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A RESEARCH ON FORMULATION AND EVALUATION OF HERBAL ETHOSOMAL GEL FOR ANALGESIC ACTIVITY

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1.ABSTRACT:

Achyranthes aspera ethosomal gel formulation will be created and assessed in this project. It aims to provide an analgesic impact that is topical. Topical medication delivery has the capacity to deliver a high concentration of the drug to the skin in compared to systemic therapy. For local action, drugs should be given topically, and Liposomes, proliposomes, and ethosomes increase the potency of drugs used topically. Recently, it was found that phospholipid vesicular networks with relatively high alcohol concentrations served as ethosomal carriers, improving cutaneous and transdermal delivery of both. substances that are hydrophilic and lipophilic. Popular herbal treatment latjeera is used to treat skin disorders, dog bites, colds, and headaches. The effectiveness of Ethosomes as innovative lipid carriers for topical delivery of Achyranthes aspera (an herbal medicine) has been assessed in the current experiment. Various phospholipid and phospholipid concentrations were used to optimise ethosomes.ethanol. Ethosomes are a brand-new type of vesicular delivery system with a lot of potential for topical and transdermal medication administration. Using a cold process, ethanol, polyethylene glycol, phospholipid, cholesterol, and filtered water were combined to create ethosomes. formulation of ethosomes with soya phosphatidylcholine (3%), and 20% ethanol was best. The vesicle size, shape, optical microscopy, entrapment effectiveness, and in-vitro release research of ethosomes were assessed. In order to create the greatest gel, carbopol 934 was utilised as a gelling agent. The ethosomes were contained in a carbopol 980 gel matrix. in varying amounts of 0.5%, 1.00%, and 1.5% w/w. The optimised Ethosomes were then mixed with a polymeric gel foundation to create Ethosomal gel, which was then tested in vitro and in vivo against traditional gel. Here, Ethosomal gel was developed and optimised using the quality by design (QbD) methodology.The components of QbD, including initial risk assessment, design of experiments (DoE), and model validation for formulation development, have all been well discussed. The improved ethosomes displayed a range of nanometric sizes, a negative zeta potential, and effective entrapment..

KEYWORDS: Ethosomal gel, Ethosomes, skin permeation, stratum corneum, Achyranthes Aspera, Topical, Analgesic, Vesicular Carrier System.

2.INTRODUCTION OF HERBAL ETHOSOMAL GEL:

Alcohol (ethanol and isopropyl alcohol) is present in relatively high concentrations in phospholipids, ethanolosomes, the lipid vesicular carrier systems, also known as alcoholic liposomes, and water. Both hydrophilic and lipophilic medicines can be transported effectively by ethosomes.Ethosomes are the preferred carriers for topical drug delivery due to their simplicity in manufacture, non-irritating nature, effectiveness in encapsulating a wide range of drug compounds, and superior stability than alternative vesicular systems. [1Although the exact mechanism by which ethosomes increase permeability is unclear, it is thought to happen in a number of different ways. They involved the stratum corneum being disrupted [2] or getting caught in the follicles (i.e., the pilosebaceous route). Phospholipids are found in ethosomes, which contain alcohol and medication solutions. In the formulations, the phosphor-lipids might range from 0.5 to 10%. Along with glycol, alcohols can act as a softener, carrier, and penetration enhancer. They make about 22–70% of ethosomal formulations.[3]. According to numerous studies, medication delivery can be adjusted by altering the alcohol and water compositions, which increases bioavailability [4]. A novel herbal analgesic called ***Achyranthes Aspera (Latjeera)*** is effective in treating headaches, colds, dog bites, snake bites, and skin conditions. The oral administration of analgesic medications results in problems like stomach or duodenal ulcer, ulcerative colitis, according to various investigations on patients receiving analgesic treatments [5]. These problems highlighted the value of other analgesic delivery methods. [6] Recently, transdermal drug delivery systems were created with the intention of achieving systemic therapeutic goals through topical application to the intact skin surface. [7] Transdermal therapy systems are described as self-contained discrete dose forms that deliver drugs to the systemic circulation through the skin at a controlled rate when applied to unbroken skin[8].A multitude of benefits, such as improved patient compliance and increased safety, can be obtained through transdermal administration. This method of drug delivery enhances patient compliance while avoiding the risks and pain of parenteral therapy [9]. In this regard, the transdermal route is an intriguing choice due to its practicality and safety [10].

3.ETHOSOMES: CONCEPTS AND ADVANTAGES:

Drugs that undergo considerable first pass metabolism, are unstable in the gastrointestinal tract, or have severe side effects when administered orally may benefit from transdermal drug delivery methods. Additionally, these systems offer better patient compliance, decreased dose frequency, and regulated medication distribution. Self-administration is also conceivable with this delivery system because it is a non-invasive method of application [11,12]. One of the new lipid vesicular systems called ethosomes has a rather high concentration of ethanol. Touitou created this ethanol vesicular system in 1996 [13]. Active pharmaceutical ingredients (API), ethanol, water, and phospholipids are the primary components of ethosomes [14]. Ethosomal vesicles have an inner aqueous core that contains the drug and a bilayer of phospholipids. Table 1 discusses the elements of ethosomes and their function in ethosome formulation.Compared to liposomal formulations, which contain up to 10% ethanol, ethanol is present in much higher concentrations in ethanolsomes (20–45%). Delivery of medicinal medicines into a deeper epidermal layer and systemic circulation is made simple and successful by the efficient penetration enhancer effect of ethanol [15]. Hydrophilic, lipophilic, and high molecular weight compounds are all capable of being captured by ethosomes [16]. Drug delivery across the skin by ethosomes is effective in both occlusive [17] and non-occlusive situations [18].

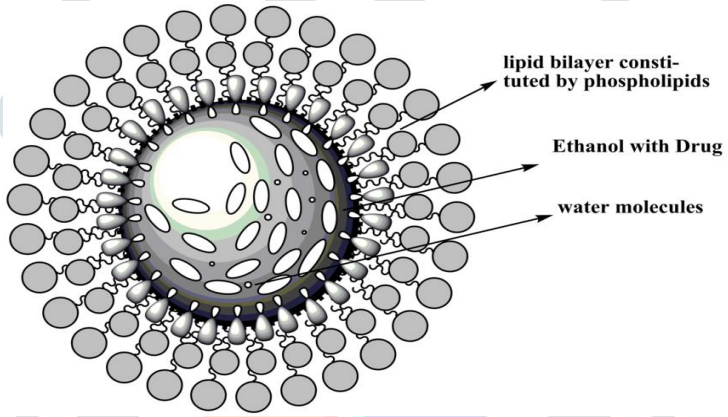
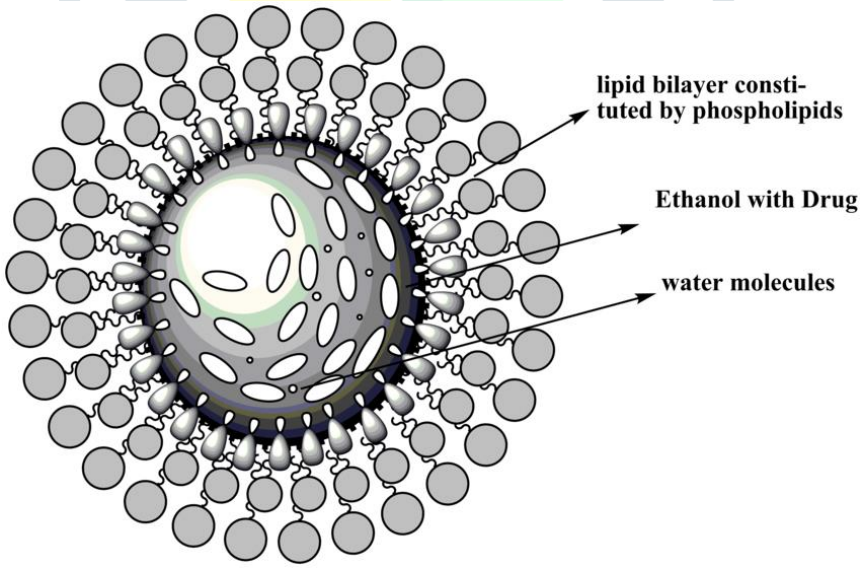


Fig 1: Structure of Ethosomes



4. TYPES OF ETHOSOMES:

On the basis of components used in the formulations, Ethosomes are of 2 types

(4.1) Classical Ethosomes:

These are adjustments to liposomes that also contain phospholipids, water, and a significant amount of ethanol (20–45%w/w). Along with ethanol, propylene glycol (PG) and other alcohols including isopropyl alcohol (IPA) may also be present in ethanolosomes [13].

(4.2) Transethosomes:

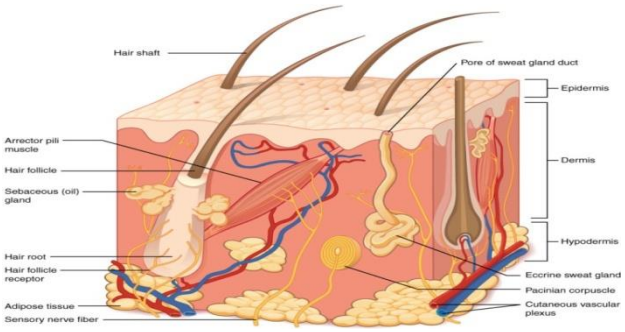
These novel Ethosomes were created by combining traditional Ethosomes with edge activators (surfactants) or penetration enhancers. Transethosomes combine the benefits of transfersomes (deformable liposomes) with traditional ethosomes [19, 20, 21]. However, given the significant risk for skin irritation caused by the combination of surfactants and a high alcohol concentration, the safety of this carrier should be carefully examined.

5. ETHOSOMAL DOSAGE FORM:

In most cases, ethosomes are investigated in their initial suspension state. However, effective drug administration through the skin is made possible by the inclusion of ethosomal systems in appropriate vehicles including gels, patches, and creams [13, 14, 19]. Achyranthes aspera (latjeera) ethosomal gels were discovered to be more efficient than commercial nonethosomal gels [23]. However, due to its low viscosity, Ethosomal suspensions released the herbal medication at a higher pace than Ethosomal gels did [24,25,26]. Even in occlusive conditions, ethosomal patches allow for the effective absorption of medications. Compared to the commercially available nonethosomal testosterone patch Testoderm, the Ethosomal testosterone patch offers efficient drug delivery. Testosterone [15], Artesunate and Febrifugine [27], Ligustarzine [28, 29], Tizanidine HCl [30], Valsartan [31], and insulin [16] are a few of the medications that various researchers have developed as ethosomal patches. Creams are also excellent at effectively delivering substances throughout the skin. Incorporating curcuma longa extract-containing ETHOSOMES onto a cream base has been investigated for its potential photoprotective [32] and anti-wrinkle [33] benefits.

6.MECHANISM OF SKIN PERMEATION BY ETHOSOMES:

Intercellular and transcellular pathways are two potential drug penetration routes through intact stratum corneum [34]. Drug distribution from topically administered vesicles into the skin is influenced by a variety of circumstances. The vesicle size and encapsulation effectiveness are two crucial factors that control the topical administration of medications. Smaller vesicles can easily penetrate the deeper layer of skin. Accepted Manuscript of skin. The quantity of ethanol and phospholipids have an impact on the size of ethosomes. In Fig. 3, the method by which ethosomes increase the penetration of medicines through the skin is depicted. The percutaneous channel via the open hair follicles and stratum corneum allowed the ethosomes to enter the skin. The vesicles in the top layer of the skin were split during percutaneous penetration, allowing the therapeutic drugs to gradually permeate while the phospholipids were kept in the upper epidermis [35]. The suggested mechanism is based on ethanol and phospholipids' synergistic activities to improve medication penetration in the ethosomal systemEffective penetration enhancers include ethanol. At physiological temperature, the SC (subcutaneous) lipid multilayer of skin is tightly packed and organised. The Tm of SC lipids is decreased by ethanol, and their fluidity is increased. Additionally, ethanol may soften and malleableize the vesicle bilayer. The disorganised SC lipid bilayers are more easily penetrated by these pliable and soft ethosomal vesicles. By fusing these vesicles in the deeper layer of epidermis, medicines are released [15].



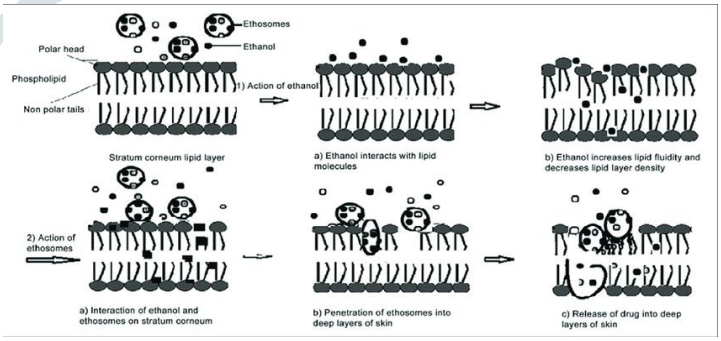


Fig 2: Structure of Skin Fig 3: Mechanism of Skin Permeation by

Ethosomal Drug Delivery System

The drug absorption probably occurs in following two phases:

(6.1)Ethanol Effect

(6.2) Ethosomes Effect

(6.1) Ethanol Effect:

Through the skin, ethanol enhances permeation. Its penetration-enhancing effect has a well-known mechanism. Ethanol permeates intercellular lipids, increasing their fluidity and decreasing the density of the cell membrane's multilayer of lipids.

(6.2) Ethosome Effect:

The ethanol in ethosomes increases the fluidity of cell membrane lipids, which increases skin permeability. In order to deliver the medications into the deep layers of skin, ethosomes fuse with skin lipids and easily penetrate deep skin layers.

MECHANISM OF ACTION OF ETHOSOMES

Ethosomes

↓

Ethanol cause skin disruption

↓

Increase lipid fluidity

↓

More permeation through skin

↓

Ethsomes permeates in side

↓

Fuse with skin lipid

↓

Release drug into deep skin layers

7. METHOD OF PREPARTION OF ETHOSOMES:

Ethosomes can be made and prepared using one of four different techniques. None of the methods require the use of any sophisticated tools or processes and are all quite straightforward and practical.

7.1 Ethosomes Can Be Formulated By Following Four Methods:

(7.1.1) Hot Method:

This technique involves heating phospholipids in water at 400 C until a colloidal solution is formed. Propylene glycol and ethanol should be properly combined in a separate vessel, which should be heated to 400°C. Into the aqueous phase, add the organic phase. Depending on the drug's solubility, dissolve it in ethanol or water. [36, 37] Using the probe sonication or extrusion approach, the vesicle size of the ethosomal formulation can be reduced to the desired extent.

(7.1.2) Cold Method:

This approach to ethosomal preparation is the most typical and popular. Phospholipids, drugs, and other lipid materials should be well stirred into ethanol in a covered vessel at room temperature to dissolve them. While stirring, add propylene glycol or another polyol. In a water bath, bring the mixture up to 300 °C. Water is heated in a different container to 300°C before being added, combined, and stirred for 5 minutes in a covered container. By employing the sonication [38] or extrusion [39] methods, the vesicle sizes of ethosomal formulation can be reduced to the desired extent. Finally, the mixture needs to be adequately refrigerated stored. [36]

(7.1.3) Classic Mechanical Dispersion Method:

In a round bottom flask, soy phosphatidylcholine is dissolved in a 3:1 mixture of chloroform and methanol. A thin lipid layer is formed on the flask wall when the organic solvents are evaporated using a rotating vacuum evaporator above the lipid transition temperature. The deposited lipid layer is then cleaned of any remaining solvent

combination by placing the container's contents under hoover for the night. By rotating the flask at the appropriate temperature, hydration is accomplished using various concentrations of a hydroethanolic mixture containing the medication. [40, 41]

(7.1.4) Classic Method:

The phospholipids and medication are dissolved in ethanol and heated in a water bath to 30°C + 1°C. In a closed vessel, the lipid mixture is added to with double-distilled water in a thin stream while being constantly stirred at a speed of 700 rpm. Through three rounds of passing through a polycarbonate membrane using a hand extruder, the resulting vesicle suspension is homogenised. [42]

8. ADVANTAGES OF ETHOSOMAL DRUG DELIVERY:

1. Ethosomal medication delivery Can Deliver Large Molecules (Peptides, Protein Molecules)
2. Enhanced transdermal drug delivery of herbal drugs through the skin.
3. The Ethosomal Drug Delivery System Is Versatile In The Pharmaceutical, Veterinary, And Cosmetic Industries.
4. Due to the semisolid form (Gel or Cream) in which the ethosomal drug is administered, patient compliance is high.
5. Compared to Iontophoresis, Phonophoresis, and Other Complicated Methods, a Simple Drug Delivery Method
6. The ethosomal system is passive, non-invasive, and ready for commercialization right away [43, 44].

9. DISADVANTAGES OF ETHOSOMES: [45, 46, 47]

1. High Blood Level Drugs Cannot Be Administered; Only Potent Molecules Needing A Daily Dose Of 10mg Or Less Can Be Used.
2. The drug must be sufficiently soluble in both lipophilic and aqueous environments in order to access the dermal microcirculation and the vascular system.
3. The drug's molecular size needs to be appropriate for percutaneous absorption.
4. Some types of skin may not respond well to adhesive.

10. MATERIALS AND METHOD:

Materials Which Are Used In Preparation Of Herbal Ethosomal Gel For Analgesic Activity Are Given In Table 1 With The Quantity.

Materials	Quantity
Achyranthes aspera (Latjeera) Herbal Drug	3gm
Ethanol	20ml
Tween 80	7-8ml
Methyl salicylate	20ml
Cholesterol	10mg
Carbopol 940	2gm
Cinnamon oil	2ml
Water	q.s

Table 1: Materials Used in Formulation

10.1 Achyranthes Aspera (Latjeera) Herbal Drug:

Achyranthes Aspera L. (Family Amaranthaceae) is known as Chirchita and Latjeera in local languageIt is a significant medicinal plant that grows as a weed all over India. It is a widely used plant medicine in Ayurveda, Unani-Tibbi, Siddha, allopathic, homoeopathic, and naturopathic treatments [48]. The plant is highly valued by traditional healers and is used to treat a variety of conditions, including asthma, bleeding, to aid in childbirth, boils, bronchitis, colds, coughs, colic, debility, dropsy, dog bites, dysentery, ear complications, headaches, leucoderma, pneumonia, renal complications, scorpion bites, snake bites, and skin diseases [49].

10.2 Classification:

Kingdom	**Plantae**
Super division	**Spermatophyta**
Division	**Magnoliophyta**
Class	**Magnoliophsida**
Subclass	**Caryophyllidae**
Order	**Caryophyllales**
Family	**Amaranthaceae**
Genus	***Achyranthes***
Species	***Aspera***

Table 2: Classification Of Achyranthes Aspera.

10.3 Botanical Characters:

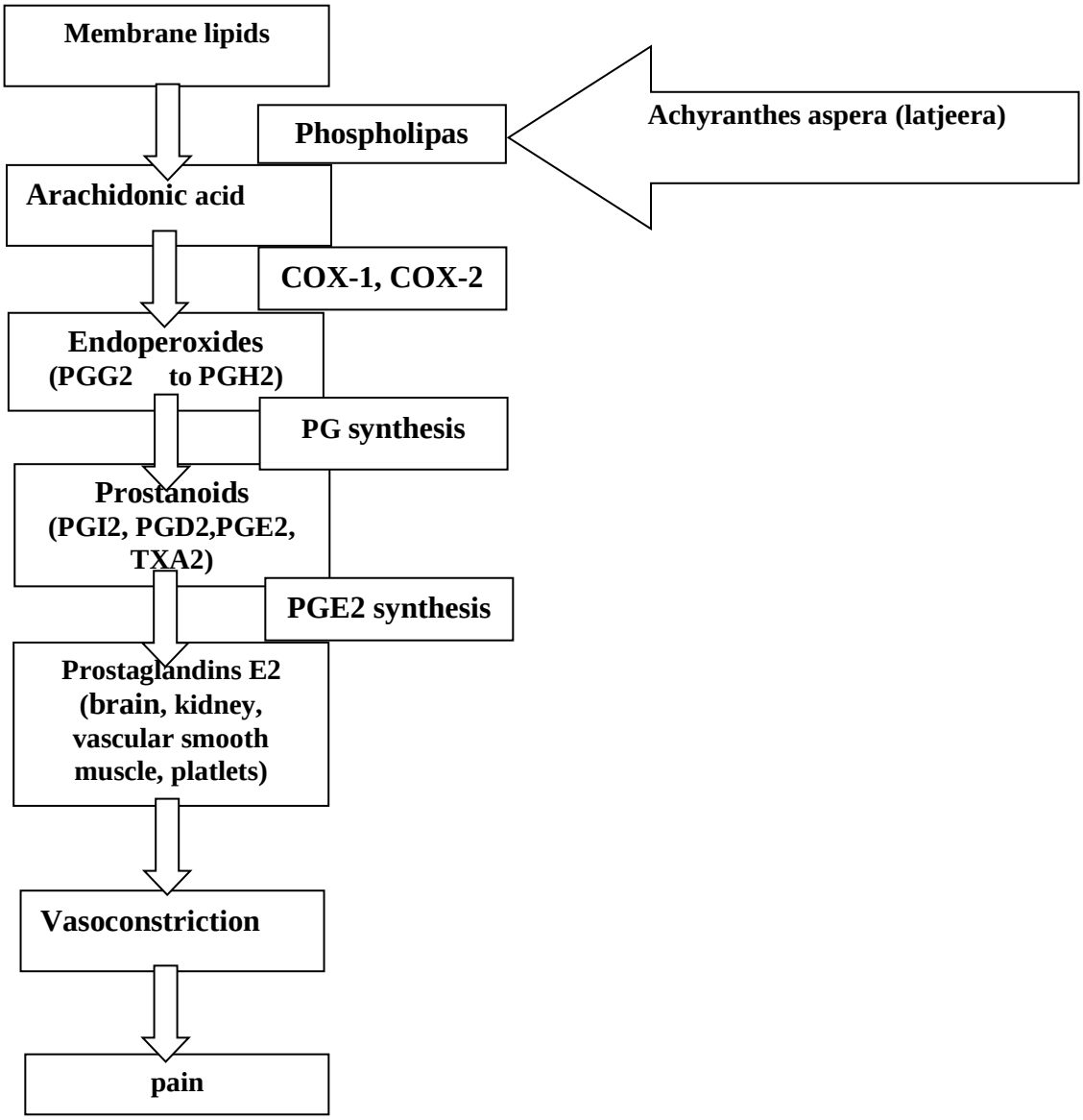
Achyranthes Aspera L. (Latjeera) is an erect or procumbent, annual or perennial herb of about 1- 2 meter in height, often with a woody base. This plant blooms in the summer and has angular, ribbed, simple, or branching stems that are frequently tinged purple [50]. The stems are square, and the leaves are broadly rhombic or elliptic in shape. The inflorescences are 8 to 30 cm tall and have numerous 3 to 7 mm broad solitary white or red blooms [51].

10.4 Chemical Constitutes:

D-glucuronic acid was discovered as saponin A and -D-galactopyranosyl ester of D-glucuronic acid as saponin B from ***Achyranthes aspera***. Other compounds, such as oleanolic acid, amino acids, and hentriacontane, were also identified along with these ones. Chemical components like 10-tricosanone, 10-octacosanone, and 4 tritriacontanone are also present in the seeds [52]. Nhexacos-14-enoic acid has been discovered in the ethanol extracts of the roots of Achyranthes aspera, and it is a novel aliphatic acid [53].

10.5 Mechanism Of Action:

One of the plants used for therapeutic purposes is Achyranthes aspera [54]. It is a perennial, stiff herb that grows between 0.3 and 0.9 metres high. It is a common plant in badlands, along highways, and in rural areas. In India, it is referred to by a number of names, including Latjira and Chirchira in Hindi, Apamargah, and Chirchitaa [55,56]. More than 10 cultivars are available. Aspera, Aspera late ovata, Aspera porphyristachya, Aspera villosior, Aspera velutina, Aspera borbonica, Aspera nigro olivacea, Aspera pubescens, and Aspera rubrofusca are common species [57]. The greenish and pinkish petals of A. aspera flowers produce rice seeds. Active substances called glycosides are found in the A. aspera seed portion. The main chemical components of A. aspera include achyranthine, linalool, oleanolic acid, arachidic, behenic, betaine, hentriacontane, and achyranthes saponins A, B. A. aspera seed powder relieves tension headaches and solidity. Achyranthes aspera's seeds and leaves exhibit pain-relieving properties [58, 57, 59, 60]. Latjira has been suggested as a potential lead for another type of anti-inflammatory agent having a double inhibitory action on phospholipase A (corticosteroid) and cyclooxygenase (COX-1, COX-2) which is responsible for pain and inflammation [61]. Headaches are primarily caused by inflammation in the brain stem. Using the Tail flick response and Hot plate procedures, an ethanol extract of A. aspera leaf (400 mg/kg) provided an analgesic effect at 30, 60, 90, and 120 minutes. When administered to albino mice in a formalin-induced pain test at a dose of 400 mg/kg, the leaf extract had an analgesic effect [62].The plant is used as a carminative, diuretic, natural blood purifier, expectorant, antidote for snakes, anti-inflammatory, antiviral, toothache, gastric tonic, nasal pollution, and analgesic. The entire plant is used to treat a variety of ailments, including gastrointestinal distention, gastritis, cough, bronchitis, colds, asthma, piles, urinary bladder stones, rheumatism, scabies, hypoglycemia, liver and kidney diseases, muscles maintenance, allergy, cardiovascular, cholera, rabies, colic, gonorrhoea, pneumonia, hydrophobia, and skin diseases [54, 56, 58, 63, 64].



10.6 Pharmacology Of Achyranthes Aspera:

10.6.1 Analgesic and antipyretic activity:

Using a heated plate and brewer's yeast to induce an analgesic and antipyretic response, a methanolic extract of leaves was used, with aspirin serving as the reference medication. [65]. Achyranthes aspera seeds and leaves, which have analgesic properties. Using the hot plate method and acetic acid-induced writhing reaction, both leaves and seeds exhibit analgesic efficacy in mice [66Using the tail flick, hot plate, and acetic acid-induced writhing methods for peripherally acting analgesic activity with aspirin as the standard medication, the hydro ethanol extract of the roots and leaves of Achyranthes aspera shows centrally acting analgesic action in adult male albino rats. There were two doses given: 200 mg/kg and 400 mg/kg. The anial that received 400 mg/kg of leaf extract demonstrated the most analgesic effect [67].

10.6.2 Anti-inflammatory and anti-arthritic activity:

The alcohol-based root extract of Achyranthes aspera exhibits anti-inflammatory action in Wistar rats when tested using the cotton pellet granuloma test and carrageenan-induced paw edoema technique [68]. Using the carrageenan-induced paw edoema technique and the formalin model, the alcoholic extracts of leaves and seeds exhibit anti-inflammatory effect in rats [66].

10.6.3 Antimicrobial Activity:

The seeds of Achyranthes aspera exhibit modest to moderate antibiotic activity against B. subtilis, E. coli, and P. aeruginosa when extracted with ethanol and chloroform [69]. The plant's callus and several leaf extracts have antibacterial action as well [70].

10.6.4 Antioxidant activity:

It is generally known that Achyranthes aspera contains phytoactive ingredients. Due to the presence of phytoactive constituents, the herbal seed powder has increased free radical scavenging activity and decreased the rate of lipid peroxidation. [71]

10.6.5 Wound Healing Activity:

Achyranthes aspera leaf extracts in both ethanolic and aqueous forms for wound healing activities. Excision wound model and incision wound model were used to study the wound healing process [72].

10.6.6 Hypoglyceamic Activity:

The whole plant powdered, which exhibits hypoglycemic action, and its aqueous and methanolic extracts. After giving different doses of Alloxan orally, the blood glucose levels of healthy and diabetic rabbits were measured [73].

Fig 4: Latjeera plant.

10.7 Uses:

Abdominal discomfort and bleeding piles can both be treated with whole plant ash. In order to clean the mouth and treat halitosis, the root is used as a toothbrush. The twig's infusion can also be used as a rinse for toothaches. For night blindness, root extract is applied as an eye drop before sleeping [74]. Alkaloids, flavonoids, saponins, steroids, and terpenoids are said to be present. Some malignancies have been demonstrated to be prevented or treated more slowly by flavonoids [75].

10.8 Ethanol:

Ethanol has the ability to disrupt the dense alignment of the cell lipid layer in the stratum corneum of the skin and lower structural density. It also has the ability to promote chemical penetration.

10.9 CARBOPOL 940:

A gelling chemical called carbopol 940 can change the physical characteristics of gel formulations. To create preparations that satisfy the requirements for gel physical qualities, namely pH, viscosity, adhesion, spreadability, organoleptic and stability, carbopol 940 concentration as a gelling-agent can be changed. Lotions, creams, and gels all include carbopol as a thickening agent. Pharmaceutical products are also stabilised, suspended, and controlled in their release using it. Herbal Ethosomal gel flows readily and feels slippery at low dosages.

10.10 TWEEN 80:

In the ethosomal system, tween 80 is employed at concentrations ranging from 10% to 50% of the total phospholipid content. Tween 80 was found to minimise vesicular size, improve system stability, and improve skin-

permeation properties in ethosomal systems. Tween 80's effects on the ethosomal system are mostly brought about by its solubilizing ability and ability to impede vesicle fusion.

10.11 CHOLESTEROL:

Because cholesterol is a hard steroid molecule, it improves the stability and drug entrapment effectiveness of ethosomal systems. In addition to preventing leakage, it lessens vesicular fusion and permeability. It is typically used at a concentration of 3%, however in some formulations it has been utilised up to 70% of the formulation's total phospholipid concentration. According to numerous research, cholesterol made ethosomal systems' vesicles larger.

10.12 CINNAMON OIL:

Due to its antibacterial properties, cinnamon essential oil (CEO), a volatile oil derived from Cinnamomum zeylanicum, has grown to be one of the most significant natural oils.

11. METHODS OF PREPARATION OF HERBAL ETHOSOMAL GEL BY COLD METHOD:

11.1 PREPARATION OF SAMPLE (A): ETHOSOMES

- Weigh accurate amount of ethanol, Tween 80, cinnamon oil, and cholesterol.
- Mix ethanol, Tween 80, cinnamon oil, and cholesterol in a beaker.
- Put the beaker on magnetic stirrer for mixing at the temperature 30°c for 45 minutes.
- Ethosomes are prepared.

11.2 PREPARATION OF SAMPLE (B): HERBAL DRUG

- Weigh accurate amount of herbal drug and transferred in a conical flask.
- Take 15ml of distil water and transferred in conical flask and mix properly for 30 minutes.

11.3 PREPARATION OF SAMPLE (C): MIXING

- Add or mix drop wise the sample (B) in sample (A) with continuous stirring.

11.4 PREPARATION OF SAMPLE (D): ETHOSOMAL GEL

- Weigh 2gm carbopol 940 and transferred in a beaker.
- Take 70 ml water and add with carbopol 940.
- Put the beaker on magnetic stirrer for mixing at the temperature 30° c for 1 hr.
- After mixing leave carbopol for swelling at room temperature for 24 hrs.
- After 24 hrs maintain the ph of sample (D) 5.5 to 6.
- Then add the sample (C) in sample (D) with continuous stirring.
- The formulation of herbal Ethosomal gel is prepared.

12. EVALUATION OF HERBAL ETHOSOMALGEL:

12.1 Physical Characteristic:

The Physical Characteristic was checked for gel formulations.

Colour: white and creamy.

Odour: acceptable.

12.2 Determination Of PH:

The pH of the herbal Ethosomal gel was measured using a digital pH metre after the pH metre was calibrated by dipping it in a buffer solution. The electrode was dipped in the gel formulation for 30 minutes until a consistent reading was obtained after one gramme of gel had been dissolved in 25 ml of distilled water. Also seen was frequent reading. Two copies of the pH measurements for each formulation were made.

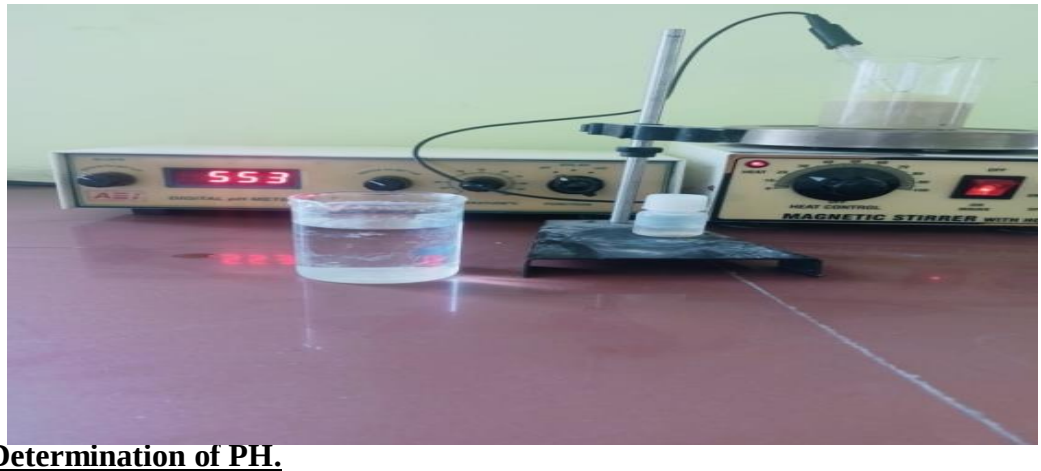
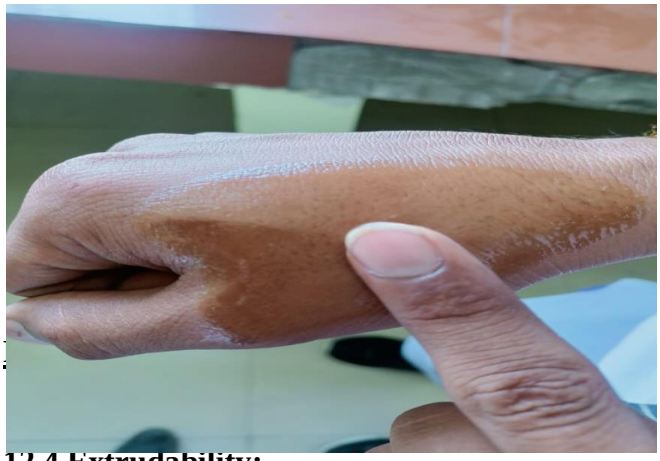


Fig 5: Determination of PH.

12.3 Washability:

On the skin, the formulation was applied, and the depth of the water wash was personally assessed.



12.4 Extrudability:

Aluminium or metal collapsible tubes were used to hold the gel formulation. The material was forced through the tubes, and the formulation's extrudability was assessed.

12.5 Spreadability:

A key need for gels is that they have strong spreadability. When a gel is applied to skin, the phrase "spreadability" refers to the area to which it spreads easily. The spreading value of a formulation affects its medicinal effectiveness as well. For the purpose of examining the spreadability of the formulations, a unique apparatus has been created. Spreadability is measured by the number of seconds it takes two slides that are separated by a load to separate from the formulation. Better spreadability is achieved with shorter gap times between two slides. It is calculated using the formula below. $s=(m*l)/t$

Where, S=Spreadability (gcm/sec), m = weight attached to the upper slide (20 grams), l= length of glass slide (6cms), t = time taken is seconds.

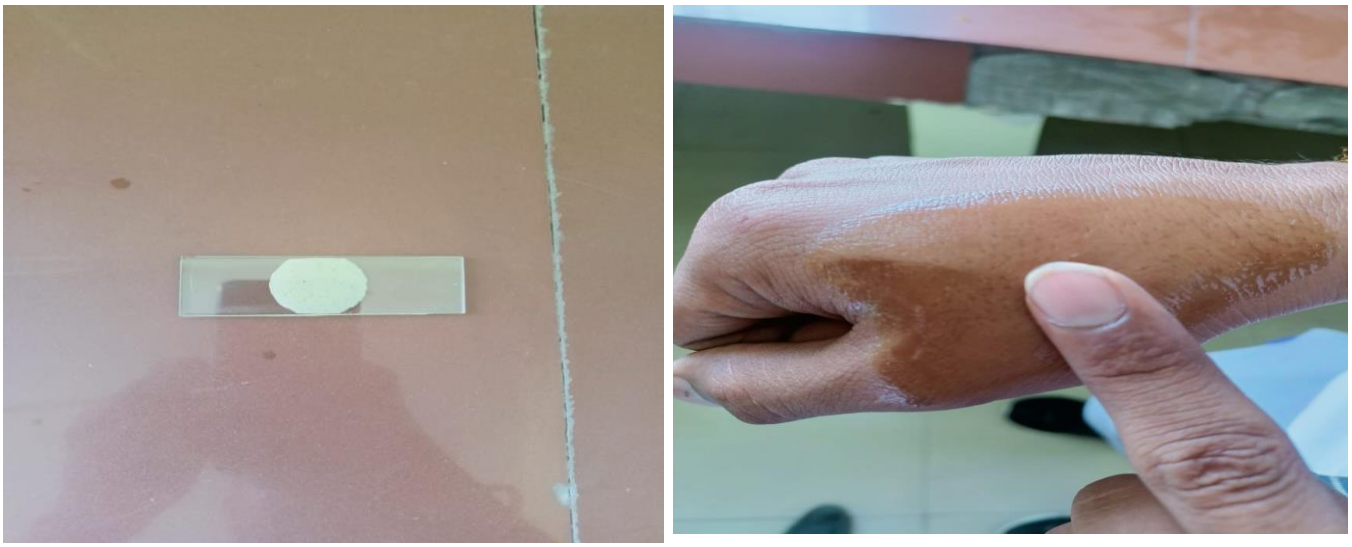


Fig :7 Spreadibility Test

12.6 Viscosity:

Using a Brookfield digital viscometer, the viscosity of the produced gel was measured. Spindle number 6 was used to measure the viscosity at 10 rpm and 250C. The proper wide mouth container was filled with an adequate amount of gel. The gel was poured into the wide-mouth container in a way that would allow the Viscometer's spindle to dip comfortably. Prior to the measurements, samples of the gels were allowed to settle for 30 min at the same temperature (25 /10C).

12.7 In-Vitro Drug Release Studies Using The Prehydrated Cellophane Membrane:

A 25 cm x 2 cm piece of cellophane membrane was extracted and cleaned under running water. It was then cleaned of any glycerine before being put on the diffusion cell for additional research and immersed in distilled water for 24 hours. Studies on drug release were conducted using a modified Franz diffusion cell. The Franz diffusion cell was mounted with the cellophane membrane. On the dialysis membrane, formulation was administered through the donor compartment. 25 cc of pH 7.4 phosphate buffer were added to the reservoir compartment. The experiment lasted eight hours at a speed of 100 rpm and a temperature of 37 1 °C. At intervals of one hour, samples were taken out of the reservoir compartment, and absorbance was calculated spectrophotometrically at 242.0 nm. The same amount of phosphate buffer with a 7.4 pH was added to the reservoir compartment each time.

Fig 7: Franz Diffusion Test.

13. CONCLUSION:

The invention of ethosomal gel has created a new opportunity for the effective local and systemic administration of medications with various physicochemical properties across skin. Ethosomal gels are lipid vesicles that have been particularly designed and contain a significant amount of ethanol, which improves skin permeability more than ordinary lipid vesicles do. Ethosomal gel are simple to make, reliable, and secure for use. Ethosomes have already demonstrated, two decades after their creation, that they may safely deliver therapeutic substances through the skin. Ethosome incorporation in appropriate vehicles, like lotions, gels, and patches, improves skin permeability and has therapeutic effects. There are numerous ethosomal preparations on the market right now. To improve ethosome stability, more research is necessary.

Their ability to provide effective therapeutic effect, topically and systemically through skin have made them an appealing and novel carrier system over time. Profound investigation has also resulted in the development of a new generation of ethosomal systems known as Transethosomes.

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