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Formulation And Evaluation Of Fast Disintegrating Tablet Of Anti Inflammatory Drug Using Natural Superdisintegrant

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Abstract:
In the development of fast disintegrating tablets, seed gum and its carboxymethyl derivatives extracted from Tamarindus indica seeds were used as pharmaceutical disintegrants. The chemical structure of the seed gum was modified through carboxymethylation.The process involved the chemical modification of the extracted gum from tamarind seeds through carboxymethylation. This modification aimed to enhance the hydrophilic nature of the gum. Additionally, calcium complexation of the carboxymethylated tamarind seed gum was carried out. Fast disintegrating tablets were then prepared using the direct compression method. The disintegration time of these tablets, containing the calcium-complexed tamarind seed gum, was compared to tablets formulated with a commercially available superdisintegrant, crospovidone. The disintegration time of the tablets with the calcium-complexed tamarind seed gum was reported to be 1 minute, approximately 32.5 seconds, and 35.2 seconds, respectively, indicating good disintegrating properties.In conclusion, the use of modified tamarind seed gum as a natural superdisintegrant in fast-dissolving tablets was found to accelerate tablet dissolution, providing a promising alternative for formulating tablets with improved disintegration properties.

Keywords: Fast disintegrating tablet, Tamarind seed gum, Disintegration time, Natural Superdisintegrant, crospovidone, Nimisulide
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Introduction

Fast Dissolving Tablets (FDTs) offer several advantages in drug delivery. They disintegrate and/or dissolve rapidly in saliva without the need for water, making them convenient for patients who have difficulty swallowing conventional tablets. FDTs can dissolve in saliva within a few seconds, providing a true fast-dissolving experience. In addition to rapid disintegration, FDTs can also incorporate taste-masking techniques, as simply adding sweeteners and flavours may not be sufficient for bitter drugs. Taste-masking methods used in FDT technologies include adsorption onto or complexation with carriers and spray coating of solid dosage forms. These techniques not only mask the taste but also increase consumer acceptance of the FDTs.[1]one of the advantages of FDTs is their potential for pregastric absorption, which occurs when the tablet disintegrates in the mouth. The drug can be absorbed through the oral cavity, pharynx, and oesophagus, bypassing the first-pass metabolism in the liver. This can lead to increased bioavailability and enhanced clinical effects of the drug. Fast dissolving drug delivery can be achieved through various techniques, including direct compression, wet granulation, compression moulding, volatization, and freeze-drying. These techniques involve the use of high amounts of hydrophilic disintegrating agents, which facilitate quick disintegration of the dosage form upon contact with saliva in the patient's mouth. Overall, FDTs offer a patient-friendly and effective drug delivery option, improving compliance and bioavailability while providing a convenient alternative for patients who struggle with swallowing conventional tablets.FDTs are especially advantageous in situations where swallowing conventional tablets may be difficult or inconvenient. For example, in cases of motion sickness, sudden allergic

attacks, or when a patient experiences coughing, it may be challenging to swallow traditional tablets. This difficulty is often more pronounced in paediatric and geriatric patients, who may have limited swallowing ability or aversions to swallowing large tablets.

Method And Material

Tamarind seed obtained from fruit of tamarind tree from local market.
Ethanol, Monochloroacetic acid, Glacial acetic acid, Sodium hydroxide obtained from
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preparation of superdisintegrant from tamarind seed gum

The tamarind seeds were used to extract the gum. Overnight, tamarind seeds were steeped in distilled water. The outer coat of the seeds was removed by crushing them in the grinder. Powder was created by separating and crushing the white component of the seeds. [2]Fig. 1 depicts a picture of tamarind seed powder. The crushed material is kept for decoction for 7-8 hours in 1000 ml of distilled water. Following complete boiling, the raw material was filtered through a muslin cloth toobtain the gum. The gum was concentrated to nearly half its volume after the marc was extracted. Fig. 3 displays the extracted tamarind seed gum. (8,10) As the concentrated gum cooled, ethanol was added until precipitates formed. Using the, the precipitates were separated.

Figure 1 Preparation of tamarind seed powder

Figure 2. method of extraction

(shows extraction of gum by Decoction. Filtrate after Filtration by muslin cloth, Obtained precipitate after ethanol Added,kept in sunlight for drying.)

Figure 3.Extracted tamarind seed gum powder.

Carboxymethylation-based modification of extracted gum

An ice-cold solution of sodium hydroxide (42%, W/W) was added to create an aqueous dispersion of tamarind seed gum (1.35% W/V). Stir continuously for 30 to 35 minutes. 22 ml of an aqueous monochloroacetic acid solution (42%, W/V) was then added. The mixture was then put in a thermostatic water bath (70°C) and stirred occasionally for 60 minutes. The resulting mass was filtered when the reaction was finished. made the mixture cool. Fig. 4 depicts the picture of carboxymethylated tamarind seed gum.(8,10)

The product was then diluted in water, balanced with glacial acetic acid, precipitated in ethanol (AR grade 90%), and washed three times with an aqueous methanol solution (80%V/V) to produce precipitates. [2]

figure 4 Calcium complexation of the carboxymethyled tamarind seed gum (CMTG)

3.5 g of CMTG were dissolved in 50 ml of distilled water. Drop by drop, water-based calcium chloride solution (5%, w/v, 50 ml) was added to the carboxymethylated gum solution with steady stirring to produce thick, homogeneous, and gelatinous precipitates as seen in Figs. 4 and 5.

Figure 5:- Calcium complexation in tamarind seeds that have been carboxymethylated

To get rid of unreacted calcium and gum, these precipitates were repeatedly washed with distilled water. These washed precipitates went through a # 80 filter after being freeze-dried.

Characterization of the superdisintegrant:

pH of the gum solution: The pH of the gum solution was determined for 1% w/v solution of the gum in distilled water. Melting Point: Melting point of pure Tamarind seed gum was determined by capillary tube method and the melting point found to be 2400C-2600C.

Swelling Index: Swelling index is describes as the amount of water absorbed by the gum when placed in water for a fixed time. It gives the % of weight achieve by the gum after absorbing water 16.

$$\text{Swelling index} = = \frac{\text{final weight of gum} - \text{initial weight of gum}}{\text{initial weight of gum}} \times 100$$

FT-IR Studies: FT-IR studies were carried out for simple gum, modified gum and the calcium complexed gum to ascertain the change in functional groups in structure of gum by Perkin Elmer FTIR.

Pre-compression studies.

These studies are conducted before compressing the compact mass of a tablet to assess the properties of the powder blend. The five steps involved in these studies are bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio.

Bulk Density:

Bulk density refers to the mass of the powder blend divided by its bulk volume. To measure bulk density, the powder blend is poured into a measuring cylinder, and the initial weight is recorded. The volume occupied by the powder blend is determined using the following formula:
Bulk density = (Mass of powder) / (Bulk volume of powder)

Tapped Density:

Tapped density is the ratio of the total mass of the powder blend to its tapped volume. Initially, the powder blend is poured into a measuring cylinder. The cylinder is then tapped gently about 500 times on a hard surface, and the tapped volume of the powder is noted. If the difference between two volumes is more than 2%, tapping is repeated 1000 times, and the tapped volume is recorded. Tapping is continued in a bulk density apparatus until the difference between subsequent volumes is less than 2%. Tapped density is expressed in g/ml and calculated as follows:

Tapped density = (Mass of powder) / (Tapped volume of powder)

Angle of Repose (θ):
The angle of repose is determined using the funnel method. The powder blend is poured through a funnel, which can be raised vertically until a specified cone height (h) is obtained. The radius of the heap (r) is measured, and the angle of repose (θ) is calculated using the formula:
θ = tan^(-1) (h/r)

Carr's Index:
Carr's index is used to determine the compressibility and flow of the powder. It is calculated using the tapped density (Dt) and bulk density (Db) of the powder:
Carr's index = (Dt - Db) / Dt × 100

Hausner Ratio:
The Hausner ratio (HR) is an indirect measure of the ease of powder flow. It is calculated by dividing the tapped density by the bulk density:

Hausner Ratio = Tapped density / Bulk density

These pre-compression studies help in understanding the flow and compressibility characteristics of the powder blend, which are crucial for the formulation and manufacturing of tablets.Pre-Compression parameters of the blend of the powders used for the formulation of the tablet by calcium salt of modified tamarind gum was noted in Table 1.

Table 1:-Precompression parameter

parameter	Formulation									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Bulk density(gm/cc)	0.49	0.42	0.48	0.47	0.49	0.39	0.37	0.49	0.43	0.42
Tapped density(gm/cc)	0.51	0.57	0.58	0.57	0.61	0.58	0.55	0.62	0.59	0.51
Angle of repose(°)	25.21	28.39	24.01	25.33	27.10	25.10	24.01	25.21	29.22	30.94
Cars index (%)	22.00	22.8	22.5	15.67	25.69	22.6	27.7	29.9	21.7	27.6
Hausners ratio	0.97	1.35	1.29	1.36	1.29	1.28	1.30	1.35	1.39	1.27

Method of preparation of tablet;-Fast dissolving tablet formulation using crospovidone as a synthetic superdisintegrant and calcium complexed tamarind seed gum as a natural superdisintegrant. The direct compression method (1) was used to create the Nimisulide and calcium complexed tamarind gum fast-disintegrating tablets. After being put through sieve no. 80, the entire amount of ingredients was combined for 10 minutes. The tablet punching machine compressed the powder to create tablets. There were eight different formulations of the tablets. Tamarind gum with a calcium combination is included in F1–F5, and crospovidone served as the disintegrating agent in F6–F10. Table 5 displays the FDTs' formulas.[3]Using NaOH and monochloroacetic acid, tamarind seed gum is carboxymethylated to add a methyl group to the carbohydrate group (COO-). As a result, the gum obtains complete hydrophilic properties.

Table 2:-Formulation of fast disintegrating tablet containing calcium complexed tamarind seed gum as natural superdisintegrant and crospovidone as synthetic superdisintegrant

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Nimisulide	45	45	45	45	45	45	45	45	45	45
Calciumcomplexed tamarind gum	2.5	5	7.5	10	12.5	-	-	-	-	-
crospovidone	-	-	-	-	-	2.5	5	7.5	10	12.5
talc	5	5	5	5	5	5	5	5	5	5
Microcrystalline cellulose	100	100	100	100	100	100	100	100	100	100
Magnesium stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Sodium saccharin	42.5	39	36.5	34	31.5	42.5	39	36.5	34	31.5
Vanilla flavour	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Total 200mg

Figure 6 :Tablet prepared by using tamarind seed disintegrant

The hardness of all the batches range from 4.3 to 5.5 kg. Friability varies from 0.68% to 1.1%. Drug content uniformity was 97% to 99.95%. Weight variation is also within limit.

The Disintegration apparatus was used to determine the Disintegration time of nimisulide tablet containing Calcium complexed Tamarind seed gum and crospovidone . The results of disintegration time for different formulation were reported in table 3.

Table 3:-Disintegration time for different formulation

Formulation	**Disintegration time(sec)**
F1	44± 6s
F2	41±7s
F3	48± 3s
F4	35± 2s
F5	37±5s
F6	44 ±3s
F7	39±2s
F8	48± 3s
F9	46±2s
F10	35± 2s

The results the Disintegration test showed that the formulation F4 containing Calcium complexed Tamarind seed gum disintegrate in shortest period as comparison to other preparations

Evaluation of Tablet

The prepared tablet is evaluations like weight variation, friability, content uniformity, hardness and disintegration studies.

Result and discussion

The pH of modified gum was found to be 5.4.
The swelling index of the gum was found to be 298%
IR spectra for pure gum showed peaks at 3425 cm-1 , 2931.8 cm-1 confirmed the presence of hydroxyl group and carboxyl group in the gum. FT-IR spectra of Pure Tamarind seed gum shown in fig 1

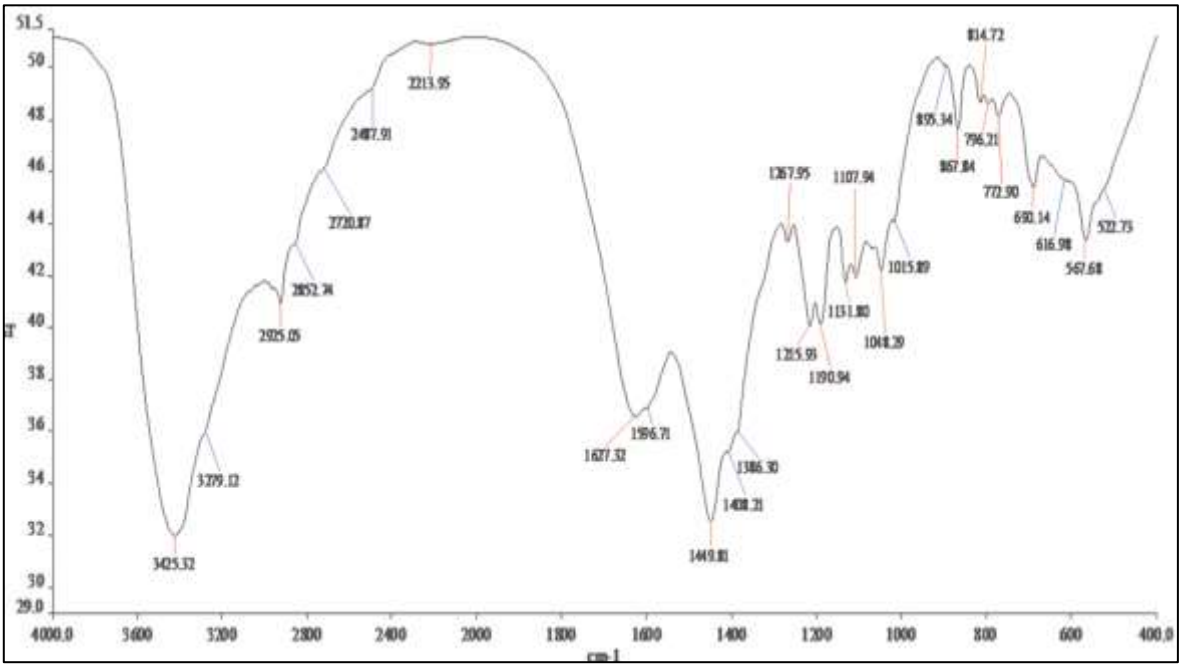

Figure 7 FTIR of tamarind seed gum

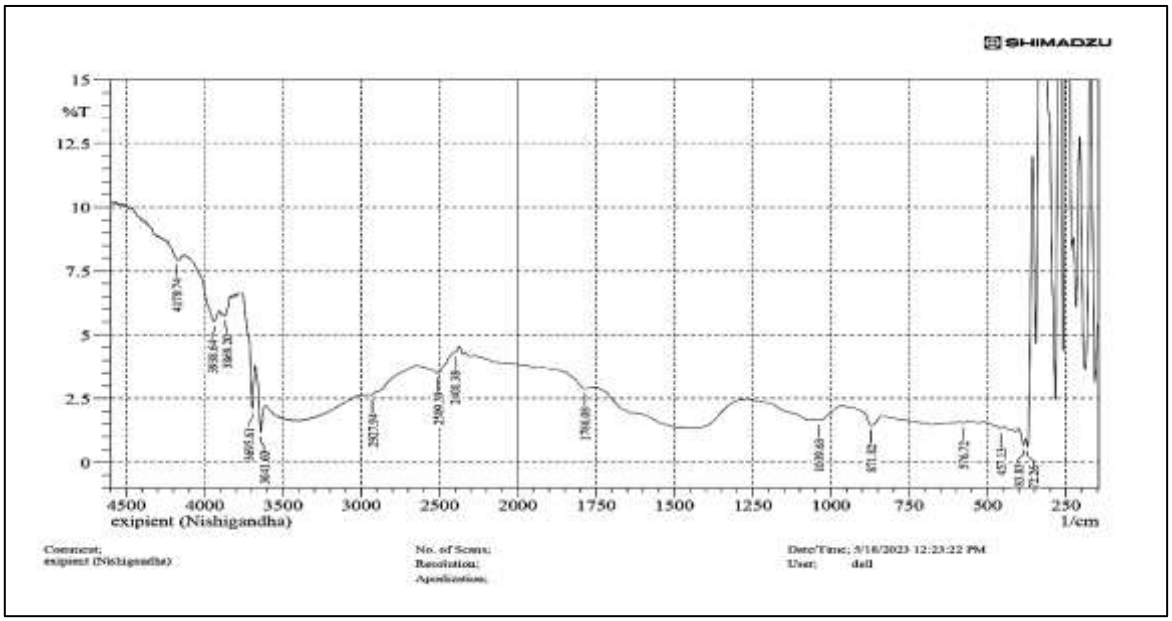

Figure 8:- FTIR of carboxymethylated tamarind seed gum

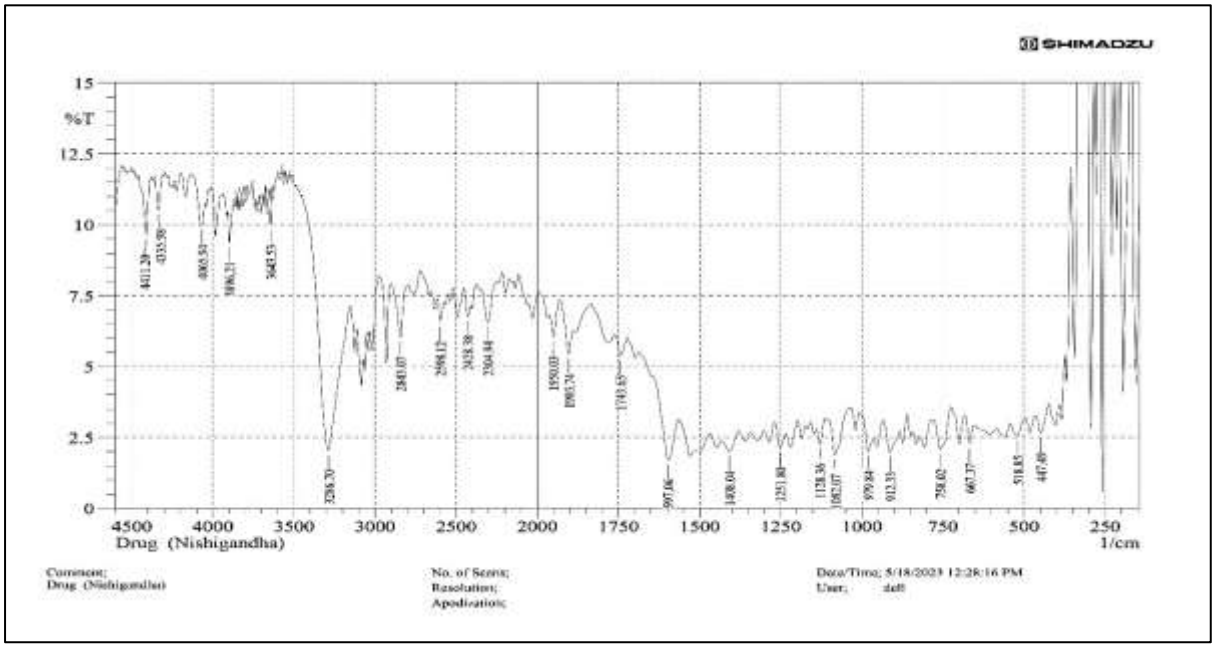

Figure 9:-FTIR of Nimesulide drug

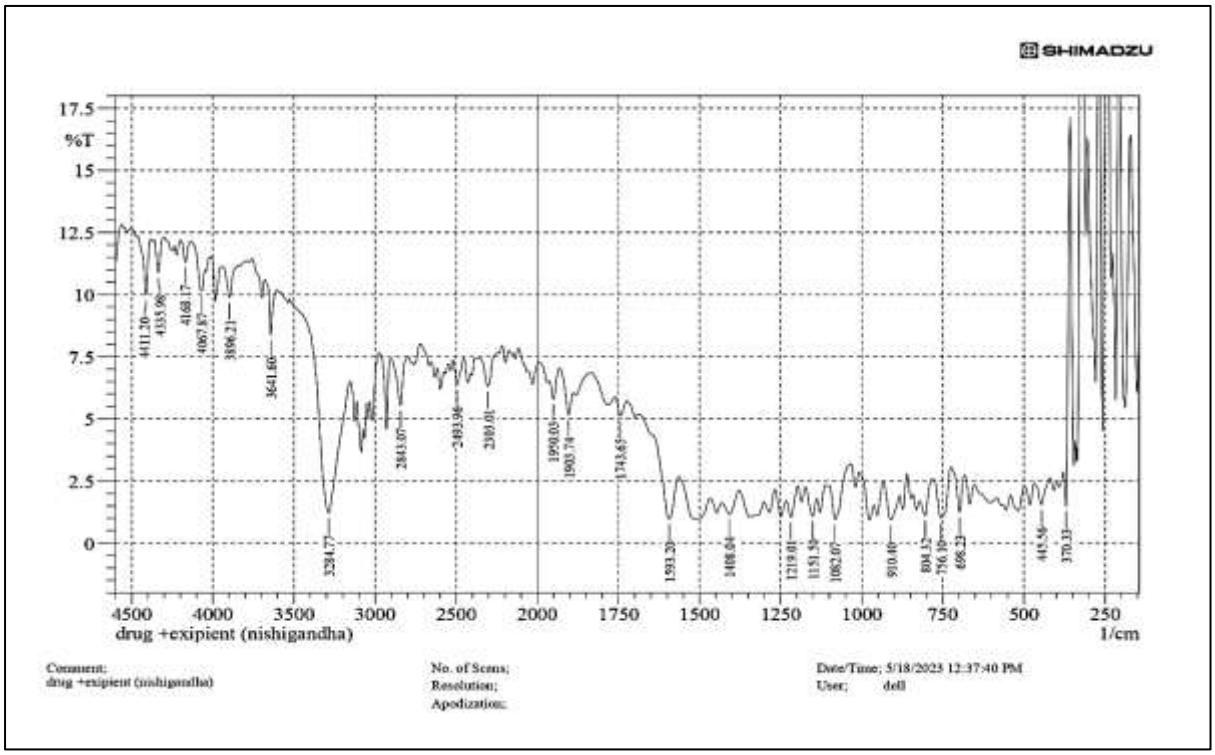

Figure 10:-FTIR of modified tamarind seed gumtamarind seed gum and nimisulide

Pre-formulation studies of gum

The fast disintegrating tablet was successfully formulated and itshowed satisfactory results. The swelling index of the gum was found to be 298% The pH of 1% w/v aqueous solution of pure extracted tamarind seed gum and calcium complexed tamarind seed gum was found to be 5.4 and 6.8. The viscosity of 1% (w/v) calcium complexed solution was found to be 9.41pa.

FTIR studies of drug and natural superdisintegrant

The provided information describes the characterization of tamarind seed gum using Fourier Transform Infrared

(FT-IR) spectroscopy. Here are the key findings:

Composition: Tamarind seed gum primarily consists of carbohydrates, which include galactose, glucose, xylopyranose, xylose, galactopyranosyl, glucuronic acid, and galacturonic acid. These components contribute to the polysaccharide structure of the gum.

Aromatic Sugar Groups: The FT-IR spectrum of tamarind seed gum revealed a medium peak at 1107.94 cm-1, indicating the presence of aromatic sugar groups. This peak suggests the existence of O-H functional groups as the main functional group in the gum. The presence of O-H groups indicates the hydrophilic nature of the polysaccharide.

C-H Stretch and Bend: A small peak at 1107.94 cm-1 was also observed, representing the C-H stretch present in galactose and rhamnose. Additionally, a broad peak at 3431.44 cm-1 indicated the presence of O-H stretches, suggesting the existence of intermolecular bonding. Another small peak at 3279.12 cm-1 indicated the C-H bend, which is a constituent of galactose and rhamnose.

C=O Stretching: A small peak at 1627.32 cm-1 indicated the C=O stretching, likely present in certain functional groups or components of tamarind seed gum.

Fig. 6, which is not provided, would presumably depict the FT-IR spectra of the pure tamarind seed gum, showing the characteristic peaks associated with its composition.Overall, the FT-IR analysis provides valuable information about the chemical constituents and functional groups present in tamarind seed gum. This characterization is important for understanding the structure and properties of the gum, which can aid in its application in various formulations and pharmaceutical products.The provided information describes the modifications made to tamarind seed gum, specifically carboxymethylation and calcium complexation, and their effects on the properties of the gum. Here are the key points:

1.Carboxymethylation: Carboxymethylation of tamarind seed gum involves the addition of a methyl group (-CH3) to the carbohydrate group (COO-). This modification makes the gum completely hydrophilic, meaning it has a strong affinity for water. This hydrophilic nature facilitates rapid disintegration of drug formulations and enhances dissolution rates. The addition of the methyl group is indicated by a shift in the peak at 2927.79 cm-1, as observed in the FT-IR spectra of carboxymethylated tamarind seed gum (CMTG), shown in Fig. 7.

2.Calcium Complexation: After carboxymethylation, the gum was further complexed with Ca2+ ions. This complexation involved the replacement of -CH- groups with Ca2+ ions, resulting in the formation of COOCa2+. This complexation increased the swelling property of the gum. The presence of calcium complexation is reflected in the shifting of IR peaks observed in the FT-IR spectra of calcium complexed tamarind seed gum, shown in Fig. 7.

3.Porous Structure and Swelling Property: The precipitates obtained after calcium complexation were found to have a porous structure. This porous structure contributes to an increased swelling property of the gum. The enhanced swelling property, along with the hydrophilic nature of the gum, promotes rapid disintegration.

4.FT-IR Spectra: The FT-IR spectra of nimisulide (a drug) and calcium complexed tamarind seed gum were also analyzed (Fig. 9). The characteristic peaks and their frequencies for carboxymethylated tamarind seed gum and calcium complexed tamarind seed gum are shown in fig no:7 These modifications, carboxymethylation, and calcium complexation, have been employed to enhance the hydrophilicity, disintegration, dissolution, and swelling properties of tamarind seed gum. These properties are desirable in pharmaceutical formulations, particularly in fast-disintegrating tablets.

Conclusion

The study found that Fast Disintegrating Tablets (FDTs) made from calcium complexed Tamarind seed gum (7.5%) exhibited faster tablet disintegration compared to the synthetic superdisintegrant Sodium starch glycolate.To enhance the hydrophilicity of the Tamarind seed gum, carboxymethylation was employed, which enables the gum to readily disintegrate in gastric fluid. Additionally, the carboxymethylated gum was complexed with calcium ions (Ca2+) to form the calcium complex gum. Consequently, the calcium complexed Tamarind seed gum exhibited superior superdisintegrant properties, providing FDTs with both good mechanical strength and the shortest disintegration time.These findings suggest that this superdisintegrant derived from

calcium complexed Tamarind seed gum can be utilized in the future for the formulation and development of FDTs. This could potentially lead to the production of tablets that disintegrate rapidly and efficiently in the oral cavity, offering benefits such as improved drug dissolution and enhanced patient compliance.

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