"STUDY OF DISINTEGRANT FROM NATURAL PRODUCT"

Submitted in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

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ABSTRACT

CONTENTS

CONTENT

LIST OF FIGURE

LIST OF TABLES

KEY WORDS AND GLOSSARY

LIST OF ABBREVIATIONS

Abbreviations	Full Form
AAL	Alpha Linolenic Acid
BD.	Bulk Density
CONC.	Concentration
Conc. H2SO4	Conc. Sulfuric Acid
D.W.	Distilled Water
GC	Gas Chromatography
Gm	Gram
HPLC	High Performance Liquid Chromatography
HPMC	Hydroxypropyl Methylcellulose
Ml	Milliliter
Min	Minute
MCC	Microcrystalline Cellulose
PVP	Pollyvinylpyrolidone
RPM	Revolutions Per Minute
TD	Tapped Density
VB	Bulk Volume
VT	Tapped Volume

Abstract

Disintegrants are the excipients used in tablets to enhance disintegration. Natural disintegrants are used for their non-toxic behavior. Flaxseed is seed obtained from *Linum Usitatissimum* (Family *Linaceae*) and rich in polysacchride. As per literature the mucilage obtained was found promising to promote disintegrant as a tableting excipient. Extraction of the mucilage from the seed needs to be done in simple and economic way. The extraction and addition of mucilage intragranularly served the purpose of disintegrant. The extracted mucilage should be free from carbohydrate and protein. The present study showed the extracted mucilage as disintegrant and its comparison with starch.

Key words: Disintegrant, Mucilage, Extraction

1 INTRODUCTION

Recent advances in Novel drug delivery system aim to enhance safety and efficacy of drug by formulating their convenient dosage forms for administration and better patient compliance.[1]
Excipients are the additives used to convert active pharmaceutical ingredients into dosage form suitable for administration to the patients.[1]

Agents which are used in the preparation of tablets which causes them to disintegrate and release their medical substances on contact with moisture are called Disintegrant. Evaluation of disintegration property can be done by the time how long the tablets take to disintegrate. They are added to formulation to promote the drug release.

For this purpose disintegration test was used. This test determines whether dosage forms such as tablet, capsule, and suppositories disintegrate within prescribed time (disintegration time) when were placed in a liquid medium under the prescribed experimental condition.

Disintegration is defined as that state in which no residue of unit under test remains on the screen of the apparatus, it consist of fragments of disintegrated parts of tablet component parts such as insoluble coating of tablets or of capsule shell, or of any melted fatty substance from the pessaries or suppositories or is a soft mass with no palpable core.[2]

There are two classes of disintegrant; Traditional disintegrates, such as starch, and Super disintegrant, which include Croscarmellose Sodium, Crospovidone and Sodium Starch Glycolate.
Today a number of researches have exposed the utility of plant-based materials as pharmaceutical excipients.

Natural excipients have easy accessibility, non-polluting, environmentally friendly nature and cost effectiveness compared to imported synthetic products.[14]

Fig 1: Flaxseed plant

Fig 2: Flaxseeds

Flaxseed is the seed of flax plant i.e. *Linum Usitatissimum* belonging to the family *Linaceae*. The mucilage of *Linum Usitatissimum* is a water soluble heterogeneous polysaccharide composed of xylose, arbinose, glucose, galactose, galacturonic acid and rhamnose. It has good water-holding capacities, owing to its marked swelling capacity and high viscosity in aqueous solution.[1, 3]

1.1 Advantages of flaxseed:

- Flaxseed is the richest source of healthy fat, antioxidant, and fibers. The seed contain protein, lignin, and the essential fatty acid alpha linolenic acid also known as ALA or omega3.[1]
- These nutrients in flaxseed may help lower the risk of diabetes, cancer, and heart disease. For this reason, it is sometimes thought of as a functional food that can be consumed to achieve health.
- Mucilage of flaxseed have a variety of application as a tablet binder, disintegrant, emulsifier, suspending agent, gelling agent, stabilizing agent, thickening agent, film forming agent,and as a sustain agent in matrix tablet.
- Research suggests that presence of omega-3 fatty acid may help prevent different types of cancer cells from growing.
- Flaxseed also contains lignans, which are antioxidant that may slow tumor growth by preventing them from forming new blood vessels.

2 REVIEW OF LITERATURE

- Global Journal of Pharmacology[7]
  8 (4): 510-514, 2014
  ISSN 1992-0075 © IDOSI Publications, 2014

Studied the **Extraction and Evaluation of *Trigonella Foenum graecum Linn* & *Linum Usitatissimum* seed Mucilage.**

This study was undertaken to isolate and evaluate the mucilage from *Trigonella foenum graecum L.* and *Linum Usitatissimum* and explore it as pharmaceutical excipients. Phytochemical characterization of *Trigonella foenumgraecum L.* and *Linum Usitatissimum* such as bulk and tapped densities, pH, swelling index, angle of repose Carr's index and Hausner's ratio were studied. Solubility behavior of both isolated mucilage and identification tests for carbohydrates, gum, mucilage, fats and oil were also studied. From the study, result conclude that *Trigonella foenum graecum L.* and *Linum Usitatissimum* seed mucilage's can be used as a pharmaceutical excipients to prepare different dosage forms and also concluded from both isolated mucilage's that fenugreek mucilage have good flow property than linseed mucilage.

- International Journal of Pharmacy & Technology[9]
  ISSN: 0975-766X

Studied the **Isolation and Evaluation of Fenugreek, Flaxseed mucilage and its use as a Pharmaceutical binder**.

Study to evaluate the binder effects of mucilage isolated from flaxseed *(Linum Usitatissimum L.)* and fenugreek seed *(Trigonella foenum graecum L.)*. The binding properties of the mucilage isolated were evaluate using lactose granules with different binder conc. levels of 3%w/v, 5% w/v, 7% w/v and 10% w/v. The results were compared with regularly used binders such as starch paste, PVP and 1:1 concentration of both FXM and FNM.

- International Journal of Pharmacy and Pharmaceutical Sciences.[10]
  Vol. 2, Suppl. 2, 2010
  ISSN- 0975-1491

Studied **To compare the disintegrating property of Papaya Starch and Sago Starch in Paracetamol Tablets.**

In this study un-ripe papaya was taken and the pulp obtained from fresh fruit was lyophilized to obtain the pulp powder. The starch was extracted from unripe papaya pulp powder and used as disintegrant in paracetamol tablets. Sago starch is used as a second disintegrant and the in vitro release data of the tablets prepared from papaya pulp powder and sago starch was compared to determine the disintegrant properties of both starches. The physical properties (bulk density and tapped density, angle of repose, swelling power and paste clarity) of both starches were also evaluated. For the comparisonof disintegrating property ten batches were prepared using different concentration of both the starch as disintegrant.

Result concluded that both papaya and sago starch posses significant disintegrating properties and can be used as disintegrating agent.

- International Journal of Pharmacy and Pharmaceutical Sciences.[10]
  ISSN- 0975-1491. Vol. 6, Issue 10, 2014

Studied **Evaluation and optimization of *Lepidium Sativum* seed mucilage as binder in tablet formulation.**

Study elaborates isolation of mucilage from *Lepidium Sativum* seeds and explores it as a tablet binder. The mucilage from seed was extracted by precipitation of soaked and blended seed in acetone. The mucilage was evaluated for its binding properties in tablets prepared by wet granulation and direct compression method. The prepared tablets were evaluated for hardness, thickness, friability, disintegrating time and in-vitro drug release and compared with established binder like starch, PVP K-30, HPMC, and MCC.

The results includes isolated mucilage from *Lepidium Sativum* seeds as a binder were very promising and indicated that mucilage is required in concentration as low as 2% for wet granulation and 4% for direct compression to give equivalent binding effect.

- International Journal of Current Research[12]
  Vol. 8, Issue, 02,
  pp. 26866-26871 February, 2016 ISSN: 0975- 833X

Studied the **Isolation and Evaluation of Mucilage from Herbal product as Pharmaceutical Excipient.**

The mucilage of plant of family of Cruciferae was collected from seeds. Seeds of the plant *Lepidium Sativum* were isolated. The result concluded that *Lepidium Sativum* mucilage has been reported to have the gel forming potential. The mucilage isolated from seeds showed the presence of carbohydrates and was found acceptable for all the tested organoleptic properties.

- Indian Journal of Research in Pharmacy and Biotechnology [15]
  ISSN: 2321-5674

Studied the **Formulation and evaluation of diclofenac sodium S.R. tablets using *Linum Usitatissimum* seed mucilage matrix.**

Study includes develop sustained release matrix tablets of Diclofenac sodium for maintaining therapeutic blood or tissue levels of the drug for extended period of time with minimized local or systemic adverse effects. Polysaccharide mucilage derived from the seeds, *Linum Usitatissimum* (family Linaceae) was investigated as sustained release matrix forming material in tablet formulations. Results of study concluded that the Flax seed (*Linum Usitatissimum*) polysaccharide mucilage can be used as an effective release retardant of drugs in matrix tablets like other established polymers.

- Indian Journal of Research in Pharmacy and Biotechnology Indranil and Jain ISSN: 2321-5674; 2320 – 3471. [15]

Studied the **Formulationand evaluation of Diclofenac Sodium S.R. tablets using *Linum Usitatissimum* seed mucilage.**

They study, Polysaccharide mucilage derived from the seeds, *Linum Usitatissimum* (family Linaceae) was investigated as sustained release matrix forming material in tablet formulations. Mucilage extracted from seeds was subjected to physicochemical characterization. Matrix tablets were prepared by wet granulation technique using isopropyl alcohol as a granulating agent. The results of study concluded that the Flaxseed *(Linum Usitatissimum)* Polysaccharide mucilage can be used as an effective release retardant of drugs in matrix tablets like other established polymers.

- Pharmaceutical and Biosciences Journal[16]
  Vol. 7(1), 09-14, 2019

Studied the **Extraction and Evaluation of Linseed Mucilage as Binding Agent in Prednisolone Tablet 20 mg.**

The Linseed mucilage was extracted and evaluated for physicochemical properties using official procedures. Tablet was prepared by wet granulation. Granules evaluation revealed satisfactory results. Three formula were prepared that contain three different percent from linseed mucilage 3%, 5% and 7%.The hardness test result show great increase in tablet hardness.

- Journal of Plant Sciences [17]
  Vol. 2, No. 1, 2014, pp. 70-76.

Studied the **Extraction and Purification of Flaxseed Proteins and Studying their Antibacterial Activities.**

Result concludes that Flaxseed contains a considerable amount of mucilage in its seed coat which interferes with the process of protein extraction from flaxseed.The antibacterial activities of flaxseed proteins as a total extract and those of the column chromatography-fractionated samples were examined against several species of G- and G+ bacteria. Flaxseed protein extract showed an antibacterial activity against the most test microorganisms specially gram negative bacteria.

- African Journal of Biotechnology [18]
  Vol.11 (4), pp. 724-731
  ISSN 1684–5315 © 2012 Academic Journals

Studied on **A Review Of The Methods Used In The Determination Of Flaxseed Components.** The study includes, the different methods used for the determination of flaxseed components are revised. The qualitative and quantitative determination of the major and minor constituents of flaxseed are carried out by GC and primarily HPLC, which are the most important two techniques widely applied for the analysis of edible oils and fats.

3 AIM AND OBJECTIVE

- **To compare the effect of disintegrate with other disintegrates (starch) at different concentration**
- **To study disintegration property of flaxseed mucilage in solid dosage form.**
- **To evaluate various parameters such as disintegration time, swelling index, angle of repose, hardness, compressibility index.**

Herbal or plant products are now used as an alternative to synthetic products due to its local accessibility and non-toxic behavior.
The main aim of this study was to isolate the mucilage from the plant seeds of Flaxseed (*Linum Usitatissimum*) and compare its disintegration properties with synthetic disintegrant.

The objective of this study toexplore Flaxseed mucilage can be used as a disintegrant in solid dosage form and to evaluate various parameters such as disintegration time, swelling index, angle of repose, hardness, thickness, and to compare it with various other synthetic disintegrant (e.g. Starch) for the same. Since, the mucilage obtained from flaxseed is rich source of polysaccharides and how remarkable swelling capacity and high viscosity, its use as a disintegrating agent has appeared logical in our current novel.

Hence the present study was concerned to explore *Linum Usitatissimum* seed mucilage for its disintegrating property by formulating tablet prepared by wet granulation, direct compression method.

4 EXPERIMENTALWORK

4.1 MATERIALS AND METHODS

I. MATERIALS:

TABLE 1: LIST OF MATERIAL

Sr. No.	Ingredients	Amount	Specification
1.	Flaxseed	400 gm	Purchased from local market
2.	Starch	30 gm	Loba Chemie Pvt. Ltd. (LR Grade)
3.	Lactose	3 gm	Loba Chemie Pvt. Ltd. (LR Grade)
4.	Talc	30 mg	Loba Chemie Pvt. Ltd. (LR Grade)
5.	Magnesium stearate	15 mg	Loba Chemie Pvt. Ltd. (LR Grade)
6.	Acetone	100 ml	Loba Chemie Pvt. Ltd. (LR Grade)
7.	Ethyl alcohol	100 ml	Loba Chemie Pvt. Ltd. (LR Grade)

All the other solvents, reagents and chemicals like Molisch's reagent, Benedict's reagent, Bromine reagent, Nutrient Agar used were of either Pharmacopoeia or analytical grade.

II. INSTRUMENTS:

TABLE 2: LIST OF INSTRUMENTS

Sr. No.	Name	Specification
1.	Single Stroke Tablet Press (Multi-cavity)	Royal Artist
2.	Hot Air Oven	Model
3.	Monsanto Hardness Tester	Bio-techno Lab
4.	Digital Tablet Disintegration Apparatus	Veego instruments Corporation, Model VTD-D
5.	Autoclave	-
6.	Balance Machine	Realtec

4.2 METHODS:

I. EXTRACTION OF MUCILAGE FROM FLAXSEEDS

Extraction involves the separation of the active constituent of plants or animal tissues from the inactive or inert component by using solvent and by using one of the standard extraction procedures.

For Extraction of mucilage, seeds of Flaxseed (*Linum Usitatissimum L.*) were used.

METHOD 1[10]:

1. 100 gm of Flaxseeds were washed with running water to remove the surface dust.
2. The whole seeds were soaked in 200 ml distilled water for 6 hr.
3. The soaked seeds were blendedand then filtered through muslin cloth.
4. Additional 200 ml water was added to the seeds and boiled at 100°C with occasional stirring till thick mass (mucilage) was obtained.
5. Mucilage wasfiltered through muslin cloth to get yield.

METHOD 2[4, 7, 9]:

1. 100 gm of Flaxseeds were soaked in 200 ml distilled water for 6 hr.
2. Whole soaked seeds were boiled about half hour to remove mucilage from seeds.
3. Decrease heat to medium-low, and boil uncovered until water begins to thicken.
4. Obtained thick mass was filtered through muslin cloth to get maximum yield.
5. 50 ml acetone was added to allow precipitation of mucilage.
6. After precipitation mass was filtered through the muslin cloth. Precipitated mucilage was dried at 50°C in hot-air oven.
7. Mucilage obtained was converted into powder by using sieve.

NOTE:

These two methods for isolation did not gave appropriate result as the separated mucilage was sticky and after drying powder was not obtained.

METHOD 3[1, 8]:

Seeds were soaked in 200 ml distilled water for 6 hours

Soaked seeds were boiled about half an hour
To remove mucilage from seeds

Re-filtered through muslin cloth

50ml of ethyl alcoholadded to the filtrate

After precipitation mass was filtered&
Dried at 50°C in hot-air oven

Powder collected sieved & stored

METHOD 4:

- Method 3 was repeated with ethyl alcohol and acetone mixture (1:1), this method was failed to provide powder form of the mucilage.

Seeds were soaked in 200 ml distilled water for 6 hours

Soaked seeds were boiled about half an hour
To remove mucilage from seeds

Re-filtered through muslin cloth

50ml of ethyl alcohol & acetone added in mixture of1:1.

After precipitation mass was filtered&
Dried at 50°C in hot-air oven

Powder collected sieved & stored

METHOD 5:

- Seed powder was used for extraction of mucilage.

1. 100 gm of seeds were washed and dried to remove dirt and impurities.
2. Then the dried seeds were blended into a mixture to get a powder of uniform size.
3. 200ml of water was taken in a beaker and 100gm of linseed powder was added and boiled to form mucilage.
4. Mucilage was filtered through muslin cloth.

NOTE:

The mucilage obtained by this process was not clear as it contains seed coat and the mucilage obtained was un-filterable.

METHOD 6:

- Use of pure form of mucilage as our disintegrating agent which was extracted by the following method.

1. 100 gm of seeds were washed and dried to remove dirt and impurities.
2. The whole seeds were soaked in 200 ml distilled water for 6 hr.
3. Soaked seeds were boiled at 100°C with occasion stirring till mucilage is removed.
4. Mucilage was squeezed through muslin cloth.

100 gm of flaxseed was washed with water.

Seeds were soaked in 200 ml D.W. for 6 hrs

Soaked seeds were boiled about half hour to release mucilage

Mucilage was squeezed through muslin cloth.

NOTE: The mucilage obtained by this process was used for further procedure.

II. MICROBIAL CONTENT[5, 2]:

Microbial content of Flaxseed Mucilage is performed by using **Nutrient Agar** as media.

- Nutrient Agar is a general purpose, nutrient medium used for the cultivation of microbes supporting growth of a wide range of non-fastidious organisms. Nutrient agar is popular because it can grow a variety of types of bacteria and fungi, and contains many nutrients needed for the bacterial growth.

➢ Process of Nutrient Agar preparation as followed:

1. 28 g of nutrient agar powder was made to suspend/dissolve in 1000 ml of distilled water.
2. Mixture was heated and stirred to dissolve all components.
3. Dissolved mixture was autoclavedat 121^{o}C for 15 minutes.
4. After autoclaving, the mixture was allowed to cool but not solidify.
5. Nutrient agar was poured into each plate and plateswere left on the sterile surface until the agar has solidified.
6. After the closing with the lid, the plate was kept in refrigerator.

i. ISOLATION OF FLAXSEED MUSCILAGE BY STREAK PLATE METHOD:

- **Requirements:**

Nutrient agar, Petri plate, Conical Flask, Beaker, Test tube, Nichrome wire loop, Glass marking pen, Autoclave, Hot air oven, Balance, Alcohol.

- **STREAK PLATE METHOD:**

  Inoculation of microbial culture to the surface of the sterile agar plate and spreading it by an inoculating wire loop is called Streak Plate **Method.**

  Streak plate technique was used for the cultivation, isolation, and separation of micro-organisms.

  This method was used to produce well separated colonies of bacteria and the size, shape, color and other physical characteristics of isolated colonies to be studied.

- **Procedure:**

1. The media for growth of respective organism was prepared and kept in autoclave at 121℃ for 15 minutes.
2. Quadrant (4) was prepared on the Petri plate before passing media into plate.
3. The sterile media was passed into sterile Petri plate in quantity of 15-20 ml.
4. Plates were then allowed to solidify under aseptic condition.
5. Using Nichrome loop, streaking was done by 4 quadrant method.
6. Plate was incubated at 37℃ for 24 hours.
7. The Growth of micro-organismsafter incubation was observed for isolated colonies and their characteristics.

III. CHEMICAL TESTS OF FLAXSEED MUCILAGE AND FLAXSEED POWDER:

i. Materials Required:

1. Glassware
2. Test tubes
3. Test tube holder

4. Water bath
5. Spatula
6. Dropper

ii. Reagents Required:

1. Molisch's Reagent
2. Benedict's qualitative reagent
3. Bromine reagent

iii. Procedure:

1) Molisch's Test:

In a test tube, 2 ml of the test mucilage solution and 2 drops of α-naphthol solution were added. Concentrated H_2SO_4 was added through the inclination of test tube by using a dropper, along the sides of the tube. Violet color at the junction of the two liquids was observed.[2, 19]

2) Benedict's Test:

In the test tube with 2 ml of Benedict's reagent, 5-6 drops ofmucilage solutionwere added and mixed well. Test tube was placed in a boiling water bath for 5 minutes and observed for any change in color or precipitate formation. Solution was then cooled and color changes were observed.[2, 19]

3) Bromine Test:

In the test tube 2 ml of the test mucilage solution and Bromine solution was added for any color change.[2, 19]

IV. FORMULATION AND EVALUATION OF TABLET:

i. FORMULATION OF TABLETS:

- For the evaluation of the Mucilage as disintegrant, Mucilage was used at different concentration i.e. 2, 4, 6, 8, 10% and mixed it with Lactose to prepare tablet formulation.

- These formulations were compared with the formulations of starch as disintegrant in the concentration range of 2, 4, 6, 8, and 10%.

ii. WET GRANULATION METHOD[10]:

- Wet granulation method was used for all tablet formulation. The calculation is made for 30 tablets in each batch.

➢ Process of Wet Granulation as follows:

1. The composition of tablet formulation containing Mucilage and Starch as shownin **Table No.7 & 8**.
2. Mucilage solution at concentration of 2%, 4%, 6%, 8%, 10% were calculated and Accurately weighed quantities of each ingredient were mixed in a mortar and an appropriate quantity of the Lactose was added as a granulating agent and mixed in a mortar to form dough (wet mass).
3. The wet mass was sieved with sieve no. 10 and dried at temperature not more than 60°C in a hot air oven.
4. The dried resultant granular masses were passed through sieve no. 44 placed up and sieve no. 60 at bottom to obtain uniform sized granules.
5. The granules were mixed with calculated equal quantity of magnesium stearate (0.5%) and talc (1%) and then evaluated for pre compression parameters.
6. The same method was followed for the preparation of tablets using starch at 2, 4, 6, 8, 10% concentration.

iii. COMPRESSION METHOD[10]:

- Granules were compressed into tablets under constant pressure with a Single Stroke Tablet Press by following Compression method.
- Tablets were compressed using 9 mm round flat punches on Single Stroke Tablet Press. The formulation of tablets at different concentration was as shownin **Table 7 and 8**.

V. EVALUATION OF FLOW PROPERTY[1,6]

i. BULK DENSITY:

The bulk density was obtained by adding a required weighed powder into a measuring cylinder. Volume was observed and recorded as Bulk Volume. The Bulk Density is calculated as Bulk Density = Mass/ V

ii. TAPPED DENSITY:

Powder Density Apparatus was used to study the tapped density for powder, granules and other bulk substances.

- Tapped Density was performed as follows:
  1. Twocleaned and dried measuring cylinder were taken.
  2. The mains of Powder Density Apparatus were switched on.
  3. Initial taps and final taps were settled by adjusting the number of strokes to 100.
  4. After setting the strokes, weighed quantity of powder was transferred into a cylinder.
  5. The two cylinders were fitted with cylinder holder plates and thestrokes were started.
  6. After completion of strokes, up and down movement of the cylinders were stopped automatically at the pre-set number.
  7. After the machine stops, the final capacity of powder in the measuring cylinder was observed.
  8. Observed volume was recorded as Tapped Volume.

The Tapped Density is calculated as

Tapped Density = Mass/ VT

iii. COMPRESSIBILITY INDEX (C %):

This was calculated using the equation:

% Compressibility = [(TD– BD)/ TD × 100]

iv. ANGLE OF REPOSE:

The angle of repose was measured by using the fixed funnel. A funnel clamped with its tip at the height (h) of 2cm above a graph paper was placed on a flat horizontal surface.

The powdered mucilage was poured through the funnel until the apex of the conical pile was formed just to touch the tip of the funnel. The mean diameter of the base of the powder cone was measured and the radius (r) was determined.

Calculated by using formula:

$$\text{Angle of repose } (\Theta) = tan^{-1}\frac{h}{r}$$

VI. POST COMPRESSION PROPERTIES

i. HARDNESS:

Hardness of tablet of each formulation was measured by MonsantoHardness tester in terms of kg/sq.cm.

- Process of Hardness test as follows:

1. Tablet was held between the jaw and nozzle in edgewise position.
2. The position of the scale (by turning the plunger clockwise) was adjusted so that the zero on the scale coincides with the pointer.
3. The screw knob was then turned slowly till the tablet breaks.
4. The pressure indicated on the dial as kg/sq.cm.
5. The hardness was recorded as kg/sq. cm.

ii. DISINTEGRATION TEST:[2,6]

Disintegration test was determined by using Digital Tablet Disintegration Apparatus. Microprocessor based Tablet Disintegration Machine was used for testing the disintegration time for tablets, capsules, and other solid dosage forms. Instrument was designed to test two batches of six tablets simultaneously.

- Process of Disintegration Test as follows:

1. Water bath was filled up to WATER LEVEL mark.
2. Both glass beakers having capacity of 1000 were placed into water bath.
3. Both the glass beakers were filled at required level. Two baskets were fixed with Bars and the basket racks werepositioned in a 1-L beaker of water.
4. The machine and heater were switched on and the instructions on screen were followed for Set Up/Run of tests.
5. Wait till the temperature reaches to 37°C.

6. One tablet containing 2% mucilage was introduced into each tube of Basket. After pressing Enter Button, bars start moving up and down.
7. After completion of test, the machine was stopped.
8. Disintegration was considered to be completed when there is no residue on the plate.
9. The final time displayed on screen was observed and recorded as disintegration time. The disintegrating tablet passes the test as no residue remains inside the tubes. The same test was repeat for 4, 6, 8, 10% concentration.

The same testwas repeated for starch tablet by using starch solution at concentration range 2, 4, 6, 8, 10% and the disintegration time was note down.

5 RESULTS

i. EXTRACTION OF MUCILAGE FROM FLAXSEEDS

TABLE 3: EXTRACTION METHOD OF MUCILAGE

METHOD 1	PROCEDURE	INFERENCE
Extraction of mucilage method	100 gm of Flaxseeds were washed ⇩ Soaked in 200 ml D.W. for 6 hr ⇩ after 6hr seeds were boiled at 100°C about half hour ⇩ Resulting material squeezed by muslin cloth	**yellow thick mass (Fig. 5)** was obtained.

***Mucilage extracted through muslin cloth (filtrate) used for following isolation method:**

TABLE 4: ISOLATION METHOD OF MUCILAGE

METHOD NO.	PROCEDURE	INFERENCE
2.	100ml Filtrate+ add50 ml of acetone ⟹ precipitated mucilage was filtered ⟹ dried at 50°C in hot air oven	**Moist form of** product was obtained. **(Fig. 6)**
3.	100ml Filtrate + 50 ml ethyl alcohol ⟹ precipitated mucilage was filtered ⟹ dried at 50°C in hot air oven	**Dried product** formed **(Fig.7)**
4.	Filtrate + add ethyl alcohol and acetone mixture (1:1) ⟹ precipitated mucilage was filtered ⟹ dried at 50°C in hot air oven	**sticky and un-filterable(Fig. 8)** Product was formed.
5.	100 gm of seeds were washed & dried ⇩ Dried seeds blended into 200ml of D.W. ⇩ 100 gm of linseed powder ⇩ Boiled to form mucilage.	Product formed was not clear and un-filterable as it **contains seed coat. (Fig. 9)**
6.	100 gm of flaxseed were washed ⇩ Seeds were soaked in 400 ml D.W. for 6 hrs ⇩ Soaked seeds were boiled about half hour ⇩ Resulting material filtered by muslin cloth	Product extracted through muslin cloth was **glossy and clear this pure form of mucilage**was used as a disintegrating agent. **(Fig.10)**

ii. MICROBIAL CONTENT:

TABLE 5: OBSERVED CHARACTERISTICS OF COLONIES OF CULTURE ON MEDIA

Colony characteristics	Nutrient Agar (Flaxseed Mucilage)
Color	Yellowish
Size	-
Shape	Circular
Margin	Entire
Elevation	Flat
Consistency	Smooth
Opacity	Opaque

iii. CHEMICAL TESTS OF FLAXSEED MUCILAGE AND FLAXSEED POWDER

TABLE 6: CHEMICAL TESTS RESULT OF FLAXSEED MUCILAGE AND FLAXSEED POWDER

Sr. no.	TESTS	OBSERVATION	INFERENCE OF MUCILAGE	INFERENCE OF POWDER
1.	MOLISCH TEST: (2ml carbohydrate solution+2 drops alpha naphthol+conc.H2SO4 from side of the test tube)	Violet ring at the junction of two liquid	Negative (carbohydrate absent)	Positive (carbohydrate present)
2.	BENEDICTS TEST: (5ml benedicts reagent +8 drops of carbohydrate solution + boil + cool)	Reddish brown color	Negative (glucose, galactose ,etc absent)	Positive (galactose , glucose, etc present)
3.	BROMINE TEST: (solution +bromine solution)	Color of bromine disappear	Negative	Positive

iv. FORMULATION OF TABLETS:

TABLE 7: Formulation of tablet prepared by using FLAXSEED MUCILAGE (Wet granulation)

	Mucilage				
Ingredients	2%	4%	6%	8%	10%
Lactose	289.5	283.5	277.5	271.5	265.5
Mucilage	6	12	18	24	30
Talc (1%)	3	3	3	3	3
Magnesium stearate (0.5%)	1.5	1.5	1.5	1.5	1.5
Total weight	300	300	300	300	300

TABLE 8: Formulation of tablet prepared by using STARCH PASTE (Wet granulation)

	Starch				
Ingredients	2%	4%	6%	8%	10%
Lactose	289.5	283.5	277.5	271.5	265.5
Starch	6	12	18	24	30
Talc (1%)	3	3	3	3	3
Magnesium stearate (0.5%)	1.5	1.5	1.5	1.5	1.5
Total weight	300	300	300	300	300

***All quantity is in mg.**

v. EVALUATION OF FLOW PROPERTY

TABLE 9: Evaluation of tablet prepared by using FLAXSEED MUCILAGE

Sr. No.	EVALUATION	2%	4%	6%	8%	10%
1.	Bulk density	0.5494	0.5839	0.6453	0.6801	0.6925
2.	Tap density	0.6993	0.7591	0.8061	0.7802	0.8122
3.	Compressibility Index (%)	21.43	23.07	19.94	12.08	14.46
4.	Angle of repose (°)	30.67	27.31	27.80	26.98	25.65
5.	Hardness (Kg/f)	5	5	5	5	5
6.	Disintegration time (min)	16.9	15.15	15.12	**15.06**	16.31

TABLE 10: Evaluation of tablet prepared by using STARCH PASTE

Sr. No.	EVALUATION	2%	4%	6%	8%	10%
1.	Bulk density	0.6131	0.6428	0.6728	0.7243	0.6982
2.	Tap density	0.8175	0.8423	0.8665	0.8947	0.8227
3.	Compressibility index (%)	25	23.68	22.35	19.04	15.33
4.	Angle of repose (°)	35.03	33.67	33.13	32.65	31.31
5.	Hardness (kg/f)	6	6	6	5	5
6.	Disintegration time (min)	20	18.54	18.20	**16.51**	22.21

vi. POST COMPRESSION PROPERTY

TABLE 11: DISINTEGRATION TIME of tablets prepared by using FLAXSEED MUCILAGE and STARCH PASTE at DIFFERENT CONCENTRATION

Concentration	Mucilage	Starch
2%	16.9	20
4%	15.15	18.54
6%	15.12	18.20
8%	**15.06**	**16.51**
10%	15.31	22.21

Fig. 3: Effect of hardness of tablet prepared by using Flaxseed mucilage and Starch paste.

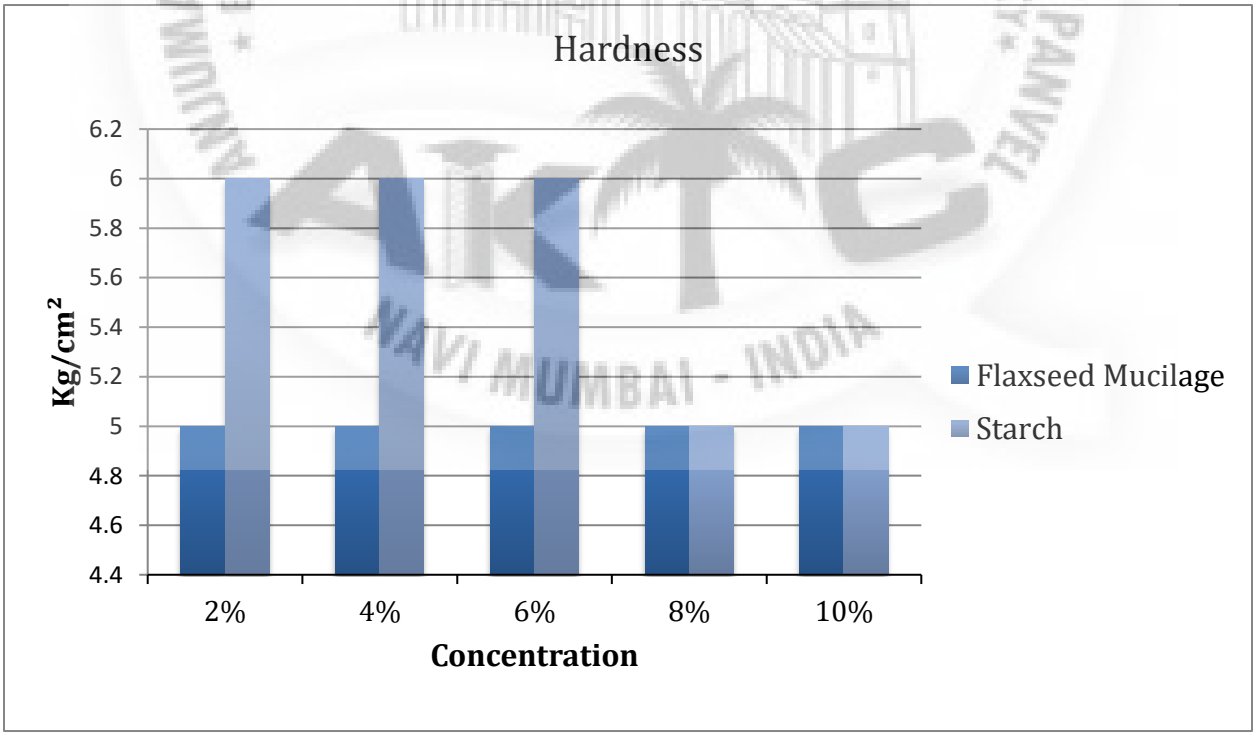
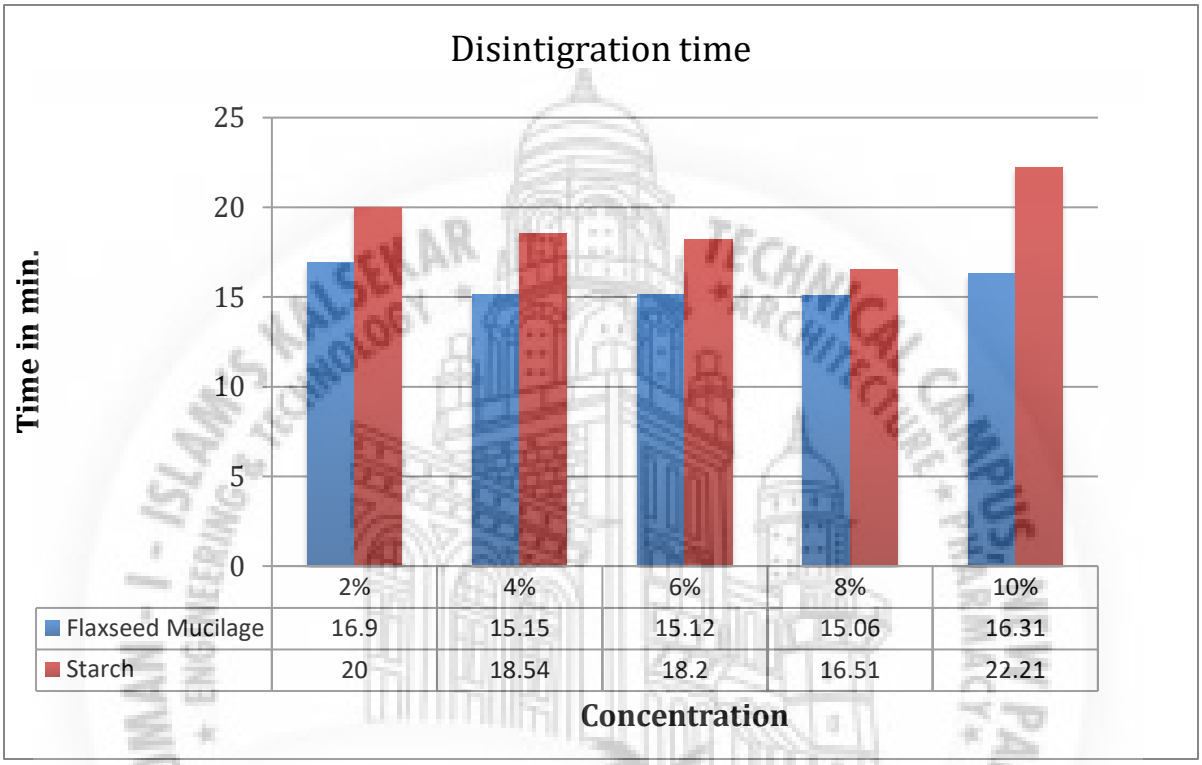


Fig. 4: Comparison of disintegration time of tablet prepared by using FLAXSEED MUCILAGE and STARCH PASTE at different concentration.



6 DISCUSSION

I. Extraction of Linseed mucilage:

As shown in **Table no.3**:

- Extraction of mucilage was done by METHOD 4 and resulting material obtained was squeezed by muslin cloth. Mass obtained was found **of yellow color with thick consistency**.**(Fig. 5)**

II. Isolation of mucilage:

As shown in **Table no.4**:

1) Followed by same process of Extraction of Mucilage (Method 1) that wassqueezed through muslin cloth was used for further isolation methods:
   Firstly by acetone was added in the filtrate to obtain dried powder form. This did not give appropriate result as the separated mucilage was not found in powdered form, **moist form of product** was obtained. **(Fig. 6)**
2) The sameprocedure was repeated by using ethyl alcohol in place of acetone and slime like consistency of mucilage was obtained which was further dried as shown in **fig. 7**, but this did not give appropriate powdered form.
3) The same procedure was repeated, but this time ethyl alcohol and acetone mixture was added in the ratio (1:1) to the filtrate still powdered
4) form of mucilage was not found. Product obtained was **sticky and un-filterable. (Fig. 8).**
5) Further mucilage was extracted from the pure powder which was prepared by blending whole dried flaxseed seeds by different method which was summarized in the above Extraction of Mucilage Method. (Method 5) The mucilage obtained by this process was not clear as it contains seed coat and the mucilage obtained was **un- filterable**. **(Fig. 9)**
6) Then lastly extraction was done by soaking the seeds in distilled water (as mentioned in Method 6), the soaked seeds were boiled to release mucilage, this **pure form of mucilage**was used for further procedure.
7) Mucilage obtained appeared **glossy and clear** and this pure form of mucilage was used as a disintegrating agent. **(Fig. 10).**

Fig. 5: Yellowish thick mass of mucilage

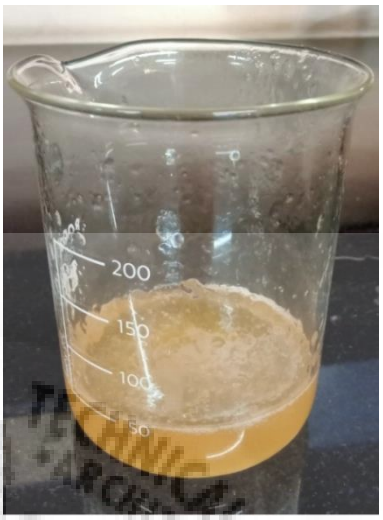


Fig. 6: Moist form of Mucilage

Fig. 7: Dried form of mucilage

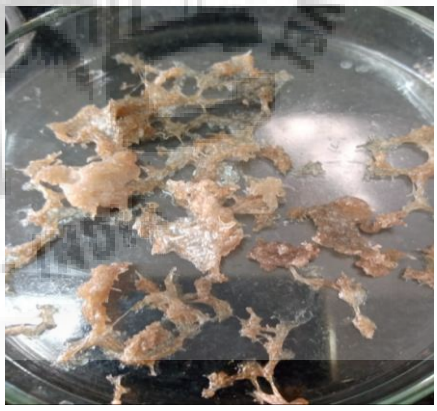
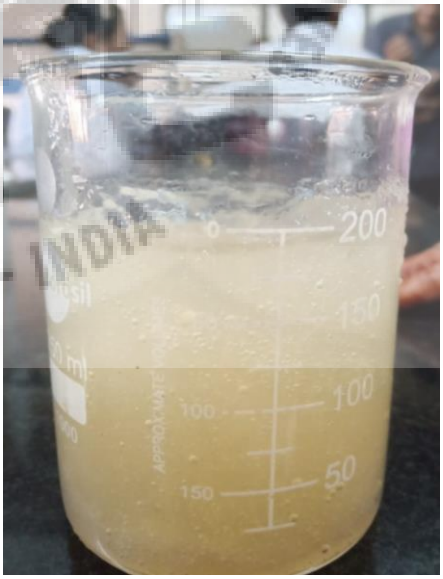


Fig 8: Sticky form of mucilage

Fig 9: Sticky and un-filterable form of Mucilage

Fig10: Pure form of mucilage



III. Microbial Content:

1) Microbial content of Flaxseed Mucilage was performed by using **Nutrient Agar** as media.
2) The cultivation, isolation, and separation of micro-organismwas done by Streak plate technique.
3) The growth of micro-organisms was observed after incubation. **(Fig. 11)**
4) The isolated colonies and characteristics such as color, size, shape, elevation,consistency, and opacity were observedas shown in **Table No. 5.**

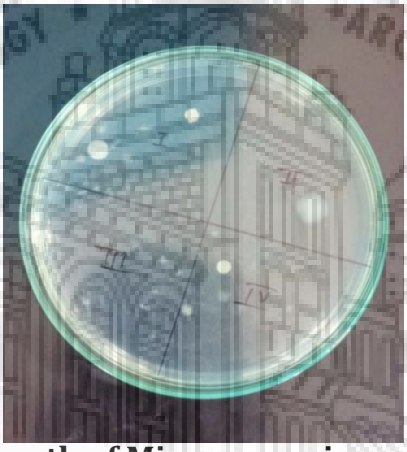


Fig. 11: growth of Micro-organisms after Incubation

IV. Chemical test of Flaxseed Mucilage and Flaxseed powder:

1) Chemical test result of flaxseed mucilage for Molisch's, Benedict's and Bromine test were found negative. Since carbohydrate, glucose, galactosewereabsent in flaxseed mucilage.
2) Similar tests were performed for flaxseed powder and the test results werefound positive; which shows presence of carbohydrate, glucose, galactose etc.

- Results observed were as shownin **Table No.6**.

V. Formulation of Tablets:

i. Tablet formulations:

1) Tablet formulations, each containing concentration of 2, 4, 6, 8, 10% of flaxseed mucilage and Starch Paste, were developed successfully as given in **Table No. 7& 8.**

ii. Wet Granulation:

1) Flaxseed mucilage was investigated as a disintegrating agent in tablet prepared by wet granulation method and its disintegrating property was compared with established disintegrant such as Starch.
2) Flaxseed mucilage and Starch paste granules were prepared by wet granulation method using Lactose as binder in sufficient quantity and evaluated for its physical characterization before compression.
3) Composition of formulation prepared by using Flaxseed mucilage and Starch paste were as shown in **Table No. 7 & 8**.

iii. Compression:

1) Tablets were compressed using 9 mm round flat punches on Single Stroke Tablet Press. The calculation was made for 30 tablets in each batch.
2) The formulations of tablets at different concentration were as shown in **Table no. 7 & 8**.

VI. Evaluation of the tablets:

i. Evaluation of Appearance

1) Tablets prepared by using Flaxseed mucilage were yellow in color, smooth, and flat shaped in appearance.
2) Tablets prepared by using Starch paste were pale white in color, smooth, and flat shaped in appearance.

VII. Evaluation of flow property

- The flow properties of the prepared granules (prepared by wet granulation) using Flaxseed mucilage and starch paste as tablet disintegrant was studied and results were shownin **Table no. 9& 10**.

i. Bulk density:

1) Bulk density of granules prepared by Flaxseed mucilage was obtained in the range of 0.54 to 0.69,
2) Bulk density ofgranules prepared by starch paste was obtained in the range of 0.61 to 0.72.

ii. Tap density:

1) Tap density of granules prepared by Flaxseed mucilage was obtained in the range of 0.69 to 0.81.
2) Tap density of granules prepared by starch paste was obtained in the range of 0.81 to 0.89.

iii. Compressibility's index:

1) Compressibility's index of granules prepared by Flaxseed mucilage formulations was obtained in the range 12.08 to 23.07%.
2) Compressibility's index of tablets prepared by starch paste formulations was obtained in the range 15.33 to 25%.

iv. Angle of repose:

1) Angle of repose of all the granules prepared by Flaxseed mucilage formulations was found to be in the range of 25.65 to 26.65.
2) Angle of repose of all the granules prepared using Starch paste was found to be in the range of 31.31 to 35.03.

- The obtained result has shown that the granules formulation prepared by using flaxseed mucilage exhibited good flow property as compared to granules formulation prepared by using starch paste.
- This result indicates that use of flaxseed mucilage as a disintegrating agent does not affect the flow property of powder.

VIII. Post compression property

i. Hardness test

1) The hardness of the entire Tablets prepared using flaxseed mucilage formulated tablet was within the limits.
2) The hardness of the Tablets prepared using starch paste varies between 5-6 kg/cm^2.
3) The hardness of the tablet was also increased with the increase in percentage of starch paste as binding agent.

4) Hardness observed in tablets prepared by using flaxseed mucilage was acceptable and comparatively better than tablets prepared by using starch paste as observed in **Fig.3**.
5) The Result shows that Flaxseed mucilage was more effective disintegrant as compared to starch paste as observed in **Table No. 9 & 10.**

ii. Disintegration test

1) The separated Flaxseed mucilage was evaluated for its disintegration action in tablets at various concentrations (2, 4, 6, 8, and 10%).
2) As per IP monograph the disintegration time for uncoated tablet must be within 15 min.
3) Disintegration time at 8% is found to be **15min 6 sec** which was within limit.
4) Also the time requires for tablets prepared by using flaxseed mucilage at 8% concentration was comparatively less than tablets prepared by using starch paste. It was found that at the equal concentration of flaxseed mucilage shows greater disintegrant property.
5) Results in **Table no. 11** indicates that disintegration time decreases with the increase in the concentration of flaxseed mucilage till 8% concentration.
6) But result shows that in more concentration (10%) tablets prepared by using flaxseed mucilage and starch paste was more effective as binder as compared at low concentration, hence the disintegration time for 10% was increased for both tablets formulation.
7) As shown in **Fig. 4** the comparative study of the tablets prepared by using Flaxseed mucilage with starch paste as disintegrant at similar concentrations revealed that Flaxseed mucilage was better disintegrant than starch paste.

7 CONCLUSION

- From the study conducted, it was concluded that *Linum Usitatissimum* seed (Flaxseed) mucilage can be used as a disintegrant to prepare solid oral dosage forms.
- Many studies carried so far (as per literature) including flaxseed in pharmaceuticals and in food industries suggested that it showed promising results as disintegrant,
- This study concluded that the mucilage separated from *Linum Usitatissimum* seed could be used as a tablet disintegrant, as it shows very good disintegrating property.
- The mucilage obtained by using mixture of ethyl alcohol and acetone (1:1) was not clear as it contained seed coat and mucilage obtained was sticky and un-filterable. Hence tablets were prepared by using direct diluted form of mucilage.
- Evaluation tests were carried out which were shown in table 9&10.As per IP monograph and it was concluded that after increase in concentration at increasing concentration ofmucilage shows binding property and worked as binder instead of disintegrant, hence formulation at 10% concentration required more time to disintegrate.
- Comparative evaluation studies proved that concentration of 8% mucilage in preparation of tablets shows least disintegration time (15.06 min) as compared to tablets prepared by starch paste.
- As the mucilage obtained was from plant origin which contained some microbial load and hence addition of preservative is required.

8 FUTURE SCOPE

- Further research can be done for comparative study of isolated mucilage with other naturally occurring disintegrant.
- Also, various active pharmaceutical ingredients can also be used for studies to know about the disintegration property and compatibility with other naturally occurring disintegrant.
- Various study regarding the shelf life and effect of microbial attack can be evaluated in presence of different excipients and preservative.
- The mucilage can be used in various pharmaceutical formulations which eventually is cost effective as compared to that of synthetic disintegrant.
- So, this mucilage can be used as a natural disintegrant in future studies to compare various parameters in presence of different excipients.

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10 APPENDIX

Now a days, a large number of pharmaceutical drugs are converted into suitable dosage form by using different types of excipients.
As natural materials are cost effective, non-toxic, stable, easily available with less regulatory issues, eco-friendly, capable of multiple chemical modifications , degradable and compatible due to their natural origin, so they have been gaining a lot of importance in the field of drug delivery.

The synthetic excipients are continuously being replaced with natural ones as recent trend towards the use of vegetable and non toxic products increased use.

The use of flaxseed as potential nutraceuticals is growing due to evidence of its various beneficial effects. The seeds of flaxseed contain high amount of soluble mucilage.

Flaxseed mucilage represents 23% of the seed and is found in the seed coat. It can be used in various formulations due to its beneficial property in reducing cancer, risk of CHD, diabetes, inflammatory diseases, to reduce serum cholesterol levels in further studies.

ACKNOWLEDGMENT

We would like to take the opportunity to express our sincere thanks to our guide **Prof. Samreen Khan**, Department of Pharmaceutics, AIKTC, School of Pharmacy, Panvel for her invaluable support and guidance throughout our project research work. Without her kind guidance & support this was not possible.

We are grateful to her for her timely feedback which helped us track and schedule the process effectively. Her time, ideas and encouragement that she gave has helped us to complete our project efficiently.

We would also like to thank **Dr. Abdul Razak Honnutagi; AIKTC, Panvel**, for his encouragement and for providing an outstanding academic environment, also for providing the adequate facilities.

We are thankful to **Dr. Shariq Syed, Dean, School of Pharmacy, Panvel** and all my B. Pharmacy Professors for providing advice and valuable guidance.

We also extend our sincere thanks to all the faculty members and the non-teaching staff and friends for their cooperation.

Last but not the least, we are thankful to all our family members whose constant support and encouragement in every aspect helped us to complete our project.

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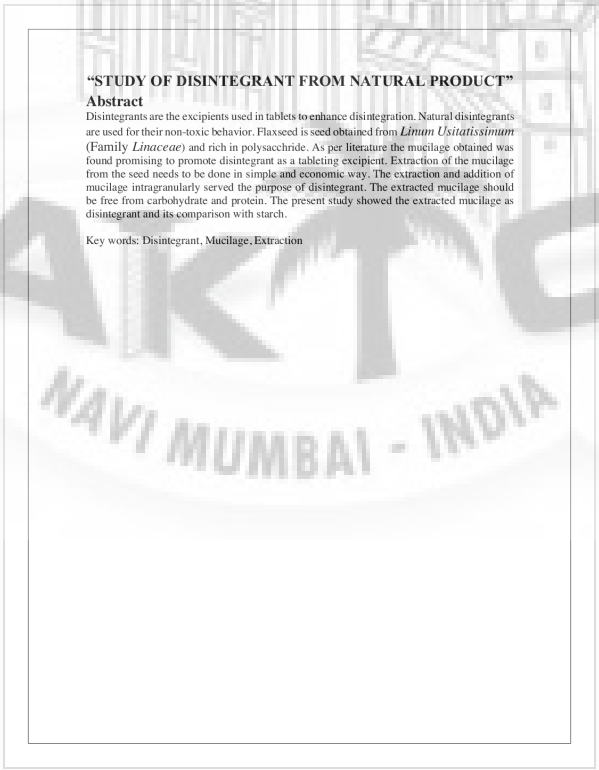

"STUDY OF DISINTEGRANT FROM NATURAL PRODUCT"

Abstract

Disintegrants are the excipients used in tablets to enhance disintegration. Natural disintegrants are used for their non-toxic behavior. Flaxseed is seed obtained from *Linum Usitatissimum* (Family *Linaceae*) and rich in polysacchride. As per literature the mucilage obtained was found promising to promote disintegrant as a tableting excipient. Extraction of the mucilage from the seed needs to be done in simple and economic way. The extraction and addition of mucilage intragranularly served the purpose of disintegrant. The extracted mucilage should be free from carbohydrate and protein. The present study showed the extracted mucilage as disintegrant and its comparison with starch.

Key words: Disintegrant, Mucilage, Extraction