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E-Mail :
editor.ijasem@gmail.com
editor@ijasem.org

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FORMULATION OF SALICYLIC ACID ETHOSOMAL GEL AND TOPICAL GEL

Ayesha Siddiqua[*], Azka Fathima[1], Akhila[2], Vamshidhar[3] Meghana[4], Rakesh[5]

Abstract:-

Salicylic acid is in a class of medications called keratolytic agents. Topical salicylic acid treats acne by reducing swelling and redness and unplugging blocked skin pores to allow pimples to shrink. It treats other skin conditions by softening and loosening dry, scaly, or thickened skin so th Topical salicylic acid comes as a cloth (a pad or wipe used to cleanse the skin), cream, lotion, liquid, gel, ointment, shampoo, wipe, pad, and patch to apply to the skin or scalp. Topical salicylic acid comes in several strengths,

The Ethosomal system is a highly efficient drug delivery system. The Salicyclic acid is used to prepare the gels.

The method described by Touitou et al., (2000) was employed with modification for the preparation of various ethosomal formulations containing concentration of ethanol (10%) by cold method. The entrapment efficiency of ethosomes containing 20% w/ Salicyclic acid has shown highest value with respect to all other formulation.

Keywords:-Salicylic acid, analgesic, 2-Hydroxybenzoic acid, salicylate.

INTRODUCTION:-

Salicylic acid is in a class of medications called keratolytic agents. Topical salicylic acid treats acne by reducing swelling and redness and unplugging blocked skin pores to allow pimples to shrink. It treats other skin conditions by softening and loosening dry, scaly, or thickened skin so the Topical salicylic acid comes as a cloth (a pad or wipe used to cleanse the skin), cream, lotion, liquid, gel, ointment, shampoo, wipe, pad, and patch to apply to the skin or scalp. Topical salicylic acid comes in several strengths, including certain products that are only available with a prescription. Topical salicylic acid may be used as often as several times a day or as infrequently as several times a week, depending on the condition being treated and the product being used. Follow the directions on the package label or your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand. Use salicylic acid exactly as directed. Do not use more or less of it or use it more often than directed on the package or prescribed by your doctor.

Bharat Institute of Technology,

Mangalpally Village, Ibrahimpatnam Mandal, Telangana 501510,

If you are using topical salicylic acid to treat acne, your skin may become dry or irritated at the beginning of your treatment. To prevent this, you may apply the product less often at first, and then gradually begin to apply the product more often after your skin has adjusted to the medication. If your skin becomes dry or irritated at any time during your treatment, you may apply the product less often. Talk to your doctor or check the package label for more information.

Apply a small amount of the salicylic acid product to one or two small areas you want to treat for 3 days when you begin to use this medication for the first time. If no reaction or discomfort occurs, use the product as directed on the package or on your prescription label.

Do not swallow topical salicylic acid. Be careful not to get topical salicylic acid in your eyes, nose, or mouth. If you accidentally get topical salicylic acid in your eyes, nose, or mouth, flush the area with water for 15 minutes.

Do not apply topical salicylic acid to skin that is broken, red, swollen, irritated, or infected.

Only apply topical salicylic acid to the areas of skin that are affected by your skin condition. Do not apply topical salicylic acid to large areas of your body unless your doctor tells you that you should. Do not cover the skin where you applied topical salicylic acid with a bandage or dressing unless your doctor tells you that you should.

If you are using topical salicylic acid to treat acne or certain other skin condition, it may take several weeks or longer for you to feel the full benefit of the medication. Your condition may worsen during the first few days of treatment as your skin adjusts to the medication.

Read the package label of the topical salicylic acid product you are using very carefully. The label will tell you how to prepare your skin before you apply the medication, and exactly how you should apply the medication. Follow these directions carefully.at it falls off or can be removed easily.

Mechanism of action

Salicylic acid directly irreversibly inhibits COX-1 and COX-2 to decrease conversion of arachidonic acid to precursors of prostaglandins and thromboxanes. Salicylate's use in rheumatic diseases is due to it's analgesic and anti-inflammatory activity. Salicylic acid is a key ingredient in many skin-care products for the

treatment of acne, psoriasis, calluses, corns, keratosis pilaris, and warts. Salicylic acid allows cells of the epidermis to more readily slough off. Because of its effect on skin cells, salicylic acid is used in several shampoos used to treat dandruff. Salicylic acid is also used as an active ingredient in gels which remove verrucas (plantar warts). Salicylic acid competitively inhibits oxidation of uridine-5-diphosphoglucose (UDPG) with nicotinamide adenosine dinucleotide (NAD) and noncompetitively with UDPG. It also competitively inhibits the transferring of the glucuronyl group of uridine-5-phosphoglucuronic acid (UDPGA) to a phenolic acceptor. Inhibition of mucopoly saccharide synthesis is likely responsible for the slowing of wound healing with salicylates.

Toxicity

Oral rat LD50: 891 mg/kg. Inhalation rat LC50: > 900 mg/m3/1hr. Irritation: skin rabbit: 500 mg/24H mild. Eye rabbit: 100 mg severe. Investigated a mutagen and reproductive effector.

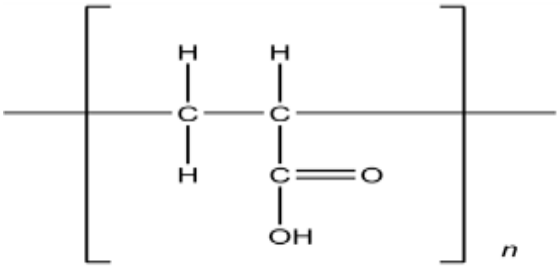
EXCIPIENT PROFILE

Carbopol 934

Chemical name Carboxyl polymethylene

Synonym Acritamer, acrylic acid polymer carboxy vinyl polymer.

Structural formula



Molecular formula $C_3 H_4 O_2$

Molecular weight 72.06266 (g/mol)

Description White, fluffy, acidic, hygroscopic powder.

Melting point 12.5^0 C.

Solubility Miscible with ethanol, ethyl ether, soluble in acetone.

Functional category Bioadhesive, emulsifying, suspending & gelling agent.

LECITHIN

Nonproprietary Names:

USP-NF: Lecithin

Synonyms:

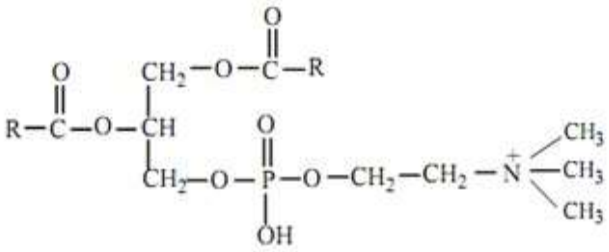
LSC 5050; LSC 6040; ovolecithin, Phosal 53 MCT; Phospholipon 100 H; soyabean phospholipids, vegetable lecithin, lecithol, vitellin, kelecin, and granulestin.

Chemical name and CAS Registry Number, Composition:

Lecithin 8002-43-5 1,2-diacyl-sn-glycero-3-phosphocholine (trivial chemical name, phosphatidyl choline).

The composition of lecithin varies enormously depending upon the source of lecithin and the degree of purification. Egg lecithin, for example contains 69% phosphatidyl choline and 24% of phosphatidylethanolamine, while soybean lecithin contains 21 % of phosphatidyl choline and 22% of phosphatidylethanolamine and 19% phosphatidylinositol, along with other components.

Structural Formula:



Lecithin

R^1 and R^2 are fatty acids, which may be different or identical. Lecithin is a complex mixture of materials. The structure above shows phosphatidylcholine, the principal component of egg lecithin, in its a-form. In the b-form, the phosphorous containing group and the R^2 group exchange positions.

Description: Brown to light yellow. When they it is exposed to air, rapid oxidation occurs, resulting in dark yellow to brown colour.

Applications of Lecithin in Pharmaceutical Formulations and Technology:

- Lecithin has emulsification and lubricant properties, and is a surfactant.
- In the pharmaceutical industry, it acts as a wetting, stabilizing agent and a choline enrichment carrier, helps in emulsifications and encapsulation, and is a

good dispersing agent. It can be used in manufacture of intravenous fat infusions and for therapeutic use.

CHOLESTEROL

Nonproprietary Names

USP-NF: Cholesterol.

Synonyms

Cholesterin; Cholesterol.

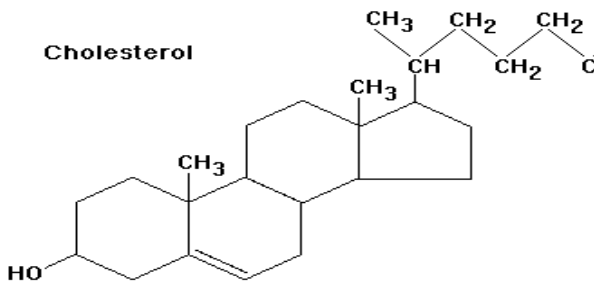
Chemical Name and CAS Registry Number

Cholest-5-en-3β-ol [57-88-5]

Empirical Formula and Molecular Weight

$C_{27}H_{46}O$ and 386.65 g/mol.

Structural Formula



Functional Category

Emollient; emulsifying agent.

Applications in Pharmaceutical Formulation and Technology

- Cholesterol is used in cosmetic and topical pharmaceutical formulations at concentrations of 0.3-5.0% w/w as an emulsifying agent. It imparts water-absorbing power to an ointment and has emollient activity.
- Cholesterol also has a physiological role. It is the major sterol of the higher animals and it is found in all body tissues, especially in the brain and spinal cord. It is also the main constituent of gallstones.

Description

Cholesterol occurs as white or faintly yellow, almost odourless, pearly leaflets, needles, powder or granules. On prolonged exposure to light and air, cholesterol acquires a yellow to tan colour.

Boiling point 360 °C (some decomposition)

Density 1.052 g/cm^3 for anhydrous form

Dielectric constant D^{20} =5.41

Melting point 147-150 °C

Solubility Cholesterol is soluble in Acetone and Ethanol.

Stability and Storage Conditions

Cholesterol is stable and should be stored in well-closed container, protected from light.

Ethyl Alcohol

Synonyms Ethyl alcohol; ethyl hydroxide; methyl carbinol.

Non Proprietary names BP: Ethanol

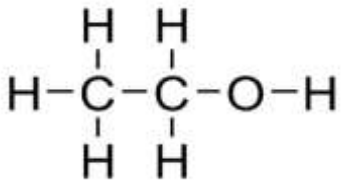
JP: Ethanol

PhEur: Ethanolum

USP: Alcohol.

Chemical Name Ethanol

Chemical structure



Molecular weight 46.07g/mol

Description Alcohol is a clear, colourless, mobile and volatile liquid with a slight, characteristic odour and burning taste.

Melting Point 78.15^0 C

Solubility Miscible with chloroform, ether, glycerine and water.

Functional category Antimicrobial preservative, Solvent, disinfectant.

SODIUM BENZOATE

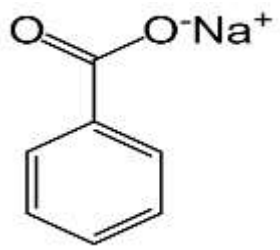
Synonyms E211, benzoate of soda

IUPAC name Sodium benzoate

Chemical formula $C_7H_5NaO_2$

Molecular weight 144.10 $g \cdot mol^{-1}$

Chemical structure



Description white or colorless, odourless crystalline powder

Density 1.497 g/cm^3

Melting Point 410 ºC

Solubility Soluble in liquid ammonia, Pyridine, water, ethanol.

Application in Pharmaceutical industry

- Sodium benzoate is a preservative.. As a food additive, sodium benzoate has the E number E211. It is bacteriostatic and fungistatic under acidic conditions.
- Sodium benzoate is used as a treatment for urea cycle disorders due to its ability to bind amino acids.

Sodium benzoate is used to treat hyperammonemia

PREPARATION OF GELS

METHOD OF PREPARATION OF TOPICAL GEL OF ETHANOLIC EXTRACT OF SALICYLIC ACID

General procedure for formulation of gels:

Topical Gels containing 10% and 20% of Salicylic acid were prepared by using different concentrations of polymer such as carbopol 934 10% and 20%w/w.

The specified amount of carbopol 934 powder was slowly added to ultrapure water and kept for 12 hours for the polymer to swell. Appropriate amount of Salicylic acid was dissolved, polyethylene glycol and sodium benzoate was added to it, this mixture is incorporated to the above mixture and was subjected to continuous stirring at 800rpm after complete addition the mixture is stirred till the homogeneous gels was obtained. These formulations were then stored in the wide mouthed bottles for stability studies and all the samples were allowed to equilibrate at room temperature.[19]

Table 1: Composition of different Topical formulations

NAME OF THE INGREDIENTS	Quantities in W/W % (100gm)	
	F1	F2
Salicylic acid	10	20
Carbopol 934 gel base (% W/V)	1	1.5
PEG 4000 (W/W)	5	5
Sodium benzoate (W/W)	1	1
Distilled water (V/V)	Q.S	Q.S

PREPARATION OF ETHOSOMAL GEL OF SALICYLIC ACID (BY COLD METHOD).

Ethosomal gels containing Salicylic acid were prepared by using the method suggested by Touitou et al., with modification. The ethosomal formulation of Ethanolic extract of Salicylic acid was formulated using different compositions of 2% phospholipid, 10% ethanol, 5% of polyethylene glycol (PEG) and 5g of cholesterol.

The Salicylic acid was dissolved separately in a covered vessel at room temperature by vigorous stirring and polyethylene glycol was added slowly to this mixture and heated to 30°C at 800 rpm. Lecithin and cholesterol dissolved in ethanol and added to the above mixture. Double distilled water was added slowly as a fine stream with constant mixing at 800 rpm.

Mixing was continued for additional 5 minutes. Ethosomes formulation was stored under refrigeration.

Ethosomal vesicles suspension were incorporated into carbopol gel (10% and 20%w/w). the specified amount of carbopol 934 powder was slowly added to ultrapure water and kept for 12 hours for the polymer to swell, tri ethanolamine was added to it drop wise

Appropriate amount of formulation of ethosomes containing Salicylic acid *is* was then incorporated into gel-base and was subjected to continuous stirring until homogenous formulation were achieved.[16]

Table 2: Composition of different ethosomal formulations

NAME OF THE INGREDIENTS	Quantities in W/W %(100 gm)	
	E1	**E2**
Salicylic acid	10	20
Lecithin (W/V)	2	2
Cholesterol (W/W)	5	5
Ethanol (V/V)	10	10
PEG 400 (V/V)	5	5
Carbopol 934 gel base (% W/V)	1	1.5
Sodium benzoate (W/W)	1	1
Distilled water (V/V)	Q.S	Q.S

MATERIALS USED

All the materials and equipments used in the formulation, evaluation and other experiments are given below.

Table 3: List of materials used with Manufacturer

S.NO	NAME OF THE MATERIAL	CATEGORY	MANUFACTURER
1.	Salicyclic acid	Organic Compound	Bharat Institute of Technology.
2.	Lecithin Cholesterol	Phospholipid	S.D Fine chemicals, Mumbai, INDIA.
3.	Polyethylene glycol	As a skin penetration enhancer	Fischer Scientific, Mumbai, INDIA.
4.	Carbopol 934	Gelling agent	Research lab fine chem. industries, Mumbai, INDIA.
5.	Ethanol	Volatile solvent	Sigma-Aldrich Corporation.
6.	Sodium benzoate	Bacteriostatic agent	Fischer Chemicals, Mumbai,INDIA.

Topical gel

Ethosomal gel

Topical gel and ethosomal gel

CONCLUSION:-

The Ethosomal system is a highly efficient drug delivery system. The Salicyclic acid is used to prepare the gels.

The method described by Touitou et al., (2000) was employed with modification for the preparation of various ethosomal formulations containing concentration of ethanol (10%) by cold method. The entrapment efficiency of ethosomes containing 20% w/w Salicyclic acid has shown highest value with respect to all other formulation.

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The Successful accomplishment of this Article would not have been possible but by the timely help and guidance rendered by many people. I would like to take this opportunity to place it in record. Though it's not possible to name all of them, I would like to mention few of them. My first salutation goes to Almighty God and my Parents for being ever so kind and courteous. It gives me an immense pleasure to acknowledge a debt of gratitude to my guide Mrs. Ayesha Siddiqua, M.Pharm, Assistant Professor, Bharat Institute of Technology for her constant encouragement, suggestions and supervision.

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