# Modified Xanthan Gum as Hydrophilic Disintegrating Excipient for Rapidly Disintegrating Tablets of Roxithromycin

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## ABSTRACT

A hydrophilic excipient that could modulate the disintegration time was developed as disintegration aid for the tablets of the model drug roxithromycin. Xanthan gum (XG) was modified by sequential processes to obtain treated xanthan gum (TXG) and co-grinded with mannitol to produce co-grounded treated xanthan gum (C-TXG) and was characterized by Scanning Electron Microscopy (SEM), Diffuse Reflectance Spectroscopy (DRS) and X-Ray Diffraction (XRD). SEM revealed structural changes attributable to processing steps without chemical modification that was established by DRS. The XRD analysis of C-TXG exhibited a crystallinity index of 87% and optimum micromeritic properties suggesting it to be amenable to direct compression. Consequently, directly compressible tablets of roxithromycin were formulated (F1–F6) using modified xanthan gum and other directly compressible hydrophilic excipients. The tablets formulated with lower level of C-TXG and higher level of microcrystalline cellulose (F4), exhibited least *in vitro* disintegration time without friability concerns. A nine fold reduction in the lag time of the optimized formulation when compared to the experimental conventional formulation was observed. The twelve months aged samples demonstrated no change in the *in vitro* drug release profile, disintegration time and were found to be stable.

**Keywords:** Roxithromycin, modified xanthan gum, micromeritic properties, crystallinity index, rapidly disintegrating tablets.

## INTRODUCTION

The demand for products that disintegrate in the mouth within seconds, quickly releasing the active ingredients for rapid relief is continually increasing. Important ingredients that are used in the formulation of Fast Disintegrating Drug Technologies (FDDTs) should allow quick release of the drug, resulting in faster dissolution. This includes both the actives and the excipients. Excipients balance the properties of the actives in FDDTs. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. These inactive food-grade ingredients, when incorporated in the formulation, impart the desired organoleptic properties and product efficacy. This organoleptic consideration is critical, especially for dosage forms designed to release the drug in the oral cavity (e.g., chewable tablets, fast disintegrating tablets, buccal tablets).[1]

Numerous scientific and patent reports on fast disintegrating excipients aim to produce a pleasant-tasting, fast-acting tablet that can be administered without the need for water that completely disintegrates within moments, with no bitterness or chalky aftertaste. GalenIQ™ 721 (Ph. Eur/BP/USP) is a high soluble agglomerated spherical isomalt for low and high dosage direct compression to produce very fast disintegrating

**DOI: 10.5530/ijper.47.4.11**

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tablets, orodispersible tablets due to excellent taste and is recommended to be used in a level of 25% w/w to enhance the tablet hardness in the formulation.[2] A commercialized excipient, Ludiflash fast-dissolving filler with a mildly sweet taste is a highly effective; disintegrant that disintegrates the tablet in the presence of very little liquid to produce a pleasantly smooth mouth feel and creamy texture.[3] Yet another patent reports a mixture of excipients that comprises at least one weakly compressible diluting agent other than trehalose and a copolymer of 1-vinylpyrrolidin-2-one and of vinyl acetate to be used as a fast disintegrating excipient.[4] Amino acids, such as L-lysine, L-alanine, L-tyrosine and glycine have also been reported as disintegration accelerators due to their excellent wetting nature, which leads to the faster disintegration of the tablet, which is suitable for fast disintegrating formulations.[5,6] Various modified poly saccharides-modified agar and guar gum,[7] modified starch (DDWMS)[8] and treated agar[9] have been evaluated and scientifically proven, as excipients that act as disintegrant and provide rapid disintegration of tablet in oral cavity. The search for simple, cost effective novel excipient(s) is a continual process.

In this context, the present study was aimed to modify, xanthan gum by simple technique, characterize, and assess its lag time reducing properties by formulating and evaluating rapidly disintegrating tablets of the model drug roxithromycin and to evaluate the effect of aging on hardness, disintegration time, drug content and *in vitro* drug release of the rapidly disintegrating tablets after storage of one year.

Roxithromycin, erythromycin 9-{O-[(2-methoxyethoxy)methyl]oxime} is a macrolide antibiotic used in the treatment of wide variety of infections like bronchitis, severe campylobacter enteritis, chancroid, diphtheria, legionnaires, pneumonia sinusitis and trench fever.[10] Following oral administration, roxithromycin is absorbed with a bioavailability of about 50% and the peak plasma concentrations are reached in about two hours, after a single dose. Absorption is reduced when taken after, but not before meals. A rapidly disintegrating tablet of roxithromycin may provide a dosage form that is easy to administer and provide rapid release of drug. Such formulation is expected to reduce $t_{max}$ and also may enhance bioavailability of the drug by pregastric absorption. Thus the project was aimed at producing and characterizing modified xanthan gum as fast disintegrating excipient followed by evaluating its efficacy by developing a rapidly disintegrating tablet of the model drug, roxithromycin.

## MATERIALS AND METHODS

### Materials

Roxithromycin was kindly supplied as a gift sample by Torrent Pharmaceuticals Ltd., Indrad, India. Spray dried lactose, xanthan gum and mannitol were purchased from S MERCK, India. Pepsin-1:3000 was procured from Titan Biotech Ltd., Rajasthan, India and potassium bromide IR grade was procured from Merck KGaA, Darmstadt, Germany. Erythriotol, PEG 6000 and MCC were purchased from S. D. Fine Chemicals Ltd. (Mumbai, India). All other chemicals used were of analytical grade.

### Preparation of modified xanthan gum

Modified polysaccharide was prepared by suspending 5 gm of selected pure polysaccharide - Xanthan gum (XG) in a beaker of 250 ml capacity, containing 100 ml of distilled water. The suspension was stirred at 500 rounds per minute using magnetic stirrer (Jindal Scientific Industries, Ambala, India), for 24 hours. Obtained swollen mass was then spread out on enameled tray (10 inches × 12 inches), and dried at room temperature for 72 hours. The dried product was scrapped out using a stainless steel spatula and subjected to crushing in a glass mortar with pestle, to obtain coarse, non-free flowing and heterogeneous particles of treated polysaccharide namely treated xanthan gum (TXG). Treated polysaccharide was then co-grounded with mannitol (1:1) in a glass pestle mortar for 20 min and passed through sieve (#22) to get the modified polysaccharide - co-grounded treated xanthan gum (C-TXG) and stored in a dessicator till further use. The swelling index and biodegradability of the modified xanthan gum were determined as reported.[11]

### Characterization of modified xanthan gum

#### *Measurement of particle size and its distribution*

Particle size distribution study for pure, treated and modified xanthan gum was carried out by the method of sieving using a nest of BSS sieves arranged in order of (# 22, 44, 60, 85, 100, 120, 200 and receiver) on a mechanical shaker (Jindal Scientific Industries, Ambala, India), for 30 min. The weight of powder retained on each sieve was used for calculation of various micromeritic parameters-mean diameter ($d_{mean}$), standard deviation[12] and IQCS (Intra quartile coefficient of skewness).[13]

#### *Evaluation for derived properties*

Derived properties were measured on pure, treated and modified xanthan gum using bulk density apparatus

(HICON®, Grover Enterprises, New Delhi, India) and the obtained values of loose bulk and tapped bulk densities were used to calculate percentage porosity. True density was determined by pycnometer (Jindal Scientific Industries, Ambala, India) using liquid (ether) displacement method. Percentage compressibility was determined using following equation

$$\% \text{ Compressibility} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100 \quad (1)$$

### Determination of flow properties

The angle of repose was determined by using a fixed base cone method, and the angle of spatula was determined by measuring the angle of powder on a spatula lifted from a powder bed and averaging that number with the angle of powder remaining on the spatula after it falls from a set of height.

### Powder x-ray diffractometry

Powder x-ray diffraction pattern of all the samples of xanthan gum (pure, treated and co-grinded), mannitol and microcrystalline cellulose were recorded on a Jeol JDX-8030 x-ray diffractometer using Ni-filtered, CuKα radiation, a voltage of 40 Kv, and a current of 25 mA (Jeol Ltd, Tokyo, Japan). The scanning rate employed was 1° $min^{-1}$ over 10° to 40° 2θ (diffraction angle) range. The crystallinity index was determined for all samples by Segal's formula:[14]

$$\% \text{ Crystallinity Index (CI)} = \frac{I_{020} - I_{am}}{I_{020}} \times 100 \quad (2)$$

Where, $I_{020}$ = Intensity at 20 and $I_{am}$ = Lowest 2θ value near 5°.

### Moisture content determination

A specimen sample weighing equivalent to 2 g (A), for each type of xanthan gum (pure, treated and modified) was kept at 105°C for 8 h, and then weighed again (B). The moisture content was calculated using the following formula:[15]

$$\text{Moisture Content} = \frac{A - B}{A} \times 100 \quad (3)$$

### Scanning electron microscopy

The shape and surface morphology of the powders i.e. pure, treated and modified xanthan gum (XG, TXG and C-TXG), was assessed by Scanning electron microscopy. Powder particles were coated with a thin gold layer by sputter coater unit (VG Microtech, West Sussex, UK) under an argon atmosphere in order to make them conductive. The surface morphology of the XG, TXG and C-TXG was analyzed by observing the captures at different magnifications (75 X, 100 X and 500 X) with FEIQuanta™ 200 scanning electron microscope (USA) operated at an acceleration voltage of 5.0 kV.

### Diffuse reflectance spectroscopy (DRS)

DRS study was carried out, using Fourier Transform Infrared Spectrophotometer (Shimadzu FTIR-8400 S) with DRS attachment (Shimadzu DRS-8000, Kyoto, Japan). The test sample was diluted with KBr IR grade to get a final dilution of 1:400 and mounted in to the instrument. The measurements were made in transmittance mode in the range of 500–4000 $cm^{-1}$ against background spectra of pure KBr IR grade.

### Determination of swelling index and biodegradability

The swelling index of the pure and modified xanthan was determined by the method reported by Sharma et al 2008. The values obtained were further subjected to statistical validation by applying Wilcoxon rank sum test.[16] The biodegradability of modified xanthan gum was observed in presence of pepsin (1:3000) at 2, 7, 24, 48, 72 and 96 hours.[17]

## Dosage form design

A formulation design was implemented in the present study for optimization of orodispersible tablets of the model drug roxithromycin is based on the concentration of modified xanthan gum (5% (w/w), 7.5% (w/w) and 10% (w/w)) and the concentration of microcrystalline cellulose (10% (w/w) and 15% (w/w)). Experimental trials were performed on all the six possible combinations (F1–F6) for modified xanthan gum (Table 1). The disintegration time and friability were measured as dependent responses.

**Table 1: Concentration of C-TXG and MCC used for development of Rapidly Disintegrating Tablets of Roxithromycin**

| S. No. | Formulation Code | Concentration of modified polysaccharide (%wt/wt) | Concentration of MCC (%wt/wt) |
|---|---|---|---|
| 1 | F1 | 5 | 10 |
| 2 | F2 | 7.5 | 10 |
| 3 | F3 | 10 | 10 |
| 4 | F4 | 5 | 15 |
| 5 | F5 | 7.5 | 15 |
| 6 | F6 | 10 | 15 |

### Blending, tabletting and evaluation of rapidly disintegrating tablets

Roxithromycin, modified xanthan gum, microcrystalline cellulose and other excipients (Table 2) were mixed in a polyethylene bag for 15 min and lubricated with finely screened (#120), PEG 6000. The powder was compressed into tablets on an electrically operated single punch machine with 8-mm punch diameter (HICON®, Grover Enterprises, New Delhi, India). Prepared rapidly disintegrating tablets (F1–F6) were evaluated for disintegration time and friability. The disintegration time (n = 12) of the rapidly disintegrating tablets were determined by employing a modified dissolution apparatus[18] and friability (n = 10) was determined using Roche type friabilator (Jindal Scientific Industries, Ambala, India).

### Selection of optimized formulation

Optimized formulation was selected on the basis of a disintegration time of less than 60 seconds and desirable friability and was subjected to wetting time and water absorption ratio determinations,[19] *in vitro* drug release and the effect of aging on orodispersion.

### *In vitro* drug release

*In vitro* drug release characteristics of optimized formulation was evaluated both in phosphate buffer pH 6.4 (salivary pH) and phosphate buffer pH 7.4 (physiological pH) separately. Dissolution studies were carried out in USP II paddle apparatus (HICON®, Grover Enterprises, New Delhi). Nine hundred mililiters of dissolution medium maintained at 37°C ± 0.5 was stirred at 100 rounds per minute and the samples withdrawn at 0, 2, 5, 7, 10, 15, 20, 25 and 30 min were replaced by fresh dissolution media. The data obtained was used to plot a graph between percentage cumulative drug release and time and compared with the drug release profile of experimental conventional tablet F7 (tablet formulated in laboratory without incorporating C-TXG).

### Effect of aging

Effect of aging was determined as per ICH $Q_1$ A stability testing guidelines for zone III. The optimized orodispersible tablets were stored at 40 ± 2°C/75 ± 5% RH[20] in aluminum capped clear glass vials for 12 months. The samples were withdrawn at the time interval of 0, 6 and 12 months and evaluated for *in vitro* disintegration time, friability and percentage drug content. The chemical stability was also evaluated by diffuse reflectance spectroscopy.

## RESULT AND DISCUSSION

### Preparation of modified xanthan gum

Hydrophilic polysaccharides interact with aqueous solutions by three-dimensional swelling, to an equilibrium value and physically entrap a significant portion of water within their structure.[21] Drying at this stage leads to evaporation of water leaving behind a porous structure. This structural modification does not allow the formation of gelatinous mass of the modified polysaccharides in water. However, the individual particles should facilitate water uptake due to the porous structure, undergo independent swelling thus facilitating the process of disintegration. Therefore, xanthan gum (XG) was subjected to sequentially controlled modifications of wetting and drying to obtain treated xanthan gum TXG that was sticky, non-free flowing aggregated lumps and presented handling problems. It is reported that grinding or milling not only reduces particle size but also causes changes in molecular behavior such

**Table 2: Formulation Design and Response Parameters of Orodispersible Tablets (F1–F6) and Experimental Conventional Formulation (F7) of Roxithromycin**

| Ingredients by weight (mg) / Response parameter | Formulation code | | | | | | |
|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 |
| Roxithromycin | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| C-TXG | 15 | 22.5 | 30 | 15 | 22.5 | 30 | – |
| Microcrystalline cellulose | 30 | 30 | 30 | 45 | 45 | 45 | 45 |
| PEG 6000 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Erythritol (%) | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Spray dried lactose q.s | 300 | 300 | 300 | 300 | 300 | 300 | 300 |
| *Disintegration time (seconds)* | *19 ± 1.8* | *24 ± 1.2* | *29 ± 2.4* | *14 ± 1.6* | *18 ± 1.4* | *23 ± 2.0* | *275 ± 3.5* |
| *Friability* | *Pass* | *Pass* | *Pass* | *Pass* | *Pass* | *Pass* | *Pass* |

as crystallinity and chemical reaction rate in the solid phase.[11] Keeping in view these facts mannitol, a directly compressible water soluble sugar alcohol was selected as a grinding assistant as it imparts a cooling sensation in mouth due to its negative heat of solution, is an orodispersion aid and improves flow property of other materials. TXG was co grinded with mannitol in 1:1 ratio to obtain free flowing, non-sticky powders of modified xanthan gum, C-TXG.

## Evaluation and characterization of modified polysaccharide

### *Measurement of particle size and its distribution*

The micromeritic data documented in Table 3 clearly indicates an increase in the $d_{mean}$ of pure xathan gum (239.26 µm) on treatment with water (255.73 µm) whereas co grinding with mannitol led to a decrease (39.37 µm) in particle size. Particle size distribution data summarized using statistical methods indicated a high degree of skewness on treatment with water, which approached zero on co grinding suggesting normalization of the particle population.[12]

### *Flow properties*

Flow properties of pharmaceutical excipients are of major concern with respect to the handling and compaction of powder materials,[22] especially for directly compressible excipients. The angle of spatula gives a relative angle of internal friction of the material and a large value indicates poor flowability. Co-grinding of the treated gum (TXG) with mannitol helped in improving the degree of flowability from passable to fair for C-TXG. Yet another flow parameter, the angle of repose, gives a qualitative assessment of internal and cohesive frictions. The angle of repose upon co-grinding was reduced from 39.10 to 36.25 indicating reduction in cohesive friction and improvement in flow properties, however; the transition was from upper limit to the lower limit of 'Fair' degree of flowability.[23,24] Angle of repose measurement is sensitive to moisture content. Moisture content of the samples was determined, and the moisture content of all the samples was found below 5.5% (Table 3) and no value exceeded 7% (w/w), as per the limits.[25] Moisture content affects the cohesiveness and hence the flow properties. Thus the treated xanthan gum with higher moisture content exhibited poor flow properties when compared to modified polysaccharide. The low values of moisture content are the indicative of higher crystallinity.[26]

Carr suggested that the compressibility of a powder material as an indicator of the tendency of the powder to flow. Accordingly, materials with Carr Index greater than 20 to 25% are classified as poor flowing powders.[27] Carr's compressibility index calculated from bulk density and tapped density was determined as 17.5% and a Hausner's ratio of 1.24 for C-TXG suggested fairly good flow properties that may be further improved by addition of flow activators. Compressibility value of 20% and above indicates that a powder is not free flowing and that it has tendency to create bridges in the hopper. Thus with a compressibility index of 17.5% for C-TXG bridge breaking measures are unnecessary.

The bulk density of XG was found to be 0.57 g/cc and that of C-TXG was found to be 0.33 g/cc. A 20–25% reduction in bulk density values of modified xanthan gum indicated a higher bulk volume and thereby higher porosity when compared to pure xanthan gum, which is desirable to support rapid disintegration.

### *Powder x-ray diffractometry*

To evaluate the effect of crystal structure of modified xanthan gum and microcrystalline cellulose on the tablet properties, the crystal state was analyzed. Figure 1 shows the X-ray diffraction pattern of a XG, TXG, C-TXG against two reference materials, namely mannitol and MCC. The intensity of diffraction peaks observed at $2\theta$ = 16.42, 19.64 and 20.10 for XG was reduced in TXG diffractogram. On co grinding with mannitol the crystalline material, C-TXG showed the diffractographic profile of crystalline material when compared to XG. The signals were intensified and the diffractogram exhibited peaks that could be associated both with TXG and mannitol. The change in the state was quantified by determination of crystallinity index.

**Table 3: Micromeritic Parameters and Moisture Content Determination**

| Type of Xanthan Gum | Micromeritic Parameters | | | | | | | | | Moisture Content (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | dmean (µm) ± S.D. | I Q C S | Bulk Density (g/c.c) | Tapped Density (g/c.c) | True Density (g/c.c) | Porosity (%) | Angle of repose (°) | Angle of Spatula (°) | % Compressibility | |
| XG | 239.26 ± 2.22 | 0.45 | 0.57 | 0.66 | 1.26 | 12.72 | 32.20 | 37.62 ± 1.2 | 13.60 ± 1 | 2.07 ± 0.23 |
| TXG | 255.73 ± 1.41 | 0.52 | 0.37 | 0.46 | 0.58 | 42.77 | 39.10 | 43.92 ± 1.9 | 19.56 ± 2 | 5.19 ± 0.68 |
| C-TXG | 39.37 ± 1.80 | 0.00 | 0.33 | 0.40 | 0.97 | 24.24 | 36.25 | 39.23 ± 0.8 | 17.50 ± 1 | 3.11 ± 0.62 |

The CI calculated by Segal's formula was found to be 86.02% for XG, which got reduced to 51.18% for TXG and further increased to 87.65% upon co grinding with mannitol. The increase in crystallinity could be attributed to the contribution made by mannitol that demonstrated a CI of 76.48%. The reference material MCC showed a CI of 87.01% comparable to CI of C-TXG hence it is presumed that the properties of compactability and compressibility associated with MCC shall be conferred upon C-TXG. However, it has been demonstrated that the mechanical strength of compacts is not always related to the crystallinity of starting materials used in the formulation.[28] The effect of morphology of particles is proposed to have a significant effect on the disintegration of the compacts.

### *Surface morphology*

Figure 2 shows scanning electron micrographs of xanthan gum (A) and treated xanthan gum (TXG) prepared by above mentioned method (B and C) and co-grounded xanthan gum (D). From the micrographs it has been observed that xanthan gum exhibited almost regular flattened particles when captured at the magnification of 75 X (Fig. 2A), but in case of TXG (Fig. 2B) the gum exhibited as large swollen particles without distortion in their shape. However at higher magnification TXG particles exhibited surface roughness, striations across the length of the particle and fine irregular pores (Fig. 2C) that are assumed to play significant role in controlling the disintegration properties.[29] A network of irregular bulk with rough surface suggests efficient swelling during initial treatment of xanthan gum. Co-grinding of TXG with mannitol, rendered the structural changes that were visualized in the microstructure of C -TXG (Fig. 2D). The particulate appearance was transformed into a network of regular amorphous structure with deep pores that can facilitate high water uptake[7] in the presence of hydrophilic fine crystals of mannitol.

### *Determination of swelling index and biodegradability*

The SI of XG (166.66%) significantly reduced after the modification, to a value of 40% for C-TXG. The reduction in SI may be attributed to higher water loading capacity of highly porous C-TXG when compared to its purer version. The water loading capacity for C-TXG (60.93%) was excellent and found to be effective disintegrant. In order to act as an efficient fast disintegrant, the modified polysaccharides the magnitude of swelling should be less than its water absorption capacity so as to avoid the formation of gelatinous mass that may retard orodispersion**.** The SI of C-TXG reduced to 75.99%, comparison to the pure xanthan gum, which assures the use of modified xanthan gum

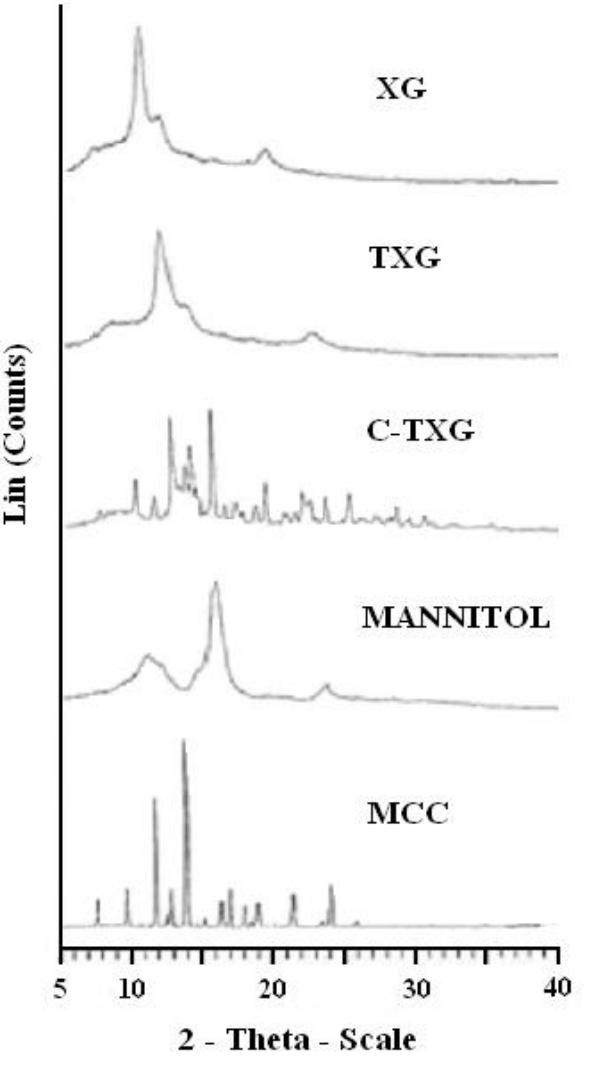


**Figure 1:** XRD diffractograms of pure (XG), treated (TXG), co-grounded xanthan gum (C-TXG), mannitol and microcrystalline cellulose (MCC).

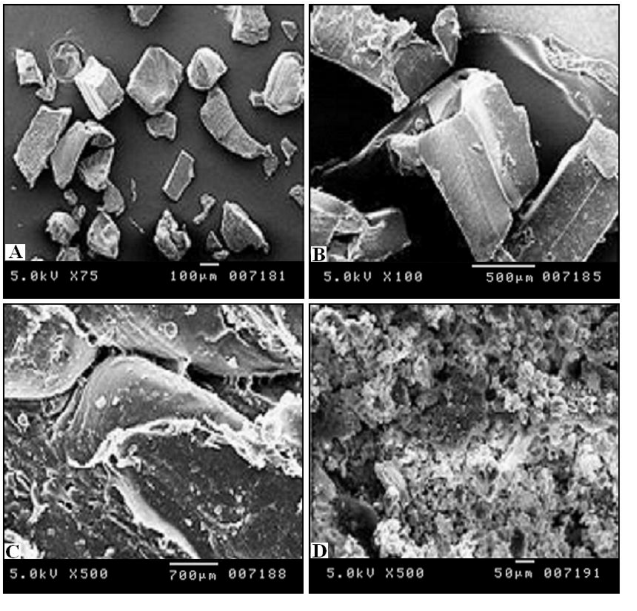


**Figure 2:** Scanning electron micrographs of (A) Xanthan gum, (B, C) Treated xanthan gum and (D) co-grinded xanthan gum.

as rapidly disintegrating excipients. The calculated Z value for XG versus C-TXG was 4.64 that is more than the tabulated Z value of 1.96 at 95% confidence level hence XG and C-TXG are assured to be statistically different in terms of their swelling capability.

Biodegradability is a primary concern when a GRAS listed excipient is subjected to modifications. Biodegradability studies on C-TXG in the presence of pepsin (1:3000), one of the enzymes present in gastric fluid exhibited gradual biodegradability within 96 hours. The modified xanthan gum lost its definite physical appearance, became bulkier within 2 hours, followed by formation of a suspension of fine particles that were digested at the end.

### *Diffuse reflectance spectroscopy*

Diffuse reflectance spectroscopy was carried out to determine the chemical changes if any, following the modifications of XG. The DRS spectra of mannitol exhibited peaks between 3000–2900 $cm^{-1}$ (C-H stretching), 3700–3600 $cm^{-1}$ (O-H stretching) and 1000−1050 $cm^{-1}$ (primary and secondary alcohols). The spectra of xanthan gum showed peaks at 1080−1150 $cm^{-1}$ (C-O-C stretching), at 2830−2700 $cm^{-1}$ (C-H stretching) and 1700–1750 $cm^{-1}$ (C=O).[30] The spectra of modified polysaccharides exhibited peaks at positions similar to that observed in the spectra of pure polysaccharides (Fig. 3) and hence, it can be concluded that the modification of the xanthan gum led to physical changes, with no evident chemical changes.

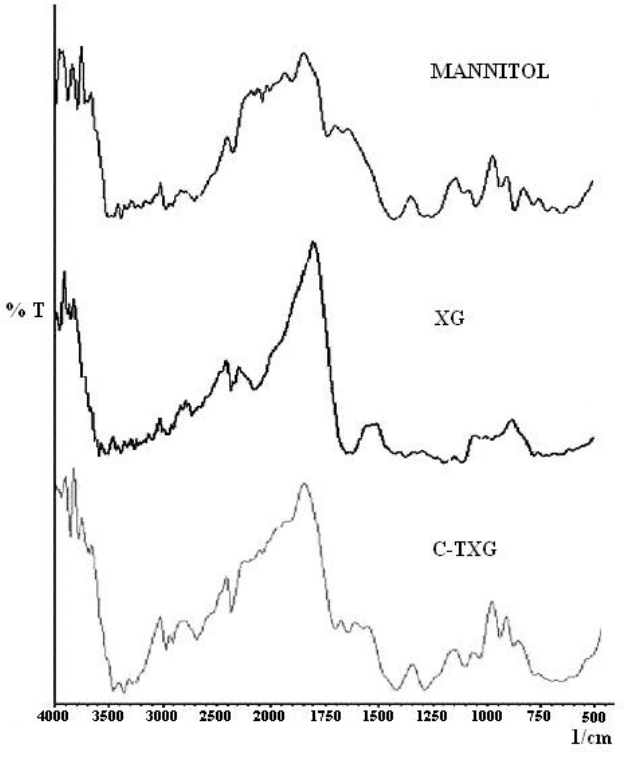


**Figure 3:** Diffuse reflectance spectrographs of xanthan gum (XG), co-grinded xanthan gum (C-TXG) and mannitol.

## Formulation considerations

The simplest technique for manufacture of tablets intended for rapid disintegration is direct compression that necessitates careful selection of excipients. The selected binding agent must be added with care, since if used in excessive amount such agents can markedly decrease the rate of disintegration. So, it was necessary to find a suitable binder with excellent compactability that could produce a suitable rapid disintegration in saliva. Microcrystalline cellulose was used as a binder that has good compressibility and compactability, according to its plastic deformation, strong hydrogen bond among hydroxyl groups, and concave-convex shape. It can also be used as disintegrants, with disintegrating properties in water attributed to either capillary action or swelling[31] thus tablets containing microcrystalline cellulose are characterized with desirable compactability and short disintegrating time. PEG 6000 was used as a lubricant which is hydrophilic in nature and aids rapid disintegration. Erythritol that exhibits good compactability was selected to enhance palatability of the tablets.

## Selection of optimized orodispersible formulation

From the results (Table 2) obtained it was observed that, all the prepared formulations exhibited a disintegration time of less than 60 sec, and all of the formulations passed the friability test. But amongst the formulations (F1–F6) prepared using C-TXG, formulation F4 exhibited least disintegration time of 14 ± 1.6 seconds and passed the friability test, hence F4 was considered as optimized formulation. Thus formulation F4 (containing lower level of modified xanthan gum and higher level of MCC) that provided optimum friability and faster disintegration was identified as optimized formulation and subjected to further evaluations. While, formulations F1, F2, F3, F5 and F6 were rejected as these formulations disintegrated beyond 15 seconds.

## Evaluation of optimized formulation

### *Determination of wetting time and water absorption ratio*

The wetting time of 6.52 ± 0.42 sec for F4 was significantly lower due to the highly porous structure of modified xanthan gum and the presence of higher levels of MCC in the formulations.[18] Water absorption ratio of the formulation F4 was found to be 1.49 ± 0.04 indicating that the formulation could uptake water

approximately up to 1.5 times of its own weight. This could be again attributed to numerous air filled pores present in modified xanthan gum that got displaced by water.

### *In vitro* drug release

*In vitro* drug release (n = 6) studies of the optimized formulation was carried out at pH 6.4 and 7.4. The pH 6.4 was selected to assess any pregastric absorption that may take place when some of the particles from rapidly disintegrating formulation get lodged into the denture and gradually may get absorbed through buccal mucosa.[32] This in turn is suggested to increase the bioavailability of roxithromycin, as the hepatic metabolism of the drug absorbed through buccal cavity, is avoided. It was evident from Fig. 4, that in phosphate buffer pH 6.4, the percentage drug release from formulation F4 was found to be 92.88% ± 2.4 at 30 min, supporting the chances of absorption of the drug through buccal cavity. At pH 7.4 the percentage drug release from formulation F4 was found to be 91.28% ± 2.8, within 30 min which was many folds higher than the drug release of 27.82% ± 1.98 from experimental conventional tablets of roxithromycin, at the same time point. Faster dissolution for rapidly disintegrating formulation was due to larger surface area available for dissolution due to rapid disintegration of the formulation when compared to the experimental conventional tablet, that required more time to disintegrate and hence to dissolute.

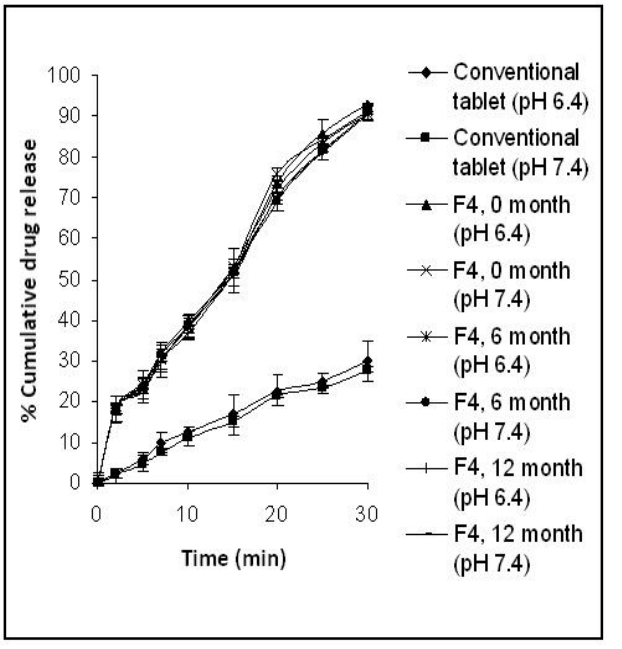


**Figure 4:** Drug release profile of fresh and aged optimized formulation (F4) and experimental conventional formulation in pH 6.4 and 7.4.

### Effect of aging

The stability studies revealed that all the formulations were chemically stable when stored at 40°C ± 2 and 75%RH ± 5 till the end of 12 months. Significant peaks of RXT at 1685 $cm^{-1}$ (ketone carbonyl), 1730 $cm^{-1}$ (lactone carbonyl), 1000 $cm^{-1}$ and 1200 $cm^{-1}$ (ethers and amine functions), 1340–1460 $cm^{-1}$ ($-CH_2$ bending) and 3400–3700 $cm^{-1}$ (hydrogen bonded −OH and water[33–34] in the DRS spectra at 0 months were retained in the samples withdrawn at sixth month and twelfth month (Fig. 5) and neither a shift, nor any new peak was observed indicating absence of any degradation product in the storage conditions tested. The tablets appeared to be physically stable and there was insignificant reduction in disintegration time, drug content and percentage drug release for both the optimized formulations (Table 4).

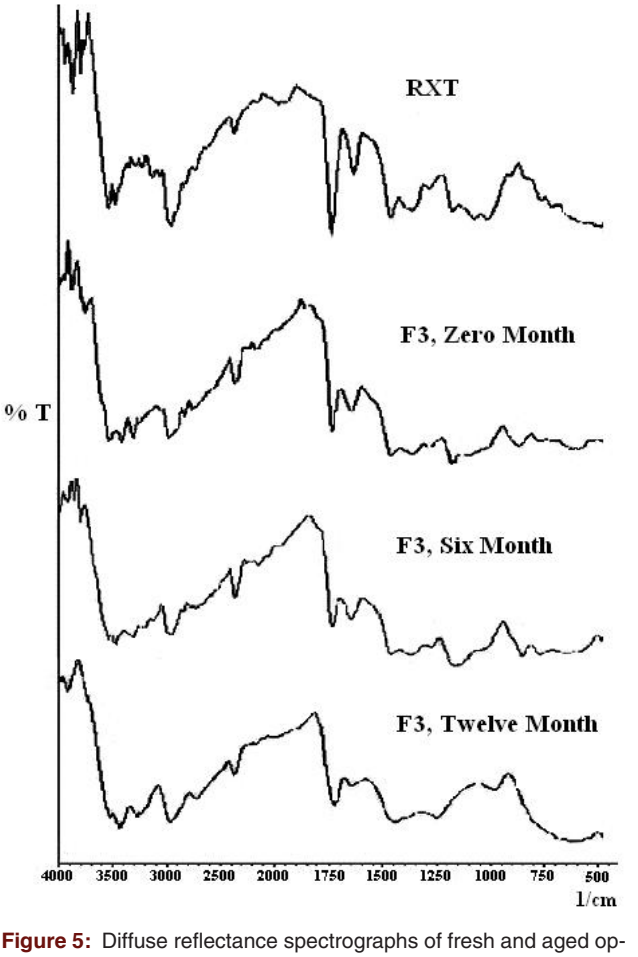


**Figure 5:** Diffuse reflectance spectrographs of fresh and aged optimized formulation (F4) against the reference spectra of roxithromycin (RXT).

## CONCLUSION

Modified xanthan gum obtained was biodegradable, directly compressible and exhibited desirable swelling dynamics to be used as a hydrophilic excipient for rapidly disintegrating tablets. The rapidly disintegrating

**Table 4. Performance Parameters for Fresh and Aged Samples of F4**

| Parameters Evaluated | Time Interval (months) | | |
|---|---|---|---|
| | 0 | 6 | 12 |
| *In vitro* disintegration time (seconds) | 25.1 ± 1.6 | 24.2 ± 1.9 | 24.1 ± 1.6 |
| Friability | Pass | Pass | Pass |
| Drug content (%) | 99.72 ± 1.3 | 99.44 ± 1.6 | 99.32 ± 0.9 |
| Percent drug release (30 min) | | | |
| *pH 6.4* | 92.88 ± 2.4 | 90.67 ± 2.7 | 90.40 ± 2.1 |
| *pH 7.4* | 91.28 ± 2.2 | 90.92 ± 1.4 | 90.91 ± 2.5 |

All values are the mean of six determinations.

tablets of roxithromycin formulated with lower level of modified xanthan gum and higher level of MCC was selected as the optimized formulation that displayed nine fold reductions in lag time, was stable for a period of 12 months and retained the rapid disintegration characteristics till the end of tested time period.

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