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A Comparative Study to Prepare and Evaluate the Effectivenes of Ibuprofen Suspension Using Natural Suspending Agent

Rushikesh Bapu Gore[1], Akhil S. kanekar[2]
[1]*Final Year B. Pharmacy of Shree Sarswati Institute of Pharmacy, Tondavali, Kankavali, Sindhudurg, Maharashtra.*
Dr. Babasaheb Ambedkar Technological University, Lonere, Raigad, Maharashtra.
[2]*Assistant Professor In Shree Sarswati Institute Of Pharmacy, Tondvali. Kankavali, Sindhudurg, Maharashtra.*
Dr. Babasaheb Ambedkar Technological University, Lonere, Raigad, Maharashtra.
Corresponding author: Rushikesh Bapu Gore

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ABSTRACT
Ibuprofen is anon-steroidal anti-inflammatory drug. It is used to relieve pain from various conditions such as headache, dental pain, menstrual cramps, muscle aches, or arthritis. Fenugreek (Trigonella foenum- graecum L.) Family Fabaceae has been traditionally used as a medicinal agent for treatment of different types of inflammation disorders, pain relief; it reduces risk of blood pressure, improves weight loss, and raises testosterone and blood sperm count. However, people have been using fenugreek in varying forms for hundreds or potentially thousands of years to treat a very wide range of conditions that is digestive problems, including constipation, loss of appetite and gastritis, childbirth pains, and breathing problems. Recently the anti-inflammatory activity of the methanolic extract of fenugreek plant at doses of 100 to 400 mg per kg were studied using carrageenan-induced edema method and result was compared with the effects of dexamethasone and ibuprofen. Medical News Today in a 2012 study, in mice suggest that the high antioxidant Flavonoids content in fenugreek seeds can reduce inflammation. Fenugreek seed have polysaccharides (galactomannans) and chemical constituent's plays important role in pharmaceutical formulations such as thickening agent, and suspending agent. By using fenugreek seed powder, as a natural suspending agent, prepared and analyzed two formulations (1%, 2%) named as F1 and F2. The method involved in this preparation is trituration method by using mortar and pestle. Evaluation tests are performed such as sedimentation volume, particle size analysis, flow rate, Determination of pH, Determination of viscosity, Assay of Ibuprofen. Phytochemical tests and swelling index for fenugreek seed powder, these tests shows that the Ibuprofen suspension F2 shows better stability than F1 formulation.

Keywords: Ibuprofen, Fenugreek, Suspending Agent , Trituration, Viscosity.

I. INTRODUCTION

Suspension are the biphasic liquid dosage forms of medicament in which finely divided solid particles ranging from 0.5 to 5 micron are dispersed in a liquid or semisolid vehicle, with aid of single or combination of suspending agent. In which solid particles acts as disperse phase where as liquid vehicle acts as continuous phase. The external phase (suspending medium) is generally aqueous in some instance, may be an organic or oily liquid for non oral use. The particle size for non oral suspension is so important to avoid grittiness to skin.

A suspension is a coarse dispersion of insoluble drug particles, generally with a diameter exceeding 1μm, in a liquid (usually aqueous) medium. Suspensions are useful for administering insoluble or poorly soluble drugs or when the presence of a finely divided form of the material in the GI tract is required. The taste of most drugs is less noticeable in suspension than in solution, due to the drug being less soluble in suspension. Particle size is an important for determination of the dissolution rate and bioavailability of drugs in suspension. In addition to the excipients described above for solutions, suspensions include surfactants and thickening agents. Surfactants wet the solid particles, thereby ensuring the particles disperse readily throughout the liquid. Thickening agents reduce the rate at which particles settle to the bottom of the container. Some settling is acceptable, provided the sediment

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can be readily dispersed when the container is shaken because hard masses of sediment do not satisfy this criterion, caking of suspensions is not acceptable. Ibuprofen chemical name is 2-[4-(2-methylpropylphenyl) propanoic acid. The suspension was prepared by mortar and pestle in lab scale method where in large scale homogenizer is used.[1], [5] [15]

The present investigation was aimed to developing oral administrable pharmaceutical suspension formulation of Ibuprofen with improved stability.

Objective

- Preparation of Ibuprofen formulation can be done by trituration method by using natural suspending agents such as fenugreek seed powder.
- Evaluation tests are performed such as sedimentation volume, particle size analysis, flow rate, Determination of pH, Determination of viscosity, In-vitro dissolution studies, Assay of ibuprofen.
- Phytochemical tests and swelling index for fenugreek seed powder, these tests shows that the ibuprofen suspension F2 had better stability than the otherF1 formulations.

The reasons for the formulation of a pharmaceutical suspension

- When the drug is insoluble in the delivery vehicle.
- To mask the bitter taste.
- To increase the drug stability.
- To achieve controlled/sustained drug release.
- To characterize the desired rheological behaviour of suspension.
- To prepare, label, and dispense a suspension.

Applications

- Suspension is usually applicable for drug which is insoluble (or) poorly soluble.

E.g. Prednisolone suspension.

- To prevent degradation of drug or to improve stability of drug.

E.g. Oxy tetracycline suspension.

- Suspension of drug can be formulated for topical application

E.g. Calamine lotion

- To mask the taste of bitter of unpleasant drug.

E.g. Chloramphenicol, Palmitate suspension.

Advantages

- Main advantages of this suspension are to improve chemical stability of certain drug
- Procaine penicillin Drug in suspension exhibits higher rate of bioavailability than other dosage forms.

Solution > Suspension > Capsule > Compressed Tablet > Coated tablet

- Duration and onset of action can be controlled.

E.g. Protamine Zinc Insulin suspension, Chloramphenicol

Disadvantage of Suspensions

- It is difficult to formulate.
- Uniform and accurate dose cannot be achieved unless suspensions are packed in unit dosage form.
- All suspensions are required to be shaken before measuring of dose.

Ideal Qualities of Good Suspension

- It should settle slowly & easily re–dispersed on shaking it should readily & evenly pour from container.
- It should prevent degradation of drug or to improve stability of drug.
- It should mask the taste of bitter of unpleasant drug.
- It should be chemically inert. It should not form hard cake.

Method of administration [14]

For oral administration, and short term use only.
Infants 6 months to 1 year: 2-5 ml, tid.
Children's 1-4 years: 5 ml tid, 4-7 years: 7.5ml tid, 7-12 years: 10ml tid.
Elderly: No special dosage modifications are required unless renal or hepatic function is impaired, in which case dosage should be assessed individually

Contraindications

1. Ibuprofen should be avoided in combination with: acetyl salicylic acid (Aspirin) was not generally recommended because of the potential increase in prostaglandin formation with further precipitation of renal failure.
2. Ibuprofen should be used with cautions in combination with: NSAIDS may reduce the effect of antihypertensive, such as ACE-inhibitors, beta blockers' and diuretics.
3. Fertility, pregnancy and lactation data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of prostaglandin synthesis inhibitors in pregnancy.

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4. Effect on ability to drive and use machines: undesirable effect such as dizziness, drowsiness, fatigue, and visual disturbances. After taking NSAIDS person should not drive or operate the machines.[10], [21]

Shelf life
36 months
Special precaution for disposal and other handling
Shake well before use
Theoretical consideration:

The particle size:
As the particle size is too much; the particles will settle faster at the bottom of the container particles (> 5 µm) impart a gritty texture to the product and also cause irritation if injected or instilled to the eye particles (> 25 µm) may cause blockage of the needle. Opposite to that very fine particles will easily form hard cake at the bottom of the container.

Wetting of the particles:
Hydrophilic materials such as No, Mg2, CO3 are easily wetted by water while hydrophobic materials i.e sulphur, charcoal are not due to the layer of adsorbed air on the surface. The use of wetting agent allows removing the air from the surface may cause to easy penetration of the vehicle into the pores as compare to hydrophobic materials because hydrophobic material are easily wetted by non-polar liquids.

Brownian movement:
The Brownian movement of particle prevents sedimentation by keeping the dispersed material in random motion. Brownian movement depends on the density of dispersed phase and the density and viscosity of the disperse medium. The kinetic bombardment of the particles by the molecules into the suspending medium will keep that particles suspending, and their size is below to the critical radius (r)

Labelling:
The labelling conditions such as; Shake well before use. Do not freeze. Protect from direct light (for light sensitive drugs). In case of dry suspensions powder the specified amount of vehicle to be mixed May indicated clearly on label. [1], [2]

Storage: Suspensions should be stored in cool place but should not be kept in a refrigerator. Freezing at very low temperatures should be avoided which may lead to aggregation of suspended particles Stored at controlled temperature from 20-25^{0}C.

Formulating Stable Suspensions
Physical stability in suspensions is controlled by,
The addition of flocculating agents to enhance particle "Dispensability" and The addition of viscosity enhancers to reduce sedimentation rate in the flocculated Suspension.
Viscosity Enhancers: The concentrations used range from 0.5% to 5%, but the needed viscosity will depend on the suspended particle's tendency to settle.
Natural hydrocolloids: Acacia, tragacanth, alginic acid, and fenugreek powder, guar gum**,** gelatine.[1] [3]

Introduction to natural suspending agent Fenugreek
Herbs have been used in all parts of the world not only as food but also as potent drugs for thousands of years. They do not work like chemical drugs and they are not substitute of them Medicinal plants are used by 80% of the world population especially in developing countries to cure and improve the general health, principally due to the common belief that plant derived drugs are without any side effects along with being economical and locally accessible Fenugreek(Trigonella foenum-graecum L)., is an annual herb grown in various countries around the world. It was thought to be indigenous. It has been used in many different cultures, especially in Asia and the Mediterranean region. Now fenugreek is widely cultivated in India, China, northern and eastern Africa, and parts of Europe and Argentina. The health promoting property of fenugreek has been long documented when it is taken as vegetables, food supplements or medicinal remedies. [16], [22]

Historical uses of fenugreek
Fenugreek has a long history as both a culinary and medicinal herb in the ancient world. Applications of fenugreek were documented in ancient Egypt, where it was used in instead to embalm mummies. The Greeks and Romans used it for cattle fodder In ancient Rome, fenugreek was purportedly used to aid labour and delivery. In traditional Chinese medicine, fenugreek seeds are used as a tonic, as well as a treatment for weakness and enema of the legs. In India, fenugreek was used as commonly.[2], [17]
Active constituents

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Fenugreek seed contains 45-60 % Carbohydrates, mainly mucilaginous fibre (galactomannans). 20-30 % Proteins high in lysin and tryptophan. 5-10 % fixed oils (lipids). Alkaloids pyridine-type, mainly trigonelline (0.2-0.3 6%), choline (0.5 %), gentianine, and carpaine. Flavonoids such as apigenin, luteolin, orientin, quercetin, vitexin, and isovitexin. Free amino acids, such as 4-hydroxyisoleucine (0.09 %); arginine, histidine, and lysine. Calcium and Iron. Saponins (0.6-1.7 %). Glycosides yielding steroidal sapogenins on hydrolysis (diosgenin, yamogenin, tigogenin, neotigogenin. Cholesterol and Sitosterol. Vitamins A, B1,C. and Nicotinic acid, and 0.015 % Volatile oils (n-alkanes and sesquiterpenes), which are thought to account for many of its presumed therapeutic effects.[16], [26]

Figure 1: Fenugreek plant

Pharmacological effects

Fenugreek is known to have several pharmacological effects such as hypoglycaemic, and Antilipidemic or hypocholestrolemic.

Mechanism of action of Fenugreek

The exact mechanism of action is still unclear. The antidiabetic effect of Fenugreek was thought to be due to formation of a colloidal-type suspension in the stomach and intestine when the mucilaginous fibre of the seeds is hydrated, therefore it affecting gastrointestinal transit, furthermore slowing glucose absorption.[19] The Antilipidemic effects of Fenugreek was thought to be due to inhibition of intestinal cholesterol absorption due to saponin-cholesterol complex formation, increased loss of bile through faecal excretion due to saponin-bile complexes, thus increasing conversion of cholesterol to bile by the liver, and effects of amino acid pattern of fenugreek on serum cholesterol. Fenugreek plant has an antioxidant action, gastro protective activity, appetite stimulation, antirheumatism.[8], [11]

II. LITERATURE SURVEY:

V. Naga Lakshmi Ponnada (2017), theoretical consideration of suspension, evaluation test for Ibuprofen suspension and mucilage test for fenugrrek seed powder.

Priyadarsini et al., (2007), determined antioxidant potential of extract of fenugreek by means of a variety of in vitro assays. The findings demonstrated that extract of seed part of fenugreek protects cell structures due to presence of anti-oxidant components. Thus, preventing oxidative damage.

Fedelic Ashish Toppo et al., (2009), review paid attention on therapeutic potential and need of Fenugreek plant reminiscent of bronchitis, fevers, asthma, lung infection, allergies, ulcers, gas, cancer, appetite, boils, sinus problem, bronchial, mucus, cholesterol, gallbladder problem, heartburn, inflammation, water retention, diabetic retinopathy, gastric disorders, anemia, throat, abscesses, anemia, eyes, uterine problems.

Meera Samantha et al., (2011), current revision has been taken to examine anti-ulcer properties of aqueous extract gained from Methika. The ulcer index was reduced by aqueous extract of plant. It proved the ulcer protective potential of methi (fenugreek) plant matter. The potential was largely because of anti-oxidant components.

B.N. malleswari et al., (2016), suspension have been characterized relatively to particle size, density and solubility. The dissolution study was

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conducted using media: buffer pH7.2, 6.8, 4, 5 and 0.1 M HCL. The result shows that 50 rpm was the adequate condition to discriminate the dissolution profile.

Jaleh varshosaz et al., (2012), objectives of the binding potential of fenugreek mucilage in formulation. Studied that the fenugreek seed was a role of fastening agent in diverse medicines.

III. MATERIAL AND METHODS:

The drug sample was viewed visually and viewed under the compound microscope for the detertminatation of its colour by use of black and white background also nature of drug sample. Observations was compared with the officials book of Indian Pharmacopoeia (IP).

Drug profile for Ibuprofen

Ibuprofen is a Non Steroidal Anti-Inflammatory drug (NSAID) used for relieving pain, helping with fever and reducing inflammatory.

It is chemically designated as 2-(4-Isobutylphenyl) propanoic acid.

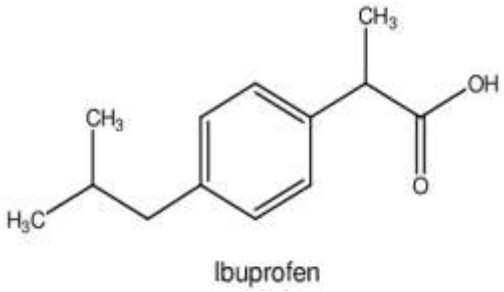

Figure: 2 structure of Ibuprofen

Molecular formula of Ibuprofen is $C_{13}H_{18}O_2$, and molecular weight is 26.2882g/mol. It is a white crystalline colourless powder. Soluble in ethanol (25mg/ml), chloroform (1:1), ether (1:2), acetone (1:1.5), aqueous solutions of alkali hydroxides and carbonates, dichloromethane, methane (5mg/ml), an ethyl acetate. Partially insoluble in water. Dissociation constant: pKa = 5.2, Melting point is 76^0C and Density is 1.03gm/ml.[15], [17]

Bioavailability		Peak plasma level	Plasma half-life	Active metabolites	Elimination
constant	90%	1 to 2 hours	2 hours	None	predominantly renal

Table 1: Pharmacokinetics

Mechanism of action of Ibuprofen:

The exact mechanism of action of Ibuprofen is still unclear. Ibuprofen is a Non Steroidal Anti-Inflammatory (NSAID) drugs work by inhibiting the COX enzymes, which convert arachidonic acid to prostaglandin H2 (PGH2). PGH2, in turn, is converted by other enzymes to several other prostaglandins which are mediators of (pain, inflammation, and fever) It works by blocking body's production of his effect helps to decrease swelling, pain, or fever[12] . Thromboxane A2 (which stimulates platelet aggregation, leading to the formation of blood clots). Ibuprofen is a non selective inhibitor of cyclooxygenase, an enzyme involved in prostaglandin synthesis via the arachidonic acid pathway. Its pharmacological effects are believed to be due to inhibition of cyclooxygenase-2 (COX-2) which decreases the synthesis of prostaglandins involved in mediating inflammation, pain, fever, and swelling. Antipyretic effects may be due to action on the hypothalamus, resulting in an increased peripheral blood flow, vasodilatation, and subsequent heat dissipation. Inhibition of COX-1 is thought to cause some of the side effects of Ibuprofen including gastrointestinal ulceration.[22]

Ibuprofen is administered as a racemic mixture. The R- enantiomer undergoes extensive inter conversion to the S-enantiomer in vivo. The S-enantiomer is believed to be the more

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pharmacologically active enantiomer like aspirin and Indomethacin, Ibuprofen is a non selective COX inhibitor, in that it inhibits two iso forms of cyclooxygenase, COX-1 and COX-2. The analgesic, antipyretic, and anti-inflammatory activity of NSAIDs appears to operate mainly through inhibition of COX-2, whereas inhibition of COX-1 would be responsible for unwanted effects on the gastrointestinal tract. The role of the individual COX iso forms in the analgesic, anti-inflammatory, and gastric damage.[1] [3]

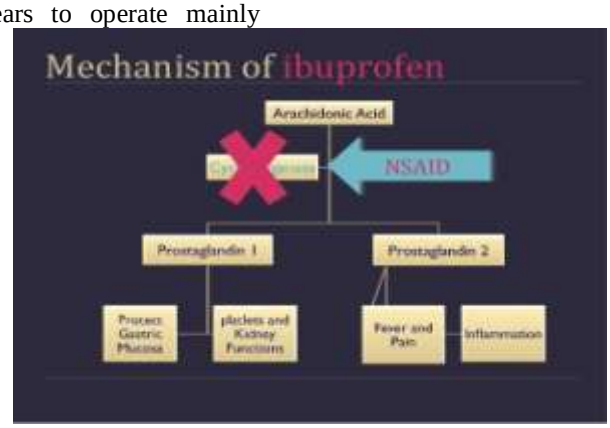

Figure: 3Mechanism of Ibuprofen

Adverse effects

- Nausea, dyspepsia, gastrointestinal ulceration/bleeding, raised liver enzymes, diarrhoea, constipation, nosebleed, headache, dizziness, rash, salt and fluid retention, and hypertension.
- NSAIDS may causes increases cardiovascular risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal.[23]
- Infrequent adverse effects include oesophageal ulceration, heart failure, hyperkalaemia, renal impairment, confusion, and bronchospasm. Ibuprofen can exacerbate asthma, sometimes fatally.
- In overdose patients risk of developing renal toxicity has been published.
- Ibuprofen may be quantified in blood, plasma, or serum to demonstrate the presence of the drug in a person having experienced an anaphylactic reaction, confirm a diagnosis of poisoning in hospitalized patients, or assist in a medico legal death investigation.[4]

Uses

- Ibuprofen helps to decrease swelling, pain, or fever.
- Ibuprofen is used to relieve pain from various conditions such as headache, dental pain, menstrual cramps, muscle aches, or arthritis.
- It is used to reduce fever and to relieve minor aches and pain due to the common cold or flu.[25]

IV. EXCIPIENTS PROFILE

1. Fenugreek seed powder

Fenugreek (Trigonella foenum-graecum) is an annual plant belongs to the family **Fabaceae**, with leaves consisting of three small obovate to oblong leaflets. It is cultivated worldwide as a semiarid crop, and its seeds are a common ingredient in dishes from the Indian subcontinent. [13] [24]

Fig 4: Fenugreek seed powder

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Morphological characteristics

Appearance: Solid- rhomboidal seeds, 3 to 5 mm long, 2 mm thick. Hard, pebble-like, Yellowish brown-light brown in colour Odour **is** characteristic spicy, Bitter and mucilaginous in taste.[29]

Macroscopic characteristics of fenugreek

Macroscopically characters Solid-rhomboidal, pebble like shape, 3 to5cm long, 2mm thick, plain surface, yellow, bitter mucilaginous taste and have characteristic odour.

The morphological evaluation was carried out for shape, size, colour, odour and taste and fracture identification of the fenugreek seed. [22]

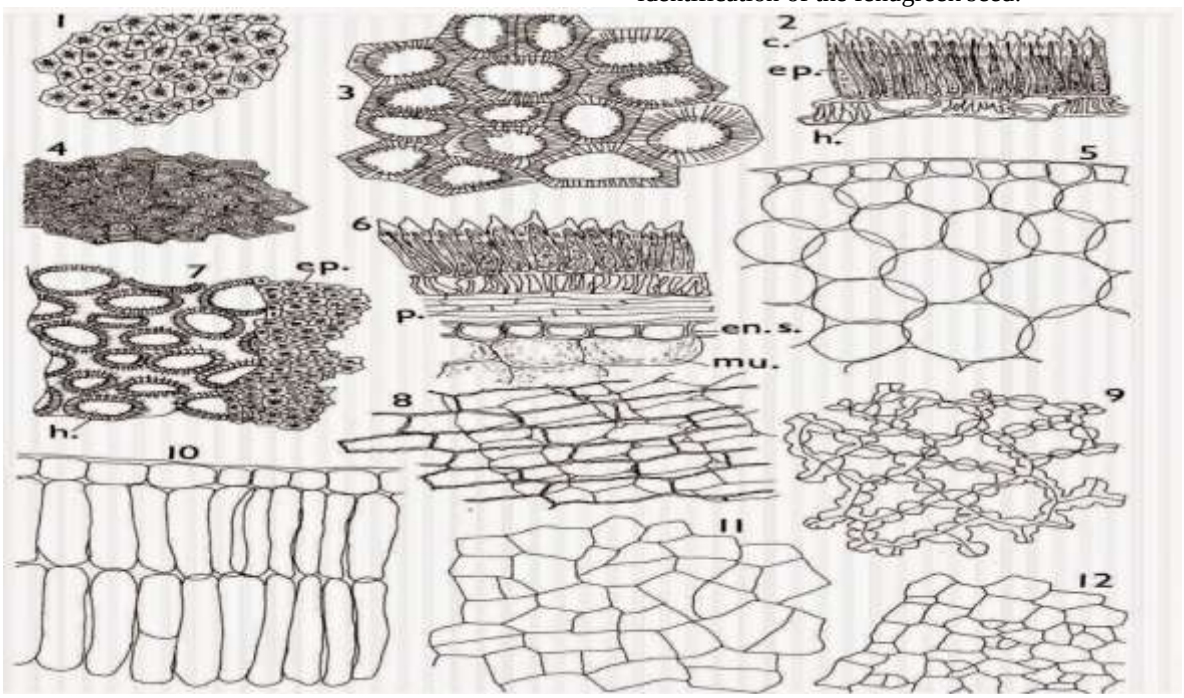

Figure: 5 microscopic view of fenugreek seed

Observations made in compound microscope

1. Epidermis of testa
2. Cuticle(c), Epidermis (ep), Hypodermis (h) of testa in sectional view
3. Hypodermis of the testa in surface view
4. Eperdemis of the testa in surface view
5. Epidermis and parenchymatous cells of the cotyledons in sectional view.
6. Part of seed showing epidermis, hypodermis and poarenchymatous layer(p) of the outermost layer (en.s) and the mucilage cell (mu) of the endosperm.
7. Epidermis (ep) and Hypodermis (h) of the testa in surface view.
8. Layers of parenchyma of the testa in surface view
9. Outermost layer of the endosperm in surface view
10. Epidermis and Palisade of the cotyledons in sectional view
11. Undifferentiated parenchyma of the cotyledons
12. A single layer of parenchyma of the testa in surface view.

Medicinal uses

The seeds are hot, with a sharp bitter taste; tonic, antipyretic, anthelmintic, increase the appetite, astringent to the bowels, cure leprosy, 'vata', vomiting, bronchitis, piles; remove bad taste from the mouth, useful in heart disease (Ayurvedic). The plant and seeds are hot and dry, suppurative, aperient, diuretic, emmenagogue, useful in dropsy, chronic cough, enlargement of the liver and the spleen. The leaves are useful in external and internal swellings and burns; prevent the hair falling off. Fenugreek seeds are considered carminative, tonic and aphrodisiac. [1], [14]

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Figure: 6 Medicinal activities of Fenugreek (Trigonella foenum graecum L.)

2. Sodium benzoate

Synonyms: Benzoic acid, sodium salt, Benzoate of soda, Natrium benzoicum, Sodium benzoic acid. The Empirical formula is $C_7H_5NaO_2$, and molecular weight is 144.1g/mol. Sodium benzoate occurs as a white granular or crystalline, slightly hygroscopic powder. It is odourless, or with faint odour of benzoin and has an unpleasant sweet and saline taste. The bulk material should be stored in a well-closed container, in a cool, dry place. [12]

Applications in Pharmaceutical Formulation

- In cosmetics, foods, and pharmaceuticals Sodium benzoate is used primarily as an antimicrobial and preservative.
- It is used in concentrations of 0.02–0.5% in oral medicines, 0.5% in parenteral products, and 0.1–0.5% in cosmetics.
- The usefulness of sodium benzoate as a preservative is limited by its effectiveness over a narrow pH range.
- Sodium benzoate is used in preference to benzoic acid in some circumstances, owing to its greater solubility; in some applications it may impart an unpleasant flavour to a product.[3]
- Sodium benzoate is used as a tablet lubricant at 2 to 5% w/w concentrations.
- Determination of liver function the solutions of sodium benzoate have also been administered, orally ors intravenously.[8]

3. Glycerin

Synonyms: Croderol, Glycerol, glycerine, glycerol, Kemstrene .Chemical Name: Propane-1, 2, 3-triol. Empirical formula is $C_2H_5NO_2$.and molecular weight: 92.093g/mol. Glycerine is a clear, colourless, odourless, viscous, hygroscopic liquid. It has a sweet taste, approximately 0.6 times as sweet as sucrose. It is categorized as Antimicrobial preservative, co solvent, emollient, humectants, Plasticizer.[4], [30]

Application

- Glycerine is used in a wide variety of pharmaceutical formulations including Oral, Otic, Ophthalmic, Topical, and Parenteral preparations.
- In cosmetics topical formulations glycerine is used primarily for its humectants and emollient properties.
- Used as a solvent or co solvent in creams emulsions.
- Additionally it is used in aqueous and non aqueous gels and also as an additive in patch applications.
- In parenteral formulations, it is used mainly as a solvent and co solvent.
- In oral solutions, glycerine is used as a solvent, sweetening agent, antimicrobial preservative and viscosity-increasing agent.
- It is also used as a plasticizer and in film coatings and gelatine in the production of soft-gelatine capsules and gelatine suppositories.
- Glycerine is employed as a therapeutic agent in a variety of clinical applications, and is also used as food additives.

Stability and Storage Conditions

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Glycerin is hygroscopic, pure glycerine is not prone to oxidation by the atmosphere under ordinary storage conditions, but it decomposes on heating with the evolution of toxic acrolein. Mixtures of glycerine with water, ethanol (95%), and propylene glycol are chemically stable. Glycerin may crystallize if stored at low temperatures; the crystals do not melt until warmed to 208^0C. Glycerin should be stored in an airtight container, in a cool, dry place.[1] , [27]

Handling Precautions

In the UK, the recommended long term work place exposure limit for glycerine mist is 10 mg/m3.Glycerin is combustible and may react explosively with strong oxidizing agent. Eye protection and gloves are recommended. [30]

4. Tween 80

Tween 80 is a synthetic compound is a viscous, water-soluble yellow liquid. Non-ionic surfactant and emulsifier often used in foods and cosmetics. Brand names: Alkest TW 80, Canarcel, Poegasorb 80 Molecular formula is $C_{64}H_{124}O_{26}$ and molecular weight is1.310 g/mol.

Uses

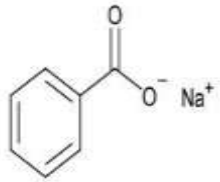
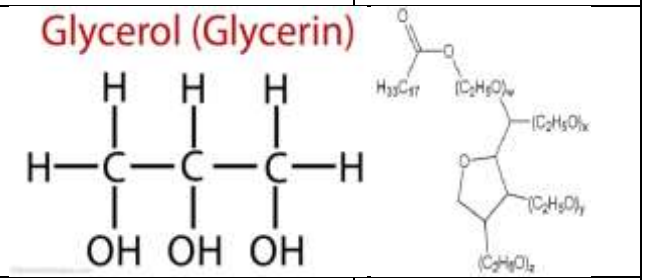
Food use: Polysorbate 80 is used as an emulsifier in foods. e.g. in ice cream, Polysorbate is added up to 0.5% (v/v) concentration to make the ice cream smoother and easier to handle, as well as increasing its resistance to melting. Adding this substance prevents milk proteins from completely coating the fat droplets. This allows them to join together in chains and nets, which hold air in the mixture, and provide a firmer texture that holds its shape as the ice cream melts.

Health and beauty use: Polysorbate 80 is used as a surfactant in soaps and cosmetics, or a solubilizer such as in a mouthwash. The cosmetic grade of Polysorbate 80 may have more impurities than the food grade.

Medicinal use: Polysorbate 80 is an excipient that is used to stabilize aqueous formulations of medications for parenteral administration, and used as an emulsifier in the manufacture of the popular antiarrhythmic amiodarone. It is also used as an excipient in some European and Canadian influenza vaccines. Influenza vaccines contain 25 µg of Polysorbate 80 per dose. [2]

It is also used in the culture of Mycobacterium tuberculosis in Middle brook 7H9 broth, and emulsifier in the estrogen-regulating drug Estrasorb. [19]

V. SUMMARY

	SODIUM BENZOATE	GLYCERIN	TWEEN 80
Synonym	Benzoate of soda	Croderol	Polysorbate
Formula	$C_7H_5NaO_2$.	$C_2H_5NO_2$	$C_{64}H_{124}O_{26}$
Structure			
Molecular weight	144.11g/mol	92.093g/mol	1,310 g/mol
Melting point	410^0C	290^0C	-21^0C
Density	1.5 g/cm^3	1.26 g/cm^3	1.06 g/cm^3
Solubility	Soluble in water, poorly soluble in alcohol	Completely soluble in water and short chain alcohols. Insoluble in hydrocarbons at	Soluble in ethanol, cottonseed oil, ethyl acetate, methanol,

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		low temperature	toluene
Uses	Antimicrobial, preservative, lubricant.	Co solvent, emollient, humactant.,plasticizer	Wetting agent, surfactant

Table: 2 Summary of Excipients

PREPARATION AND EVALUATION OF IBUPROFEN SUSPENSION BY USING NATURAL SUSPENDING AGENT

A. Preparation of Suspension

Formula for preparation of suspension

Ingredient	**F1**	**F2**	**Uses**
Ibuprofen	2gm	2gm	Anti-inflammatory
Fenugreek seed powder	1gm	2gm	Natural suspending agent
Simple syrup	10ml	10ml	Sweetening agent
Sodium benzoate	0.1gm	0.1gm	Preservative
Tween 80	0.1gm	0.1gm	Wetting agent
Glycerine	10ml	10ml	Viscosity enhancer
Water	Upto 100 ml	Upto 100 ml	Vehicle

Table 2: Composition for preparation of suspension

Preparation (Trituration method)

i. Suspension of ibuprofen was prepared by trituration method using above ingredients.
ii. Weighed quantity of Ibuprofen was taken into a dry motor and triturated until fine powder is obtained.
iii. Add the tween 80 and mixed to form uniform suspension, and then add methyl cellulose and triturate again.
iv. To the above mixture glycerin was added and mixed to form a uniform suspension.
v. Finally, to this suspension simple syrup followed by sodium benzoate dissolved in few ml of water in a separate beaker.
vi. This is mixed thoroughly and transport into measuring cylinder.
vii. The volume is made with the water.

EVALUATION OF SUSPENSION

1. Calibration curve for Ibuprofen

Calibration curve of ibuprofen was constructed by using a series of standard solution containing 11,12,13,14 and 15µg of Ibuprofen per ml.

The solution was scanned in the region 200-400nm using ELICO –SL 159 UV spectrophotometer.

Finally the absorbance of the solution was measured at 221nm using p^H 7.2 phosphate buffers as a blank.

Calibration curve of ibuprofen was plotted Concentration vs. Absorbance. [5], [9]

2. In-vitro dissolution studies

Preparation of 7.2pH phosphate buffer: 173.5 ml of 0.2N NaOH and 250ml of 0.2N potassium dihydrogen phosphate buffer using UV visible specto-photometry at 221nm.

Parameters for dissolution process: Apparatus - paddle type dissolution; apparatus medium- 7.2 pH; phosphate buffer Stirrer- paddle at 50 rpm;Temperature- 37^0c ± 0.5^0 C; Duration - 30 min; Total no of samples is 6, Wave length -221[5], [6]

3. Particle size analysis

Firstly, calibrate the eye piece. Place a drop of lotion on a glass slide and covered with a cover slip without any air bubbles. The slide was observed under the microscope. Each particle

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diameter was measured and recorded for at least 100 particles. [1], [2]

4. Determination of sedimentation volume

Prepared Ibuprofen suspension was transferred into a measuring cylinder and kept aside without disturbing it. Then observe the height of the sediment at a regular time interval of 0, 10, 20, 30, 40, 50, 60, and calculate the sedimentation volume by using the following. F = 100 Hu/Ho. [10]

5. Measurement of viscosity

The viscosity (M.pa×sec) of the sample was determined at 24^0 C using Brookfield Synchro electric viscometer; at 12 RPM (spindle T Shaped). All determinations were made in at least triplicate and the results obtained are expressed as the mean values. [5]

6. Determination of flow rate

The time required for each suspension sample to flow through a 10 ml pipette was determined and the apparent viscosity was calculated using the equation. Flow rate = Volume of pipette (ml) / Flow time (s)

7. Determination of pH

The P^H of suspension is determined by using digital pH meter.

8. Assay of Ibuprofen

5ml of ibuprofen suspension was transferred into a conical flask. To this add 2ml of methanol and was triturated against 0.1N NaOH by using phenolphthalein as an indicator. The end point was colourless to pale pink. Equivalent factor**:** each ml 0.1N NaOH = 0.02063 gm of Ibuprofen.[22], [24]

9. Determination of Swelling Index

The natural suspending agent 1g was taken in a China dish and then 10 ml of distilled water was added and the mixture was shaken and allowed to stand for 1 hour. After 1 hour the remaining water in China dish was discarded and the weight increase of the natural suspending agent was calculated.

Swelling index% = W1 – W2 /W1 × 100

Where, W1= Weight of tablet at time;

W2= Weight of tablet at time t. [6], [8]

10. Phytochemical tests for fenugreek (Trigonella foenum graecum)

Preliminary tests were performed to confirm the nature of mucilage obtained. In view of phytochemical test, fenugreek mucilage contains carbohydrates, alkaloids and proteins.[28], [29]

VI. RESULT

1. Calibration curve for Ibuprofen

Sr.no.	Concentration (µg/ml)	Absorbance
1	2	0.113
2	4	0.212
3	6	0.304
4	8	0.403
5	10	0.510

Table: 3 Calibration curve

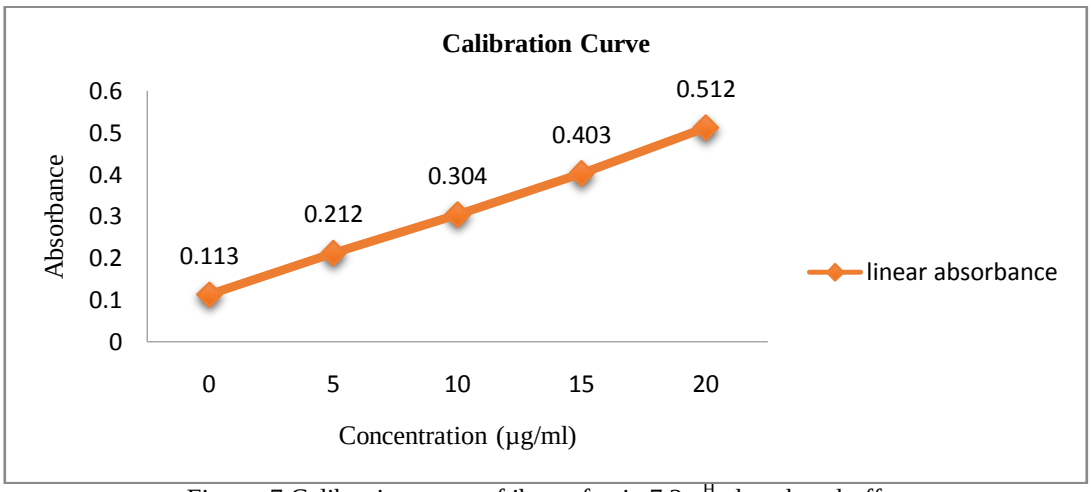

Figure: 7 Calibration curve of ibuprofen in 7.2 p^H phosphate buffer

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The different concentration of 2, 4, 6, 8 and 10 µg/ml used respectively, the absorbance was measured at 221 nm against blank by UV spectrophotometer.

2. Particle size analysis

	10	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**
10	2	3	3	4	4	7	5	7	6	1
20	2	7	5	6	7	3	4	1	2	4
30	2	5	2	5	2	4	1	2	3	5
40	3	4	4	2	5	5	3	3	1	3
50	1	3	3	2	4	4	2	3	4	4
60	4	6	1	7	2	2	7	2	1	2
70	3	5	2	3	3	5	4	5	1	1
80	5	4	3	9	8	6	3	3	3	7
90	4	5	4	7	7	8	2	2	2	2
100	3	3	5	3	5	4	1	2	1	1

Table 3: Particle size analysis for F1 formulation

Size range	**Mean size (d)**	**No. of particle (n)**	**n × d**	**%** n	**Cumulative frequency under size**	**Cumulative frequency over size**
0-5	0-5	84	210	84%	84%	100%
5-10	5-10	16	120	16%	100%	84%
10-15	10-15	0	0	0	0	0
15-20	15-20	0	0	0	0	0
20-25	20-25	0	0	0	0	0
25-30	25-30	0	0	0	0	0
30-35	30-35	0	0	0	0	0
35-40	35-40	0	0	0	0	0
40-45	40-45	0	0	0	0	0
45-50	45-50	0	0	0	0	0
		∑n=100	∑nd=330			

Table 4: Calculation of particle size analysis for F1 formulation

Average diameter = $\sum n \times d / \sum n$
= 330/100

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= 3.3 µ

0	**10**	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**
10	3	1	2	1	0	1	4	5	1	2
20	1	2	3	5	4	1	2	2	3	6
30	3	2	1	4	2	1	3	5	1	3
40	0	2	1	4	2	3	1	5	6	2
50	7	2	1	3	2	1	3	2	1	4
60	2	1	3	1	6	2	1	3	2	1
70	3	2	1	1	0	2	2	3	7	1
80	1	3	7	3	2	0	1	2	3	2
90	2	1	2	1	2	4	0	2	1	2
100	3	2	4	2	1	6	2	1	3	2

Table 5: Calculation of particle size analysis for F2 formulation

Size range	**Mean size (d)**	**No. of particle (n)**	**n × d**	**% n**	**Cumulative frequency under size**	**Cumulative frequency over size**
0-5	0-5	94	235	94%	94%	100%
5-10	5-10	6	45	6%	100%	94%
10-15	10-15	0	0	0	0	0
15-20	15-20	0	0	0	0	0
20-25	20-25	0	0	0	0	0
25-30	25-30	0	0	0	0	0
30-35	30-35	0	0	0	0	0
35-40	35-40	0	0	0	0	0
40-45	40-45	0	0	0	0	0
45-50	45-50	0	0	0	0	0
		∑n=100	∑nd/=280			

Table: 6 Calculation of particle size analysis for F2 Formulation

Average diameter = ∑n × d/ ∑n
= 280/100
= 2.8µ

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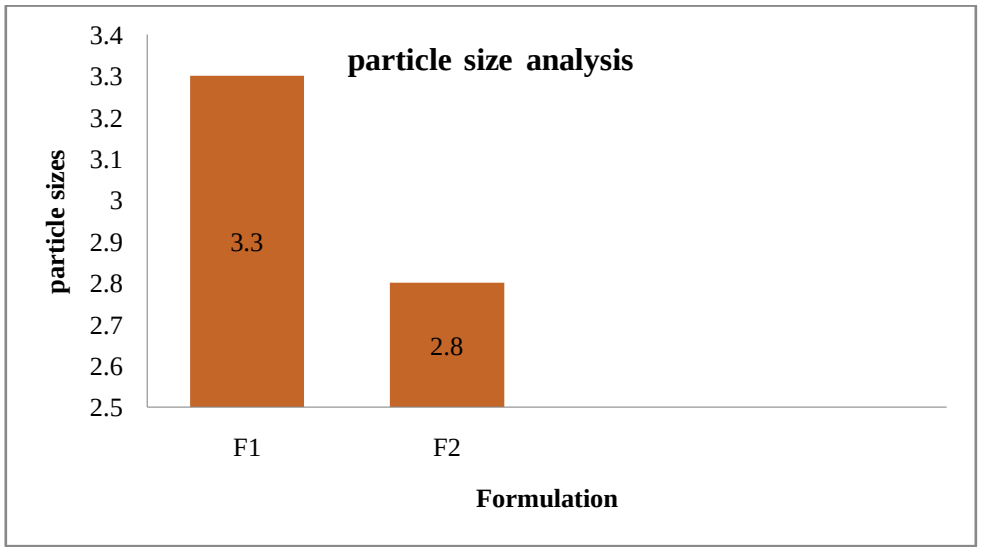

Figure: 8 Comparison graph of Particle size analysis of ibuprofen suspension

Particle size distribution for F2 is 2.8µ. By this, we concluded that F2 has better homogeneity, easily absorbable as compared to F1 formulation.

2. Sedimentation volume

Time	Hu/Ho F1	Hu/Ho F2
0	1	1
5	0.96	0.97
10	0.95	0.95
15	0.94	0.95
20	0.95	0.93
25	0.92	0.9
30	0.9	0.89
45	0.89	0.89
60	0.85	0.88

Table 7: Sedimentation volume for F1 and F2

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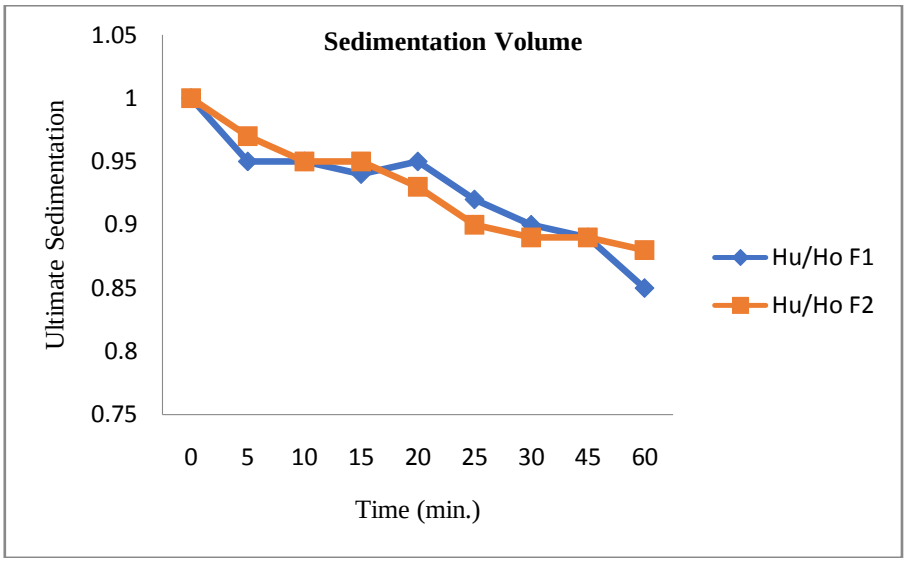

Figure: 9 comparision of sedimentation volume between F1 and F2 formulation

By comparing the sedimentation volume of 2 formulations we concluded that F2 is more stable than F1formulation. As it is higher volume of sedimentation ratio indicates its higher suspendibility.

3. Viscosity

The viscosity of F1 and F2 formulation is 690.1 Mpa×sec, and 693.2 Mpa×sec.

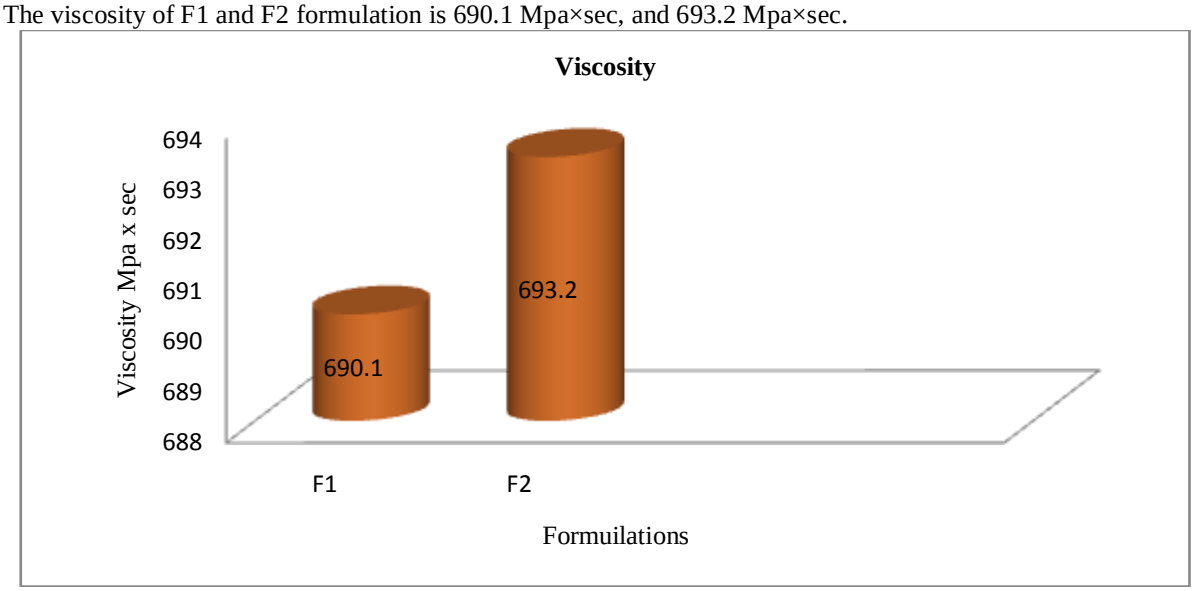

Figure: 10 Comparision between viscosity of ibuprofen suspension formulation F1 and F2

From the above results, it was concluded that F2 formulation having the high stability because it showing high viscosity and show high sedimentation volume among F1formulation.

4. Flow Rate

The flow rate of F1, F2 formulation is 0.87 ml/sec and 0.25 ml/sec.

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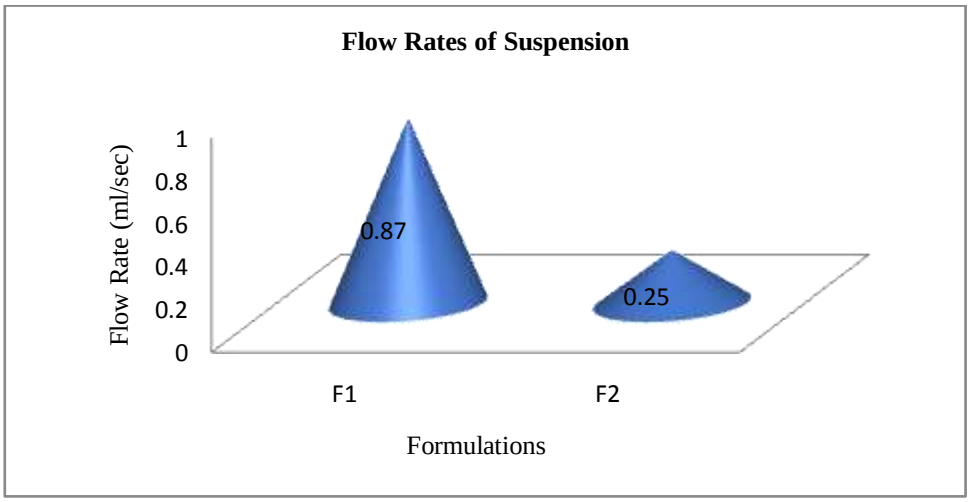

Figure: 11 comparision between Flow rates of Ibuprofen suspension formulation F1 and F2

From the above results, it was concluded that F2 formulation having the high stability because it showing the lowest flow rate than the F1 formulation.

5. P^H of the Ibuprofen suspension.

The PH of Ibuprofen suspension Formulation F1 is 4.7 and F2 is 4.8.

6. Assay of ibuprofen suspension

In the assay of Ibuprofen suspension the Formulation F1 had 93.11%, and F2 had 96.22% drug content.

From the above result, it was concluded that F2 formulation having high percent of drug content than other formulation.

7. Swelling index of fenugreek seed

Swelling index % (SI) = (W1-W/W1) x100
= 25-10/10 x100
= 150%

Result show that as time increases, swelling index was increased. This is because weight gain by mucilage was proportional to rate of hydration. The direct relationship observed between swelling index and mucilage concentration. Mucilage concentration is directly proportional to swelling index.

8. Phytochemical screening of mucilage of fenugreek seeds

Sr. No.	TESTS	OBSERVATION	RESULT
1	Molisch's test	Carbohydrates	Positive
2	Fecl3 test	Tannins	Negative
3	Ninhydrin test	Proteins	Positive
4	Wagner's test	Alkaloids	Positive
5	Keller- killani test	Glycosides	Negative
6	Ruthenium red test	Mucilage	Positive
7	Shinoda test	Flavonoids	Negative
8	Fehling test	Reducing sugar	Negative

Table 8: Phytochemical screening of mucilage of fenugreek seeds

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The preliminary and phytochemical test was performed to confirm the nature of mucilage obtained, mucilage contains carbohydrates, alkaloids and proteins were observed.

VII. CONCLUSION

From the above research review formulation of Ibuprofen suspension, Two formulations F1 and F2 with different concentrations of natural suspending agent Fenugreek seed powder that have good anti-inflammatory activity. It is seen that F2 has better stability as compare to F1 formulation.

Data presented in this study possesses most significant, therapeutically efficacious suitable suspending agent, with high potential.

It is better and significant way to formulate medicines by using fenugreek as suspending agent to obtain better In vitro dissolution study partical size, dispersibility, p^H, flow rate, viscosity, and stability of suspension. So is to stable and good for topical applications.

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