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FORMULATION AND EVALUATION OF HERBAL DRUG LOADED TOPICAL DRUG DELIVERY SYSTEM FOR BETTER TREATMENT OF WOUNDS

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ABSTRACT

Herbal formulations are dosage forms that contain one or more herbs or processed herbs in specific amounts to provide specific nutritional or cosmetic benefits, and are intended for use to diagnose, treat, or mitigate diseases in humans. Emulgel, also known as gelified emulsions (of the oil-in-water or water-in-oil type), is created by the addition of a gelling agent. Powdered drug was treated with different reagents and the colour changes were observed and tabulated in table. Physico-chemical Characters of Linum usitatissimum seed extract Total ash, Acid insoluble ash, Water insoluble ash, Loss on Drying was found to be 10.61, 1.25, 6.35 and respectively 4.5 w/w. Different Physicochemical evaluation parameters of formulated emulgel were examined by standard methods and results were shown in table. The formulation FE-3 was found to have good spreadibality, viscosity and Stability study and can be further used for wound healing. Further examinations should be possible to assess the various investigations on Linum usitatissimum various parts.

KEYWORDS: Herbal, Linum usitatissimum, Emulgel, skin, wound healing.

INTRODUCTION

The utilization of helpful plants across many societies has been irrefutable, and this use has happened even without an exhaustive comprehension of the compound creation and exact physiological activities of the plants.[1] Considering that plant drugs have been utilized for centuries, there is a high predominance of home grown treatment because of social acknowledgment.[2] There are somewhere in the range of 1:200 and 1:400 home grown medication professionals per 100,000 individuals in countries like Zambia, Tanzania, and Uganda. In any case, there are something like 1:20,000 professionals of western medication.[3] As per a 1991 review, there are 100 to 1 additional sub-Saharan African conventional specialists than western practitioners.[4] as opposed to costly western prescription, natural medication has kept on being reasonable.[5] The provincial populace in overpopulated countries, similar to India, has basically no admittance to present day therapy; subsequently, they are compelled to depend on natural medication for their fundamental clinical prerequisites.[6]

Skin

Skin has three significant purposes: insurance, guideline, and feeling. It is a layer of commonly delicate, adaptable external tissue that covers the body of a vertebrate creature.[7] Originally, "skin" exclusively applied to ready and tanned creature stow away, while the expression "stows away" was utilized to portray human skin. Old Norse skinn, signifying "creature stow away, fur," and the Proto-Indo-European root *sek-, and that signifies "to cut," are the wellsprings of "skin."[8]

Structure in humans

Mammal skin consists of two main layers:

- The epidermis, which waterproofs and acts as an infection barrier.
- The dermis, which is where the skin's protrusions are located.

Wound

An injury is a physical issue with an unexpected beginning that includes penetrated or cut skin (a serious injury) or an injury (a contained injury) brought about by pressure or gruff power injury. An injury is a serious sore in pathology that influences the skin's epidermis.[9]

Types of wounds

A wound's amount of contamination determines its classification :

- Clean wound – produced in sterile settings, where no organisms are present, and the skin is likely to recover well.
- Contaminated wound – Usually the consequence of an accident, the wound contains harmful organisms and other objects.
- Infected wound – Pathogenic organisms are present and growing in the wound, showing clinical indications of infection (yellow appearance, soreness, redness, oozing pus).
- Colonized wound – a persistent condition with harmful organisms that is challenging to repair (e.g. bedsore).[10]

Management

The nature, etiology, and profundity of the injury, as well as whether different designs other than the skin (dermis) are impacted, all influence the general course of treatment. Ongoing gashes require assessment, wound purging, and conclusion. Minor wounds like injuries will normally recuperate, and skin staining will frequently disappear in 1 fourteen days. However long the district is kept spotless, first with cleanser and water, scraped areas, which are wounds with solid skin (non-infiltration through dermis to subcutaneous fat), frequently needn't bother with any dynamic treatment. Contingent upon the level of entrance, stabbings might be helpless to contamination. To permit microorganisms or garbage to be eliminated from inside the cut, the entry is left open.[11]

Benefits of the topical route of drug administration[12]

Topical medication administration has a wide range of advantages. The use of a topical medication delivery system has the following five advantages.

- An alternative to oral dosage
- Less likelihood of experiencing digestive issues
- Less chance of misuse
- Convenient to use
- Lessening of hospital traffic

Collection of plant material

Linum usitatissimum was taken from the National Botanical Research Institute's Botanical Garden in Lucknow, Uttar Pradesh, and cleaned with pure water. The plant's dried-out and diseased components were removed.

Preparation of the extracts

The extract was concentrated below 60^0C after being extracted in a Soxhlet apparatus with a maximum temperature of 60^0C. The gathered seeds were cleaned, air dried, and ground. For powder microscopy, the gathered fine powder is employed.

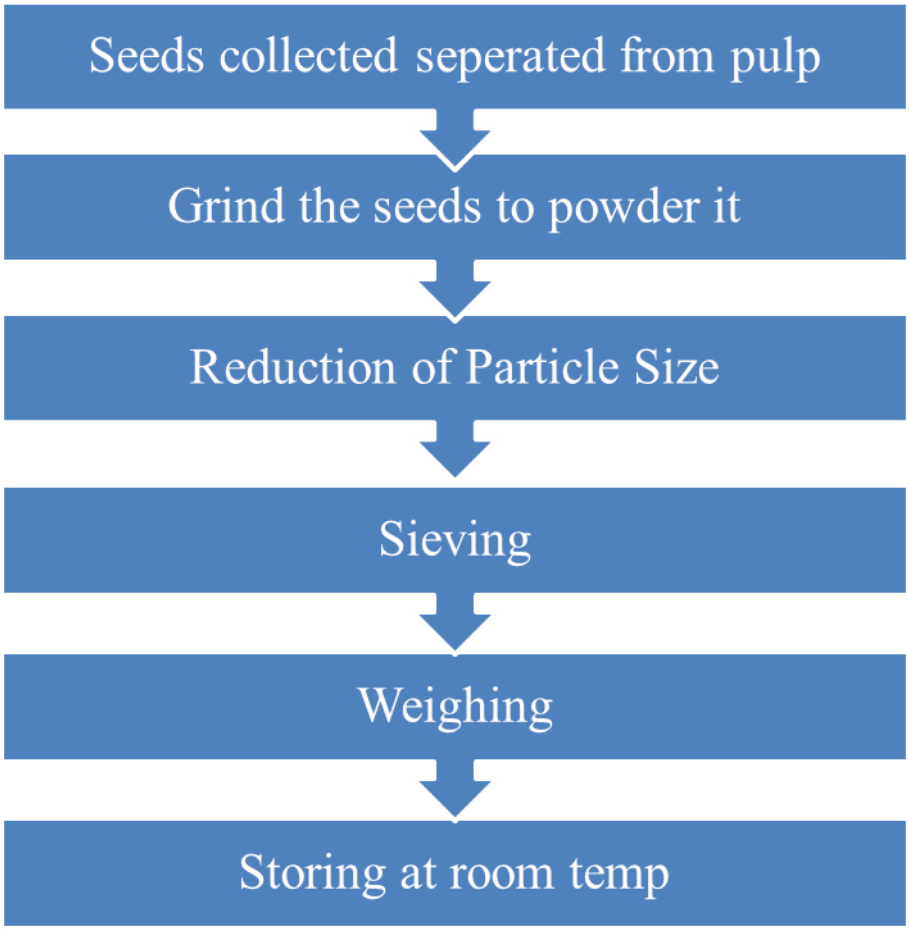


Figure 1: Preparation of the extracts.

Standardization of extract

According to procedures outlined in the Indian Pharmacopoeia, macroscopical aspects related to form, size, texture, colour, surface properties, and fracture were tested for sample identification and purity using various chemical solvents.[13]

Determination of Ash Values

Just the appraisal of debris esteem considers the assessment of unrefined prescriptions. Debris values can be utilized to survey the virtue and nature of a rough drug, especially on the off chance that it is accessible in powdered structure. The motivation behind ashing unrefined drugs is to dispose of any natural garbage that could obstruct a scientific outcome.

The debris that outcomes from consuming unrefined meds commonly contains carbonates, phosphates, and silicates of sodium, potassium, calcium, and magnesium. Higher debris focuses show conceivable defilement, debasement, replacement, or carelessness in the development of the crude prescription. The three following strategies were utilized for investigation.[14]

Total ash value

A silicon cauldron that had been tarred, lit, and cooled prior to getting an example of approximately 2-3 gms of exactly gauged, finely powdered root powder was utilized to compute the complete debris esteem. The temperature of the pot was held under 5000C. Subsequent to being chilled in a desiccator for 30 minutes, the subsequent buildup was gauged. Up until a consistent weight was felt, the whole interaction was rehashed. To register the complete debris esteem, the air-dried material was utilized as a kind of perspective. How much debris in a rough medication lets you know how cautiously it was made. Especially when silica might be available or when the medication's calcium oxalate focus is especially high, a more noteworthy constraint of corrosive insoluble debris is added. Prior to ashing, a few examinations prompted joining acids like sulphuric corrosive with the powdered unrefined drug as sulphated debris is frequently less combustible than ordinary ash.[15]

Water solvent debris

The total debris from the principal stage was warmed in 25 cc of water for 5 minutes. The obtained insoluble material will next be accumulated utilizing debris free channel paper. Yet again washed in steaming hot water, it is then lighted for 15 minutes at a temperature no higher than 4500C, let to cool, and gauged. This weight was deducted from the general measure of debris' weight. The level of water solvent debris will be figured regarding the air-dried medicine and the water dissolvable debris esteem was gotten from the weight distinction.[16]

Acid insoluble values

The subsequent value was delicately warmed for 5 minutes in a pot finished off with a watch glass with 30 cc of weakened hydrochloric corrosive. Around 5.0 cc of heated water were available in the watch glass, and this boiling water was put to the cauldron. On channel paper with no debris, the insoluble debris will be accumulated. The procured buildup was cleaned with heated water, set ablaze, permitted to cool in a desiccator, and afterward gauged. Concerning the medication that has been air dried, the extent of corrosive insoluble debris

still up in the air. The buildup that stayed insoluble was moved to the first cauldron, dried on a hot plate, and consumed to a reliable weight. After the buildup had cooled in a reasonable desiccator for 30 minutes, it was promptly gauged. How much corrosive insoluble debris in every gram of the air-dried material was assessed.[17]

Extractive Values

To explore the dissemination of a few Linumu Usitatissimum seed items and the definition's all's unrefined components, the extractive qualities in liquor and water were recorded. The amount of the dynamic fixings in the unrefined prescription was determined utilizing this methodology. The extractive worth is utilized to evaluate unrefined drugs that are hard to survey utilizing different methods. For example, the extractive worth of every rough medication has a characterized range; a reduction in that worth suggests the expansion of unwanted or depleted material to the first medication or ill-advised handling of the medication during the drying, stockpiling, and so on processes. The buildup was quickly weighed in the wake of drying at 105°C for 6 hours and cooling in a desiccator for 30 minutes.

Water soluble extractive

100 ml of chloroform water and 5 g of previously weighed air-dried medication were put to a stoppered conical flask. On an electric shaker, it was shaken constantly for 4 hours before being filtered quickly to prevent solvent loss. A little over 25 ml of the filtrate was dried to dryness in a petri dish with a flat bottom and tar, dried at 1000°C, chilled, and weighed. With reference to the air-dried medication, the extractive will be determined as a percentage weight-for-weight.[18]

Alcohol soluble extractive

Five grammes of powdered medication were weighed in a weighing vial, transferred to a conical flask measuring 250 millilitres, and 90 percent alcohol was added till the delivery mark in a graduated flask. Flask was corked and left for 24 hours while being periodically shook throughout. After filtering, 25 ml of the filtrate was transferred to a thin porcelain plate that was weighed in order to determine the ash value. This filtrate was dried to dryness on a water bath, dried further at a temperature below 1000C in an oven, chilled in a desiccator, and weighed. The extractive value was computed using the drug's % w/w after it had been air dried.[19]

Moisture Content (Loss on Drying)

A thin porcelain dish that had previously been weighed was filled with around 1.5 g of the powdered medication. It was maintained in a desiccator to cool after being dried in an oven set to 100 to 550°C. The required moisture content was the weight loss. To determine the constant value, the experiment was repeated.[20]

Determination of foreign organic matter

A white tile was evenly wetted with 250 g of the sample without going over it. The sample was examined by unassisted eyes or with a lens (5x or above). The alien biological material was painstakingly isolated. The substance was weighed again after full separation, and the percentage of weight present in the sample was calculated.

Preparation of Emulgel formulation

Carbopol 934 and Tween 80 were dissolved in 50 cc of distilled water in a 1:2 ratio while being continuously stirred. The necessary amount of propylene glycol was dissolved in 5 cc of distilled water by boiling on a water bath and then cooling. preparation of an ethanol-based emulgel formulation.[21]

Table 4.4 Formulations of Gel containing ethanolic extract of linumu usitatissiumum seed extract.

Ingredient	FM-1	FM-2	FM-3
linumu usitatissiumum seed Ethanolic Extract (% w/w)	2.0	2.0	2.0
Carbopol 934	2.0	2.0	2.0
Ethanol(% w/w)	30	30	30
Tween 80(% w/w)	10	10	10
Propylene glycol (%w/w)	15	15	15
Distilled Water	100ml	100ml	100ml

Stability study

Initially For three days, Three distinct formulations (FM1–FM3) were created and kept in an incubator at 25 °C. The formulation FM 2,3 was one of the Three formulas that was quite stable. FM-2,3 was also used for the stability research. Three samples of Formulation FM-2,3 were created and stored at four different temperatures and relative humidity levels: 8°C, 25°C, 40°C, and 50°C + 75% RH. These were examined organoleptically for a month at

various intervals, looking at colour, homogeneity, phase separation, and liquefaction. The samples' pH levels were also examined.[22]

Spreadability study[23]

The instrument, which consists of a wooden block with a pulley at one end, was used to measure spreadability. By using this technique, spreadability was assessed based on the gels' properties of slip and drag. Mutimer et al recommended.'s equipment was used to measure spreadability. It consists of a block of wood with a pulley attached to one end of it. Spreadability was assessed using the "drag" and "sleep" approach. After that, gel was placed between this glass slide and another glass slide with a hook and a set ground slide dimension. For five minutes, a one kilogramme weight was put on top of the two slides to force air out and create a homogenous gel coating between them. On this block, a ground glass slide was mounted. On this slide, test emulgel (4 g) was applied. After that, an additional glass slide with a hook and the same fixed ground side dimension was placed between these two slides, containing the emulgel. The top of this slide was then loaded with weight (50 g). The top slide's time (in seconds) to travel a distance of 6 cm was recorded. Next, spreadability was determined using the formula below.

$S = M.L/T$

where:

S = spreadability,

M = Weight tied to upper slide,

L = Length of glass slides

T = Time taken to separate the slides completely from each other

Viscosity/Rheology[24]

Initially, the spindle number 04 of a brook field viscometer was used to measure the viscosities of eight freshly created formulations (FE-1 to FE-5). Making sure the spindle did not contact the beaker's bottom, the spindle was dropped perpendicularly into the middle of the emulgel mixture and revolved at a speed of 2.5 rpm for five minutes. It was observed the viscosity measurement. After then, four samples of the stable formulation FE-5 were separated (i.e. FE5a, FE-5b). The four samples underwent further viscosity testing, and they were periodically monitored for a month.

Measurement of pH

With the use of a digital pH metre, the pH of several gel compositions was measured. In 100 ml of distilled water, one gramme of gel was dissolved before being let to stand for two hours. Each formulation's pH was measured three times, with the average value being computed.

RESULT

5.1 Organoleptic characteristics of Linum usitatissimum seed extract

Table 5.1 Powdered drug was treated with different reagents and the colour changes were observed.

S.no	Parameter	Result
1.	Odour	Odourless
2.	Powder as such	Light brown
3.	Colour	Brownish
4.	Texture	Rough
5.	Taste	Tasteless
6.	Consistency	Powdered

5.2 Determination of Physico-Chemical Parameters

This phase involved determining different Physico-chemical parameters of chosen plants using accepted practises (Table below). To identify phytochemical ingredients, Linum usitatissimum seed extract was put through physio-chemical and phytochemical screening in the current work. Total ash, acid-insoluble ash, and water-soluble ash values are all included in the ash value. Below is a presentation of the results for moisture content and foreign organic materials. 8.24 percent was found to be the moisture content.

Table 5.2 Physico-Chemical Characters of Linum usitatissimum seed extract.

S.no	Properties	Linum usitatissimum seed extract (w/w)
1.	Total ash	10.61
2.	Acid insoluble ash	1.25
3.	Water insoluble ash	6.35
4.	Loss on Drying	4.5

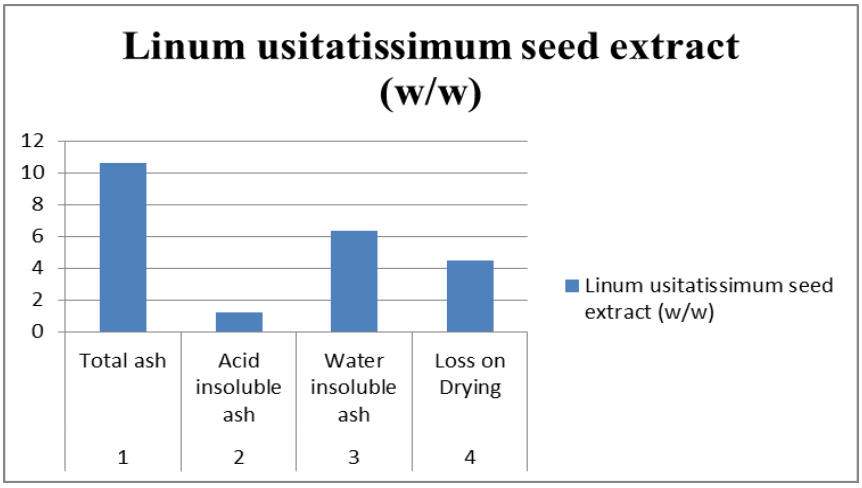


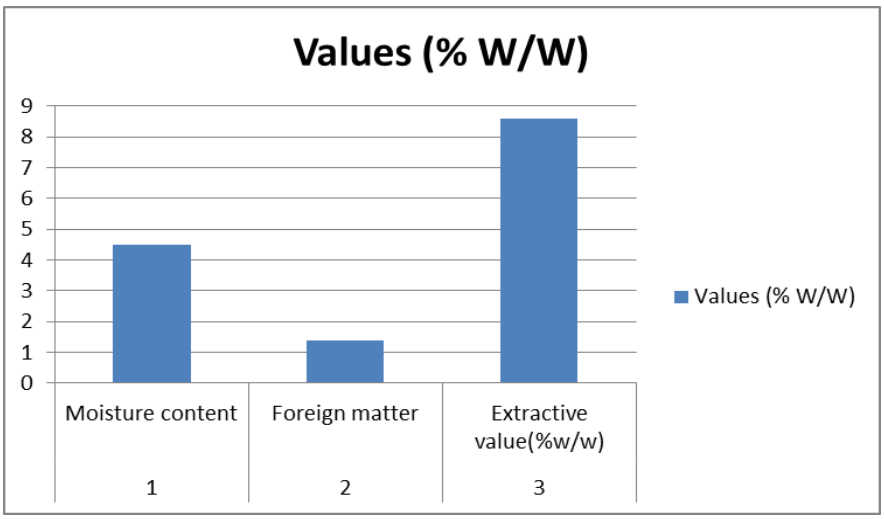
Figure 5.1 Graph of physico-chemical Characters of Linum usitatissimum seed extract.

5.3 Physical constant values of extracts

The table below lists the percentage yields for the powdered Linum usitatissimum seed extracts that were chosen for extraction. The extractive values were calculated using the percentage yield of each extract, and 8.57 percent weight-for-weight with ethanol was found to be the extractive value.

Table 5.3 Extract physical constant values.

S.No	Physical Constant	Values (% W/W)
1.	Moisture content	4.5
2.	Foreign matter	1.37
3.	Extractive value(%w/w)	8.57



5.4 Physicochemical Evaluation of Formulated emulgel

Different Physicochemical evaluation parameters of formulated emulgel were examined by standard methods and results were shown in table:

Table 5.4 Physicochemical evaluation of formulated emulgel.

S.no	Parameters	FM-1	FM-2	FM-3
1.	Colour	creamish white	creamish white	creamish white
2.	Consistency	Smooth	Smooth	Smooth
3.	Odour	Characteristic	Characteristic	Characteristic
4.	Non irritancy	Non irritant	Non irritant	Non irritant
5.	Ph	6.1	5.9	6.1
6.	Washability	Good	Good	Good
7.	Stability study	Stable	Stable	Stable

5.5 Spreadability study

Spreadability describes how readily the emulgel may be applied and how little shearing is required to get it out of the container. Table 3 lists the average spreadability values for various formulations. Better spreadability on the skin is indicated by a larger spreadability coefficient value. All selected formulations' spreadability values were in the following order: FE1 > FE2 > FE3. The spreadability values did not differ significantly across any of the formulations. The average spreadability value for FE-3 was 22.94, whereas FE-3 had the second-highest value at 19.34. The low level of gelling agent is what causes the high value of spreadability. High spreadability value may also be caused by low levels of liquid paraffin.

Table 5.5 Spreadability.

S.no	Parameters	Spreadability (gm-cm/sec)
1.	FM-1	15.54
2.	FM-2	19.34
3.	FM-3	22.94

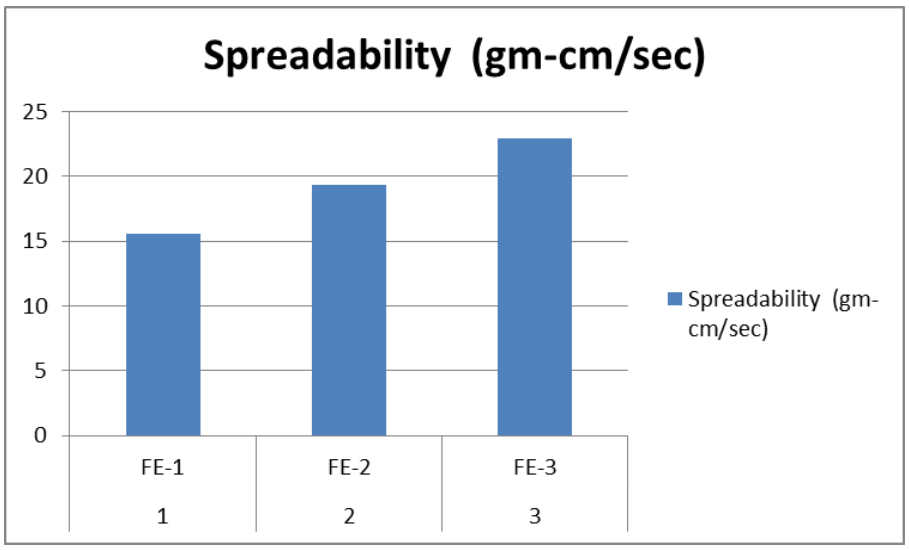


Figure 5.3 Graph showing spreadability.

5.6 Viscosity

Viscosity is a crucial criterion to assess since it is mostly responsible for the uniformity of the dosage form and the release of the drug's payload. All formulations' viscosities were measured using a brook field viscometer. The table below contains values. FM-3 was the formulation with the highest viscosity (12500 cp). This is caused by the mixture's high gelling agent content, low emulsifying agent content, and low liquid paraffin content. The viscosities of the three samples of formulation FE-3 that were kept at different temperatures for one month—FM-3 (kept at 25 °C), FE-2 (kept at 40 °C), and FM-3 (kept at 40 °C + 74 percent RH)—did not differ from one another. but the viscosities of formulation FB8A differed significantly from FE-3 and FE-2 (p 0.05). Viscosities decreased more quickly at 40 °C and 40 °C + 75% RH. According to Li et al., such a drop in viscosities is invariably linked to a rise in temperature. According to his research, a rise in temperature (from 25°C to 32°C) caused a decrease in viscosities. This indicates that the emulgel's fluidity and spreadability would be greater at 32 °C than they would be at 25 °C when applied to the skin's surface. It's crucial to check the viscosity of a formulation to see if patients would accept it. Here, the inverse relationship between viscosities and temperature is explained by two mechanisms: first, water molecules diffuse from the scattered aqueous phase to the continuous aqueous phase, and second, numerous globules break under the influence of osmotic pressure.

Table 5.6 Viscosity.

	Viscosity FE-1	Viscosity FE-2	Viscosity FE-3
0 hour	13500	13500	13500
12 hour	12480	12465	11350
24 hour	12340	12330	11450
48 hour	11345	11365	11000

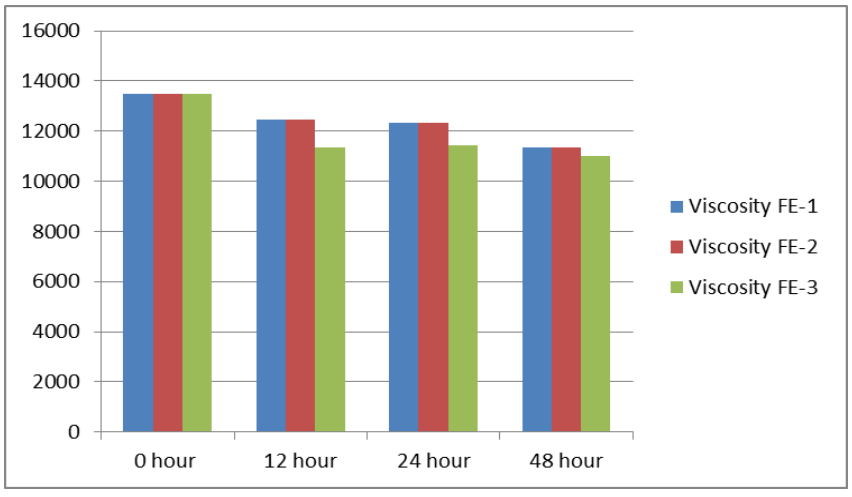


Figure 5.4 Viscosity graph.

5.7 Stability study

In order to test for colour, phase separation, homogeneity, consistency, and liquefaction, all three samples of the stable formulation FE-1,2,3 were stored for one month under various storage circumstances. Phase separation was not visible at first, and all formulations were thick, smooth, and yellowish green in hue. The pH of freshly made formulations was 6.13, which is considered acceptable for skin, which has a pH between 5 and 6. Regarding the aforementioned criteria, all samples were confirmed to be stable. A minor phase separation and a modest shift in colour to a somewhat blackish hue were visible in the sample held at 40 °C and 75 percent RH. This shift in hue can be caused by the oily phase's separation, which is encouraged at higher temperatures. The pH of the three samples was also determined at various time intervals, including 0, 12, 24, 1, 2, 3, and 4 weeks. Student t tests were performed on each pH value. There was no detectable change in pH ($p > 0.05$). The average pH of the formulation's three samples was between 5 and 6, which is considered to be within the acceptable range to reduce the risk of skin irritation when used topically. Up to one month, a very modest pH decline was seen, however this change was within the typical pH range of skin. The generation of very acidic by-products from any of the oil constituents, or diffusion of water (pH 5 to 7) from the internal phase to the exterior phase, may be to blame for the pH dropping over time.

CONCLUSION

According to several research, Linum usitatissimum is used to cure a variety of illnesses and ailments. The characteristics of active phytocompounds must be studied. Organoleptic qualities of Linum usitatissimum seed remove discoveries are accounted for in table above. Absolute debris, corrosive insoluble debris, water-dissolvable debris and Loss on Drying values are 10.61, 1.25, 6.35, 4.5 w/w Respectively. The table above records the rate yields for the powdered Linum usitatissimum seed extricates that were picked for extraction. The extractive qualities were determined utilizing the rate yield of each concentrate, and 8.57 percent weight-for-weight with ethanol was viewed as the extractive worth. Different Physicochemical assessment boundaries of figured out emulgel were analyzed by standard techniques and results were displayed in table above. Consequently the Linum usitatissimum seed extricate formed as emulgel showed every one of the adequate qualities and it was tracked down viable in treatment of wound withdrawal. Further examinations should be possible to assess the various investigations on Linum usitatissimum various parts.

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