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FORMULATION AND EVALUATION OF IBUPROFEN SUSPENSION USING NATURAL AND SYNTHETIC SUSPENDING AGENTS

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1. ABSTRACT

Ibuprofen is a non steroidal anti-inflammatory drug. It is used to relieve pain from various conditions such as headache, dental pain, menstrual cramps, muscle aches, or arthritis. By using synthetic suspending agents such as methyl cellulose and using natural suspending agents such as fenugreek seed powder, prepare 1%, 2% formulations F1, F2, F3, F4. 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 p^H, Determination of viscosity, In-vitro dissolution studies drug, Assay of Ibuprofen. Phytochemical tests and swelling index for fenugreek seed powder, these tests shows that the Ibuprofen suspension F4 shows better stability than other three formulations.

KEYWORDS: Ibuprofen, fenugreek seed powder, methyl cellulose.

2. INTRODUCTION

Suspension

Suspensions 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.[1]

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. An example of the latter is the treatment of "frothy bloat" with dimethyl polysiloxanes, which relies on a dispersion of finely divided silica in the fore-stomach of ruminants. 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 determinant 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 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.[2]

Advantage of Suspensions

Advantage of suspension can improve chemical stability of certain drug.

E.g. 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.

E.g. Chloramphenicol.

Disadvantage of Suspensions

- Disadvantage of suspension Physical stability, sedimentation and compaction can causes problems.
- 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.
- The storage of suspension may lead to changes in disperse system especially, when there is a fluctuation in temperatures.

Ideal Qualities of Good Suspension

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

TYPES OF SUSPENSIONS

Flocculated Suspension

Flocculated suspension in this type, solid particles are loosely aggregates themselves, means individual particles are come in contact with each other to forms network like structure called as a floccules. These flocs are light, fluffy in nature, which are held together by weak vanderwaals force of attraction. Aggregation is achieved by adding flocculating agent. These suspensions will readily sediments. These suspensions possess better physical stability but less bioavailability as compared to deflocculated suspension due to dissolution of floccules.

Deflocculated Suspension

Deflocculated suspension in this type of suspension, individual particle exits as a separate entity, means particles carry finite charges on their surface. Hence particles approaches each other, they experience repulsive forces. These forces create a high potential barrier, which prevents an aggregation of particles. During storage, these suspension shows a sedimentation at slow rate, due to that particles forms a close packing arrangement. So that it is difficult to re-dispersed on agitation & forms a cake or claying which is hard in nature. This type of suspension has shorter shelf life but high bioavailability as compared to flocculated suspension.[3]

Properties of flocculated suspension

Flocculated Suspension having particles form loose aggregates & forms network like structure. Particles experience attractive forces. Supernatant liquid is clear. The rate of sediment is high. Sediment is rapidly formed. Sediment are loosely packed, hence hard cake is not formed. The sediment is easy to re-disperse on shaking. Bioavailability is comparatively less. Bioavailability is relatively high. The suspension is not pleasing in appearance.[4]

Properties of de-flocculated suspension

De-flocculated suspension having Particles exist as separate entities. Particles experience repulsive forces. Supernatant liquid is cloudy. The rate of sediment is slow. Sediment is slowly formed. Sediments are closely packed, hence hard cake is formed. Sediment is difficult to re-disperse on shaking (Due to formation of hard cake). The suspension is pleasing in appearance.

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
- Characterize the desired rheological behavior of suspension
- Prepare, label, and dispense a suspension.[5]

Formulating Stable Suspensions

Physical stability in suspensions is controlled by

(1) The addition of flocculating agents to enhance particle "Dispersability" and

(2) The addition of viscosity enhancers to reduce sedimentation rate in the flocculated suspension.

Flocculating agents are electrolytes which carry an electrical charge opposite that of the net zeta potential of the suspended particles. The addition of the flocculating agent, at some critical concentration, negates the surface charge on the suspended particles and allows the formation of floccules or clusters as particles are held loosely together by weak Vander Waals forces. Since the particles are linked together only loosely, they will not cake and may be easily re-dispersed by shaking the suspension. Floccules have approximately the same size particles; therefore a clear boundary is seen when the particles settle. [6] The rate of sedimentation of a suspended phase depends on several factors which may be controlled by pharmaceutical manipulation. Assuming that all dispersed particles are of uniform shape and size and that the particles are sufficiently far apart so that the movement of one does not affect the neighbouring particles, the rate of sedimentation can be estimated by Stoke's equation.

$$V = \frac{d^2 (\rho_1 - \rho_2) g}{18 \eta_o}$$

where **V** is the sedimentation rate (cm/sec), d the diameter of the suspended particles (cm), r_1 its density and r_2 is the density of the medium (g/cm^3), g is the acceleration of gravity (980.7 cm/sec^2) and η_o is the viscosity of the external phase in poises (g/cm sec).

Although the Stokes' equation does not consider all the variables which affect the stability of a suspension, it gives an approximation of the settling rate and an appreciation of the variables governing the sedimentation process. For example, by reducing the particle size or by increasing the viscosity and density of the external phase, the rate of sedimentation can be retarded.

As we can see from Stroke's Law, if we apply flocculation as a means of preventing caking, then we will increase the particle diameter, and thus increase the rate of sedimentation. Now we need some means to reduce this rate of settling, so that the suspension can be accurately dosed before it begins to settle. Practically speaking, the viscosity of the dispersion medium is the only other Stokes's variable affecting sedimentation rate over which the pharmacist can exert any control. Suspending or thickening agents are added to suspensions to thicken the suspending medium, thereby reducing the movement (sedimentation) of suspended particles and physically stabilizing the product. This is particularly important in flocculated systems in which rapid particle settling is the primary factor leading to physical instability and lack of dosage uniformity in the product.

Ideally, the system should (rheological) be pseudo plastic; that is, it should have high viscosity at low shear rates (during storage) and low viscosity at high shear rates (during shaking, pouring, or spreading). Suspending agents which are thixotropic as well as pseudo plastic are desirable, since they recover slowly from the deformation that occurs through shearing (i.e. upon shaking, they remain fluid long enough to be poured and spread). [6]

Viscosity Enhancers

Viscosity enhancers include agents from each of the following categories. Typically, 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, fenugreek powder, guar gum, gelatin.
- **Semi synthetic hydrocolloids**
- Methylcellulose, sodium carboxy methylcellulose
- **Synthetic hydrocolloids:** Carbopol
- **Clays:** Bentonite, Veegum

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
- To mask the taste of bitter of unpleasant drug. E.g. Chloramphenicol, palmitate suspension. Suspension of drug can be formulated for topical application e.g. Calamine lotion.

Theoretic considerations

Particle size of any suspension is critical and must be reduced within the range. -Too large or too small particles should be avoided. Larger 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 block the needle. Too fine particles will easily form hard cake at the bottom of the container.

Wetting of the particles: Hydrophilic materials (talc, ZnO, Mg_2CO_3) are easily wetted by water while hydrophobic materials (sulphur, charcoal) are not due to the layer of adsorbed air on the surface. Thus, the particles, even high density, float on the surface of the liquid until the layer of air is displaced completely. The use of wetting agent allows removing this air from the surface and to easy penetration of the vehicle into the pores. However hydrophobic materials are easily wetted by non-polar liquids.

Brownian movement: (Drunken walk) 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 of the suspending medium will keep the particles suspending, provided that their size is below critical radius (r)

Labelling: 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.

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^{O}C.

INTRODUCTION TO NATURAL SUSPENDING AGENT

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-groecum* L., is an annual herb grown in various countries around the world. It was thought to be indigenous to the countries bordering on the eastern shores of the Mediterranean, but now 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. It has been used in many different cultures, but especially in Asia and the Mediterranean region.

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 incense and to embalm mummies. The Greeks and Romans used it for cattle fodder (hence the Latin *foenum graecum* meaning Greek hay). In ancient Rome, fenugreek was purportedly used to aid labor and delivery. In traditional Chinese medicine, fenugreek seeds are used as a tonic, as well as a treatment for weakness and edema of the legs. In India, fenugreek is commonly.[7]

Active constituents

Fenugreek seed contains 45-60 % carbohydrates, mainly mucilaginous fiber (galactomannans); 20-30 % proteins high in lysine and tryptophan; 5-10 % fixed oils (lipids); pyridine-type alkaloids, mainly trigonelline (0.2-0.3 6%), choline (0.5 %), gentianine, and carpaine; the flavonoids 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.[8]

Pharmacological effects and mechanisms of action

Fenugreek is known to have several pharmacological effects such as: hypoglycemic, and antilipidemic or hypocholestrolemic. However, 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 intestines when the mucilagenous fiber of the seeds is hydrated, therefore affecting gastrointestinal transit, slowing glucose absorption.[9] 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 fecal 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. Furthermore, this plant has an antioxidant action, gastroprotective activity, appetite stimulation, and antirheumatism.[10]

3. REVIEW OF LITERATURE

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.

J.D.Sharma and Anjula Bhinda et al., (2005), studied and reported100 % negative result in case of fertility with treatment of fenugreek. Hence, extract of fenugreek show antifertility and anti estrogenic potential in rats.

Saravanan et al., (2009), investigates dethanolic extract of fenugreek plant for its ant diabetic potential. The diabetes was induced in rats by alloxan drug. The extract was given orally in a dose of 50mg/100g up to 48 days. Parameters checked were SGOT, amount of glucose in blood, amount of cholesterol in serum and level of SGPT in alloxan treated and healthy rats. It can be seen that application of extract prepared from plant showed greater reduction in amount of glucose in blood, amount of cholesterol in serum, level of SGOT and level of SGPT.

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, paid attention of the people on this matter.

Manoj M Nitalikar et al., (2010), examined a study technique for division of husk part of T. foenum graecum (fenugreek). A variety of physicochemical criteria counting angle of repose, distribution of particle and swelling factor were determined. As a binder husk of fenugreek in tablets was studied. To optimize the binding potential of dispersion of methi husk in tablets, as a sculpt drug ibuprofen was chosen. Assessment of dispersion of husk with paste of starch was done. The greatest amount needed of the dispersion of husk was 4-6% as a binder, which is comparatively less in contrast to standard. Dispersion of methi husk was established to be advanced over paste of starch.

Meera Sumanthet et al., (2011), endeavor of 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 componants.

Payal Dande and Suraj Patil et al., (2012), examined antifertility potential of seeds of fenugreek containing saponins. Three diverse investigational models were taken like estrogenic activity, anti implantation and anti estrogenic activity. In anti implantation potential saponin extract showed greater prominent action. At the similar instance it depicted less estrogenic potential in rats. It can be accomplished that antifertility potential was proved by the saponin extract of Fenugreek.

Hawazen A. Lamfon et al., (2012), studied the result on testicular toxicity induced by carbendazim using extract of seeds of methi. It was accomplished that testicular toxicity gets advanced by means of fenugreek extract. The findings can be as of antioxidant potential of plant matter.

Jaleh Varshosaz et al., (2012), intention of the nearby examination was to assess the binding potential of fenugreek mucilage in formulation. Mucilagenous part of fenugreek seed was secluded and employed in a role of fastening agent in all diverse medicines. Model drugs chosen were theophylline, ibuprofen, Calciumacetate. The consequences demostrated that a 2.5% amount of the novel binder in contrast to typical binders studied.

Neha Sharmaet al., (2014), an attempt was made to reveal the possible beneficial results of Trigonella foenum graecum extract and glibenclamide in regulation of diabetes mellitus and hepatic lipid peroxidation. Combined effects of TFG and GLB compared with that of individual treatments for regulation of alloxan induced hyperglycemia, hepatic LPO and to the changes in the status of antioxidants. HPLC was also performed to find out the concentrations of major active compounds. Combined administration of TFG and GLB not only inhibited LPO and glucose to a great extent, but also ameliorated the alloxan induced decrease in insulin and antioxidants in contrast to the individual drugs. HPLC analyses of the test extract revealed the presence of trigonelline, quercetin and rutin. Fenugreek seed extract, when added along with glibenclaimide may ameliorate diabetes mellitus to a greater extent as compared to monotherapy.

Minna Helin-Tanninen et al(12 July 2012): In order to comply with the pharmacopeia test for content uniformity, suspensions compounded with methylcellulose 1% syrup NF or hypromellose 1% require mixing by invertin the bottle 10-15 times. In contrast, the commercial suspension vehicles passed the test if the bottle was inverted only three times.

Robert lundqvist et al, (31 Jan 2007) A study of the rheology of aqueous solutions of methylcellulose is presented with the aim of supporting the previously suggested physics, referred to as laminar dynamics, of the viscosity increasing effect per unit volume of particles with extended shape on a flowing suspension. Since it is essential that appropriate flow is employed in order to utilize the proposed model enabling absolute values of the particle's weight average axial ratio a_w to be derived from the intrinsic viscosity [η], the shear requirement is studied extensively. It is demonstrated how these universal functions can be used for absolute determination of a_w and subsequent calculation of such values as molecular weight, size, Mark-Houwink constant, critical ("overlap") concentration c*, and radius of gyration $R_{g,w}$. In addition, a universal suspension characteristic termed critical specific viscosity η_{sp}* is identified.

Sc Marriott et al, (1991 Sep; 66(9): 1037–1042.) A double blind trial was conducted to determine the dose of Ibuprofen suspension, which is effective in reducing the body temperature. The principal measure of efficacy was a reduction in auxiliary temperature of 1 degree C or more three hours after dosing. A second objective of the trial was to compare the incidence and severity of side effects and the palatability of a range of Ibuprofen doses. Ninety three children were included in the analysis. All four doses of ibuprofen studied (0.625 mg/kg-5 mg/kg) were associated with temperature reduction and only the lowest dose failed to satisfy the principal measure of efficacy.

Jc Revera levya et al, 2012 Jul; In vitro dissolution studies for solid oral dosage forms have recently widened the scope to a variety of special dosage forms such as suspensions. For class II drugs, like Ibuprofen, it is very important to have discriminative methods for different formulations in physiological conditions of the gastrointestinal tract, which will identify different problems that compromise the drug bioavailability. In the present work, two agitation speeds have been performed in order to study ibuprofen suspension dissolution. The suspensions have been characterised relatively to particle size, density and solubility. The dissolution study was conducted using the following media: buffer pH 7.2, pH 6.8, 4.5 and 0.1 M HCl. For quantitative analysis, the UV is spectro-photometry was used because this

methodology had been adequately validated. The results show that 50 rpm was the adequate condition to discriminate the dissolution profile. The suspension kinetic release was found to be dependent on pH and was different compared to tablet release profile at the same experimental conditions. The ibuprofen release at pH 1.0 was the slowest.

4. AIM AND OBJECTIVE

AIM

- The aim is to comparison of natural and synthetic suspending agents in Ibuprofen suspension.
- Preparation of Ibuprofen formulation can be done by trituration method by using natural suspending agents such as fenugreek seed powder and synthetic suspending agent such as methyl cellulose.

OBJECTIVE

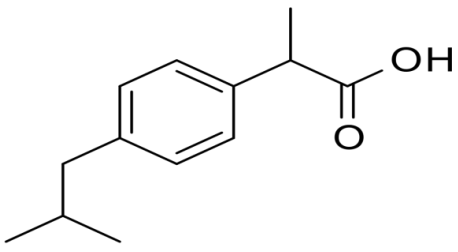
- Evaluation tests are performed such as sedimentation volume, particle size analysis, flow rate, Determination of p^H, Determination of viscosity, In-vitro dissolution studies, Assay of ibuprofen. Phytochemical tests and swelling index for fenugreek seed powder, these tests shows that the ibuprofen suspension F4 had better stability than the otherF1, F2, F3 formulations.

5. DRUG PROFILE

IBUPROFEN

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) used for relieving pain, helping with fever and reducing inflammation.

Structure



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

Molecular formula: $C_{13}H_{18}O_2$

Molecular weight: 26.2882g/mol

PHYSICAL CHARACTERS

State: white crystalline powder

Colour: colourless

Solubility: Soluble in ethanol(25mg/ml),chloroform(1:1),ether(1:2), acetone(1:1.5),aqueous solutions of alkali hydroxides and carbonates, dichloromethane, methanaol(5mg/ml),an ethyl acetate. Partially insoluble in water.

Dissociation constant: pKa = 5.2

Melting point: 76^0 c

Density: 1.03gm/ml

Pharmacokinetics: Table no.1

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

Pharmacological propertie

Nonsteroidal anti-inflammatory drugs such as Ibuprofen 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) and to thromboxane A2 (which stimulates platelet aggregation, leading to the formation of blood clots).

The exact mechanism of action of Ibuprofen is unknown. Ibuprofen is a nonselective 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, vasodilation, and subsequent heat dissipation. Inhibition of COX-1 is thought to cause some of the side effects of Ibuprofen including gastrointestinal ulceration. Ibuprofen is administered as a racemic mixture. The R-enantiomer undergoes extensive interconversion to the S-enantiomer *in vivo*. The S-enantiomer is believed to be the more pharmacologically active enantiomer Like aspirin and Indomethacin, Ibuprofen is a nonselective COX inhibitor, in that it inhibits two isoforms 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.[40] However, the role of the individual COX isoforms in the analgesic, anti-inflammatory, and gastric damage effects of NSAIDs is uncertain and different compounds cause different degrees of analgesia and gastric damage.

Adverse effects

Adverse effects include nausea, dyspepsia, gastrointestinal ulceration/bleeding, raised liver enzymes, diarrhea, constipation, nosebleed, headache, dizziness, rash, salt and fluid retention, and hypertension.

Infrequent adverse effects include esophageal ulceration, heart failure, hyperkalemia, renal impairment, confusion, and bronchospasm. Ibuprofen can exacerbate asthma, sometimes fatally.

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 medicolegal death investigation. A monograph relating ibuprofen plasma concentration, time since ingestion, and risk of developing renal toxicity in overdose patients has been published.

Uses

Ibuprofen is used to relieve pain from various conditions such as headache, dental pain, menstrual cramps, muscle aches, or arthritis. It is also used to reduce fever and to relieve minor aches and pain due to the common cold or flu. Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID). It works by blocking your body's production of certain natural substances that cause inflammation. This effect helps to decrease swelling, pain, or fever.

6. EXCIPIENTS PROFILE

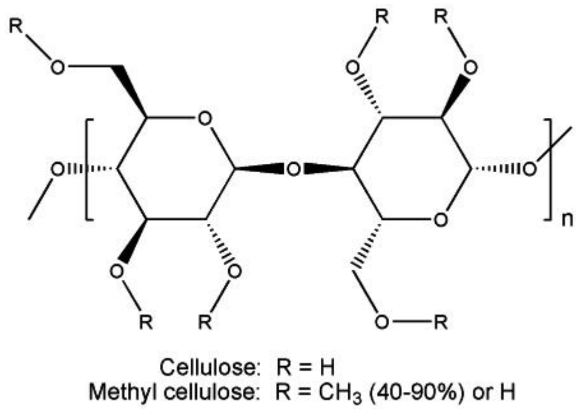
METHYL CELLULOSE

Synonym: Cellulose methyl ether.

Chemical name: Methyl ether cellulose, cellulose methyl ether.

Formula: $C_6H_7O_2$ (OH)x(OCH_3)y.

Molecular structure



Definition: The methyl ether of cellulose, prepared from wood pulp or cotton by treatment with alkali and methylation of the alkali cellulose with methyl chloride.

Description: Hygroscopic white or off-white, odourless fine granules, filaments or powder, thickening agent, emulsifier, stabilizer.[12]

Pharmaceutical specification:

Solubility: swelling in water, producing a clear to opalescent, viscous, colloidal solution; insoluble in ethanol, ether and chloroform; soluble in glacial acetic acid.

P^{H} : 5 to 8.

USES OF METHYL CELLULOSE

Treating constipation and restoring regularity. It may also be used for other conditions as determined by your doctor. Methylcellulose is a bulk-forming laxative. It works by absorbing water and swelling in the intestines. [13]

Thickener and emulsifier

Methyl cellulose is very occasionally added to hair shampoos, tooth pastes and liquid soaps, to generate their characteristic thick consistency. This is also done for foods, for example ice cream or croquette. Methyl cellulose is also an important emulsifier, preventing the separation of two mixed liquids because it is an emulsion stabilizer.

Lubricant

Methyl cellulose is used as a variable viscosity personal lubricant; it is the main ingredient in K-Y Jelly.

Clinical

The lubricating property of methyl cellulose is of particular benefit in the treatment of dry eyes (Keratoconjunctivitis Sicca). Dry eyes are common in the elderly and are often associated with rheumatoid arthritis. The lacrimal gland and the accessory conjunctival glands produce fewer tears. Methyl cellulose may be used as a tear substitute.

Artificial tears and saliva

Solutions containing methyl cellulose or similar cellulose derivatives are used as substitute for tears or saliva if the natural production of these fluids is disturbed.

Nutritional supplement capsules

Methyl cellulose is used in the manufacture of capsules in nutritional supplements; its edible and nontoxic properties provide a vegetarian alternative to the use of gelatin.

FENUGREEK SEED POWDER

Fenugreek (***Trigonella foenum-graecum***) is an annual plant in 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.[11]

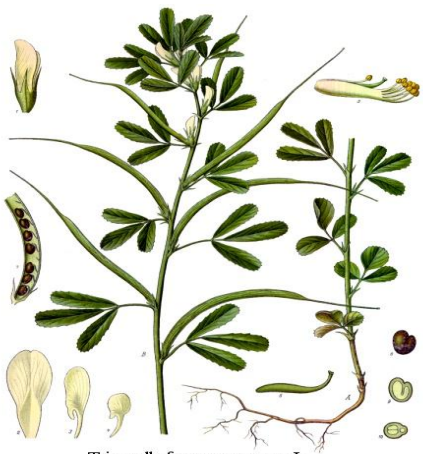
Morphology

1. Appearance: Solid- rhomboidal seeds, 3 to 5 mm long, 2 mm thick. Hard, pebble-like.

2. Colour: Yellowish brown-light brown.

3. Odour: characteristic spicy.

4. Taste: Bitter and mucilaginous.



Trigonella foenum-graecum L.
Image processed by Thomas Schoepke
www.plant-pictures.de

PHYTOCHEMISTRY

Seed

Fenugreek Seeds are aromatic, bitter, carminative, galactogouge, antibacterial and may be eaten raw or cooked. Bulk of the seed is dietary fiber (50%) and protein (30%) both of which have no taste or flavor. The chemical components of fenugreek seeds include a large carbohydrate fraction (mucilaginous fiber, galactomannan); 20-30% proteins high in tryptophan and lysine; pyridine-type alkaloids; flavonoids; free amino acids (4-hydroxyisoleucine, arginine, lysine, histidine); saponins; glycosides; vitamins, minerals, (28%) mucilage, (22 %) proteids, 5 % of a stronger-smelling, bitter fixed oil. volatile oils. Bitterness is mainly due to the oil, steroidal saponins and alkaloids. Historically used as a culinary and medicinal herb, recent research studies have shown its effectiveness in reducing blood glucose levels, promoting lean body mass, lowering cholesterol, [14] and treating gastrointestinal disorders. Studies with type 2 diabetics have shown a blood glucose normalizing effect and decreased insulin resistance. Preliminary research with type-1 diabetics suggest that fenugreek may aid insulin secretion and may reduce total cholesterol and LDL cholesterol levels.[15]

Seeds contain 0.1% to 0.9% diosgenin and are extracted on a commercial basis. Plant tissue cultures from seeds grown under optimal conditions have been found to produce as much as 2% diosgenin with smaller amounts of gitongenin and trigogenin. The seeds also contain the saponinfenugrin B. Several coumarin compounds have been identified in fenugreek seeds as well as a number of alkaloids (eg, trigonelline, gentianine, carpaine). A large proportion of the trigonelline is degraded to nicotinic acid and related pyridines during roasting. These degradation products are, in part, [16] responsible for the flavor of the seed. The seeds also yield as much as 8% of fixed, foul-smelling oil. Three minor steroidal sapogenins also have been found in the seeds: smilagenin, sarsapogenin, and yuccagenin.

PHARMACOGNOSTICAL STUDIES

The macroscopy of the seeds were studied by comparing their macroscopical characters mentioned in the literature. Size was measured using a graduated ruler in millimetres which was used for the measurement of the length, width and thickness of seed samples. Since, the seeds are quite small in size they are measured by aligning 10 of them on a sheet of calibrated paper, with 1mm spacing between lines, and dividing the result by 10.[17] The colour was examined by exposing the untreated seed sample under diffuse daylight, and the colour of the

seed sample was studied. For analysing the surface characteristics, texture and fracture characteristics the untreated seed sample were examined using a magnifying lens (6X to 10X), seed surface was touched to determine the texture whether soft or hard; bend or ruptured and to obtain information on brittleness and the appearance of the fracture plane-whether it is fibrous, smooth, rough granular, etc. [18] The odour was analysed by placing a small portion of the crushed seed sample (25g) in a 100ml beaker and then pouring a small quantity of boiling water onto the crushed seed sample. Determined the strength of the odour (none, weak, distinct, strong) and then the odour sensation (aromatic, fruity, musty, mouldy, rancid, etc.).[20]

1. Macroscopic characteristics of fenugreek

- **Macroscopical characters**

The morphological studies were carried out for shape, size, color, odour and taste and fracture identification of the fenugreek seed.[21]

- **Macroscopical evaluation**

The macroscopical characters of seeds are -Solid-rhomboidal, pebble like shape, 3- 5cm long, 2mm thick, plain surface, yellow, bitter mucilaginous taste and have characteristic odour.[22]

- **Medicinal uses**

The seeds are hot, with a sharp bitter taste; tonic, antipyretic, anthelmentic, increase the appetite, astringent to the bowels, cure leprosy, “vata”, vomiting, bronchitis, piles; remove bad taste from the mouth, useful in heart disease[23] (Ayurvedic).1, 3 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.[24] 1, 3 Fenugreek seeds are considered carminative, tonic and aphrodisiac. Several confections made with this the article are recommended for use in dyspepsia with loss of appetite, in the diarrhea of puerperal women, and in rheumatism.[25]

MEDICINAL STUDIES

Anticancer Activity

Fenugreek seeds showed potential protective activity against 7, 12-dimethylbenz(a) anthracene (DMBA)-induced breast cancer in rats at 200mg/kg body weight. Fenugreek seeds extract significantly inhibited the DMBA-induced mammary hyperplasia and decreased its incidence. [26] Epidemiological studies also implicate apoptosis as a mechanism that might mediate the Fenugreek's antibreast cancer protective effects.[27] The ethanolic extract of *Trigonella foenum-graecum*, with an ED50 less than10µg/ml in the brine shrimp cytotoxicity assay, was also observed to possess anti-tumour activity in A-549 male lung carcinoma, MCF-7 female breast cancer and HT-29 colon adenocarcinoma cell lines.[28] The extract gave negative results in the mutagenicity test. *Trigonellafoenum-graecumhas* appreciable anti-cancer activity.[29] Flavonoids seem to be most likely candidates eliciting study establishes anti-tumorigenic effect.[30]

SODIUM BENZOATE

Synonyms

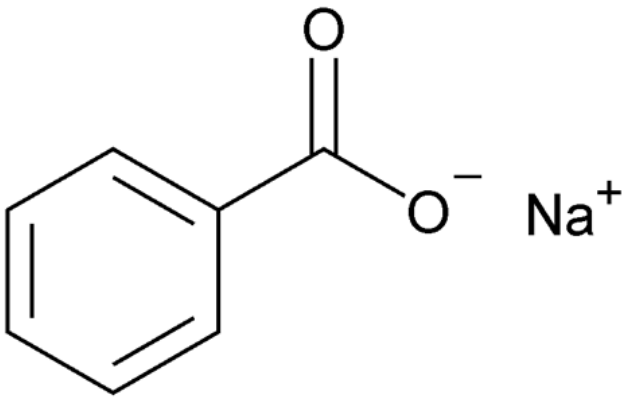
- Benzoic acid sodium salt;
- Benzoate of soda;
- Natrium benzoicum;
- Sodium benzoic acid.

Empirical Formula: $C_7 H_5 NaO_2$.

Molecular Weight: 144.11g/mol

Functional Category: Antimicrobial preservative; tablet and capsule lubricant

Structure



Applications in Pharmaceutical Formulation or Technology

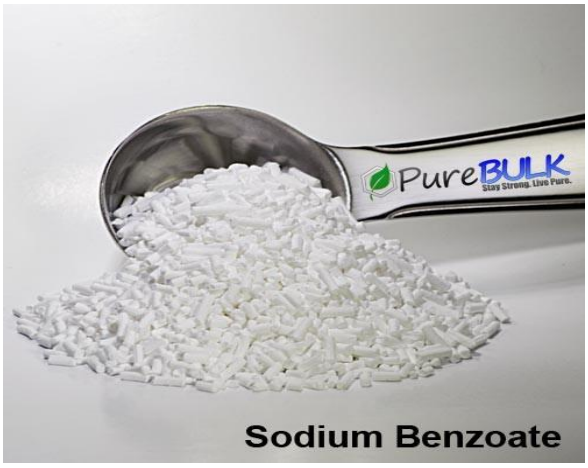
Sodium benzoate is used primarily as an antimicrobial preservative in cosmetics, foods, and pharmaceuticals. It is used in concentrations of 0.02–0.5% in oral medicines, 0.5% in parenteral products, and 0.1–0.5% in cosmetics. The usefulness of sodium benzoate as a preservative is limited by its effectiveness over a narrow pH range. Sodium benzoate is used in preference to benzoic acid in some circumstances, owing to its greater solubility. However, in some applications it may impart an unpleasant flavor to a product. Sodium benzoate has also been used as a tablet lubricant at 2–5% w/w concentrations. Solutions of sodium benzoate have also been administered, orally or intravenously, in order to determine liver function.[31]

Description

Sodium benzoate occurs as a white granular or crystalline, slightly hygroscopic powder. It is odorless, or with faint odor of benzoin and has an unpleasant sweet and saline taste.[32]

Stability and Storage Conditions

Aqueous solutions may be sterilized by autoclaving or filtration. The bulk material should be stored in a well-closed container, in a cool, dry place.[33]



Incompatibilities

With quaternary compounds, gelatin, ferric salts, calcium salts, and salts of heavy metals, including silver, lead, and mercury. Preservative activity may be reduced by interactions with kaolin or nonionic surfactants.[34]

GLYCERIN

Synonyms

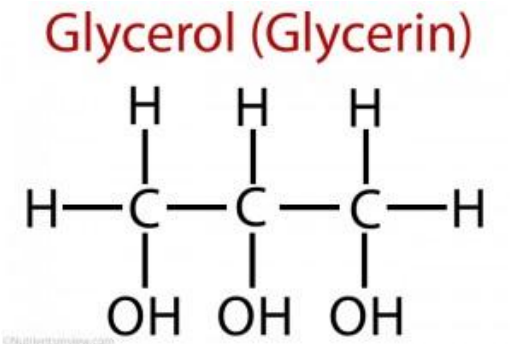
- Croderol;
- glicerol;
- glycerine;
- glycerolum;
- Kemstrene;

Chemical Name: Propane-1, 2, 3-triol

Empirical Formula: $C_2H_5NO_2$.

Molecular Weight: 92.093g/mol

Structural Formula



Functional Category: Antimicrobial preservative; cosolvent; emollient; humectant; plasticizer;

Solvent: Sweetening agent; tonicity agent.

Applications in Pharmaceutical Formulation or Technology

Glycerin is used in a wide variety of pharmaceutical formulations including oral, otic, ophthalmic, topical, and parenteral preparations. In topical pharmaceutical formulations and cosmetics, glycerin is used primarily for its humectant and emollient properties. Glycerin is used as a solvent or cosolvent in creams and emulsions. Glycerin is additionally used in aqueous and nonaqueous gels and also as an additive in patch applications. In parenteral formulations, glycerin is used mainly as a solvent and cosolvent. In oral solutions, glycerin is used as a solvent, sweetening agent, antimicrobial preservative and viscosity-increasing agent. It is also used as a plasticizer and in film coatings. Glycerin is used as a plasticizer of gelatin in the production of soft-gelatin capsules and gelatin suppositories. Glycerin is employed as a therapeutic agent in a variety of clinical applications, and is also used as a food additive.[35]

Description

Glycerin is a clear, colorless, odorless, viscous, hygroscopic liquid; it has a sweet taste, approximately 0.6 times as sweet as sucrose.

Stability and Storage Conditions

Glycerin is hygroscopic. Pure glycerin 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 glycerin 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 208C. Glycerin should be stored in an airtight container, in a cool, dry place.

Incompatibilities

Glycerin may explode if mixed with strong oxidizing agents such as chromium trioxide, potassium chlorate, or potassium permanganate. In dilute solution, the reaction proceeds at a slower rate with several oxidation products being formed. Black discoloration of glycerin occurs in the presence of light, or on contact with zinc oxide or basic bismuth nitrate. An iron contaminant in glycerin is responsible for the darkening in color of mixtures containing

phenols, salicylates, and tannin. Glycerin forms a boric acid complex, glycerol boric acid, which is a stronger acid than boric acid.

Method of Manufacture

Glycerin is mainly obtained from oils and fats as a by-product in the manufacture of soaps and fatty acids. It may also be obtained from natural sources by fermentation of, for example, sugar beet molasses in the presence of large quantities of sodium sulfite. Synthetically, glycerin may be prepared by the chlorination and saponification of propylene.

Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and gloves are recommended. In the UK, the recommended long-term work place exposure limit for glycerin mist is 10 mg/m3. Glycerin is combustible and may react explosively with strong oxidizing agents.

TWEEN 80

Definition: nonionic surfactant and emulsifier often used in foods and cosmetics. This synthetic compound is a viscous, water-soluble yellow liquid.[36]

Brand names

- Alkest TW 80
- Scattics
- Canarcel
- Poegasorb 80

Molecular formula: $C_{32}H_{60}O_{10}$

Molecular weight: 604.8128g/mol

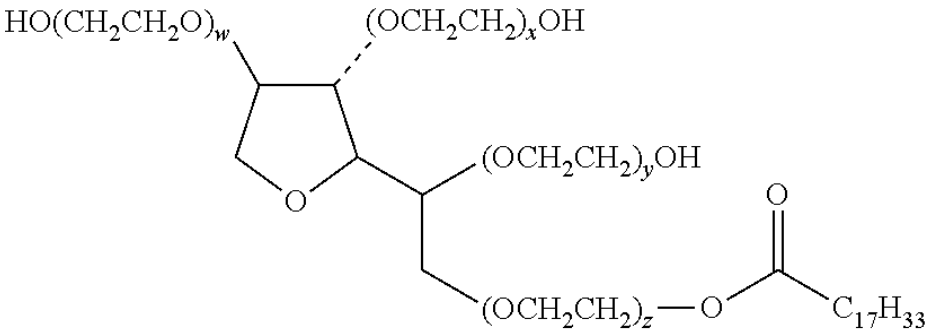
Chemistry

Polysorbate 80 is derived from polyethoxylated sorbitan and oleic acid. The hydrophilic groups in this compound are polyethers also known as polyoxyethylene groups, which are polymers of ethylene oxide. In the nomenclature of polysorbates, the numeric designation following polysorbate refers to the lipophilic group, in this case the oleic acid.

The full chemical names for polysorbate 80 are:

- Polyoxyethylene (20) sorbitan monooleate
- (x)-sorbitan mono-9-octadecenoate poly(oxy-1,2-ethanediyl)

Structure



Polysorbate 80
(Sum of w, x, y, and z is 20)

Food use

- Polysorbate 80 is used as an emulsifier in foods.
- For example 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 also 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.

Medical 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. It is also used in the culture of *Mycobacterium tuberculosis* in Middlebrook 7H9 broth. It is also used as an emulsifier in the estrogen-regulating drug Estrasorb.

Laboratory use

- Some mycobacteria contain a type of lipase (enzyme that breaks up lipid molecules). When added to a mixture of polysorbate 80 and phenol red, they cause the solution to change colour, so this is used as a test to identify the phenotype of a strain or isolate.

7. PREPARATION AND EVALUATION OF IBUPROFEN SUSPENSION BY USING NATURAL AND SYNTHETIC SUSPENDING AGENT

7.1 Preparation of Suspension

7.2 Evaluation of suspension

A. Calibration curve of Ibuprofen.

B. In-vitro dissolution studies.

C. Particle size analysis

D. Sedimentation volume

E. Viscosity

F. Flow rate

G. P^H

H. Assay of Ibuprofen.

I. Swelling index of fenugreek seeds

J. Phyto-chemical tests for fenugreek seeds

Preparation of suspension

Table no.2: Formula of Ibuprofen suspension.

Ingredients	F1	F2	F3	F4	Uses
Ibuprofen	2gm	2gm	2gm	2gm	Anti inflammatory
Methyl cellulose	1gm	2gm	_	_	Suspending agent
Fenugreek seed powder	_	_	1gm	2gm	Natural Suspending agent
Simple syrup	10ml	10ml	10ml	10ml	Sweetening agent
Sodium benzoate	0.1gm	0.1gm	0.1gm	0.1gm	Preservative
Tween 80	0.1gm	0.1gm	0.1gm	0.1gm	Wetting agent
Glycerin	10ml	10ml	10ml	10ml	Viscosity enhancer
Water	q.s	q.s	q.s	q.s	Vehicle

Preparation

Suspension of ibuprofen were prepared by tituration method using above ingredients .weighed quantity of Ibuprofen and taken into a dry motor and titurated until fine powder is obtained. Add the tween 80 and mixed to form uniform suspension, and then add methyl cellulose and titurate again. To the above mixture glycerin was added and mixed to form a

uniform suspension. Finally to this suspension simple syrup followed by sodium benzoate dissolved in few ml of water in a separate beaker. This is mixed thoroughly and transport into measuring cylinder. The volume is made with the water.

7.2 Evaluation of suspensions

A. Calibration curve of ibuprofen

100mg of drug was weighed and dissolved in small quantity of methanol and makeup upto 100ml with 7.2pH phosphate buffer. Which gives 1000µg per ml from that concentration 1ml is pipetted out and the volume is made upto 100ml with phosphate buffer which gives 100µg per ml which is a stock solution. From that stock solution prepare different concentration of 2, 4, 6, 8, 10µg/ml. by using UV spectro-photometer at 221nm. Note the absorbance of the prepared concentration. Finally plot a graph between concentration Vs absorbance.[37]

B. 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 [38]

Parameters for dissolution process

- Apparatus – paddle type dissolution apparatus
- Medium- 7.2pH phosphate buffer
- Stirrer- paddle at 50 rpm
- Temperature- $37^{o}c \pm 0.5^{o}c$
- Duration - 30 min.
- Total no of samples = 6

- Wave length = 221nm

Procedure: Fill the vessel with 7.2 pH phosphate buffer upto 900ml and maintain the temperature of the vessel at 3.7^{o}c ± 0.5^{o}c place 5ml of Ibuprofen suspension in the vessel .The samples of 5ml was collected at a predetermined time intervals. Replace the 5ml of sample with 5ml of 7.2pH phosphate buffer to maintaining sink condition. The samples were diluted if necessary and note the absorbance of the sample by using UV visible spectro-photometer at 221nm.

C. Particle size analysis

Firstly calibrate the eye piece. Place a drop of lotion on a glass slide and was covered with a cover slip without any air bubbles and was observed under microscope. Each particle diameter was measured and recorded for at least 100 particles.

D. Determination of sedimentation volume

Transfer the prepared ibuprofen suspension into a measuring cylinder and was kept aside without disturbing observe the height of the sediment at a regular time intervals of 0, 10, 20, 30, 40, 50, 60, and calculate the sedimentation volume by using the following.

F = 100 Hu/Ho

E. Measurement of viscosity using Brookfield viscometer

The viscosity (M.pa×sec) of the sample was determined at 24^{O}C using Brookfield Synchro-electric viscometer; at 12 RPM (spindle T Shaped).[40] All determinations were made in at least triplicate and the results obtained are expressed as the mean values.

F. 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[41]

$$\text{Flow rate} = \frac{\text{Volume of pipette (ml)}}{\text{Flow time (s)}}$$

G. Determination of p^{H}

The p^{H} of suspension is determined by using digital p^{H} meter. [42]

H. 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 phenophthalein as an indicator. The end point was colourless to pale pink. [43]

Equivalent factor: each ml 0.1N NaOH = 0.02063 gm of Ibuprofen

I. 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 rated. [44]

$$swelling\ index\% = \frac{w1-w2}{w1} \times 100$$

W1= Weight of tablet at time '0'

W2= Weight of tablet at time 't'

J. Pytochemical 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.[45]

8. RESULTS AND DISCUSSION

A. CALIBRATION CURVE OF IBUPROFEN

Table no.3: Calibration curve.

Concentration (µg/ml)	Absorbance
2	0.112
4	0.212
6	0.306
8	0.402
10	0.508
12	0.612

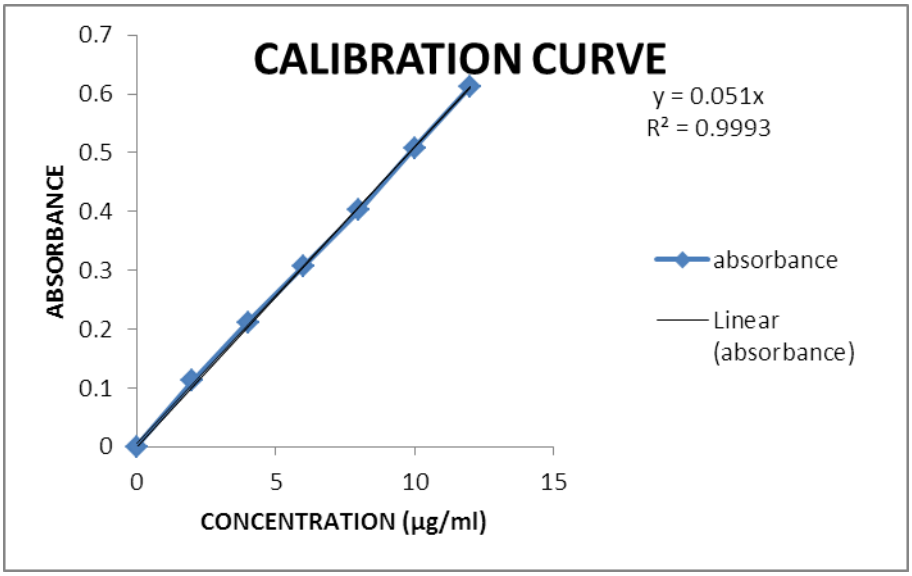


Fig no.1: Calibration curve of Ibuprofen.

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

B.IN-VITRO DISSOLUTION STUDIES.

Table no. 4 Drug Release for F1 Formulation.

Time	Absorbance	Dilution Factor	Actual Absorbance	Amount	Conc	%Drug Release
5	0.206	10	2.06	41.2	37.08	37.08
10	0.225	10	2.25	45	40.05	40.05
15	0.312	10	3.12	62.4	56.16	56.16
20	0.386	10	3.86	77.2	64.98	64.98
25	0.407	10	4.07	81.4	73.26	73.26
30	0.465	10	4.65	93	83.7	83.7

Table no. 5: Drug Release for F2 Formulation.

Time	Absorbance	Dilution Factor	Actual Absorbance	Amount	Conc	%Drug Release
5	0.225	10	2.25	45	40.5	40.5
10	0.254	10	2.54	50.8	45.72	45.72
15	0.325	10	3.25	65	58.5	58.5
20	0.397	10	3.97	79.4	71.46	71.46
25	0.424	10	4.27	85.4	76.86	76.86
30	0.512	10	5.12	102.4	91.8	91.8

Table no.6: Cumulative drug release of F1 and F2 formulation.

S.NO	TIME	F1 (cumulative % drug release)	F2 (cumulative % drug release)
1	5	37.08 ±0.05	40.5 ±0.21
2	10	40.05 ±0.21	45.72 ±0.35
3	15	56.16 ±0.32	58.5 ±0.45
4	20	64.98 ±0.41	71.46 ±0.52
5	25	73.26 ±0.46	76.86 ±0.61
6	30	83.7 ±0.54	91.8 ±0.76

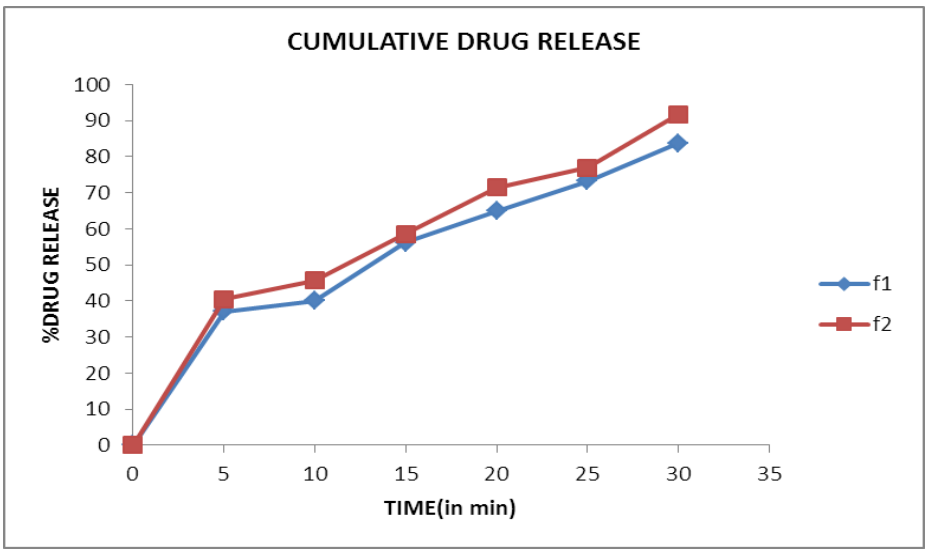


Fig. no. 2: Cumulative drug release for F1 & F2 Formulations.

Table no. 7 Drug Release for F3 Formulation.

Time	Absorbance	Dilution Factor	Actual Absorbance	Amount	Conc	%Drug Release
5	0.256	10	2.56	51.2	46.08	46.08
10	0.298	10	2.98	59.6	53.64	53.64
15	0.315	10	3.15	63	56.7	56.7
20	0.399	10	3.99	79.6	71.64	71.64
25	0.435	10	4.35	87	78.3	78.3
30	0.523	10	5.23	104.6	94.14	94.14

Table no. 8: Drug Release for F4 Formulation.

Time	Absorbance	Dilution Factor	Actual Absorbance	Amount	Conc	%Drug Release
5	0.279	10	2.79	55.8	50.22	50.22
10	0.299	10	2.99	59.8	53.82	53.82
15	0.32	10	3.2	64	57.6	57.6
20	0.405	10	4.05	81	72.9	72.9
25	0.446	10	4.46	89.8	80.28	80.28
30	0.548	10	5.48	109.6	98.64	98.64

Table no.9: Cumulative drug release of F3 and F4 formulation:

S.NO	TIME	F3 (cumulative % drug release)	F4 (cumulative % drug release)
1	5	46.08 ±0.02	50.22 ±0.09
2	10	53.64 ±0.14	53.82 ±0.16
3	15	56.7 ±0.29	57.6 ±0.25
4	20	71.64 ±0.31	72.9 ±0.274
5	25	78.3 ±0.42	80.28 ±0.72
6	30	94.14 ±0.51	98.64 ±1.02

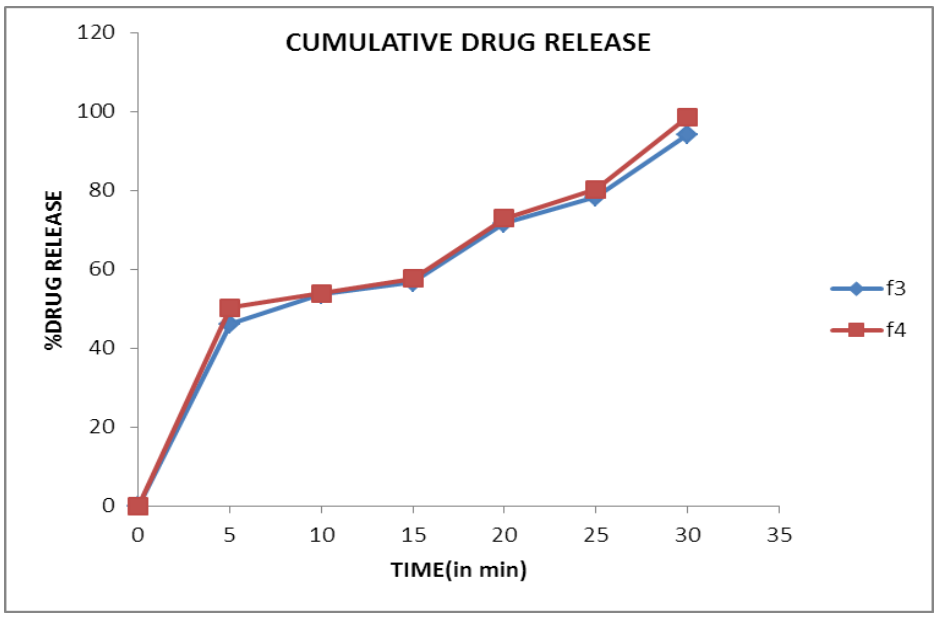


Fig. no.3: Cumulative drug release for F3 & F4 Formulations.

Table no.10: Cumulative drug release for Four Formulations (F1, F2, F3, F4):

S.NO	TIME	F1 (cumulative% drug release)	F2 (cumulative % drug release)	F3 (cumulative % drug release)	F4 (cumulative% drug release)
1	5	37.08 ±0.05	40.5 ±0.21	46.08 ±0.02	50.22 ±0.09
2	10	40.05 ±0.21	45.72 ±0.35	53.64 ±0.14	53.82 ±0.16
3	15	56.16 ±0.32	58.5 ±0.45	56.7 ±0.29	57.6 ±0.25
4	20	64.98 ±0.41	71.46 ±0.52	71.64 ±0.31	72.9 ±0.274
5	25	73.26 ±0.46	76.86 ±0.61	78.3 ±0.42	80.28 ±0.72
6	30	83.7 ±0.54	91.8 ±0.76	94.14 ±0.51	98.64 ±1.02

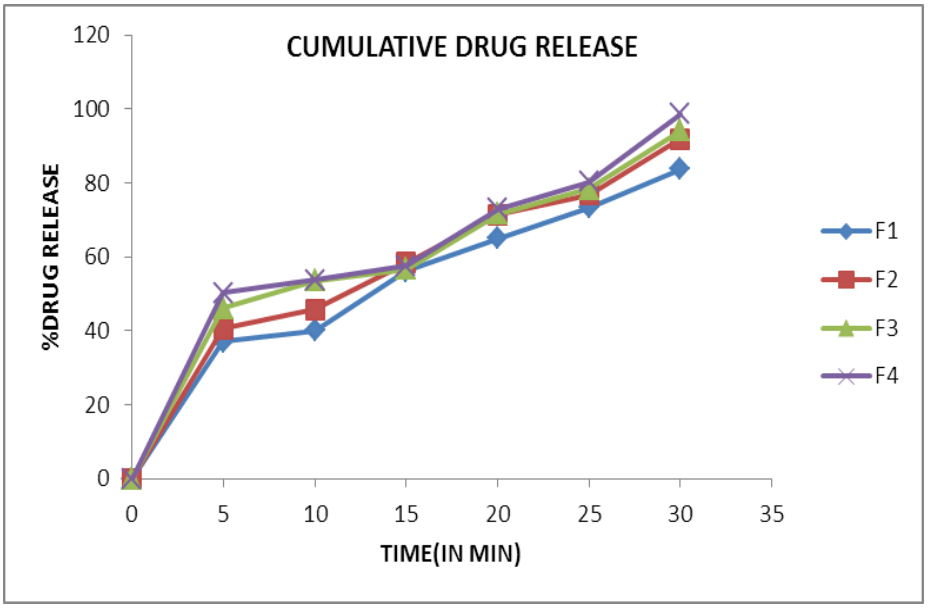


Fig. no.4: comparison of Cumulative drug release forF1, F2, F3 & F4 formulations.

The In-vitro release of all the formulations was found to be 83.7, 92.16, 94.14, 98.64 for F1, F2, F3, & F4 formulations respectively, the formulation F4 showing the better drug release (98.64) at the end of 30min. as compared to other formulations.

C. PARTICLE SIZE ANALYSIS

Table no.11 Particle size analysis for F1 formulation.

0	10	20	30	40	50	60	70	80	90	100
10	4	3	4	1	1	4	2	2	7	9
20	6	1	1	7	6	9	7	7	5	6
30	6	2	5	4	3	2	4	2	3	2
40	1	2	4	3	6	8	9	2	2	2
50	5	3	2	1	4	2	3	2	2	3
60	2	4	5	6	7	4	6	5	3	3
70	5	2	2	4	3	7	6	5	1	4
80	3	4	6	7	4	3	5	1	2	2
90	2	2	3	4	6	1	4	2	2	1
100	3	1	3	4	2	2	6	3	4	1

Table no.12 Calculation of particle size distribution for F1 formulation:

Size range	Mean size(d)	No. of particles (n)	n×d	% n	Cumulative frequency under size	Cumulative frequency over size
0-5	2.5	68	170	68%	68%	100%
5-10	7.5	29	217.5	29%	97%	32%
10-15	12.5	3	37.5	3%	100%	3%
15-20	17.5	0	0	0	0	0
20-25	22.5	0	0	0	0	0

25-30	27.5	0	0	0	0	0
30-35	32.5	0	0	0	0	0
35-40	37.5	0	0	0	0	0
40-45	42.5	0	0	0	0	0
45-50	47.5	0	0	0	0	0
		∑n=100	∑nd=425			

$$average\ diameter = \frac{\sum n \times d}{\sum n}$$

$$= \frac{425}{100}$$

= 4.25 µ

Table no.13 Particle size analysis for F2 formulation.

0	10	20	30	40	50	60	70	80	90	100
10	7	5	4	2	4	2	9	7	8	2
20	4	5	7	8	9	6	9	4	3	5
30	4	2	5	6	7	2	6	4	2	7
40	5	4	6	9	7	4	6	3	9	8
50	5	3	2	6	3	3	5	4	5	7
60	5	0	1	3	4	2	2	3	5	6
70	4	4	6	7	2	2	5	1	5	4
80	3	2	7	3	4	9	4	8	5	2
90	2	0	2	5	6	3	2	7	3	6
100	5	4	2	1	3	5	2	4	2	5

Table no.14 Calculation of particle size distribution for F2 formulation.

Size range	Mean size(d)	No. of particles (n)	n×d	% n	Cumulative frequency under size	Cumulative frequency over size
0-5	0-5	70	175	70%	70%	100%
5-10	5-10	30	225	30%	100%	70%
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=400			

$$average\ diameter = \frac{\sum n \times d}{\sum n}$$

$= \frac{400}{100}$

= 4.00 µ

Table no.15: Particle size analysis for F3 formulation.

0	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 no.16: Calculation of particle size distribution for F3 formulation.

Size range	Mean size(d)	No. of particles (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			

$$average\ diameter = \frac{\sum n \times d}{\sum n} = \frac{330}{100}$$

= 3.3 µ

Table no. 17: Particle size analysis for F4 formulation.

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	0	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 no 18: Calculation of particle size distribution for F4 formulation.

Size range	Mean size(d)	No. of particles (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			

$$average\ diameter = \frac{\sum n \times d}{\sum n}$$

$$= \frac{280}{100}$$

= 2.8µ

Table no 19: Comparison of particle size analysis for formulations.

S.NO	F1	F2	F3	F4
1	4.25	4.00	3.3	2.8

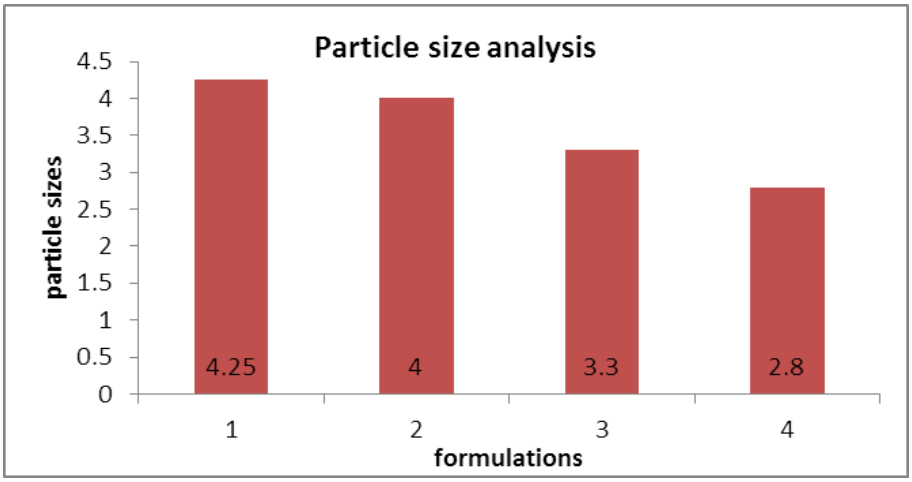


Fig. no. 5: Particle size graph of ibuprofen suspension.

Particle size distribution for F4 is 2.8µ. By this, we concluded that the F4 has better homogeneity, easily absorbable as compared to other formulations.

D. SEDIMENTATION VOLUME

Table no. 20: Sedimentation volume for F1 & F2.

TIME	H_U/H_O F1	H_U/H_O F2
0	1	1
5	0.98	0.98
10	0.96	0.97
15	0.92	0.96
20	0.89	0.96
25	0.85	0.95
30	0.78	0.94
45	0.75	0.91
60	0.7	0.8

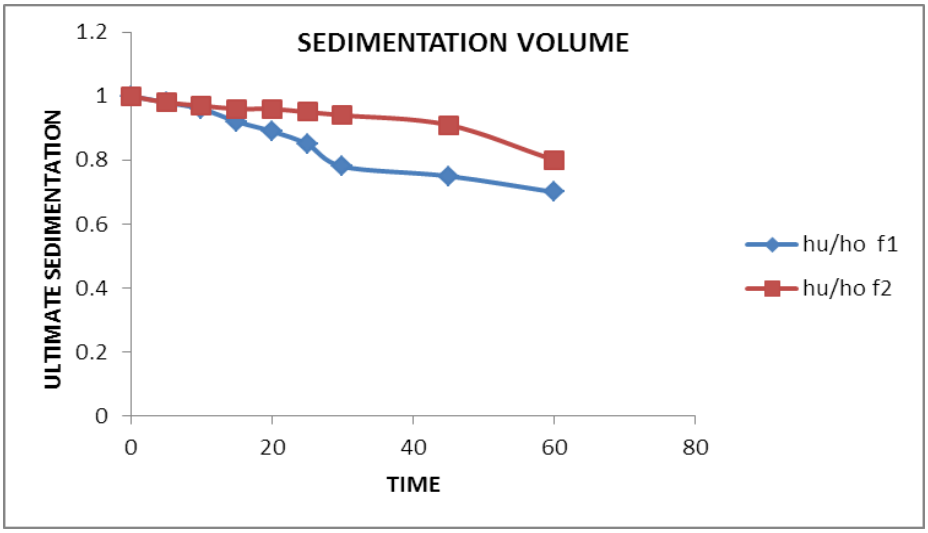


Fig.no.6: Comparison of sedimentation volume between F1 and F2 formulations.

B. Table no: 21 Sedimentation Volume for F3 & F4.

TIME	Hu/H_o F3	H_u/H_o F4
0	1	1
5	0.98	0.98
10	0.96	0.96
15	0.95	0.96
20	0.94	0.92
25	0.92	0.9
30	0.9	0.89
45	0.88	0.88
60	0.84	0.87

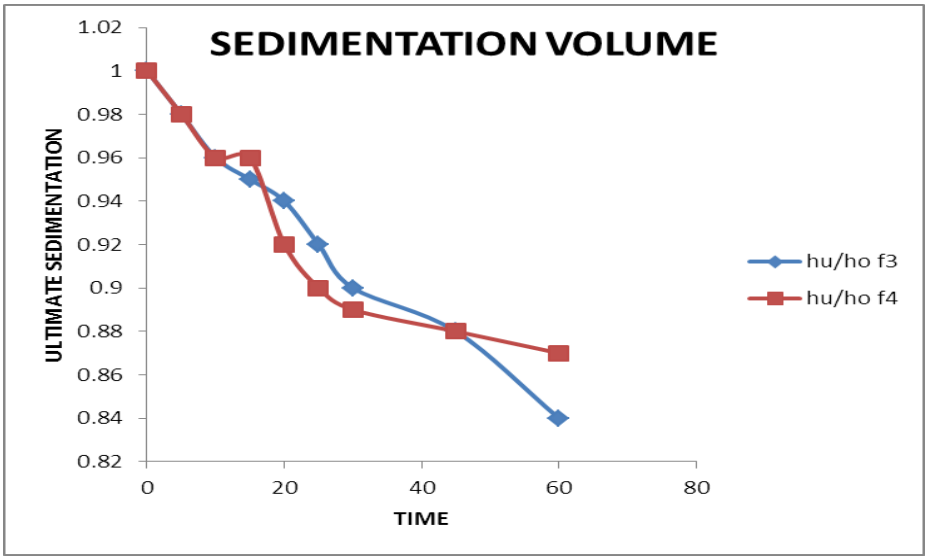


Fig no.7 Comparison of sedimentation volume between F3 and F4 formulation.

Table no.22 Comparison of sedimentation volume for four formulations.

TIME	F1 (H_U/H_O)	F2 (H_U/H_O)	F3 (H_U/H_O)	F4 (H_U/H_O)
0	1	1	1	1
5	0.98	0.98	0.98	0.98
10	0.96	0.97	0.96	0.96
15	0.92	0.96	0.95	0.96
20	0.89	0.96	0.94	0.92
25	0.85	0.95	0.92	0.9
30	0.78	0.94	0.9	0.89
45	0.75	0.91	0.88	0.88
60	0.7	0.8	0.84	0.87

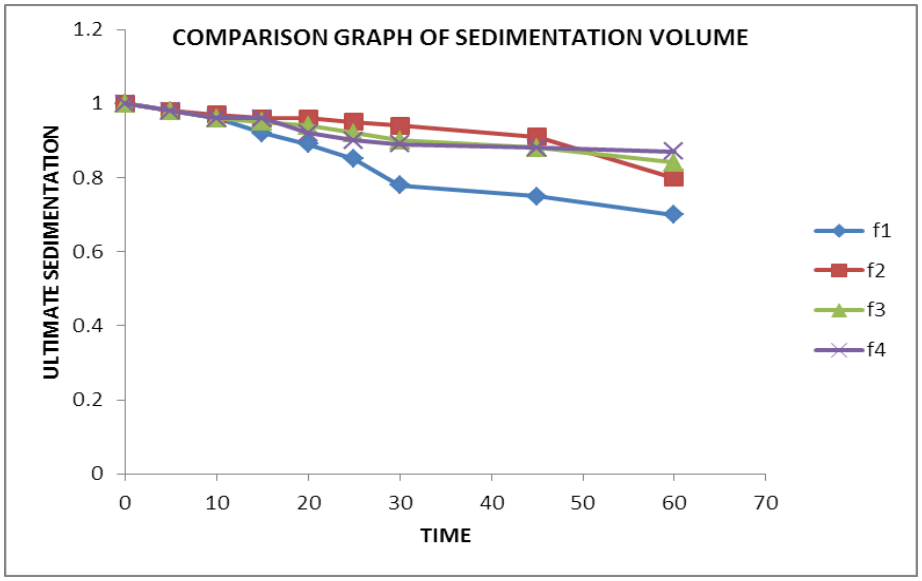


Fig no 8: Comparison graph Sedimentation volume of ibuprofen suspension.

By comparing the sedimentation volume of all the four formulations we concluded that F4 is more stable than other formulations F1, F2, F3, as it has higher volume of sedimentation ratio indicating that it has higher suspendibility.

E. VISCOSITY

Table no 23: Viscosity for ibuprofen suspension.

S.NO	F1	F2	F3	F4
1	652.2mpa×sec	673.9mpa×sec	689.3mpa×sec	692.8mpa×sec

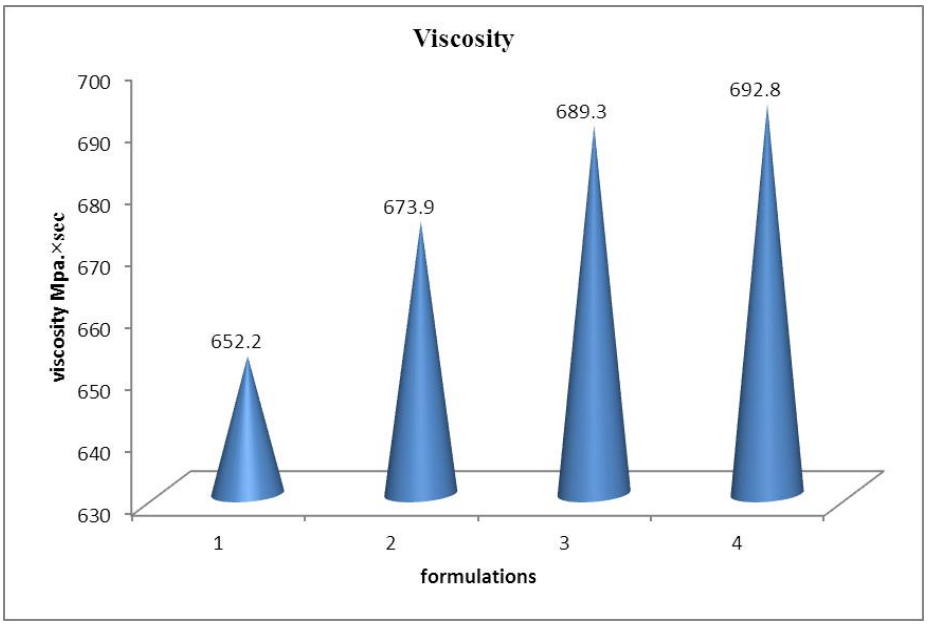


Fig. no 9: Viscosity of Ibuprofen suspensions.

From the above results, it was concluded that F4 formulation having the high stability because it showing high viscosity show that high sedimentation volume among the all the formulations.

F. FLOW RATE

Table no: 24 Flow rate of ibuprofen suspension.

S.NO	F1	F2	F3	F4
1	1.666 ml/sec	1.204 ml/sec	0.86 ml/sec	0.24 ml/sec

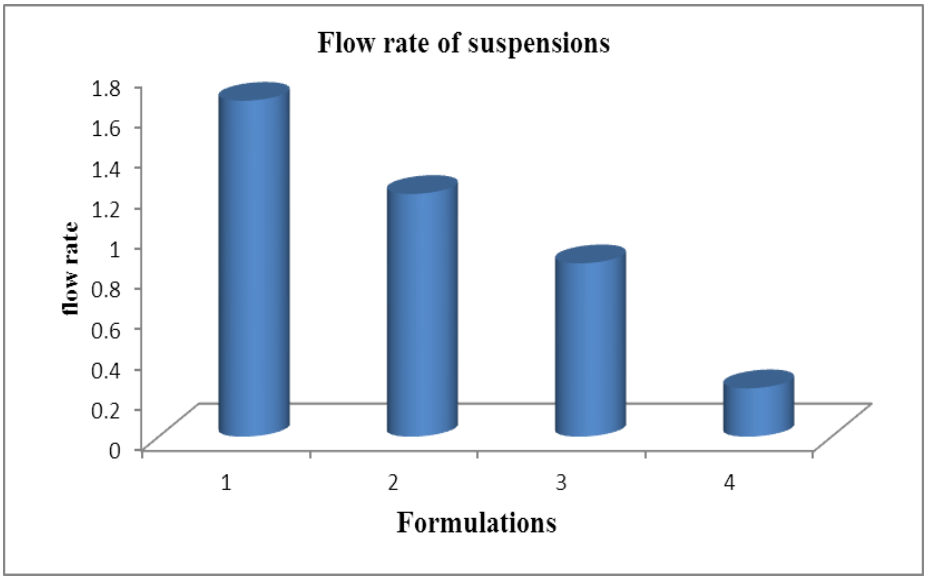


Fig. no: 10 Flow Rates of Ibuprofen Suspensions.

From the above results, it was concluded that formulation F4 having the high stability because it showing the lowest flow rate than the other formulations.

G. P^H OF THE IBUPROFEN SUSPENSIONS.

Table no: 25.

F1	F2	F3	F4
3.9pH	4.6pH	4.7pH	4.8pH

H. ASSAY OF IBUPROFEN SUSPENSIONS.

Table no: 26.

F1	F2	F3	F4
92.28%	92.7%	93.11%	96.22%

From the above results, it was concluded that formulation f4 formulation having the high percent of drug content than the other formulations.

I. Swelling index of fenugreek seeds

Swelling Index % (SI) = (W2 – W1/W1) x 100

$= \frac{25-10}{10} \times 100$

= 150%

W_1= weight of fenugreek powder at "time o", W_2= weight of fenugreek powder at "time t"

Result shows that the time increase, swelling index was increased, because weight gain by mucilage was proportional to rate of hydration. The direct relationship was observed between swelling index and mucilage concentration, as mucilage concentration increase swelling index increased

J. Phytochemical test for the fenugreek seeds

The qualitative analysis was carried out to determine the compounds of selected natural suspending agent to fenugreek.

Table no 27: Phytochemical screening of mucilage of fenugreek seeds.

S.NO	TESTS	OBSERVATION
1	Test for carbohydrates(molisch's test)	Positive
2	Test for tannins (ferric chloride test)	Negative
3	Test for proteins (ninhydrin test)	Positive
4	Test for alkaloids (wagner's test)	Positive
5	Test for glycosides (keller-kiliaini test)	Negative
6	Test for mucilage (ruthenium red test)	Positive
7	Test for flavonoids (shinoda test)	Negative
8	Test for reducing sugar (fehling's test)	Negative
9	Mounting in the iodine starch	Absent

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

9. CONCLUSION

Ibuprofen is a non steroidal anti-inflammatory drug. It is used to relieve pain from various conditions such as headache, dental pain, menstrual cramps, muscle aches, or arthritis.

The ibuprofen suspension was successfully prepared using the natural and synthetic suspending agents.

Sedimentation volume of F1 is 0.7, F2 is 0.8, F3 is 0.84, and F4 is 0.87. The particle size analysis of F1 is 4.25µ, F2 is 4.00µ, F3 is 3.3µ, and F4 is 2.8µ. Viscosity of F1 is 652.2m.pa× sec, F2 is 673.9 m.pa× sec, F3 is 689.3 m.pa× sec, and F4 is 692.8 M.pa × sec. Flow rate of F1 is 1.666ml/sec, F2 is 1.204ml/sec, F3 is 0.86ml/sec, and F4 is 0.24ml/sec. pH of F1 is 3.9, F2 is 4.6, F3 is 4.7, F4 is 4.8.

By performing these evaluation tests, we concluded that F4 formulation is better compared to all other formulations.

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