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Research article

### Monoherbal Formulation Development for Laxative activity

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#### ABSTRACT

The Ayurvedic Pharmacopoeia specifically approves flaxseed as a poultice for boils externally and demulcent or laxative internally. In this study monoherbal formulation development for laxative activity of flaxseed was undertaken. The plant *Linum usitatissimum* has showed higher percentage of total ash as well as alcohol soluble extractive values. The aqueous extract of *Linum usitatissimum* was prepared by using pilot scale extraction plant and spray drying unit. The qualitative phytochemical studies reveal the presence of amino acids, carbohydrates, vitamins and proteins. From the available literatures it was found that *Linum usitatissimum* contains more number of amino acids. The formulated tablets showed acceptable pharmacopoeial limits and complies with specifications for thickness, hardness, friability and weight variation. The formulation has showed better laxative activity indicating additive property of the combined phytoconstituents of the plant.

**Keywords:** Flaxseed, *L.usitatissimum*, Laxative activity.

#### INTRODUCTION

Constipation is common in 1-6 % middle aged and 20-80% of the elderly people. It is a main symptom of irritable bowel syndrome in all ages; the functional constipation is the most common type without any specific etiology. Dietary fiber has been suggested to be the first line treatment for irritable bowel syndrome starting from 1970's to 1980's and reported that the addition of 7 grams of fiber in the form of wheat bran to the diet of such patients for six weeks resulted in significant improvement in symptoms.<sup>1</sup> Flaxseed is rich in  $\alpha$ -linolenic acid and soluble and insoluble fiber and is therefore of considerable nutritional value<sup>2</sup>. During the last decade, there has been an increasing interest in the use of flaxseed (*Linum usitatissimum* L., Linaceae) in the diet in order to improve the nutritional and health status.

Flaxseed contains secoisolariciresinol di glucoside (SDG), a potent antioxidant and known precursor of the mammalian lignans, enterolactone and enterodiol<sup>3</sup>. These compounds have other pharmacological properties including phytoestrogens properties, similar to isoflavones. SDG

prevents the development of hypercholesterolemic atherosclerosis. New technologies can produce products that extend the nutraceutical properties described to flax seed with minimizing drawbacks associated with the consumption of whole flaxseed which are usually consumed with baked goods which damages the EFA's and other healthful components. Correctly processed raw flaxseed can have reduced levels of the strong laxative for the purgative effects normally associated with cyanogenic glycoside mucilage components of flaxseed. The fibre content in flaxseed has significant positive impacts in reduction of total cholesterol and low-density lipoprotein (LDL) cholesterol levels by 22% and 24.38% respectively. Besides that, flaxseed has anti-inflammatory and laxative effects. It is also postulated that flaxseed relieves menopausal symptoms, for example hot flashes and vaginal dryness, and osteoporosis<sup>4</sup>. Flaxseed consists of 40 to 45% of oil, 20 to 25% of fibres, 20 to 25% of proteins, and 1% of SDG<sup>5</sup>.

The Ayurvedic Pharmacopoeia specifically approves flaxseed external use as a poultice for

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boils and internal use as a demulcent or laxative<sup>6</sup>. From the available plethora of literatures, it's evident that there is a need for the development of proper medication and dosage form for the

treatment of constipation. Hence the project monoherbal formulation development for laxative activity was undertaken using flaxseed seed.

## Plant Profile



Figure 1. Image of *Linum usitatissimum* seeds.

### *Linum usitatissimum* Linn<sup>7</sup>.

Synonym	: Flaxseeds, linseed
Tamil	: Allivirai
Family	: Linaceae
Hindi	: Alsi, Tisi.
Kanada	: Alasibija

## MATERIALS AND METHODS

### Collection of plant material

*Linum usitatissimum* Linn., was purchased from Yucca Enterprises Mumbai. The flax seeds were coarsely powdered and stored in a suitable container for further studies.

### Physiochemical Constant Determination

The physiochemical constants like ash values (total ash, acid insoluble ash and water soluble ash) and extractive values (alcohol soluble and water soluble extractives) were carried out and reported<sup>8</sup>.

### Extraction of linseed by pilot scale extraction plant

The linseed raw material was cleaned, washed and crushed into coarse powder. 10 kg of coarse powder was soaked with 80 liters of purified water (1:8) and kept aside for overnight. The perforated plate of the extractor in the extraction plant was covered with coir mate and the coir mate was covered with cotton cloth to filter the decoction and retain the material for further extraction. The soaked raw material was transferred into the extractor, the extractor was made up of stainless steel with steam jacketed (Seico Enterprises with 100 lit capacity). The content of the extractor was boiled by using steam, which is generated

through the boiler. The water circulation for the condenser was started from the cooling tower. The temperature was maintained at 100<sup>0</sup>C throughout the experiment. The first extraction was carried out for 4 hrs and the decoction was removed and transferred into the concentrator. Once again 40 liters of water was added to the extractor and the extraction was carried out for another 2 hours. The decoction was removed from the extractor and transferred to the concentrator. The first and second volume of decoction was mixed and concentrated upto 30% of solid content.

### Spray drying of Linseed extract<sup>9</sup>

The decoction was transferred into the feed tank of pilot scale spray drying unit (Hemraj Enterprises Mumbai - 4 lts/hr capacity). The body of the drying chamber was heated by keeping the required temperature at 120<sup>0</sup>C inlet temperature and 130<sup>0</sup>C outlet temperature. The temperature was set in the panel board and the inlet and outlet fan was switched on. The spraying efficiency was checked with water before transferring the decoction. After adding the decoction, the spraying efficiency was checked once again in the outside. Once the outlet temperature reached at 100<sup>0</sup>C, the nozzle was placed into the chamber from the top. The mechanism of the drying was co-current, both the

hot air and the spray takes place in the same direction. The dried powder was separated from cyclone separator and collected in the plastic jar. The excess air was exhausted by the exhaust motor through the scrapper tank. The size of nozzle used was 1.5 mm.

### Formulation Development

The chewable tablets containing known quantities of the selected excipients were prepared by wet granulation technique using a rotary tableting machine<sup>10</sup>. The quantity of extract and the excipients used for formulating 250 tablets is tabulated in table 1.

**Table 1. Composition of chewable tablet formulation**

<b>Ingredients</b>	<b>Qty (mg)</b>
<i>Linum usitatissimum</i> extract	750
Starch paste	20
Sugar	15
Sodium benzoate	1
Micro crystalline cellulose	10
Starch	579
PVP	20
Ethyl cellulose	20
Color (tartrazine yellow)	5
Sodium starch glycolate	10
Aerosil	20
Sodium saccharine	25
Flavor (Banana flavor)	10
Talc	10
Magnesium stearate	5
Total Weight (mg)	1500

### Pre-formulation Studies of the Granules.

The overall objective of pre-formulation testing is to generate information useful to the formulator in developing stable and bioavailability dosage form, which can be mass-produced obviously, the type of information needed depend on the dosage form to be developed. In the present work the pre-formulation studies viz: angle of repose, bulk density, fines and loss on drying was carried out<sup>11</sup>.

### Evaluation of Formulation

The prepared tablet formulations were subjected to various physical evaluations like weight variation, hardness, friability test and disintegration time as per the procedure given in Indian Pharmacopoeia and reported<sup>12</sup>.

### Pharmacological Screening

#### Acute Toxicity Study

The acute toxicity study was carried out by OECD guideline no.423 (OECD guideline 423, 2000)<sup>13</sup> for aqueous extract of *linum usitatisimum*. It was

observed that the test extract was not lethal to the rats even at 2000 mg/kg dose.

### Laxative Screening

The experiment was performed according to Capasso et. al. (Capasso et. al., 1986)<sup>14</sup> with slight modifications. Albino rats of Wistar strain, either sex were used to evaluate the laxative activity. The animals were fasted for 12 hour before the experiment, but provided with water ad libitum. The animals were divided into 4 groups of six in each and were placed individually in cages lined with clean filter paper. The animal groups were treated orally with Control (Group I Normal saline, 2 ml p.o.), reference standard drug agar-agar (Group II 300 mg/ kg, p.o.) and tablet formulation (Group III 750 mg/kg, p.o) respectively. Immediately after dosing, the animals were separately placed in cages suitable for collection of faeces. After 8 hour of drug administration, the faeces were collected and weighed. Thereafter, food and water were given to all rats and faecal

outputs were again weighed after a period of 16 hour<sup>15, 16</sup>.

### Statistical Studies

Data were expressed as mean  $\pm$  SEM. The differences were compared using one-way ANOVA followed by student's t-test.  $P < 0.05$ .

## RESULTS AND DISCUSSION

### Physicochemical Constant Determination

To establish the identity and purity of the raw material used for the various physicochemical parameters such as ash values and extractive values were evaluated and reported in table 2&3. The results revealed that the plant *Linum usitatissimum* shows higher percentage of total ash (3.212% w/w) as well as alcohol soluble extractive values (7.61% w/w) compared to other parameters.

Table 2. Different ash values of *Linum usitatissimum*

S.No	Ash values	Ash value in %w/w <i>Linum usitatissimum</i>
1	Total ash	3.212
2	Water soluble ash	0.294
3	Acid insoluble ash	2.677
4	Sulphated ash	0.241

Table 3. Different extractive values of *Linum usitatissimum*

S.No	Types of extractives	Extractive value in %w/w <i>Linum usitatissimum</i>
1	Alcohol soluble extractive	7.610
2	Water soluble extractive	4.211

### Extraction and Spray drying

The percentage yield of the flaxseed extract was found to be 4.6% w/w

### Formulation Development

#### Pre-formulation Studies

The pre-formulation studies were carried out for the prepared granules like angle of repose, bulk density, moisture content, fineness ratio and the results are complying with pharmacopoeia standards. The results suggested that the granules were of good physical properties like flow and cohesion. The results are tabulated in table 4.

Table 4. Results of pre-formulation studies

Formulation	Angle of repose ( $\theta$ )	Loose bulk density (g/ml)	Tapped bulk density (g/ml)	Carr's index (%)
Granules	24.52	0.432	0.482	12.19

### Evaluation of Formulations

The physical parameters like average weight, hardness, friability test and disintegration time were carried out for tablet formulation. All the

parameters were complies with Indian Pharmacopoeia standards. The formulated tablets were found to have good physicochemical properties and the results are reported in table 5.

Table 5. Physical evaluation of the tablets

Formulation	Thickness (mm)	Hardness (kg/cm <sup>2</sup> )	Friability (%)	Weight variation (%)	Disintegration Time (Min)
Tablet	4.0	5.4	0.65	1.852	13.05

### Laxative Activity

The laxative activity of the tablet formulation was evaluated by observing the faecal output. It was observed that after 8 hours of treatment, tablet treated group (1000 mg/kg p.o.) exhibited higher faecal output (126.41±1.038) compared to control (36.55±0.756) but lower faecal output when

compared to agar-agar (166±2.720). After 8-16 hours test drug exhibited increase in faecal out-put (214.52±1.072), while agar-agar treated groups showed less faecal output (164.46±1.230). Hence, tablet formulation showed significant laxative activity (P<0.01) at 750 mg/kg dose level when compared to the control. The results are tabulated in table.6.

**Table 6. Laxative activity of *Linum usitatissimum***

<b>Faecal Output (mg) after drug administration</b>		
<b>Treatment</b>	<b>8 hours</b>	<b>8-16 hours</b>
Control (Normal Saline)	36.55±0.756	96.51±1.186
Tablet (750 mg/kg)	126.41±1.038*	214.52±1.072*
Agar-agar (300 mg/kg)	166±2.720	164.46±1.230

**Values are Mean ± SEM, n = 6, \* P <0.05**

### CONCLUSION

The plant *L.usitatissimum* has showed higher percentage of total ash as well as alcohol soluble extractive values. *L.usitatissimum* extract was prepared by using pilot scale extraction plant and spray drying unit. The formulated tablets showed acceptable pharmacopoeia limits and complies with specifications for thickness, hardness, friability and weight variation. The formulation has showed better

laxative activity indicating additive property of the flaxseed.

*Linum usitatissimum* seed has a tremendous scope on further studies mainly in the area of nutraceuticals and dietary supplements, because it contains many amino acids, carbohydrates, fatty acids, vitamins and minerals etc., therefore further research work to be carried out on this plant towards above said field.

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