32.01° | 31.2° | 29.05° | 28.7° | 32.8° |
| Bulk density (g/cc) | 0.39 | 0.39 | 0.36 | 0.56 | 0.55 | 0.52 |
| Tapped density (g/cc) | 0.50 | 0.52 | 0.45 | 0.69 | 0.73 | 0.66 |
| Carr's compressibility Index (%) | 21.88 | 23.81 | 17.64 | 18.92 | 24.66 | 20.83 |
| Hausner's ratio | 1.28 | 1.31 | 1.21 | 1.24 | 1.33 | 1.26 |

**Table 4.** POST- FORMULATION PARAMETERS: Evaluation of mechanical properties of tablets.

| Parameters | Fp1 | Fp2 | Fp3 | Fd1 | Fd2 | Fd3 |
|---|---|---|---|---|---|---|
| Crushing Strength (N) | 48.64 | 54.44 | 53.15 | 51.68 | 74.63 | 50.12 |
| Friability (%) | 0.55 | 0.455 | 0.644 | 0.365 | 0.392 | 0.432 |
| CSFR | 88.44 | 119.65 | 82.53 | 141.59 | 190.38 | 116.02 |
| Tensile strength ($N/mm^2$) | 0.562 | 0.667 | 0.641 | 1.455 | 2.106 | 1.36 |

Two different laboratory developed methods were tried for the isolation of seed mucilage from seed powder. Defatting method using soxhlet apparatus yielded 10% and filtration method yielded 24%. The mucilage powder obtained was a light brown fine powder. The physico-chemical and microbiological properties of mucilage were determined and the extracted mucilage was evaluated for microbial count and pH. The microbial count for both bacteria and fungi were within the limits. Since the pH of the seed gum is 6.5, it may be less irritating the GIT and it may be suitable for uncoated tablets. Swelling capacity of the gum favored it to be a good granulating agent. The density parameters of the gum from both the methods were found to be within the official limits.

The pre-compression parameters like bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio have showed that paracetamol and diclofenac granules prepared using *cassia roxburghii* gum were well within the limits and comparable to those prepared using standard starch paste as binder.

Post compression parameter shows Higher CSFR value stronger the tablet. According to CSFR Ranking, *c.roxburghii* filtered gum> *c.roxburghii* defatted gum>starch. With regard to CSFR and tensile strength, formulations with filtered *C.roxburghii* gum showed more mechanical strength than those with starch paste and *C.roxburghii* defatted gum showed comparable results to those with starch paste. As regard to the disintegration time, tablets prepared with *C.roxburghii* gum, showed an increase in disintegration time when compared to those with starch paste. The tablets prepared with *C.roxburghii* gum showed better properties in terms of mechanical and binding properties than standard starch paste especially in paracetamol tablets. Capping in paracetamol tablets were also minimized in tablets prepared with *C.roxburghii* gum. Comparable properties in diclofenac tablets were observed with respect to standard starch paste.

The *in vitro* dissolution profile shows that drug release decreased in the order, tablets prepared by Starch>*C.roxburghii* defatted>*C.roxburghii* filtered in both paracetamol and diclofenac formulations. This study revealed that the drug release from tablets prepared by *C.roxburghii* seed gum was more than 85% in 2 hours and did not meet with official specifications (figure 1 and 2).

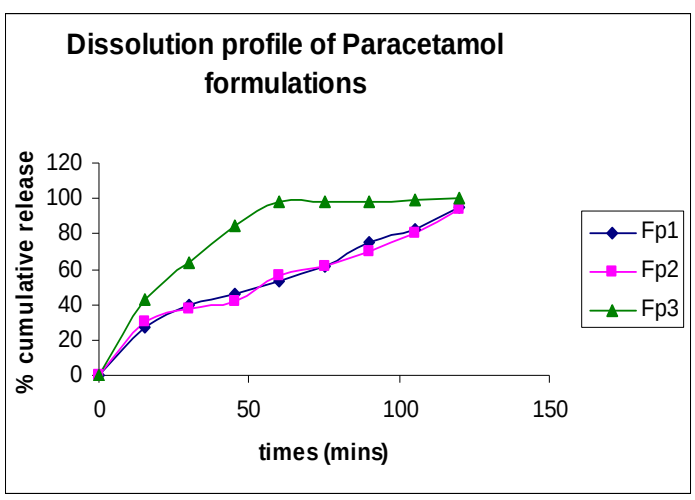


**Fig 1.**

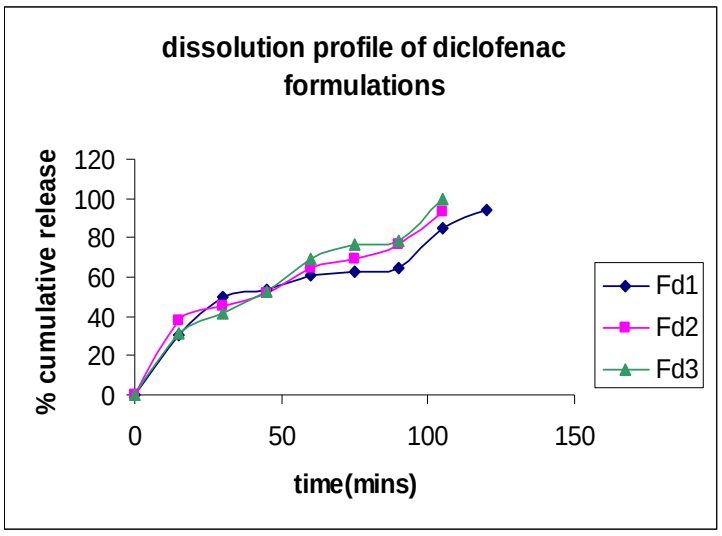


**Fig 2.**

**Effect of Disintegrants in Paracetamol Formulations**

- Rank order of starches in case of disintegration

  Sodium starch glycolate >pre-gelatinized starch> wheat starch

- The rank order of Crushing strength for different modes of addition

  External>internal-external>internal.

- The rank order of disintegration time for different modes of addition

  External>internal-external>internal.

- CSFR/DT ratio has been suggested as a better index of measuring tablet quality than CSFR because in addition to measuring the tablet strength (hardness) and weakness (friability), it simultaneously evaluates all negative effects of these parameters on disintegration time. Higher CSFR/DT ratio indicates a better balance between binding and disintegration properties.

- Considering CSFR/DT ratio rank order of starches and modes of addition in paracetamol tablets using filtered *c.roxburghii* seed gum.

  Sodium starch glycolate >pre-gelatinised starch> wheat starch.

  External>internal-external>internal.

  The *in vitro* dissolution study was done for paracetamol formulations with sodium starch glycolate and the dissolution profile shows all the three formulations met with official specifications. Tablets with external mode of addition showed faster release than those with internal-external mode of addition which in turn showed faster release than internal mode of addition.

## Conclusion

The present study indicates that the *c.roxburghii* gum may be a better binder for paracetamol and diclofenac tablets since it has minimized capping tendency without adversely affecting other crucial properties of the tablets. Considering the mechanical and binding properties of tablet formulations, filtered *c.roxburghii* gum was found to be better than defatted *c.roxburghii* gum. *C.roxburghii gum* produced tablets with stronger mechanical properties and longer disintegration and dissolution times than tablets with standard starch binder. This suggests that *c.roxburghii gum* could be useful as a binding agent, especially when higher mechanical strength and slower dissolution rates are desired.

*C.roxburghii gum* can be also be used in conventional tablets with an efficient disintegrant in an appropriate mode of addition. Use of the CSFR/DT ratio indicates that sodium starch glycolate has the best overall disintegrant property for the three modes of disintegrant addition employed. The external mode of disintegrant addition resulted in the balance between binding and disintegration properties of *c.roxburghii gum* in paracetamol tablets. From the *in vitro* study of paracetamol formulations with sodium starch glycolate, it can be concluded that external mode of disintegrant addition resulted in a faster release than other modes of addition. The present study reveals that filtered *c.roxburghii gum* has excellent mechanical, binding and release properties in paracetamol and diclofenac tablet formulations with the addition of sodium starch glycolate as an external disintegrant.

## References


Ashok Katdare, and Mahesh V Chaubal. Excipient development for pharmaceutical, biotechnology and drug delivery system. *Informa Healthcare*. **12:** 109-110 (2007).

Avachat A, Gujar KN, Kotwal VB, Patil S. Isolation and evaluation of fenugreek seed husk as granulating agent. *Indian J Pharm Sci.* **69:** 676-79 (2007).

Bhogi B Sheth et al., Compressed Tablets. Pharmaceutical Dosage Forms: Tablets. Lieberman H, and Lachman L. Marcel Dekker Inc. New York and Basel. **1:** Pp109-185 (1979).

Bradley Morris J. Legume genetic resources with novel "value added" industrial and pharmaceutical use: Perspectives on new crops and new uses. 196-201 (1999).

British Pharmacopoeia. London. Hal &Chapman . **2:** A157 (1993).

Ghule BN, Darwhekar GD, Jain DK, Yeole PG. Evaluation of binding property of eulophia campestris wall Mucilage. *Indian J Pharm Sci*. **68:** 566-69 (2006).

Keith Marshall, Compression and Consolidation of Powdered Solids. In: The Theory and Practice of Industrial Pharmacy. Lieberman, Lachman, and Kanig, eds., 3rd Edition, Marcel Dekker Inc. New York and Basel. **3:** Pp66-99 (1986).

Kohli DPS, and Shah DH. *Drug formulation manual*. Delhi, **3:** 78 (2005).

Kokate CK, Purohit AP, and Gokhale SB. Text book of pharmacognosy. Nirali Prakashan. Pune. **16:** (2008).

Kunle A, Dorothy O, Ajani A, Odeku OA, Itiola OA. Effect of pigeon pea and plantain starches on the compressional mechanichal and disintegraton properties of paracetamol tablets. *Drug Dev and Ind Pharm.* **32:** 357-65 (2006).

Loyd V Allen, Nicholas G Popovich, and Howard C Ansel. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Baltimore. Lippincott Williams & Wilkins. **8** Pp109-185 (2005).

Mathur NK, and Mathur GM. Fenugreek Galactomannan: An Emerging Industrial Polysaccharide. *Science Tech Entrepreneur* (2006).

Mehta RM. Text book of Pharmaceutics. Pp 226-53 (2008).

Odeku AO, and Itiola OA. Evaluation of effects of khaya gum on mechanical and release properties of paracetamol tablets. *drug deve and ind pharm*. **29:** 311-20 (2003).

Oknlola A, Babatunde AA, Oluwatoyin A. Evaluation of pharmaceutical and microbial qualities of some herbal medicinal products in south western Nigeria. *tjpr*. **6:** 661-70 (2007).

Parikh DM. Handbook of pharmaceutical granulation technology. Pp 512 (1997).

Patent Storm / US Patent 5847109 - Galactomannan products and compositions containing the same.

Patel DM, Prajapati DG, Patel NM. Seed mucilage from ocimum americanum Linn. As disintegrent in tablets : separation and evaluation. *Indian J Pharm Sci.* **69:** 431-35 (2007).

Pharmpedia/ formulation of tablets.