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SALICYLIC ACID IN DERMATOLOGY AND COSMETOLOGY FROM NATURAL ORIGIN: BENEFITS AND THERAPEUTIC APPLICATION

Dr. D. Nagavalli[1], M. S. Kumudhapriya[2]*, Nandhagopal[3]

[1]M. Pharm, Ph. D., Professor and H.O.D. Department of Pharmaceutical Chemistry, Adhiparasakthi College of Pharmacy, Melmaruvathur-603319, Affiliated to The Tamil Nadu Dr. M.G.R Medical University, Chennai-600032, Tamil Nadu, India.

[2]M. Pharm. (PG Scholar), Department of Pharmaceutical Analysis, Adhiparasakthi College of Pharmacy, Melmaruvathur-603 319, Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, 2 Chennai-600032, Tamil Nadu, India.

[3]M. Pharm, Assistant Professor, Department of Pharmaceutical Chemistry, Adhiparasakthi College of Pharmacy, Melmaruvathur-603319, Affiliated to The Tamil Nadu Dr. M.G.R Medical University, Chennai-600032, Tamil Nadu, India.

***Corresponding Author: M. S. Kumudhapriya**
M. Pharm. (PG Scholar), Department of Pharmaceutical Analysis, Adhiparasakthi College of Pharmacy, Melmaruvathur-603319, Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, 2 Chennai-600032, Tamil Nadu, India. **DOI:** https://doi.org/10.5281/zenodo.21157040

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ABSTRACT
Salicylic acid is a naturally occurring beta-hydroxy acid that has been used for many years in medical, cosmetic, and pharmaceutical fields. It was originally found in willow bark and other plant sources. This acid has several beneficial properties like keratolytic, comedolytic, anti-inflammatory, and antimicrobial effects, which make it a key treatment in dermatology and skincare. This review provides an overview of the historical background, sources, biosynthesis, chemical properties, mechanism of action, and various applications of salicylic acid. The review also discusses its use in the treatment of conditions such as acne, psoriasis, dandruff, hyperpigmentation, and other skin issues, as well as its role as a component in the production of aspirin. The article covers therapeutic indications, contraindications, side effects, and the common forms of salicylic acid used in treatment. Additionally, it summarizes various analytical methods, especially those based on high-performance liquid chromatography (HPLC), used to measure and assess the quality of salicylic acid. Due to its effectiveness, versatility, and well-established safety profile when used correctly, salicylic acid remains an important ingredient in modern pharmaceutical and cosmetic products. Ongoing research is being conducted to enhance its delivery and improve its therapeutic results**.**

KEYWORDS: *Salicylic Acid, Pharmaceutical Applications, HPLC Analysis, Skin Exfoliation, Hyperpigmentation, Topical Formulations.*

INTRODUCTION
Salicylic acid has a long history of use in medicine and the chemical industry. The journey of its therapeutic applications is quite fascinating.

Sources and Derivation of Salicylic Acid
Natural Origin
Salicylic acid is a naturally occurring **β-hydroxy acid** found in several plants. It was first isolated from the bark of the willow tree (Salix species), from which its name is derived. Natural sources of salicylic acid include willow bark, wintergreen leaves, sweet birch bark, and meadowsweet plants. In plants, salicylic acid acts as a natural hormone involved in growth regulation and defense against pathogens. Due to its keratolytic, anti-inflammatory, and antimicrobial properties, naturally derived salicylic acid is widely used in cosmetic and pharmaceutical formulations, particularly for the treatment of acne, dandruff, warts, and other skin disorders.

Natural sources

Salicylic acid is primarily found in willow bark. It is also present in wintergreen leaves, sweet birch, myrtle, and meadowsweet flowers. In addition, it can be found in almonds, water chestnuts, peanuts, mushrooms, and many fruits and vegetables such as blackberries, blueberries, and broccoli.

Dietary sources

Salicylic acid is found naturally in plants. Studies show that some of this acid can be obtained through diet. Foods rich in this acid include tea, coffee, fruits, vegetables, sweet potatoes, nuts, and olive oil. Some people may be sensitive to salicylic acid in their diet, and they might experience symptoms such as asthma, rhinitis, stomach discomfort, or diarrhea**.**

Chemical reactions of Salicylic acid

➢ **Biosynthesis of Salicylic acid**

This figure shows how plants make salicylic acid (SA), which is a key signaling molecule that helps plants respond to threats.Salicylic acid is created through two main pathways: the Isochorismate pathway and the Phenylalanine pathway.

1. Isochorismate Pathway

This pathway starts with shikimic acid, which is transformed into 3-enolpyruvyl shikimate-5-phosphate (EPSP) and then into chorismic acid.

Chorismic acid is a critical point where different aromatic compounds are made.

- Isochorismate synthase (ICS) changes chorismic acid into isochorismate.
- Isochorismate pyruvate lyase (IPL) then turns isochorismate directly into salicylic acid.

This pathway is the main way plants produce salicylic acid, especially when they are infected by pathogens.

2. Phenylalanine Pathway

Chorismic acid can also be used to make phenylalanine through various steps.

- Phenylalanine ammonia-lyase (PAL) converts phenylalanine into trans-cinnamic acid.
- Trans-cinnamic acid can go through two different paths:

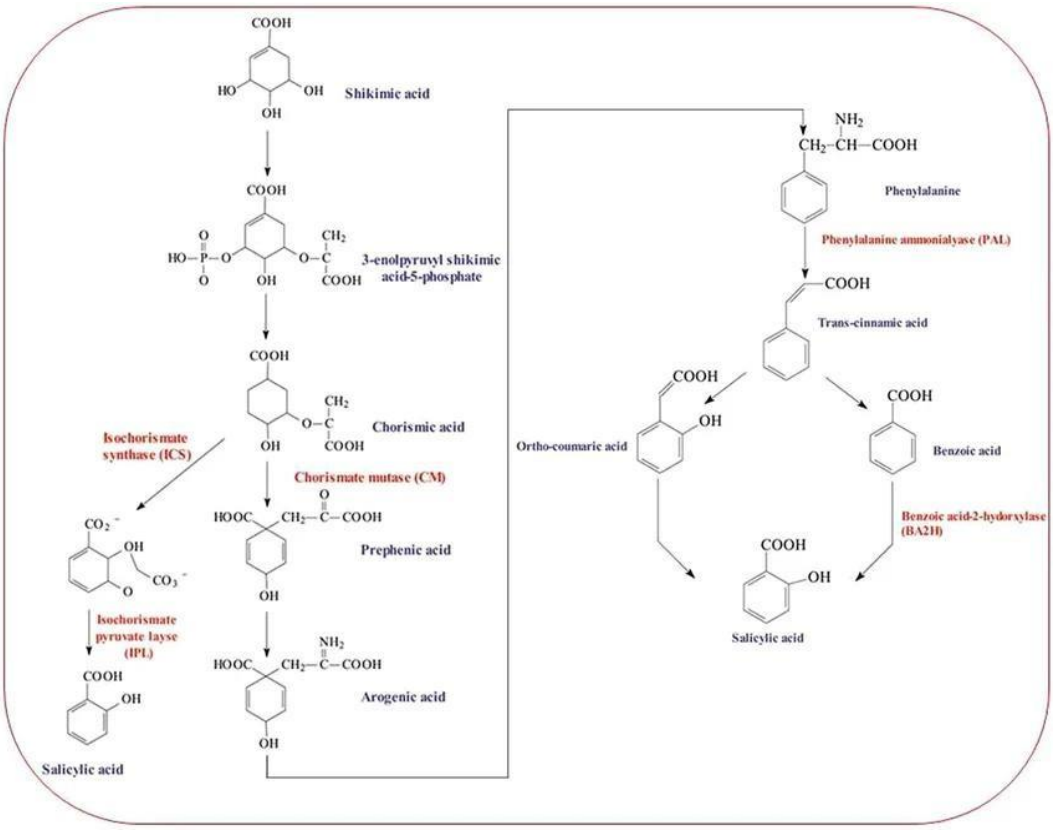
o It can be changed into benzoic acid, which is then modified by benzoic acid 2-hydroxylase (BA2H) to become salicylic acid.

o It can also become ortho-coumaric acid, which is further processed into salicylic acid.

Biological Significance

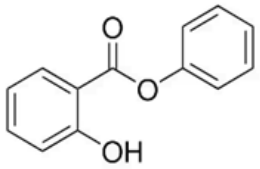
Salicylic acid acts as a plant hormone that

- Helps activate the plant's defense systems against harmful organisms.
- Controls how genes related to defense are expressed.
- Triggers systemic acquired resistance (SAR), offering long-lasting protection across the entire plant.



Chemical synthesis

- When heated, salicylic acid undergoes condensation to form phenyl salicylate (salol), releasing carbon dioxide and water



$2\ HOC_6H_4CO_2H \rightarrow + CO_2 + H_2O$

- Further heating of the product leads to the formation of xanthone derivatives.
- Salicylic acid and its conjugate base also act as chelating agents, showing a strong affinity for iron(III) ions.
- At temperatures around 200–230 °C, salicylic acid slowly decomposes into phenol and carbon dioxide:
  $C_6H_4OH(CO_2H) \rightarrow C_6H_5OH + CO_2$
- In addition, all isomers of chlorosalicylic acid and dichlorosalicylic acid are known. Among them, 5-chlorosalicylic acid is commonly prepared by the direct chlorination of salicylic acid.

Ultrasound Reaction

1. $C_6H_5OH + NaOH \rightarrow C_6H_5ONa + H_2O$

   Phenol Sodium phenoxide

2. $C_6H_5ONa + CO_2 \xrightarrow{\text{(Ultrasound)}} C_6H_4(OH)COONa$

   Sodium salicylate

3. $C_6H_4(OH)COONa + HCl \rightarrow C_6H_4(OH)COOH + NaCl$

   Salicylic acid

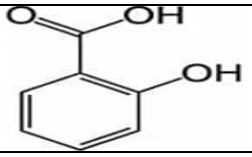
Photosynthesis Reaction

1. $6CO_2 + 6H_2O \xrightarrow{\text{Light/Chlorophyll}} C_6H_{12}O_6 + 6O_2$

   (Photosynthesis)

2. $C_6H_{12}O_6 \xrightarrow{\text{Shikimate Pathway}}$ Chorismate
3. Chorismate $\xrightarrow{\text{Isochorismate Synthase}}$ Isochorismate
4. Isochorismate $\xrightarrow{\text{IPL/PBS3 Pathway}}$ Salicylic Acid ($C_7H_6O_3$)

Physiochemical properties

Chemical structure	
Chemical Formula	$C_7H_6O_3$
IUPAC Name	2-Hydroxybenzoic acid.
Molecular Weight	138.13g/mol
Boiling point	211 ºC
Melting point	158-160ºC
Colour	White, nearly white or colourless
Odour	Odourless
Solubility	Salicylic acid is freely soluble in methanol, ethanol, acetone and diethyl ether while it is slightly soluble in water
Physical state	Solid, needle like crystals or powder form

General Mechanism of Action

- Salicylic acid influences the activity of the COX-1 enzyme, which helps decrease the production of pro-inflammatory prostaglandins.
- Salicylate may also interfere with the formation of prostaglandins in a competitive manner.
- When applied to the skin, salicylic acid causes the outer layer of skin cells to shed more easily, preventing pores from becoming clogged and allowing new skin cells to grow.
- It works by competing with NADH to block the oxidation of uridine-5-diphosphoglucose (UDPG), and it also competes with UDPG to prevent the transfer of the glucuronyl group from uridine-5-phosphoglucuronic acid to a phenolic acceptor.
- The effect of salicylates in slowing wound healing is

likely because they reduce the production of mucopolysaccharides**.**

Mechanism of Salicylic acid Cosmetic

1. Keratolysis (Exfoliation)

- Salicylic acid breaks down the intercellular lipid structure in the outer layer of the skin by weakening the desmosomes — the protein bridges that hold skin cells together.

- This process loosens and removes dead skin cells, resulting in smoother skin texture and unclogged pores.

- Because it is oil-soluble, it can penetrate deep into the hair follicle, which is something that AHAs cannot do.

2. Comedolytic Action (Anti-acne)

- Since salicylic acid can dissolve into sebum and travel down the hair follicle,
- It dissolves the keratin plug that forms the core of blackheads and whiteheads.
- It reduces follicular hyper keratinization — the abnormal accumulation of cells within the pore.
- It prevents the formation of new comedones.

3. Anti-inflammatory Effect

Salicylic acid is structurally similar to aspirin (acetylsalicylic acid) and acts in a similar way by:

- Inhibiting the cyclooxygenase (COX) enzymes, leading to lower prostaglandin production.
- Reducing the activity of pro-inflammatory cytokines such as IL-1 and TNF-α.
- This makes it especially effective against inflammatory acne, such as papules and pustules.

4. Sebostatic Effect

- At higher concentrations, salicylic acid can slightly reduce the production of sebum, helping to create a less oily skin appearance — useful in anti-acne and mattifying products**.**

5. Antimicrobial Action

- Salicylic acid creates a mildly acidic environment that is not favorable for Cutibacterium acnes (formerly known as P. acnes) and Malassezia (a fungus that causes dandruff).
- At effective concentrations, it can damage the cell membranes of these microorganisms.

6. Skin Brightening

By speeding up cell turnover through keratolysis, salicylic acid indirectly

- Removes skin cells that contain excess melanin more quickly.
- Reduces post-inflammatory hyperpigmentation (PIH) over time.
- It is often used alongside niacinamide or vitamin C to enhance skin brightening effects.

Percentage of Salicylic Acid in Pharmaceutics and Cosmetic Products

Concentration range	Formulation/ Brand	Primary Use	Category
0.1-0.5%	Toner, serum- **paula's Choice**	Preservative	Cosmetic
0.5-2%	Facewash, gel, cream- **Cetaphil, Neutrogena**	Daily skincare, acne prevention	Cosmetic/OTC
2-3%	Acne gel, lotion- **Acnemoist, Salicex**	Active acne treatment, dandruff	OTC Pharmaceutical
3-6%	Shampoo, cream- **Sebowash**	Psoriasis, seborrheic dermatitis	Prescription/Professional
6-10%	Ointment, gel- Salex- **Keralyt**	Hyperkeratosis, thick plaques	Prescription
10-20%	Plaster, Solution- **Duofilm**	Warts, calluses, corns	OTC/Prescription
20-40%	Peel solution- **Obagi,Professional peels**	Chemical peels, stubborn warts	Professional only
40-50%	Medicated plaster- **Mosco**	Severe hyperkeratosis	Medical only

BENEFITS OF SALICYLIC ACID IN COSMETIC

Salicylic acid is widely used in cosmetic and skincare products because of its exfoliating, anti-inflammatory, and oil-controlling properties. It belong to the group of beta hydroxy acids (BHAs).

Common Cosmetic Uses

Benefits	Its Mechanisms
Acne treatment	Salicylic acid helps unclog pores by dissolving excess oil and dead skin cells. It is commonly found in face washes, spot treatments, and acne creams.
Exfoliation	It removes dead skin cells from the skin surface, promoting smoother and brighter skin. This makes it useful in exfoliating cleansers and peeling solutions.
Control of oily skin	Because it penetrates oily pores effectively, salicylic acid helps reduce excess sebum production and shine.
Blackhead and whitehead removal	It clears blocked pores and prevents the formation of comedones.
Anti-inflammatory action	Salicylic acid reduces redness and swelling associated with acne and irritated skin.
Treatment of dandruff and scalp conditions	It is used in medicated shampoos to remove scalp flakes and reduce scaling.
Management of psoriasis and keratosis pilaris	In higher concentrations, it softens thickened skin and helps remove scales.
Skin renewal and texture improvement:	Regular use can improve uneven skin texture and mild pigmentation.

Cosmetic Products Containing Salicylic Acid

Salicylic acid is commonly included in

- Cleansers and face washes
- Toners
- Serums
- Acne spot treatments
- Chemical peels
- Exfoliating pads
- Anti-dandruff shampoos
- Body lotions for rough skin

Precautions

- Excessive use may cause dryness, irritation, or peeling.
- Sunscreen should be used because exfoliated skin becomes more sensitive to sunlight.
- People with very sensitive skin or aspirin allergy should use it cautiously

BENEFITS OF SALICYLIC ACID IN PHARMA-CEUTICS

1. Keratolytic Agent

Salicylic acid softens and removes the outer layer of skin by breaking down keratin.

Used in

- Corn and callus removers
- Wart treatments
- Psoriasis preparations
- Dandruff and seborrheic dermatitis shampoos

2. Acne Treatment (Comedolytic Action)

It penetrates oily skin and helps unclog pores.

Benefits

- Reduces blackheads and whiteheads
- Decreases excess oil
- Prevents formation of acne lesions

Found in

- Cleansers
- Gels
- Creams
- Toners and face washes

3. Anti-inflammatory Activity

Salicylic acid is chemically related to aspirin and shows mild anti-inflammatory effects**. Used in:**

- Topical pain-relief products
- Irritated skin formulations
- Some dermatological ointments

4. Antifungal and Antimicrobial Preparations

It creates an unfavorable environment for fungal growth and helps remove infected skin layers.

Applications

- Athlete's foot preparations
- Medicated soaps
- Antifungal creams and powders

5. Pharmaceutical Intermediate

Salicylic acid is an important raw material in drug synthesis.

Most notable example

- Manufacture of Aspirin

Reaction

- Acetylation of salicylic acid produces aspirin.

6. Preservative and Stabilizing Functions

Historically, salicylic acid was used as a preservative because of antimicrobial properties, though modern preservatives are now preferred.

- Stability of topical formulations
- Prevention of microbial contamination in some preparations

7. Cosmetic and Dermatological Formulations Used in

- Chemical peels
- Exfoliating creams
- Anti-aging products
- Skin renewal therapies

Because it is oil-soluble, it penetrates sebaceous glands effectively.

Common Dosage Forms
Salicylic acid is formulated as

- Ointments
- Creams
- Gels
- Lotions
- Medicated shampoos
- Collodion paints
- Transdermal/topical patches

Precautions
Excessive use can cause

- Skin irritation
- Dryness and peeling
- Salicylate toxicity (rare, with large-area application)

Avoid high concentrations in

- Infants
- Broken skin
- Patients allergic to salicylates
- Here is a revised and polished version of your text with improved grammar, clarity, and scientific style suitable for academic or professional use.

SAR of Salicylic Acid and Its Derivatives
Basic Structure of Salicylic Acid

- Core structure: Benzoic acid with ortho-OH group
- Chemical formula: $C_7H_6O_3$

Structure-Activity Relationship (SAR)

1. Position of Hydroxyl Group

- Ortho-OH (salicylic acid): Most active - forms intramolecular H-bond, enhances activity
- Meta-OH: Less active
- Para-OH (p-hydroxybenzoic acid): Weak/inactive as anti-inflammatory

2. Carboxyl Group (-COOH)

- Essential for anti-inflammatory activity
- Responsible for acidic properties
- Important for COX enzyme inhibition
- Removal = loss of activity

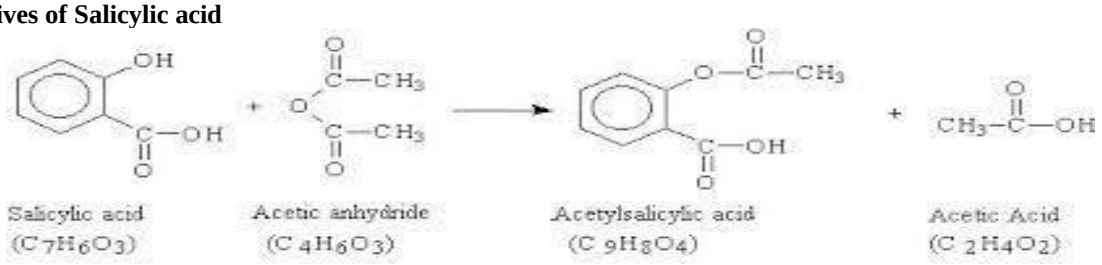
3. Esterification of -COOH

- Methyl salicylate: Prodrug, converted to salicylic acid in vivo
- Used topically (counterirritant, rubefacient)

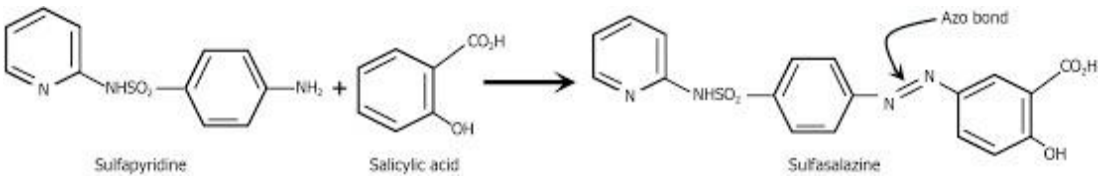
4. Acetylation of -OH Group Aspirin (Acetylsalicylic acid)

- Acetyl group at ortho position
- Increased anti-inflammatory activity
- Improved antipyretic and analgesic effects
- Antiplatelet activity (irreversible COX-1 inhibition)
- More GI irritation (but better tolerated than salicylic acid).

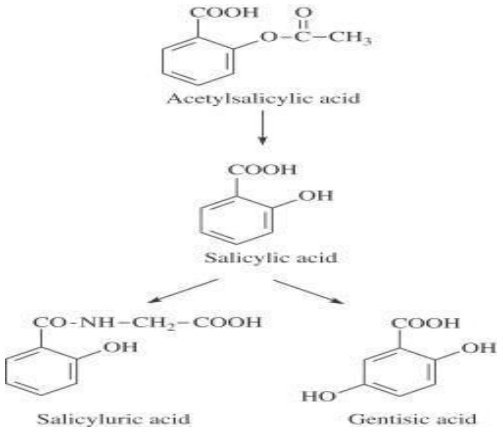
Derivatives of Salicylic acid



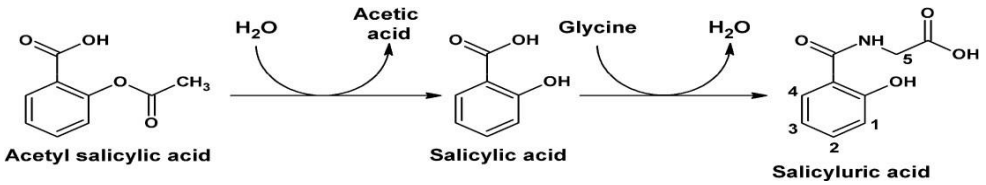
1. Synthesis of Aspirin from Salicylic acid.



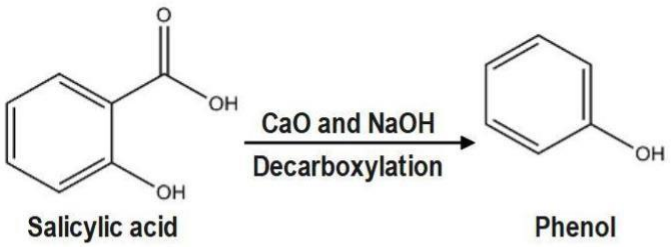
2. Synthesis of Sulfasalazine from Salicylic acid.



3. Synthesis of Gentisic from salicylic acid.



4. Synthesis of Salicyluric acid from salicylic acid.



5. Synthesis of Phenol from Salicylic acid.

Indications and Contraindications for Salicylic Acid Treatment

Indications for Salicylic Acid Exfoliation

Salicylic acid peels are commonly recommended for the treatment of:

- Acne vulgaris, including comedonal and papulopustular acne, even during active flare-ups
- Rosacea
- Superficial wrinkles, pigmented and atrophic scars, stretch marks, and signs of premature skin ageing
- Rough, inflexible skin with reduced firmness
- Hyperpigmentation disorders such as melasma, lentigines, freckles, sun-induced pigmentation, and post-inflammatory hyperpigmentation
- Enlarged pores, keratosis, and seborrhoea
- Various skin types, including oily, combination, impure, mature, and seborrhoeic skin
- Psoriasis

Relative Contraindications

Salicylic acid exfoliation should be used with caution in individuals with

- Current use of medications such as anti-inflammatory drugs, antibiotics, diuretics, cardiovascular medications, steroids, or hormonal contraceptives
- Herbal supplementation, particularly chamomile or St. John's wort
- Skin disorders such as atopic dermatitis or rosacea
- Chronic sinusitis
- Frostbite or cold-related skin damage
- Excessive tanning or tanning addiction (tannorexia)
- Skin or sebaceous gland atrophy
- Use of alcohol, smoking, or recreational drugs
- Continuous or excessive sun exposure
- Recent cosmetic or dermatological procedures that may interfere with chemical peeling
- Treatment during spring or summer, especially when high concentrations are used, due to increased risk of sunburn and hyperpigmentation

Absolute Contraindications

Salicylic acid exfoliation must not be performed in cases of:

- Active viral, bacterial, or fungal infections
- Active herpes simplex infection
- Pregnancy or breastfeeding
- Known allergy or hypersensitivity to salicylic acid or salicylates
- Severe skin irritation, redness, or open wounds such

as cuts and abrasions
- History or tendency toward keloid or excessive scar formation
- Current oral isotretinoin therapy or within six months after treatment completion
- Use of antidepressants or photosensitising medications
- HIV infection
- Ongoing chemotherapy, liver disease, or kidney disorders
- Phototherapy treatment
- Severe emotional or psychiatric disorders, including depression
- Conditions associated with impaired wound healing, such as diabetes mellitus or autoimmune diseases.

ANALYTICAL MEHODS OF SALICYLIC ACID

STUDY	COLUMN	FLOW RATE	MOBILE PHASE	WAVELENGTH
Direct Spectrophotometric Determination of Salicylic Acid, Acetylsalicylic Acid, Salicylamide, Caffeine, and Phenacetin in Tablets or Powders	-	-	Acetonitrile: Water	**296nm** 226m,
Simultaneous determination of salicylic acid and acetylsalicylic acid by First derivative UV Spectrophotometry in pharmaceutical preparation	-	-	1 % Citric acid	**286nm** 318nm
Simultaneous determination of salicylic acid and acetylsalicylic acid in Aspirin tablet by second derivative UV Spectrophotometry	Nucleosil C18, (Alltech, 5 mm, 250×4.6 mm).	1.5 ml/min	Acetonitrile: Formic acid	328nm **292nm**
Simultaneous RP-HPLC determination of salicylamide, salicylic acid and deferasirox in bulk dosage form	C18(250cm *4.6mm I.D.,5m)	1.0ml/min	Acetonitrile: Potassium dihydrogen phosphate 40:60	245nm
Simultaneous analysis of dehydroacetic acid, benzoic acid, sorbic acid and salicylic acid in cosmetic products by solid phase extraction and HPLC	TSK gel ODS-8Otm colume (5µm, 150*4. 6mm I.D)	1.0ml/min	Methanol: Water (65:35)	235nm
RP-HPLC Development and validation for the combination of Imiquimod and salicylic acid	C18(250cm *4.6mm I.D.,5m)	1.0ml/min	Acetonitrile: Potassium dihydrogen phosphate 45:55	234 nm and **226nm**
Simultaineous determination of salicylic acid and their related compounds in diprosalic lotion	150nm*4.6mm I.D.YMC J'sphere ODS-H8o column	-	Methanesulfonic acid: Acetonitrile	240nm
Stability indicating analytical method development and validation of salicylic acid and tolnaftate inpharmaceutical ointment by HPLC	Merck C-18 column	1.5ml/min	Acetonitrile: Methanol: water 50: 20: 30	245nm

RESULT AND DISCUSSION

Salicylic acid (SA) is a versatile compound widely used in cosmetic and pharmaceutical products due to its keratolytic, anti-inflammatory, and antimicrobial properties. It is highly effective in treating acne, improving skin texture, and managing conditions such as warts, psoriasis, and dandruff. SA is also an important ingredient in various topical formulations and is commonly analyzed using RP-HPLC methods. Although generally safe and effective, improper use may cause skin irritation and other side effects. Overall, salicylic acid remains an important therapeutic and cosmetic agent with significant potential for future formulation advancements.

CONCLUSION

Salicylic acid is a widely used dermatological agent with keratolytic, comedolytic, anti-inflammatory, and antimicrobial properties. It is effective in treating acne, hyperpigmentation, photoaging, seborrhoea, and psoriasis, particularly in oily and acne-prone skin due to its ability to penetrate sebaceous follicles. It is also commonly used in chemical peels and skincare products because of its proven efficacy and safety. However, proper patient selection, treatment protocols, and sun protection are essential for optimal results. Contraindications such as pregnancy, active infections, hypersensitivity, isotretinoin use, and poor wound healing must be considered. Ongoing research aims to improve

formulations and delivery systems to enhance its effectiveness and safety.

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