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Modified Okra Gum with Silica: A Novel Superdisintegrant for Fast Disintegrating Tablet

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ABSTRACT

The present work on the fast disintegrating tablet of Atenolol was done to formulate a dosage form which can release the active ingredient at the faster rate. The fast disintegrating tablet was made by wet granulation method, the natural gum was used (Modified Okra Gum (*Abelmoschus esculentus*)). The gum in a modified form is a combination with the silica which increases the disintegration rate of the gum. The swelling index of Modified gum was found as 205. The pH of the gum was found as 6.1, in the gum no microbial growth was found during the study. In the contact with the water, due to high porosity, the tablet mass get swell hence it helps in the faster drug release. The water absorption ratio was found best in F4 formulation that was 84%. The eight formulations were studied for the drug content or the drug release, the drug release of the formulations F1 to F8 was found in the range of 90to 98%. Since the present was done using the natural disintegrating agent, so it was also subjected to study for the efficiency. In the present study the disintegration time of Modified Okra Gum containing tablet was compared with the synthetic disintegrating agent (Sodium Starch Glycolate). Disintegration time of Modified Okra Gum was found best in F4 formulation as 2min 10 sec. whereas tablet containing sodium Starch Glycolate was found as 2 min 34sec.

Keywords: Okra gum, Silica, Super-disintegrant, Modified gum.

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INTRODUCTION

Tablet is a solid dosage form that is used to deliver the active pharmaceutical ingredient to the body to make a pharmacological action; the tablet is consisting of the active drug ingredient, binder, disintegrating agent, lubricant, glidant, flavouring agent etc. and compressed into a compact mass that is known as the tablet.

The oral dosage form should ideally dispersed into small particles to deliver it's mechanism of action in the body. To disintegrate the tablet in the biological fluids mostly disintegrating agents are used, most of them are synthetic in nature but now a days, the natural products are used in other words natural super-disintegrating agents are used. In the recent years many of the super-disintegrating agents are developed and are used in the pharmaceutical industries, the main category of super-disintegrants that are used - synthetic, semisynthetic and the natural. [2, 3]

Oral drug delivery system is usually preferred over the other routes because it is convenient and used for the all age category of people, but having the low bioavailability as compare to the IV route, and sometimes the tablets takes the long time to deliver the active drug to the body so disintegrating agents are used to disintegrates the tablets at the faster rate and super-disintegrants are agents that usually causes the fast disintegration of tablets, there some market preparations as well which causes the tablets to disintegrants at the 5 minutes or even less than that. In most of the tablets the super-disintegrants are used in combination or sometimes alone as well. Therefore novel drug delivery system has developed many of the dosage forms to conveniently deliver the active drug to the body without any inconvenience. Sometimes the tablets dosage forms become difficult for some people, like difficulty in swallowing the tablets, and irritation in oral cavity. Super-disintegrating tablets dissolves rapidly in the oral cavity. [4, 5, 6]

Faster the drug dissolution faster will be the mechanism of action and sometimes the drug absorbs in the oral cavity, pharynx and oesophagus. And finally reaches to the site of

action in the body. When the tablets administered in the body it becomes like soft paste and liquid form in the oral cavity as a result of that it easily get dissolved in the body, and ready for the action in the body. The quantity of the disintegrating agent is very significant in this case, because more you will add more would be the faster action of the tablets. Before the final packaging of the drug dosage form the tablets are checked for the friability, weight variation, hardness, drug content and the disintegrating time of the tablet. The evaluations of the tablets are very time consuming and lengthy procedure. [2, 3, 6]

MATERIAL AND METHOD

The materials and methods used in formulation of fast disintegrating tablet of atenolol using okra gum was Abelmoschus esculentus (okra) gum (Purchase from local market), Atenolol (Chemisynth Labs Uttrakhand), Sodium hydroxide (Ranken Laboratory, new Delhi), Isopropyl alcohol (Avantor Performance Material India, Ltd. Gujrat), Methanol (Avantor Performance Material India, Ltd. Gujrat), Sodium starch glycolate (Himedia Laboratories Pvt, Ltd, Mumbai), Talc (Central drug house, Mumbai), Magnesium stearate (Central drug house, Mumbai), Microcrystalline cellulose (Thermo fischer scientific India, Pvt, Ltd. Mumbai), Lactose (CDH Laboratory reagents, New Delhi), Acetone (CDH Laboratory reagents, New Delhi), KBr (Himedia Laboratories Pvt, Ltd, Mumbai).

Preparation of super-disintegrating from Okra gum – Okra gum is a sticky, mucilaginous, and pale yellowish coloured gum. The preparation of the gum is consisting of the four steps. The final step is quite lengthy and it takes up to 2 weeks to complete.

Washing - For the extraction of the mucilaginous gum from the okra, the 1Kg okra was obtained from the local market and it was washed completely to remove the soil and dirt particles. Then it was dried to remove water. The okra was thinly sliced or it was chopped into the small pieces. The seeds were removed from the okra because it consists of no mucilage.

Filtration - After the cutting of the okra, the smaller pieces were soaked into the water. The okra was soaked overnight in the water to extract out the mucilage. After thickening of the mucilage, the muslin cloth was used to filter out the gummy material from the rest of the part of okra.

Precipitation – In the third step the precipitation of the gum was done. For the precipitation of the gum, the acetone was added at a ratio of 3 parts of acetone to 1 part of gum extract. This results in the precipitation of the gummy material.

Drying - After the complete precipitation of the gum, then it was dried in a desiccator containing anhydrous $CaCl_2$ for approximate two week when the gum was dried to remove excess of water then the gum was stored in the air tight container, to avoid contamination. The prepared okra gum was then treated with the silica in the presence of the 2 M HCl to make in modified form.

Formulation of Fast disintegrating Drug (Atenolol) and modified okra gum - The fast disintegrating tablet of the Atenolol was made by the wet granulation method. The formulation of the FDT is consisting of the no. of ingredients that are explained below: The formulation of fast disintegrating tablet of atenolol and okra mucilage was prepared by the direct compression method. The drug and excipients were passed through sieve no. 80 to ensure better mixing, natural superdisintegrants okra gum were used in different proportions. The powders were compressed into tablets on tablet punching machine (Cadmach, India) using 9mm punch and weight of the tablet is 500mg. as shown in **Table 1.**

The formulation of the tablet was formed in seven formulations, which is up to F1 to F8; these formulations were varying in okra gum quantity. In F1 to F4 the disintegrating agent used was okra gum and in F5 to F8 the disintegrating agent was Sodium Starch glycolate.

Table 1: Formulation of Fast Disintegrating Tablet

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8
Atenolol	40	40	40	40	40	40	40	40
AeM.	50	52	54	56	-	-	-	-
Sod. Starch glycolate	-	-	-	-	50	52	54	56
Talc	5	5	5	5	5	5	5	5
Microcrystalline cellulose	100	100	100	100	100	100	100	100
Mag. Stearate	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Lactose	84.5	82.5	80.5	78.5	84.5	82.5	80.5	78.5

EVALUATION

Stability studies of the gum - Prepared gum was stored in glass containers (well stoppered) for one month in the incubator temperature (25±1°C). This was checked after preparation and month throughout a week of period. Physical evaluation of stability of the prepared gum formulation was carried out by appearance, odour, swelling ratio, FTIR, pH and DSC studies.

Swelling index - The swelling index of the gum was carried out to find out the swelling capacity of the okra gum. The Swelling index of Okra gum was determined by placing one gram of powder in a measuring cylinder. The initial volume of the powder in a measuring cylinder was noted and then the volume was made up to 100ml mark with 0.1N HCl (pH 1.2) at room temperature. The cylinder was stoppered shaken gently and set aside for some time.

$$\text{Swelling index} = \frac{W_t - W_o}{W_t} \text{ X } 100$$

Where, S.I. = Swelling index

W_t = Height occupied by swollen gum after 24hrs

W_o = Initial height of the powder in graduated cylinder

FTIR of Modified Okra gum -The Okra gum was mixed with the silica to improve the porosity of the jelly structure of the gum. The addition of the silica in the gum has changed the FTIR spectra of the okra gum. The okra gum is mainly consists of the galactose, rhamnose, and galacturonic acid were determined in the spectrum of FTIR analysis as shown in **Fig. 1:** A broad peak at 1102.90 cm^{-1} was found in the spectrum, indicating the presence of aromatic sugar groups with O–H as the main functional group, which was found in the 3 main components of Okra. O–H groups are able to bind

with water molecules and produce bound moisture to the polymer components. The presence of the silicates group in the gum changes the FTIR of the Okra gum. The existence of O–H groups represents the hydrophilic characteristic that is present in the polysaccharide. The medium peak that is visible at 1102.09 cm^{-1} represents C–H stretch that exists in galactose and rhamnose. The small peak at 3421.31 cm^{-1} shows the presence of C=O stretches that can be found in the constituent of galacturonic acid while the identical small peak at 3221.54cm^{-1} indicates C–H bend which is a constituent of galactose and rhamnose. The frequency of 3432.01cm^{-1} indicates C–O stretch bonds which are present in the aromatic compounds of galactose, rhamnose, and galacturonic acid. The methyl, carbonyl, and hydroxyl functional groups that are present in the chemical structure of Okra are constituents of carbohydrate molecule, which is concluded to be the main backbone of the polymer.

DSC of Modified Okra gum- Okra gum contains moisture and when it get mixed with the silica, the porosity of the gum get increased, the moisture content was detected from the moisture content analysis; therefore, in order to measure the moisture activity of the molecules, thermal analysis with DSC was conducted using a pan with a hole in its lid. A broad peak was distinguished at 96.04°C as can be seen in **Fig. 2:** This broad peak represents the evaporation activity of bound moisture in the Okra gum with silica during the DSC run and it was released through the hole of the aluminium lid. The evaporation temperature is slightly higher than boiling temperature as more amount of heat is needed to break up the ionic bond between water molecules and the polysaccharide linkage.

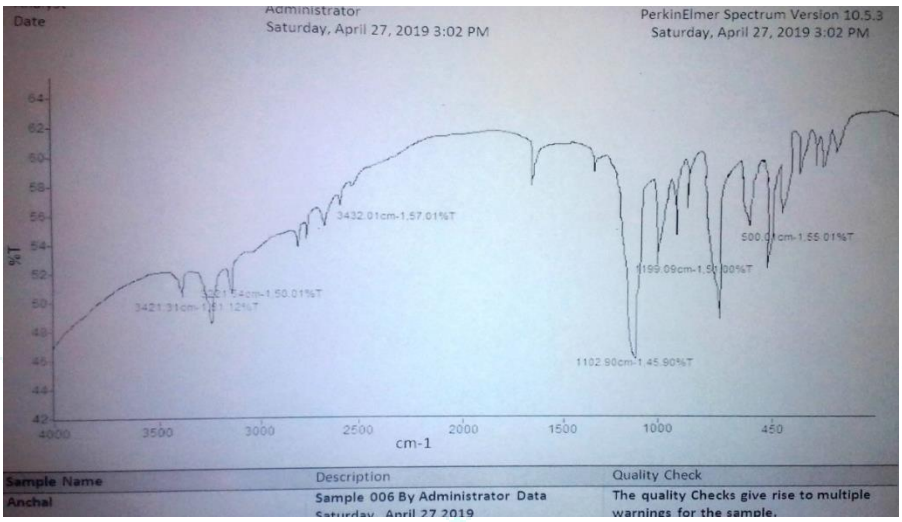

Fig. 1: FTIR of Modified Okra gum

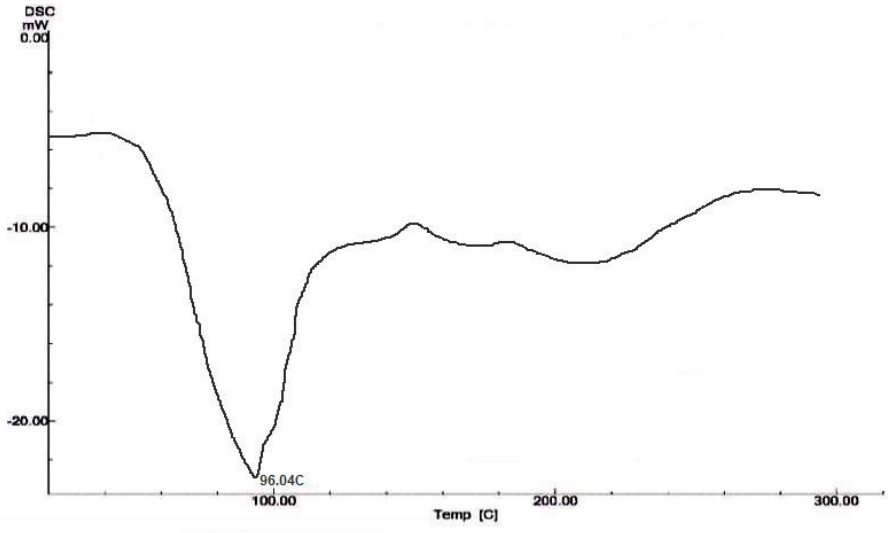

Fig. 2: DSC of Modified Okra gum

Pre-formulation studies of the drug

The Pre-formulation studies of the drug consist of the various parameters, as shown below.

Bulk density - It is a ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume

and by this way the bulk density was calculated according to the formula mentioned below.

$$\text{Bulk density} = \frac{M}{V_b}$$

Where, M is the mass of powder V_b is the bulk volume of the powder.

Tapped Density: It is a ratio of total mass of the powder to the tapped volume of the powder, Volume was measured by tapping the powder for 500 times and the tapped volume was noted, if the difference between these two volumes was less than 2%. If it was more than 2%, tapping was continued for 1000 times and tapped volume was noted. Tapping was continued until the difference between successive volumes was less than 2% (in a bulk density apparatus).

It was expressed in g/ml and was explained as:

$$\text{Tapped density} = \frac{M}{V_t}$$

Where, M is the mass of powder V_t is the tapped volume of the powder.

Angle of Repose (θ): The friction forces in the loose powder were measured by the angle of repose (θ). It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane, the angle of repose was found out by this way.

$$\text{Angle of repose} = \text{Tan}\theta = \frac{h}{r};\ \theta = \text{Tan}^{-1} = \frac{h}{r}$$

Where, θ is the angle of repose.

Carr's index (or) % compressibility: It indicates powder flow properties. It is expressed in percentage and is explained as:

$$\text{Carr's index} = \frac{D_t - D_b}{D_t} \text{ X } 100$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Hardness - Hardness of the tablets was measured using the Pfizer hardness tester. A significant strength of ODT is difficult to achieve due to the specialized processes and ingredients used in the manufacturing so the limit of hardness for the ODT is usually kept in a lower range to facilitate early disintegration in the mouth.

Friability – The friability of a sample of six tablets was measured using a USP type Roche friabilator (Pharmalab, Ahmedabad, India). Pre-weighed tablets were placed in a plastic chambered friabilator then this device subjects tablets to the combined effect of abrasions and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Pre weighed sample of 6 tablets was placed in the Friabilator, which was then operated for 100 revolutions. Tablets were dusted and weighed. The friability was determined using following formula:

$$\text{Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \text{ X } 100\ \%$$

Weight variation: In the study Fast disintegrating tablet were subjected to study for weight variation. The weight of a tablet being made is routinely measured to ensure that a tablet contains proper amount of drug so Firstly weight of 20 tablets was determined. From that average weight was calculated and then individual tablets were weighed and the individual weight was compared with an average weight.

Water Absorption Ratio: A piece of tissue paper folded twice was placed in a small Petri dish containing 5 ml of water. A tablet was put on the tissue paper and allowed to completely wet then wetted tablet was then weighed. Water absorption ratio, R, was determined by using following equation:

$$\text{Water absorption ratio} = \frac{W_a - W_b}{W_b} \text{ X } 100$$

Where, W_b = Weight of tablet before water absorption, W_a = Weight of tablet after water absorption.

Disintegration test (Comparison) - The okra mucilage as a disintegrating agent was compared with the Sodium starch glycolate which also act as a disintegrating agent but it's a synthetic disintegrating agent. The dosage form was compared in the manner of Disintegration Time and Dissolution time. Disintegration of orally disintegrating tablets usually achieved in the mouth by the action of saliva, however amount of saliva in the mouth is limited so *in vitro* tests are done for study. A method was used to determine disintegration time of the tablets, a cylindrical vessel was used in which 10 mesh a screen was placed in such way to determine disintegration time, 500ml of buffer 6.8 pH, was placed inside the vessel. Tablet was placed on the sieve and the whole assembly was then placed on a shaker and then time at which all the particles pass through the sieve was taken as a disintegration time of the tablet. Six tablets were chosen randomly from the samples and the average value was determined carefully.

% Drug content uniformity – The drug content of the tablet was determined by the spectrophotometric method. It was done for the eight formulations F1 to F8. The mean value and the standard deviation of the all formulations were calculated. The drug content of the tablet was found in the range of 89.9% to 99.3%. The % drug content is mentioned in table below.

RESULT AND DISCUSSION

The Fast disintegrating tablet was successfully formulated and it had all the satisfactory results. The gum was studied for the stability and no unusual changes were found in the gum, it was found as compatible with silica in the combination form. The swelling index of the modified gum was found as 205, which indicates that the gum has good selling capacity. The Pre-compression studies of the gum were done and it had all the satisfactory results the pre-compression studies were found in the range and as shown in **Table 2.** The post compression studies of the gum were had all the satisfactory results, the post-compression studies were found in the range and shown in **Table 3.** The disintegration time of the eight formulations was compared the compared formulation has shown that formulation F4 has shown the lowest disintegrating time which means that the Modified Okra gum works better than the synthetic disintegrant and it is as shown in **Table 4.** The percentage drug content uniformity of the eight formulations were determined, it was observed that the F4 formulation has best result, the drug content was found as the 99.3% and shown in **Table 5.**

Table 2: Pre-compression studies

Formulations	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose (^{0})	Carr's index (%)	Hausner's ratio
F1	0.54	0.65	27	16.2	0.95
F2	0.57	0.71	30.2	21.4	1.21
F3	0.56	0.70	31.2	22.4	1.25
F4	0.57	0.75	31.38	22.8	1.38
F5	0.52	0.72	28.3	22.9	1.29
F6	0.56	0.76	27.7	22.6	1.28
F7	0.57	0.74	32	27.7	1.35
F8	0.58	0.75	30.5	24.1	1.33

Table 3: Post-compression studies

Formulations	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Weight variation	Water absorption ratio (%)	Disintegration time (sec.)
F1	4.8±0.01	3.1±0.34	0.29	320±0.65	37	46±5s
F2	4.7±0.23	3.5±0.21	0.42	322±0.55	58	44±5s
F3	4.2±0.21	3.4±0.21	0.51	310±0.58	69	39±5s
F4	4.1±0.21	3.5±0.01	0.58	319±0.69	84	35±5s
F5	4.7±0.60	2.9±0.67	0.62	323±0.63	20	50±5s
F6	4.5±0.69	3.2±0.32	0.67	312±0.57	35	44±5s
F7	4.1±0.21	3.5±0.42	0.68	322±0.58	48	41±5s
F8	3.9±0.43	3.5±0.42	0.70	321±0.55	57	39±5s

Table 4: Disintegration time of formulations (Comparison)

Disintegration time	F1	F2	F3	F4	F5	F6	F7	F8
Modified okra gum	2min 42sec.	2min 20sec.	2min 16sec.	2min 10sec.	-	-	-	-
Sodium starch glycolate	-	-	-	-	3min 2sec.	2min 56sec.	2min 40sec.	2min 34sec.

Table 5: Percentage drug content

S no.	Formulations	% Drug content
1	F1	92.2
2	F2	93.0
3	F3	97.9
4	F4	99.3
5	F5	89.9
6	F6	90.8
7	F7	98.5
8	F8	98.3

CONCLUSION

The present work on Fast Disintegrating Tablet was done to formulate to provide the immediate release of drug (Atenolol). Atenolol is a drug that is mainly used in the hypertension treatment and other heart diseases. The main gum that was used in the formulation was Okra gum (*Abelmoschus esculents*) in a modified form with silica. which was used to fasten the drug release, which increased the swelling ratio of the gum. The gum was subjected for the stability studies before the final dosage form formulations. In the gum on unusual changes was found during the study. The gum was tested for the various things like swelling index which was found as 205. The tablet granules were made by the intra-granulation method, the gum was included in the tablet blend to provide a better a dosage form. The okra gum worked by the swelling mechanism, the main function of the (*Abelmoschus esculents*) Okra gum was that to provide a better porosity in the tablet mass. In the contact with the water, due to high porosity, the tablet mass get swell hence it helps in the faster drug release. The sole purpose of gum was to increase the swelling capability of the tablet by increasing the porosity of the tablet.

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CONFLICT OF INTEREST

The authors report no conflicts of interest.

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