



**International Journal of Biology, Pharmacy  
and Allied Sciences (IJBPA S)**  
*'A Bridge Between Laboratory and Reader'*

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## IMPROVEMENT OF MINIATURE EMULSION-BASED TOPICAL GEL PREPARATION IN ANTHELMINTIC ACTIVITY FOR TOPICAL APPLICATION

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Received 26<sup>th</sup> Dec. 2021; Revised 25<sup>th</sup> Jan. 2022; Accepted 12<sup>th</sup> March 2022; Available online 1<sup>st</sup> Dec. 2022

<https://doi.org/10.31032/IJBPA S/2022/11.12.6679>

### ABSTRACT

Microemulsions are a superior strategy in clever medication conveyance frameworks in light of their properties like long timeframe of realistic usability, further developed medication solubilization easily of planning and organization. Microemulsions are thermodynamically reliable and optically isotropic fluid plans of oil-water and amphiphile. Microemulsions have an incredible scope of utilizations and utilize, for example, in drugs, agrochemicals, cutting oils, biotechnology, food, beauty care products, scientific applications, ecological detoxification, and so on Since the disclosure of microemulsions, they have achieved expanding importance both in essential exploration and in various modern fields. Contemplating their captivating properties, unequivocally, ultralow interfacial strain, titanic interfacial locale, thermodynamic obvious quality, and the capacity to solubilize paying little notification to immiscible fluids.

The utilizations and uses of microemulsions are various in the compound and natural fields. The microemulsion system vows to be one of the flexible approach methodologies which connect with the control of their molecule properties, for example, instruments of particle size control, calculation, morphology, homogeneity, and surface area Because of their stand-out properties, specifically, ultralow interfacial strain, colossal interfacial area, thermodynamic unfazed quality, and the capacity to solubilize notwithstanding immiscible

fluids. The reason for this review was to foster a miniature emulsion-based gel plan for skin conveyance to expand the solvency and skin penetrability of the medication. The primary target of this audit paper is to examine microemulsion Gel as an Enhancer for Skin Permeation of potential applications.

**Keywords - Microemulsion, Novel Drug delivery, Surfactants, Co-surfactants, Solubility**

## **INTRODUCTION -**

The detailing and improvement of an original medication conveyance framework with the idea of upgrading the viability of existing medications is a continuous interaction in drug research. Since there are many kinds of drug movement systems that have been created [1]. The microemulsion thought was presented as are minutely scattered. Most analysts in the right on time as the 1940s by Hoar and Schulman who field concur anyway that for a microemulsion to be created a reasonable single-stage arrangement by titrating a framed framework should contain some smooth emulsion with hexanol. Schulman and unequivocal microstructure, toward the day's end, there is a teammate (1959) who subsequently established the term indisputable breaking point between the oil and water stages microemulsion, and it has since been defined and at which the surfactant is located. To gain an indeed redefined on many occasions. For the comprehension of the purposes behind microemulsion stances of this survey, nonetheless, the microemulsion development, it is first critical to consider

the properties definition given by Danielsson and Lindman in of amphiphiles, such as surfactants, in solution. 1981 will be utilized as Conventional surfactant particles involve a Microemulsions are along these lines characterized as an arrangement of polar head bunch area and an apolar tail district, the water, oil and amphiphile which is a solitary optically last option having the bigger atomic volume especially isotropic and thermodynamically stable fluid arrangement [2].

Skin transport structures for drugs make the confined relationship of the game plan any spot in the body through ophthalmic, vaginal, skin, and rectal courses. Effective definitions include a wide assortment of plans planned for corrective or dermatological application, to solid just as sick skin. Medications might be managed for limited or fundamental impacts. Effective arrangements can be figured with differing physicochemical properties, as strong, semisolid, or fluid. The microemulsion of the medication is ready and consolidated into an emulgel, having an original skin drug conveyance framework as a double delivery control

framework. Miniature emulsions are micronized; thermodynamically consistent frameworks having low interfacial strain ready by adding co-surfactant has two or three parts like additionally evolved porousness, uncommon thermodynamic security, and delayed movement. Emulgel draws out the medication discharge, expands patient consistency and dependability of the emulsion. The arranged emulgel is investigated for different cut-off centers like pH, consistency, globule size; spreadability, etc through while the little emulsion is assessed for different cut-off points like thickness, pH, zeta-potential, and so forth [3].

Over the most recent couple of years, the treatment of disease has been cultivated by directing the medications to the human body through different courses, to be specific, oral, sublingual, rectal, parental, and so forth The skin drug conveyance framework is and large utilized where different frameworks of medication organization fall flat or it is chiefly utilized in nearby skin diseases like contagious contamination. Skin drug conveyance can be characterized as the utilization of a medication containing definition to the skin to straightforwardly treat cutaneous turmoil [3].

#### **ADVANTAGES OF MICROEMULSION SYSTEM -**

I) microemulsions can administer APIs in liquid form.

II) Microemulsion further develops bioavailability and steadiness through little drop sizes.

iii) It solubilize and passes on both hydrophilic and lipophilic meds.

iv) It shapes unexpectedly with somewhat basic beginning ingredients<sup>4</sup>.

#### **DISADVANTAGES OF MICROEMULSION SYSTEMS -**

I) The requirement for chemically OK fixings restricts the decision of microemulsion parts (e.g., oil, surfactant, and cosurfactants) prompting troubles in the detailing.

II) The blend of surfactants and co-surfactants utilized should be saved low for toxicological reasons.

III) Microemulsion further develops bioavailability and dependability through little bead sizes.

IV) For intravenous use, the demand of toxicity on formulation is rigorous and very few studies have been reported so far [4].

#### **FORMULATION EXCIPIENTS OF MICROEMULSION-**

##### **I) Surfactants:-**

Surfactants are the particles which when present in low fixation will adsorb to the outer layer of marks of collaboration of a System and change the interfacial energies of the System. The interfacial energy is the work expected to make a unit

space of a mark of interactions assembly of surfactants and co-surfactants utilized should be saved low for toxicological reasons. The real motivation behind surfactant is to bring down the interfacial strain to an insignificant worth that works with the course of scattering during the readiness of microemulsion. I used to stabilize the system; -non-ionic, zwitterion, cationic or anionic [5].

## II) Co-surfactant:-

It decreases the interfacial tension; - and increases the microemulsion region; alcohols, amines, and cholesterol. Generally, single-chain surfactants alone are missing to lessen o/w interfacial strain to the point of planning a microemulsion. Attributable to its amphiphilic nature, a co-surfactant amasses considerably at the interfacial layer, expanding the smoothness of interfacial film by infiltrating the surfactant layer. Short to medium chain length alcohols are everything viewed as added as co-surfactants helping no perspiration of the spot of correspondence. Amonshort chain alkanols, ethanol is

completely abused as a drenching enhancer. Medium-chain alcohols 1-butanol was addressed to be the best enhancer. The surfactant and co-surfactant proportion is a critical element for stage properties [5].

## III) Oils:-

The determination of oil depends on the idea of the medication just as the course of the organization. The screened oil should have solubilization potential for the arrangement. The oil impacts the ebb and flow and can grow the tail gathering of surfactant. Soaked and unsaturated fats have infiltration upgrading action of their own. The unsaturated fats increment the porousness by disturbing thickly gotten lipids and occupying together in extracellular spaces of the layer corneum. Among unsaturated fats, oleic harming is a strong skin entrance enhancer. Hydrocarbon oils such as heptane or -cyclic oils like cyclohexane the droplets i.e., internal phase [5].

## COMMON EXCIPIENTS USED IN MICROEMULSIONS-

Oil Phase	Surfactant	Co-surfactant
Oleic acid	Tween 80	PEG 400
Caprylic Acid	Span 80	Ethanol
Carol 90	Translator	Transcutol P
Isopropyl Myristate	Span 40	Propylene glycol

## CLASSIFICATION OF MICROEMULSION-

Three sorts of microemulsions are doubtlessly going to be illustrated relying on the strategy

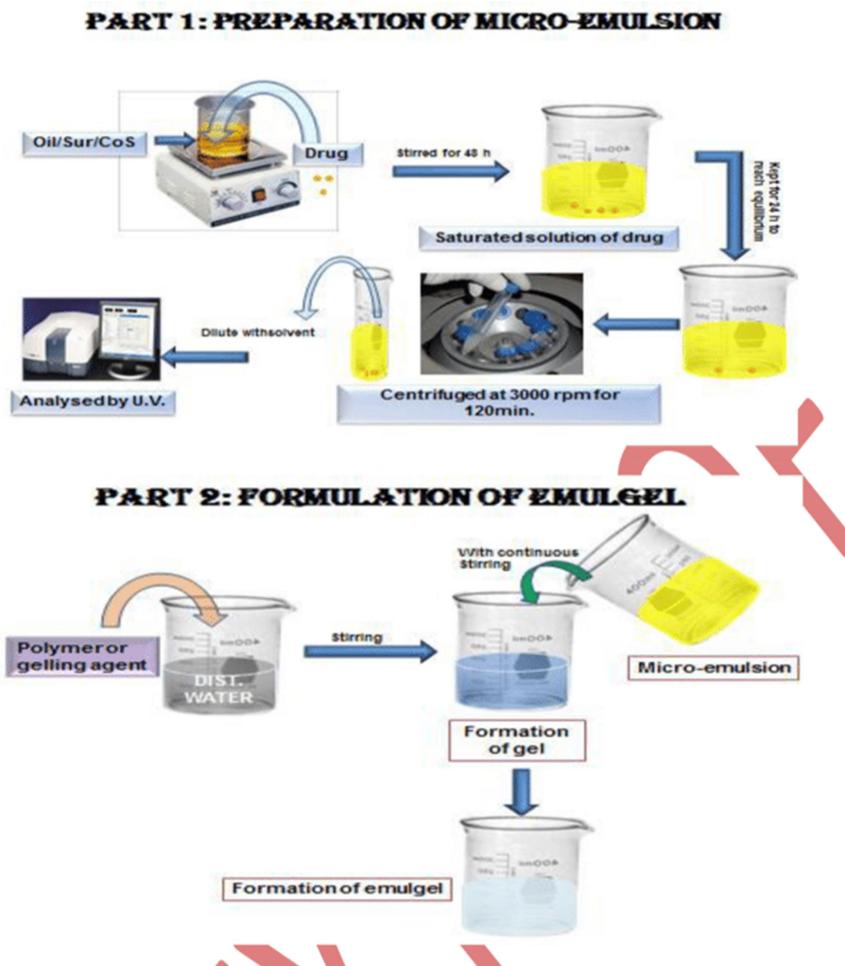
I. Oil in water microemulsions wherein oil spots are dissipated in the dependable watery stage.

ii. Water in oil microemulsions wherein water spots are scattered in the reliable oil stage.

iii. Bi-consistent microemulsions where in microdomains of oil and water are blended inside the arrangement.

iv. In every one of the three kinds of microemulsions, the association point is offset by a fitting mix of surfactants and co-surfactants [5].

## METHOD OF FORMULATIONS



### 1 Phase titration method:-

Microemulsions are prepared by the unconstrained emulsification strategy which is tended to with the help of stage charts. Stage outline development is a reasonable way to deal with concentrating on complex series of connection that

happens when various parts are blended. The part of the stage chart is stage harmony and outline of stage limits. Most frequently pseudo-ternary stage charts are developed to sort out the microemulsion zone as the quaternary stage outline is tedious and hard to decipher [5].

2) Phase inversion method:-

Stage reversal of microemulsion changes upon the expansion of an abundance of the scattered stage. Stage reversal prompts revolutionary actual changes as an adjustment of molecule size that modifies drug discharge. During cooling, this framework crosses the mark of zero unconstrained arch and negligible surface pressure, inciting the arrangement of finely scattered oil beads. Microemulsions can be ready by the

controlled movement of lower alkanols (butanol, pentanol, and hexanol) to smooth emulsions to deliver straightforward arrangements including scatterings of one or the other o/w or w/o or colloidal scatterings. The lower alkanols are called co-surfactants. They bring down the interfacial strain among oil and water adequately low for practically unconstrained development [5].

ANTHELMINTIC ACTIVITY-

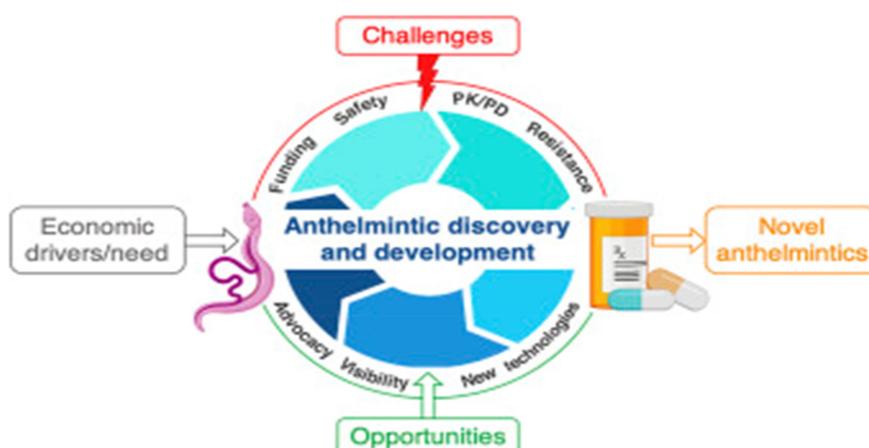


Fig.: Challenges and Opportunities on the path of New Anthelmintic Activity

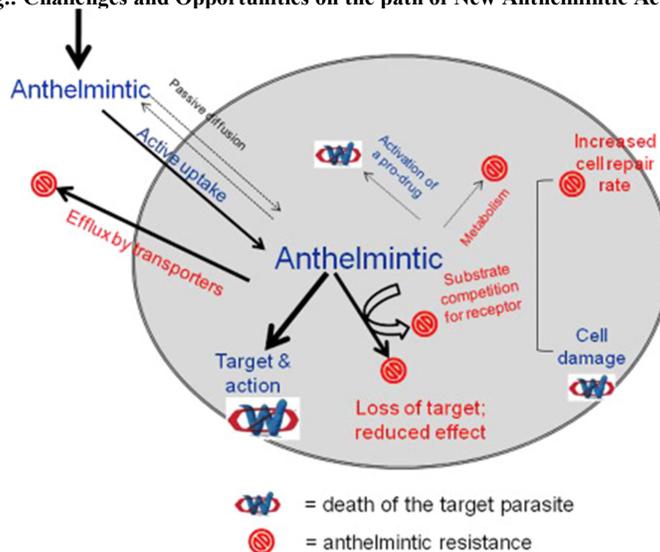


Fig.: Mechanism Anthelmintic activity

Helminth diseases are among the commonest contaminations in man, influencing a huge extent of the total populace. In emerging nations, they represent a significant danger to general wellbeing and add to the pervasiveness of lack of healthy sustenance, paleness, eosinophilia, and pneumonia. Anthelmintics are drugs that either kill or dispose of overpowering helminths and the gastrointestinal pack is the spot of different helminths, albeit some likewise live in tissues, or their hatchlings move into tissues. They hurt the host by denying him food, causing blood misfortune, injury to organs, digestive or lymphatic check, and discharging poisons. Helminthiasis is seldom deadly yet is a significant reason for grimness [6].

Anthelmintic are drugs that are utilized to treat contaminations with parasitic worms. This solidifies the two flatworms, e.g., fiascoes and tapeworms, and roundworms, i.e., nematodes. They are essential for human tropical medications and veterinary medication. The World Health Organization overviews that a stunning 2 billion individuals harbor parasitic worm pollutions. Parasitic worms furthermore taint creatures and yields, impacting food creation with a resultant money-related impact. Additionally of significance is the disease of homegrown pets. Without a doubt, the friend creature

market is a significant monetary thought for creature wellbeing organizations undertaking drug disclosure programs [7].

Anthelmintics or antihelminthics are a group of antiparasitic drugs that expel parasitic worms (helminths) and other internal parasites from the body by either stunning or killing them and without causing significant damage to the host. They may in like way be called vermifuges (those that shock) or vermicides (those that kill). Anthelmintics are utilized to treat individuals who are debased by helminths, a condition called helminthiasis. These medications are likewise used to treat contaminated creatures [8].

Pills containing anthelmintics are utilized in mass deworming tries of school-created young people in various green nations. The arrangements of decision for soil-sent helminths are mebendazole and albendazole; for schistosomiasis and tapeworms, it is praziquantel [9].

#### **ANTHELMINTIC RESISTANCE-**

Anthelmintic resistance in parasites is now widespread. It is a significant danger to the supportability of current ruminant domesticated animals creation, bringing about diminished efficiency, compromised animal wellbeing and government assistance, furthermore extended ozone hurting substance releases through extended parasitism and farm inputs. An informational collection of disseminated

and unpublished European AR research on gastrointestinal nematodes was assembled in 2020. A sum of 197 distributions was accessible for investigation, addressing 535 examinations in 22 nations and traversing the period 1980–2020. Brings about sheep and goats beginning around 2010 uncover a normal pervasiveness of protection from benzimidazoles of 86%, macrocyclic lactones except moxidectin 52%, levamisole 48%, and moxidectin 21%. All major gastrointestinal nematodes genera endure treatment in different assessments. In cows, the prevalence of anthelmintic block vacillated between anthelmintic classes from 0–100 percent (benzimidazoles and macrocyclic lactones), 0–17% (levamisole), and 0–73% (moxidectin), and both *Cooperia* and *Ostertagia* suffer treatment.

The capacity of parasites to endure medicines that are for the most part compelling at the prescribed dosages is a huge risk to the future control of worm parasites in little ruminants and horses. This is especially true of nematodes and has helped spur the development of aminoacetonitrile derivatives for treatment against drug-resistant nematodes, as well as exploration of doxycycline to kill their endosymbiotic *Wolbachia* bacteria [10].

#### **TOPICAL ACTIVITY-**

#### **Microemulsion delivery through skin-**

This is the most settled different evened out course for which the microemulsion strategy was used. In transdermal conveyance, the objective of the dose structure is to expand the transition through the skin into the foundational dissemination. A valuable system for further developing percutaneous transition is to work on the convergence of medications or pick a suitable vehicle that can upgrade transdermal conveyance. The strong transdermal vehicle of ketoprofen, apomorphine, estradiol, and lidocaine, utilizing microemulsions has been tended to. Human skin inciting influence examinations of a lecithin microemulsion gel and lecithin liposomes have been performed. Soybean phosphatidylcholine (lecithin) microemulsion gels offer promising elements for conceivable use as plans in transdermal steady frameworks. To outline the skin irritancy capacity of the gel, remarkable and outright upsetting tests were acted in human subjects. This layout shows an astoundingly low power and a low combined irritancy potential for the soybean lecithin microemulsion gel making it a competitor framework for transdermal strong frameworks in like way under toxicological viewpoints [11].

#### **TOPICAL PATHWAYS-**

There are two crucial pathways by which meds can cross the skin and show up at the fundamental stream. The clearer

course is known as the transcellular pathway.

### **I) Transcellular pathway -**

By this course, drugs get the skin by clearly going through both the phospholipids films and the cytoplasm of the dead keratinocytes that fuse the layer corneum. Albeit this is the way of most brief distance, the medications experience huge protection from penetration. This opposition is caused because the medications should cross the lipophilic film of every cell, then, at that point, the hydrophilic cell substance containing keratin, and from that point the phospholipid bilayer of the cell without a doubt. This series of steps is rehashed on various occasions to navigate the full thickness of the layer corneum [12].

### **II) Intercellular pathway:-**

The other more standard pathway through the skin is using the intercellular course. Drugs crossing the skin by this course should go through the little spaces between the cells of the skin, making the course more convoluted. In any case, the thickness of the layer corneum is around 20  $\mu\text{m}$ , the certifiable diffusional strategy for most particles crossing the skin is on the requesting for 400  $\mu\text{m}^3$ . The 20-overlap expansion in the real way of saturating particles extraordinarily lessens the pace of medication entrance [14].

The ongoing examination has set up that the intercellular course can be drastically improved by taking care of the actual science of the framework solubilizing the dynamic drug fixing, delivering a significantly more productive conveyance of payload, and empowering the conveyance of most mixtures through this course [15, 16].

### **OBSTACLES –**

Albeit the skin is a huge and intelligent objective for drug conveyance, its fundamental capacities limit its utility for this reason. The skin capacities principally to shield the body from the outside entrance (by for example hurtful substances and microorganisms) and to contain all body liquids.

There are two huge layers to the human skin (1) the Epidermis and (2) the Dermis. For the transdermal new development, meds should go through the two sublayers of the epidermis to appear at the microcirculation of the dermis.

### **EVALUATION OF TOPICAL MICROEMULGEL:-**

#### **I) Solubility:-**

The solvency information demonstrates that has the most elevated dissolvability in explicit oil followed by among the oils tried. The solvency profile in various oils can be seen as in Supplementary. As requirements are, oils

were picked to set up the microemulsions and make the pseudo-ternary stage follows.

### III) Viscosity and pH –

The solvency profile in various oils can be viewed as in Supplementary. Thusly, oils were picked to set up the microemulsions and foster the pseudo-ternary stage follows. The consistency was made by utilizing a Brookfield viscometer. The shaft number 2 was dunked in microemulsion and turned at 5, 10, 20, and 50 rpm at room temperature. For the thickness of the gel, shaft number 6 was plunged in readiness and turned at 5, 10, 20, and 50 rpm at room temperature. The thickness of little emulsion-based gel was facilitated by using a Brookfield viscometer. For thickness assurance of miniature emulsion-based gel, 175 g of miniature emulsion-based gel was filled in a 250 ml compartment and the consistency was surveyed by utilizing Spindle number LV4. The pH was determined using a digital pH meter. Microemulsion-based gel (2.5 g) was weighed conclusively and scattered in 25 ml of refined water. The pH meter was changed before each use with a cushion blueprint of pH 4.0, 7.0, and 9.0. The estimation of pH of the plan was done three-fold and mean qualities were determined [17].

### III) Droplet size determination-

The globule size of microemulsion definitions was formed by Photon relationship spectroscopy that disengaged the movements in light dispersing because of Brownian progress of the particles 13 utilizing a Zetasizer. The microemulsion formulation sample was diluted to 1: 2000 and ready in separated deionized water in the weakening scope of 1:2000. A couple of drops of the weakened example were then added to a glass cuvette containing separated deionized water, situated between the laser light and identifier for actually looking at light power in the scope of 50, 000 to 1, 00, 0000 of the dispersed particles.

Light dispersing was observed at 25 o C at a 3. , 30.1o, 62.5o, and 90pointsnt. Since the power of light is point subordinate since particles dissipate light to an alternate point with various forces [18].

### IV) Refractive Index:-

The Refractive record of not set in stone utilizing an Abbes type refractometer at 25±0.5 o C [19].

### V) HPLC assay:-

HPLC test technique for Drugs was created and approved. The maintenance time was set by the Drugs. The restriction of location (LOD) and cut off of evaluation (LOQ) is diverse as per material, individually. The adjustment bend was direct inside a particular fixation [19].

### VI) Stability:-

The substance in the new plans examined by HPLC. Microemulsion and microemulsion gel plans were overseen at 5 °C, 25 °C, 40 °C/75 % RH (relative submersion) chambers. The actual capacity of the microemulsion plans was assessed through h appearance check (stage detachment, shading change). Besides, any progressions in molecule size and PDI of the microemulsions were additionally assessed during the solidness trial. Compound secure qualities in the details were examined by HPLC following multi-week, one-month, and 90 days of capacity at the previously mentioned dependability conditions. HPLC tests were ready by dissolving the definitions in methanol. Momentarily, precisely gauged plans were first added to the volumetric carafes, and afterward methanol was added. The carafes were sonicated for 30 min for complete extraction of medication from the details lastly separated through 0.45  $\mu$  PTFE needle channels (Fisher Scientific; USA) into the HPLC vials. Item shades of the soundness tests were additionally outwardly contrasted and the new examples [19].

#### VII) Permeation Through Membrane:-

Franz dispersing cells and planned polysulfone films were utilized to take a look at the in vitro layer invasion of ivermectin from the microemulsion gel plans. Twofold walled Franz spreading

cells were set on a multistage attracting stirrer and related with a water circulator. Hydro-alcoholic arrangement (70 % (v/v) phosphate cushion saline (PBS; pH 7.4) and 30 % (v/v) methanol) was utilized as receptor liquid to keep up with sink condition. Receptor liquid was set in the receptor chamber. The temperature of the water circulator was set at 33 °C with the valid that temperature of the receptor liquid remained mindful of at  $32 \pm 0.5$  °C. The layer was set in the partner chamber and receptor chamber. The accomplice chamber was filled the microemulsion gel or clear microemulsion gel or reference standard. The speed of the attracting the stirrer was set at 300 pm. Tests from the receptor liquid were accumulated through the looking at the port at 0.5, 1, 2, 3, 4, 5, and 6 h for HPLC assessment of entered.. Effective gel-type items don't remain on the skin for more than a couple of hours (under 6 h). In this manner placement tests of the gel, plans were facilitated for 6 h. During test combinations, the interfacing with stirrer was traded off, 2 mL new receptor fluid was presented from the base port, the initial 1 mL test was disposed of and the following 1 mL test was gathered in the HPLC vial from the top examining port lastly, the magnetic stirrer was again switched on. The honesty of the films was

affirmed under the magnifying lens later the fulfilment of the penetration study [19].

#### **VIII) Zeta potential measurement:-**

It should be negative or unbiased, which indicate that beads of a microemulsion have no charge, and henceforth the framework is steady. Zeta potential is determined by using Zetasizer. Zeta potential is essentially useful for assessing flocculation since electrical charges on particles influence the rate of flocculation [20].

#### **IX) Measurement of electrical conductivity:-**

The electrical conductivity of microemulsions was evaluated with a conductivity meter outfitted with an inbuilt magnetic stirrer. This is done by using a conductivity cell consisting of two platinum plates separated by desired distance and having liquid between the platinum plates acting as a conductor [20].

#### **CONCLUSION-**

Choice of oils, surfactants, co-surfactants and development of stage diagram(s) are essentials for the advancement of microemulsion based definitions of any medication. As drug has poor watery dissolvability, the oils were chosen dependent on their solubilisation ability so that limited quantity of oil utilized in the microemulsion formulations can break down 1 %. Diff oil were viewed as appropriate for this reason. Stage charts

were successfully built on these oils utilizing distinctive surfactant/co-surfactant organizations and microemulsion districts were distinguished. Stable stacked microemulsion and microemulsion gel definitions were arranged dependent on the chose organizations from the stage graphs. The microemulsion gel details showed essentially higher film penetration of Drug (i.e., higher medication discharge from the microemulsion-gels) than advertised item. The result of this review can be used for following three purposes.

I) Significantly lower level of Drug content in the microemulsion gel plans might give same or then again preferable viability over Soolantra because of higher film pervasion. This will lessen cost and may diminish results of the item.

ii) Some parasites (e.g., parasites for scabies, onchocerciasis) also reside inside the skin (epidermis and dermis) and subcutaneous tissues. Penetration of drug through stratum corneum can help to act on those parasites. Therefore, the microemulsion based formulations should be more effective (due to higher membrane permeation of Drug) than Other for topical treatment of parasites.

iii) High membrane permeation (or drug release) of these microemulsion based formulations can be utilized to develop topical/transdermal delivery systems of

other BCS class II drugs for systemic actions.

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