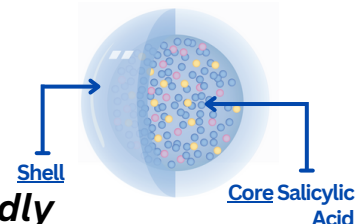


SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly



Why do you need this technology?

SalSphere® Even Skin is a unique technology that enables the easy use of salicylic acid in most topical formulations. It presents a formulation-friendly solution to the poor water solubility of salicylic acid, encapsulated for maximum efficacy. Regular use of salicylic acid treatments maintain clear skin and evens natural skin tone, leading to brighter, rejuvenated, and more youthful skin.

Unique natural delivery technology

SalSphere® Even Skin is an advanced encapsulated form, allowing easy use of salicylic acid. The timed release of salicylic acid derives from adhesion of the polymer shell to the lipid domains on the skin, allowing the lipophilic core to deliver its therapeutic benefit efficiently and efficaciously. The modulated release of salicylic acid reduces irritation commonly experienced with use of acids on the skin.



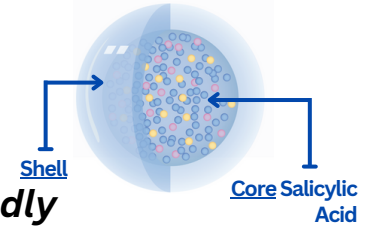
Cosmetic and dermo-cosmetics have used beta-hydroxy acids (BHAs) such as salicylic acid to repair skin issues for ages. Salicylic acid, like most acid treatments, break down the connections between skin cells, dissolving skin debris that clogs pores. It helps lift the intracellular "glue" that holds skin cells together and expedites treatment of red, inflamed pimples. Once the pimple is exfoliated, oxygen penetrates the pores or hair follicles, eliminating the growth of the anaerobic *Propionibacterium*, the cause of acne vulgaris.

In dermatology and cosmetics, BHAs such as salicylic acid are best for the treatment of dermatitis, acne, psoriasis, calluses, dandruff, and more. Regular use at cosmetic levels lead to skin toning, brightening, scar and pore reduction, excess sebum reduction, blemish removal, and skin smoothing for younger and brighter appearing skin.

SalSphere® Even Skin (Fig 1) is available at 30% salicylic acid.



Fig 1: SalSphere® Even Skin is a transparent liquid that can be easily mixed with various surfactants and thickeners to form clear washes, serums and lotions.



SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Skin Testing

Method 1: The effect of SalSphere® Even Skin version 04 on the pH of the skin was measured with a Hanna Skin pH meter on the forearm of the volunteers (Fig 2). Volunteers used both arms to assess the pH. One arm was washed with a commercial wash, with free SA at 2%, and the other arm was washed with the same final concentration of SA using SalSphere® Even Skin version 04.

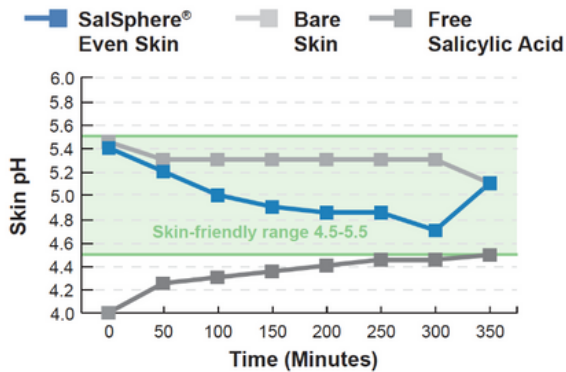


Fig 2: Washing with free SA dropped the pH to 4 and gradually increased to 4.6 over 6 hours. The skin treated with SalSphere® Even Skin version 04 showed a pH of 5.4 upon application; gradually, the pH dropped to 4.6 over 5 hours and was rebalanced. SalSphere® Even Skin is a more skin-friendly solution. The gradual release (time-release) of SA drops the pH but is still at the friendly range.

Method 2: Exfoliation was assessed by coloring the skin and using a Cutaneous Colorimeter before and after the wash with 6.67% SalSphere® Even Skin version 04 (Fig 3).

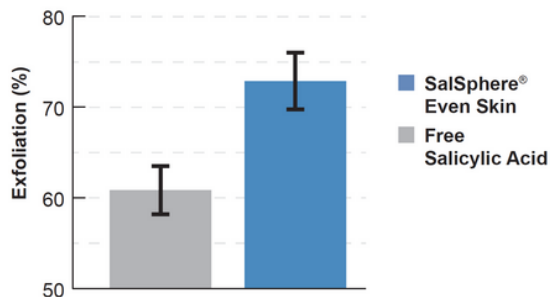


Fig 3: SalSphere® Even Skin Version 04 provides a significant 20% increase in exfoliation compared with free salicylic acid (n=21).

Method 3*: In the following study, panelists used a facial wash containing 2.0% Salicylic Acid (6.67% SalSphere® Even Skin version 04) daily for 7 days.

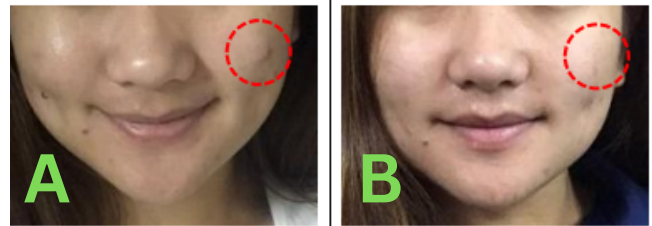


Fig 4: Volunteer 1: Before (A) and after (B) 7 days of treatment to reduce acne.



Fig 5: Volunteer 2: Before (A) and after (B) 7 days of treatment to reduce acne.



Fig 6: Volunteer 3: Before (A) and after (B) 7 days of treatment to reduce acne.

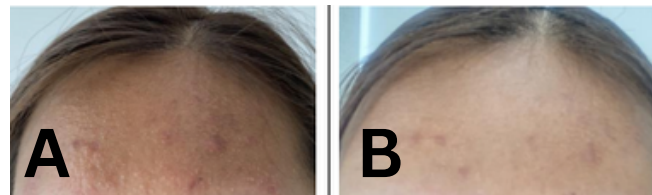
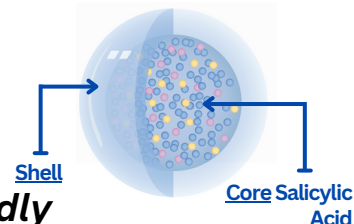


Fig 7: Volunteer 4: Before (A) and after (B) 7 days of treatment to reduce acne.

SalSphere® Even Skin is very effective in fighting acne and smoothing the skin.

*data is courtesy of AlphaTech Science, Thailand
Formula listed on SalSphere® Even Skin Formulation Tips Document



SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Technical Data Sheet

Property	Specification
Appearance	Translucent to hazy liquid
Form @RT	Liquid
Color	Light to dark amber
pH (neat)	3.0 - 5.0
SA Assay %wt (HPLC) (Ver -04)	27.0 - 33.0

SA Dosage Limits

Application	% SA Limit	%Wt Even Skin -04
Cosmetic	< 0.50	Up to 1.67
OTC anti-acne	0.5 - 2.0	1.67 - 6.67
Rx anti-acne	2.0 - 6.0	6.67 - 20
Anti-dandruff	1.8 - 3.0	6.0 - 9.0

INCI - Version 04, 30% SA

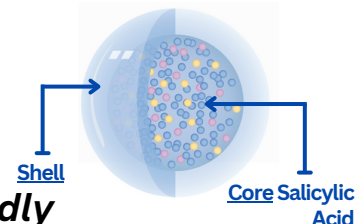
Salicylic Acid, PEG-8, Isosteamamidopropyl Ethyldimonium Ethosulfate, Sodium Hydroxide, Propylene Glycol, *Olea Europaea* (Olive) Fruit Oil, *Carthamus Tinctorius* (Safflower) Seed Oil

Dermatological applications of SA

%wt SA	Uses	Reference
0.5 - 10	Anti-Acne	Hjorth N. Traditional topical treatment of acne. Acta Derm Venereol Suppl (Stockh). 1980;Suppl 89:53-6. PMID: 6451127.
3.0 - 6.0	Hyperkeratotic skin disorders (psoriasis, ichthyosis, keratosis pilaris)	Bikowski J. Hyperkeratosis of the heels: treatment with salicylic acid in a novel delivery system. Skinmed. 2004 Nov-Dec;3(6):350-1. doi: 10.1111/j.1540-9740.2004.04056.x. PMID: 15538090.
5.0 - 40.0	Warts, corns	Bowe WP, Shalita AR. Effective over-the-counter acne treatments. Semin Cutan Med Surg. 2008 Sep;27(3):170-6. doi: 10.1016/j.sder.2008.07.004. PMID: 18786494.
20.0 - 30.0	Superficial chemical peel (facial)	Arif T. Salicylic acid as a peeling agent: a comprehensive review. Clin Cosmet Investig Dermatol. 2015 Aug 26;8:455-61. doi: 10.2147/CCID.S84765. PMID: 26347269; PMCID: PMC4554394.
50.0	Actinic damage and pigmented lesions	Swinehart JM. Salicylic acid ointment peeling of the hands and forearms. Effective nonsurgical removal of pigmented lesions and actinic damage. J Dermatol Surg Oncol. 1992 Jun;18(6):495-8. doi: 10.1111/j.1524-4725.1992.tb03311.x. PMID: 1534332.

Regulatory compliance:





SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Formulation Tips

The viscosity of SalSphere® Even Skin depends on its concentration and on type of the thickener used in the formula (Fig 1). For formulas using carbomers as thickeners, SalSphere® Even Skin must be added before the neutralization of the carbomer.

For other thickeners, SalSphere® Even Skin can be added at any stage of the formulation process at a temperature below 40°C.

The recommended pH of the final formula has to be a minimum of 4.5.

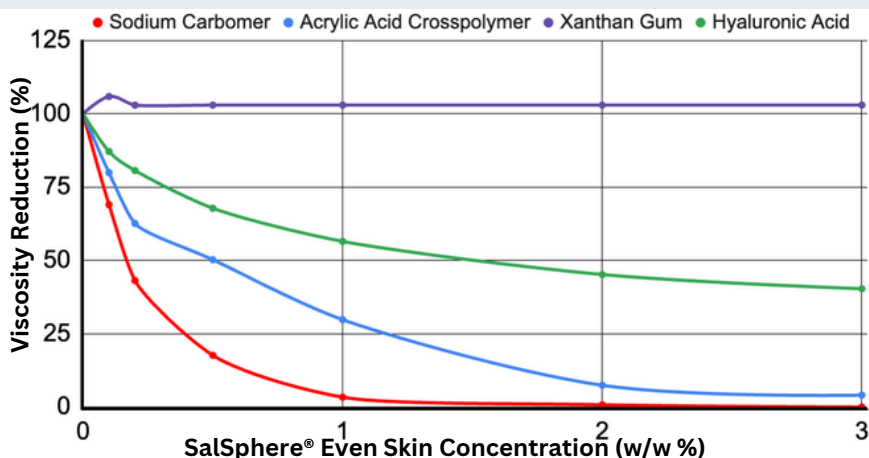


Fig 1: The effect of SalSphere® Even Skin dosage on viscosity using 4 different thickeners. Sodium Carbomer is the most sensitive to viscosity breakdown, and the least sensitive is Xanthan Gum

Anti-Acne Formula (Used in clinical study)		
	INCI	%WT
A	Water	72.68
A	Acrylates/C10-30 Alkyl Acrylate Crosspolymer	1.20
A	Disodium EDTA	0.10
B	Water	10.00
B	Diglycerin	3.00
B	SalSphere Even Skin 8894-04	6.67
B	Polysorbate 80	0.50
B	1, 2-Hexanediol	3.00
C	Triethanolamine	2.85
	Total	100.00

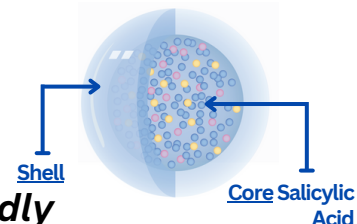
Procedure

1. Add phase A to an appropriate container and mix at 300-500 rpm
2. Add B to A and mix thoroughly
3. Next, add C and adjust the pH.

Refreshing Face Wash (PID: 11005)		
	INCI	%WT
A	Xanthan Gum	0.70
A	Glycerin	5.00
B	Water	Q.S.
B	Aloe Barbadensis Leaf Juice	5.00
B	Hamamelis Virginiana (Witch Hazel) Extract	5.00
C	Cocamidopropyl Betaine	15.00
D	Preservative	Q.S.
D	SalSphere Even Skin 8894-04	5.00
D	HydroSal SalCool 8278-04	1.00
D	Propanediol (and) Aqua (and) Calendula Officinalis Flower Extract	1.50
D	Citrus Grandis (Grapefruit) Peel Oil	0.25
	Total	100.00

Procedure

1. Mix Phase A together and disperse the mixture into phase B.
2. Mix until homogenous.
3. Slowly add phase C, make sure pH is below 5.3.
4. Add phase D and mix until uniform, homogenize using an Ulta Turrax Homoginizer.



SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Formulation Tips

Foaming Face Mask

INCI		%WT
A1	<i>Isostearyl Isostearate</i>	0.40
A2	<i>Glyceryl Stearate</i>	0.60
A3	<i>Hydroxystearic Acid</i>	0.20
A4	<i>Cetearyl Alcohol (and) Cetearyl Glucoside</i>	0.80
A5	<i>Cetearyl Alcohol</i>	0.60
A6	<i>Squalane</i>	0.40
A7	<i>Stearic Acid</i>	0.30
B	<i>Water</i>	18.00
C1	<i>Water</i>	Q.S.
C2	<i>Zea Mays (Corn) Starch</i>	2.00
C3	<i>Propanediol</i>	2.50
C4	<i>Xanthan Gum</i>	0.75
C5	<i>Cocamidopropyl Betaine</i>	5.00
C6	<i>Disodium Cocoyl Glutamate</i>	5.00
C7	<i>Preservative</i>	Q.S.
C8	SalSphere Even Skin 8894-04	1.67
Total		100.00

Procedure

1. Heat phase A to 75C under mixing in Vessel
2. Heat phase B to 75C in a separate vessel
3. Slowly add phase B to phase A at a rate of 20% per minute.
4. Begin cooling the batch to 60C.
5. Premix Keltrol and Propanediol.
6. Charge phase C in vessel #3, and heat to 45C under mixing.
7. Slowly add phase C to vessel #1 at a rate of 20% per minute with propeller mixing. Begin cooling batch.
8. Once batch is below 35C, add phase D with propeller mixing.
9. Use an ice bath to cool batch. Once below 20C, add phase E with slow sweep stirring until uniform.
10. Adjust pH with 20% Lactic Acid or 20% L-Arginine Solution.

Face Cleanser

INCI		%WT
A	<i>Water</i>	36.49
A	<i>Preservative</i>	Q.S.
A	<i>Sodium Lauroyl Sarcosinate</i>	29.41
A	<i>Coco Betaine</i>	14.72
A	<i>Cocamidopropyl Betaine</i>	9.80
B	SalSphere Even Skin 8894-04	1.47
C	<i>20% Lactic Acid Soln</i>	7.61
Total		100.00

Procedure

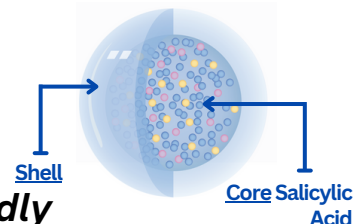
1. Add phase A to an appropriate container and mix at 300-500 rpm
2. Add B to A and mix thoroughly
3. Next, add C and adjust the pH to 5.25

Anti-Acne Gel

INCI		%WT
A	<i>Water</i>	87.25
B	<i>Glycerin</i>	5.00
B	<i>Carbomer 940</i>	0.50
B	<i>Hyaluronic Acid</i>	0.25
C	SalSphere Even Skin 8894-04	3
D	<i>Other ingredients (moisturizers, humectants, extracts, etc.)</i>	3.00
D	<i>Preservative</i>	Q.S.
Total		100.00

Procedure

1. Mix phase A to an appropriate container and at 300-500 rpm
2. Premix B and add to A. Mix thoroughly to hydrate the carbomer (15-30 minutes)
3. Next, add C and adjust the pH to 6-7
4. Add phase D and mix well if desired



SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Formulation Tips

Anti-Acne Clear Toner (PID: 11002)		
INCI		%WT
A	Water	Q.S.
A	Disodium EDTA	0.10
B	Glycerin	0.30
B	Butylene Glycol	2.00
B	Fragrance	Q.S.
B	Caprylyl/Capryl Glucoside & Water & Sodium Cocoyl Glutamate & GlycerylCaprylate & Citric Acid & Polyglyceryl-6 Oleate & Sodium Surfactin	3.00
B	Preservative	Q.S.
C	Hamamelis Virginiana (Witch Hazel) Extract	3.50
C	Trehalose	0.10
C	Sodium Hyaluronate (and) Water	0.10
D	SalSphere Even Skin 8894-04	6.67
Total		100.00

Procedure

1. Combine phase A under mixing until dissolved
2. Mix phase B in a separate vessel.
3. Combine phase A and phase B under mixing.
4. Add phase C under mixing in order until homogenous.
5. Add phase D and Adjust pH to 5.5 with lactic acid or 20%NaOH.

Anti-Blemish Face Wash (PID: 11004)		
INCI		%WT
A1	Water	Q.S.
A2	Hydroxypropyl guar hydroxypropyltrimonium chloride	0.10
A2	Glycerin	1.00
A3	Oryza Sativa (Rice) Extract	1.00
A4	Sodium Lauryl Sulfosuccinate (and) Sodium Laureth Sulfosuccinate	18.00
A5	Sodium(C14-C16) Olefin Sulfonate	5.00
A6	Cocamidopropyl Betaine	5.00
A7	Disodium EDTA	0.10
A8	Citrus Grandis (Grapefruit) Peel Oil	0.05
A9	Tartaric Acid	0.05
A10	SalSphere Even Skin 8894-04	5.00
A11	Preservative	Q.S.
A12	Fragrance	Q.S.
Total		100.00

Procedure

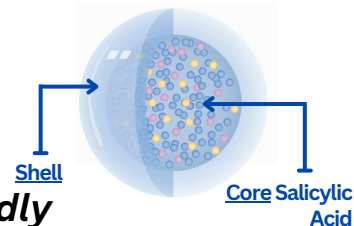
1. Combine PHASE A in order listed in main kettle while mixing with medium prop mixing @500rpm.
2. Mix for 5 minutes @RT in between each addition. Mix an additional 15 minutes @RT.
3. Check pH and adjust if necessary with 20% Lactic Acid or 20% Arginine.
4. Adjust viscosity with Sodium Chloride.

Regulatory compliance:



SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly



Claim Support

Main benefit of the technology

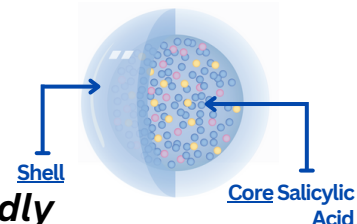
A delivery system for a blend of salicylic acid and enzymes* to provide the benefit of improving and rejuvenating skin conditions in a less irritating and time-released formulation.

Additional claims and unique features

- Helps to unblock and clean pores to combat acne
- Reduces sebum production of the skin to combat acne
- Exfoliates the skin with no to minimal irritation
- Helps to improve skin tone and smoothness
- Minimal to no irritation or skin barrier damage
- Time-released and long lasting
- Easy to formulate

References

1. Tsai, Thomas & BS, & Hantash, Basil. (2008). Cosmeceutical Agents: A Comprehensive Review of the Literature. Clinical Medicine Insights : Dermatology.
2. Arif, T. (2015). Salicylic acid as a peeling agent: a comprehensive review. Clinical, Cosmetic and Investigational Dermatology, 455. doi:10.2147/ccid.s84765
3. Saint-Léger, D., Lévêque, J.-L., & Verschoore, M. (2007). The use of hydroxy acids on the skin: characteristics of C8-lipo-hydroxy acid. Journal of Cosmetic Dermatology, 6(1), 59–65. doi:10.1111/j.1473-2165.2007.00296.x
4. Bissett, D. L. (2009). Common cosmeceuticals. Clinics in Dermatology, 27(5), 435–445. doi:10.1016/j.clindermatol.2009.05.006
5. Chen, Y.-Y., Lu, Y.-H., Ma, C.-H., Tao, W.-W., Zhu, J.-J., & Zhang, X. (2017). A novel elastic liposome for skin delivery of papain and its application on hypertrophic scar. Biomedicine & Pharmacotherapy, 87, 82–91. doi:10.1016/j.biopha.2016.12.076
6. Lourenço, C. B., Ataíde, J. A., Cefali, L. C., Novaes, L. C. d. L., Moriel, P., Silveira, E., ... Mazzola, P. G. (2016). Evaluation of the enzymatic activity and stability of commercial bromelain incorporated in topical formulations. International Journal of Cosmetic Science, 38(5), 535–540. doi:10.1111/ics.12308
7. Ramli, A. N. M., Aznan, T. N. T., & Illias, R. M. (2016). Bromelain: from production to commercialisation. Journal of the Science of Food and Agriculture, 97(5), 1386–1395. doi:10.1002/jsfa.8122

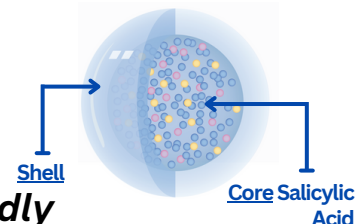


SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Claim Support

Claims	Literature Substantiation
Helps to unblock and clean pores to combat acne	“SA is most commonly employed in the treatment of acne, where its lipophilicity allows penetration into the pore and subsequent exfoliation of dead skin; excess oil build up is also diminished. Numerous studies have shown that SA decreases follicular plugging and progression to inflammatory acne lesions.” [1]
Reduces sebum production of the skin to combat acne	“[Salicylic acid] also decreases secretion of sebum in patients with acne, which adds to its therapeutic effect in these patients. Marczyk et al studied the effect of 50% pyruvic acid and 30% SA peels on skin lipid film in patients with acne vulgaris, and concluded that SA had a greater sebometric effect than pyruvic acid.” [2]
Exfoliates the skin with no to minimal irritation	<p>“It has been found that SA, being an organic acid, extracts desmosomal proteins including desmogleins. As a result of this action, the cohesion of epidermal cells is lost, leading to exfoliation...Imayama et al studied histological changes in the skin... [and] concluded that peeling with SA can lead to alterations in the underlying dermal tissue without directly wounding the skin.” [2]</p> <p>“...creams containing 2% SA or C8-LHA were found to enhance the shedding of corneocytes and reduce the thickness of the stratum corneum. Ultrastructural studies of the skin show that hydroxy acids target in particular the central desmosomes in the stratum disjunctum, resulting in a reduced coherence between the layers of corneocytes but leaving the corneocytes in sheets. The penetration of SA and the AHAs is relatively rapid and consequently the breakdown of central corneosomes occurs throughout the stratum corneum.” [3]</p>
Helps to improve skin tone and smoothness	<p>“Taking salicylic acid as an example, human testing on forearm skin (dansyl chloride method) reveals increased stratum corneum turnover with topical 1.5% salicylic acid of 18.5 days vs 21.5 days for the vehicle control. More rapid turnover leads to improvement in facial skin smoothness and color as assessed by test volunteers themselves and by image analysis and expert grader assessment.” [4]</p> <p>“SA also has been shown to protect against ultraviolet (UV) B radiation and photoaging, as well as improve the appearance of photo-induced skin dyspigmentation. In a study of 268 patients, weekly facial peels of SA 30% used for 8 weeks improved the appearance of melasma, post-acne scars, post-inflammatory hyperpigmentation (PIH), fine lines and wrinkles.” [1]</p> <p>“The capacity of the hydroxy acids to stimulate the division and maturation of keratinocytes has been suggested for a number of years...It now seems more certain that the effect of low concentrations of hydroxy acids does not evoke an inflammatory response and indeed SA may even be anti-inflammatory. In animal models, topically applied GA and SA have been found to increase epidermal cell division and in some experiments, a wave of cell proliferation has been observed 12–16 h after topical application.” [3]</p>

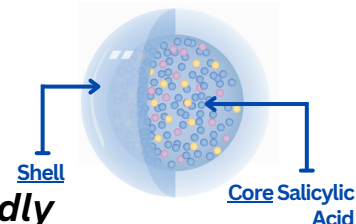


SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Claim Support

Claims	Literature Substantiation
<p>Minimal to no irritation or skin barrier damage</p>	<p>“Taking salicylic acid as an example, human testing on forearm skin (dansyl chloride method) reveals increased stratum corneum turnover with topical 1.5% salicylic acid of 18.5 days vs 21.5 days for the vehicle control...No significant redness or TEWL changes were associated with the salicylic acid treatment.” [4]</p> <p>“[Salicylic acid] is lipophilic and easily enters the epidermis and membrane of adnexal structures such as sebaceous glands via hair follicle pores...The lipophilic nature of SA helps limit its clinical effect to the superficial epidermis leading to fewer side effects in comparison to α-hydroxy acids, which penetrate deeper into the dermis.” [1]</p>
<p>Proteolytic enzymes to assist in reduction of blemishes and rejuvenating skin</p>	<p>“Papain, a cysteine protease isolated from the latex of <i>Carica papaya</i> fruit, has been widely used in the medical field for centuries. This proteolytic enzyme has biological activity of antiinflammatory, anti-bacterial, anti-oxidant, and degradation of protein and collagen. It has been used in dermatology for wound treatment to remove injured tissues and stimulate the cicatrisation process, and recently it was applied for scar treatment.” [5]</p> <p>“In cosmetics, bromelain is used as an active ingredient in skincare products, owing to its exfoliating properties that decreases the thickness of the stratum corneum, it is effective in...reducing the intensity of skin blemishes and promoting skin renewal.” [6]</p> <p>“Resulting in gentle peeling of the skin, bromelain is used as an active ingredient in cosmetic products. Bromelain can be used to treat skin complications such as wrinkles, acne and dry skin. Bromelain works by gently digesting the protein layer of dead cells, allowing the dead cells to be replaced with younger skin cells.” [7]</p>
<p>Time-released and long lasting</p>	<p>In vitro tests on porcine skin show that SalSphere® Even Skin maintains salicylic acid on skin for a longer duration than unencapsulated salicylic acid</p>



SalSphere® Even Skin

Skin rejuvenation with BHA: easy to use and skin friendly

Claim Support

Application, claim	Reference
Chemical peeling is a safe, efficacious, and cost-effective procedure for treating various skin disorders and for enhancing cosmetic appearance.	Salicylic acid as a peeling agent: a comprehensive review Tasleem Arif, Clinical, Cosmetic, and Investigational Dermatology Volume 8, 2015
Peeling with SA can lead to alterations in the underlying dermal tissue without directly wounding the skin	ImayamaSUedaSIsodaMHistologic changes in the skin of hairless mice following peeling with salicylic acidArch Dermatol20001361390139511074703 [Crossref], [Web of Science ®], [Google Scholar]
SA also has anti-inflammatory properties. The concentration at which the anti-inflammatory action of SA is most pronounced is between 0.5% and 5% (w/w)	BurkeASmythEFitzgerald GarretAAAnalgesic antipyretic and anti-inflammatory agentsBruntonLLLazoJSParkerKGoodman and Gilman's The Pharmacological Basis of Therapeutics11th edNew York, NY, USAMcGraw-Hill2006 [Google Scholar]
Salicylates and their derivatives have been used in sunscreen formulations. The aromatic benzene ring in the salicylate converts ultraviolet radiation into longer wave radiation that is felt as heat, which explains the mechanism of action in sunscreen preparations.	AdamBHJulioCCDanaMKAndrewNLAagents used for treatment of hyperkeratosisWolvertonSEComprehensive Dermatologic Drug Therapy3rd edNew York, NY, USAElsevier Saunders2013 [Google Scholar]
SA also has antimicrobial and antifungal properties. Whitfield's ointment, which contains benzoic acid and SA, has been used for its antifungal properties.	AdamBHJulioCCDanaMKAndrewNLAagents used for treatment of hyperkeratosisWolvertonSEComprehensive Dermatologic Drug Therapy3rd edNew York, NY, USAElsevier Saunders2013 [Google Scholar]
50% SA ointment paste containing buffered methyl salicylate and croton oil for the treatment of actinically damaged skin, lentigines, and pigmented keratosis on the forearms and dorsal aspect of the hands, and reported excellent results.	SwinehartJMSalicylic acid ointment peeling of the hands and forearms. Effective nonsurgical removal of pigmented lesions and actinic damageJ Dermatol Surg Oncol1992184954981534332 [Crossref], [Google Scholar]
SA peels are a good therapeutic option for comedonal acne , and can be a good adjunctive modality for treating open and closed comedones, post-acne erythema, and hyperpigmentation .	MonheitGDChastianMAChemical and mechanical skin resurfacingBolognaJLJorizzoJLRapiniRPDermatologyPhiladelphia, PA, USAMosby2003 [Google Scholar]
The efficacy of SA in the treatment of photoaging and acne has been described in patients with Fitzpatrick skin types I-III as well as in skin types V and VI.	BourellyPELotsikas-BaggiliAJChemexfoliation and superficial skin resurfacingBurgessCMCosmetic Dermatology1st edHeidelberg, GermanySpringer-Verlag2005 [Crossref], [Google Scholar]
Improvement in surface roughness and pigmented lesions, along with a reduction in fine lines .	KligmanDKligmanAMSalicylic acid peels for the treatment of photoagingDermatol Surg1998243253289537006 [Crossref], [Web of Science ®], [Google Scholar]