

Formulation and Evaluation of a Skin Crack Repair and Peeling Gel Solution for the Treatment of Dry and Fissured Skin

Vibha Chandeliya¹, Nayana Borole²

¹Student of M.Sc. Beauty Cosmetology, School of Design, Sandip University, Nashik - 422213, India, vibhachandeliya@gmail.com ²Assistant Professor, Cosmetic Science and Cosmetology, School of Design, Sandip University, Nashik - 422213, India, kalenayana08@gmail.com

ABSTRACT

Dry and fissured skin can be defined as rough, dry, flaky, non-elastic skin with cracks that cause pain. They are usually observed on the legs, heels, hands, elbows, and knees due to uneven pressure, exposure to the weather, and improper skin care. Such a condition may frequently lead to the formation of open fissures, resulting in irritation and infection. There are a few moisturizing creams and ointments designed to eliminate this problem. However, not all of them are suitable for daily use since they may lack certain beneficial ingredients. Therefore, this study aims to prepare a skin crack-repairing and peeling gel solution that will address this issue efficiently by combining the properties of hydrating, peeling, and barrier-protective dosage forms.

The composition that will be prepared for the experiment will contain all the necessary ingredients for repairing and softening dry, cracked skin. A sufficient amount of humectants will be introduced to the solution to help retain moisture in the skin. Emollients and skin conditioning agents are also essential due to their ability to moisturize, smooth, and make the skin less rough and flaky. Moreover, the gel-like substance should include mild keratolytic and peeling agents to remove the top layer of dead and damaged skin. Lastly, some film-forming and soothing agents can be added to the solution to improve its texture and therapeutic features. The final product will have a convenient form that allows it to spread easily and uniformly on the surface of the skin, penetrate it deeply, and not leave noticeable traces after rubbing.

The physical and chemical properties of the prepared medication will be analyzed to observe its organoleptic properties, pH, homogeneity, viscosity, spreadability, washability, stability, skin compatibility, and moisturizing ability. The experiment will also determine the effect of the gel-like composition on the cracks, roughness, and dryness of the skin. In addition, the stability of the final product will also be observed to estimate its possible application in cosmetics. The gathered results will help conclude the ability of the created composition to heal, moisturize, and protect the skin from external irritants.

In general, this research aims to find an effective, safe, and convenient method to repair and maintain the skin with cracks. The expected outcome of this study is to elaborate on a composition that will combine the beneficial effects of several therapeutic skin treatments. The obtained solution would be helpful for persons who suffer from fissured and dry skin areas that leave marks on the epidermis after regular treatment. This experiment is also expected to show how such a composition may become a viable alternative to traditional heavy creams and ointments that can be overly greasy and difficult to remove from the skin. Ultimately, this study will demonstrate how a gel solution can help treat and prevent fissured skin while providing a better cosmetic finish than a standard moisturizing cream.

Keywords: Fissured skin, crack-repairing gel, keratolytic agents, humectants, skin barrier, topical formulation, spreadability.

INTRODUCTION

Skin is the largest and most complex organ of the human body that forms the body's outer surface. It plays a protective role against the external environment, prevents dehydration, regulates temperature, and provides sensation. The skin's appearance depends on the amount of water in it, the state of the lipid layer, the renewal of the cells that make up the epidermis, the action of the environment, and the protection provided by the skin.

The surface of the skin is designed to retain water in the body while allowing for free removal. The natural moisturizing factors, intercellular lipid layers, sebum, and the special structure of corneocytes are responsible for the balance of water and protection from the outside. A disturbance of this balance leads to dryness, roughness, flakiness, and reduced elasticity of the skin. As a consequence of dryness and the natural process of keratinization, the skin loses its elasticity and sheds in flakes. With the increased load on the skin, cracks also appear, which penetrate into the skin's depth.

Most often, dryness and cracks occur on the legs and feet, less often on the arms and hands. Such changes in the skin can be caused by dry air, cold weather, excessive water, soap, hardening, lack of massage, friction, and a decrease in the amount of moisture due to the shedding of the top layer of the epidermis. The thickened and rough skin of the heel is subject to cracks due to the constant load on the feet. In addition, the decreased elasticity of the skin contributes to the formation of fissures that are difficult to heal.

The available moisturizing creams, pastes, and salves cannot solve the problem of fissures. To achieve good results, a product is needed that would remove the dry and rough layer of the skin, moisturize, soften, protect, and renew the upper layers of the epidermis, restoring the integrity of the skin. The main idea of the work is to develop a multifunctional skin crack-repairing and peeling gel-solution that would restore the skin's protective barrier and eliminate the roughness caused by the accumulation of dead cells.

The research work "Formulation and Evaluation of a Skin Crack Repair and Peeling Gel-Solution for the Treatment of Dry and Fissured Skin" is devoted to the creation of a cosmetic product that would effectively solve the problem of dryness and fissures. The goal of this work is to develop a cosmetically acceptable composition that would repair the skin and remove the rough and dead layer of the epidermis.

FORMULATION TABLE

Table 1: Formulation table

Sr.No.	Ingredients	100g	20g	Properties of Ingredients
1	Water	Qs to 100g	Qs to 20g	Vehicle, Base
2	Urea	25g	5g	Keratolytic agent
3	Polyvinyl Alcohol	10g	2g	Peel off
4	Polyvinyl Pyrrolidone	6g	1.2g	Film former
5	Propylene Glycol	8g	1.6g	Humectant
6	Glycerine	6g	1.2g	Humectant
7	Salicylic Acid	1g	0.2g	Exfoliant
8	2-Phenoxyethanol	0.5g	0.1g	Preservative
9	Disodium EDTA	0.1g	0.02g	Chelating agent
10	Carbomer	0.3g	0.06g	Viscosity modifier
11	Triethanolamine	Qs to adjust pH	Qs to adjust pH	Neutralizer

METHOD OF PREPARATION

1. Cleaning and weighing. All glassware is cleaned and rinsed with purified water. Each ingredient is weighed on the analytical balance using glazed paper. The carbomer is weighed quickly as it is very fine. The balance is tared before each addition.
2. Preparation of Phase A (PVA solution). The PVA is sprinkled gradually into the first portion of water while under magnetic stirring to prevent lumping. The beaker is placed directly on the hot plate and heated under continuous stirring with a thermometer immersed in the solution until the solution becomes clear. The temperature remains moderate throughout the heating with continuous stirring, as direct contact with the hot plate will cause intense local heating over the beaker base, leading to scorching and discoloration of the polymer at the contact point with glass, especially if the mixture is left stagnant. On reaching clarity, the solution is taken off the heat and cooled down to room temperature.

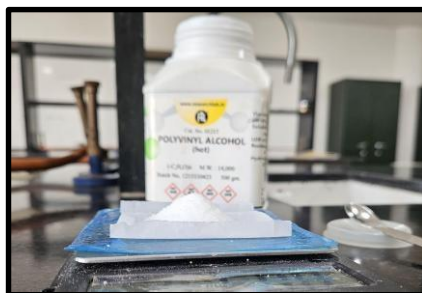


Fig. 1: Preparation of Phase A

3. Preparation of Phase B (carbomer dispersion). In the second beaker, the carbomer is sprinkled into the second portion of water under low to moderate continuous stirring. It is added in small portions rather than all at once (since rapid addition leads to lumping that is difficult to break up later). The beaker is capped and left alone to completely hydrate with no lumping present. During this stage, the polymer coils absorb the aqueous phase and swell, but full thickening will occur later at the stage of neutralization.



Fig. 2: Preparation of Phase B

4. Phase C: Preparation of aqueous auxiliary solution. In a third beaker, the PVP is dissolved in a small portion of purified water with gentle stirring. The solution is then charged with the urea, glycerine, and disodium EDTA in succession, with thorough stirring after each addition, until the solution is clear with no visible undissolved material.



Fig. 3: Preparation of Phase C

5. Phase D: Preparation of active ingredient solution. The salicylic acid is ground to a fine powder using a mortar and pestle. The powder is transferred to a beaker and dissolved in the propylene glycol, gently stirring and warming on the hot plate as needed. The solution is continuously stirred until no crystals are visible, and it has been cooled as needed for use.



Fig. 4: Preparation of Phase D

6. Combining Phases A + C into Phase B. Using an overhead mechanical stirrer at low speed, the mixture of phases A + C (PVA solution + PVP, urea, glycerine and EDTA solution) is slowly added into the hydrated Phase B (carbomer dispersion). Slow pouring down of phases A + C (again via small steady flow) is continued until all are combined. Slow-speed stirring is maintained to avoid entrapment of air.



Fig. 5: Combining two phases

7. Incorporating Phase D (salicylic acid in propylene glycol) is slowly added into the mix under continued stirring as a thin stream to keep the salicylic acid from precipitating upon contact with the aqueous base.



Fig. 6: Incorporation of Phase D

8. Adding the preservative. The mixture is cooled at room temperature, and 2-phenoxyethanol is added and mixed in until evenly distributed (The preservative is only added after all heating steps, to prevent loss by evaporation or degradation).
9. Neutralization and gel formation. The neutralizer is added dropwise under slow ongoing stirring on the overhead stirrer. The speed of the overhead stirrer is reduced gradually as viscosity builds up.
10. pH adjustment. The pH is measured using a calibrated pH meter, and time is given for the reading to stabilize in the gel. Further

neutralizer or a drop of acid can be added to reach the target pH as required. Carbomer gels are rheologically stable over approximately pH 5.0–8.0, so the target is selected within this mildly acidic, skin-compatible range suitable for salicylic acid. stable over approximately pH 5.0–8.0, so the target is selected within this mildly acidic, skin-compatible range suitable for salicylic acid.

11. Volume make-up. The remaining purified water is added to bring the final mass, and the gel is gently stirred until thoroughly smoothed.
12. De-aeration. The gel is left to stand in an ultrasonic bath for a time to remove bubbles (This step is important as bubbles will affect subsequent measurements of clarity and viscosity).



Fig. 7: Process for Deaeration of prepared formulation

13. Packaging. The gel is transferred into a clean/dry container, filling it slowly with a spatula or syringe to avoid entrapment of air. The container is then closed securely.



Fig. 8: Final product

EVALUATION PARAMETERS

1. **Organoleptic properties.** Appearance, colour, clarity, homogeneity, odour and texture were assessed visually and by touch. Appearance and colour were examined on a glass slide against white backgrounds in natural light, clarity against dark and light backgrounds, homogeneity by pressing the gel between thumb and forefinger and spreading it on a slide, and texture by rubbing a small amount on the back of the hand.

Table 2: Organoleptic Evaluation Observation Table

Sr. No.	Parameter	Method of evaluation	Final observation
1	Appearance	Visual examination against a white background	Smooth, Semi-solid gel
2	Colour	Visual examination against a white tile	Colourless/Slightly cloudy
3	Clarity	Visual examination against dark and light backgrounds	Clear
4	Homogeneity	Manual spreading between fingers and on glass slide	Homogeneous, Free from lumps
5	Odour	Direct sensory examination	Mild, Characteristic
6	Texture	Application and rubbing on the skin	Smooth, easily spreadable

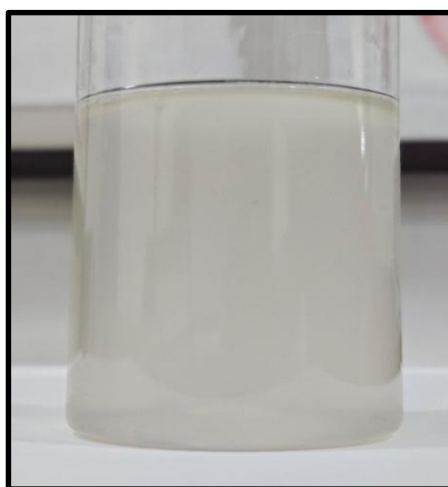


Fig. 9: Final peeling gel-solution

- pH.** Approximately 1 g of gel was dispersed in distilled water, and the pH was read with a digital pH meter. The measured pH was found to be in the range of 5.78

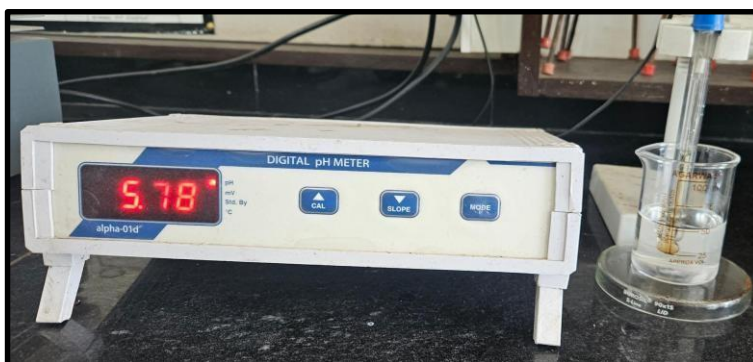


Fig. 10: pH determination using a digital pH meter

3. **Spreadability.** Spreadability was measured by the glass-slide method. About 0.5 g of gel was placed on a glass plate and covered with a second plate; uniform pressure was applied, and the distance spread was measured.

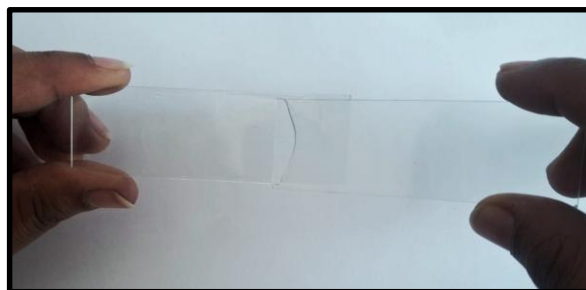


Fig. 11: Spreadability evaluation using the glass slide method.

4. **Specific gravity.** Specific gravity was determined with a pycnometer as $(W3 - W1)/(W2 - W1)$, where $W1$, $W2$, and $W3$ are the weights of the empty pycnometer, the pycnometer filled with distilled water, and the pycnometer filled with gel. The specific gravity was found to be 1.12



Fig. 12: Determination of specific gravity using pycnometer.

5. **Skin compatibility (patch test).** A small amount of gel was applied to the skin, and the site was observed for redness, itching, burning sensation, and inflammation.



Fig. 13: During application



Fig. 14: During waiting period



Fig. 15: After peeling

Observation Table:

Table 3: Patch Test Observation Table

Sr. No.	Parameter	Observation
1	Redness	Not observed
2	Itching	Not observed
3	Burning sensation	Not observed
4	Inflammation	Not observed

6. **Accelerated stability.** Gel samples in the product container were stored under accelerated conditions and examined on days 1, 7 and 15 for appearance, colour, clarity, homogeneity, odour, pH, viscosity, and spreadability.

Observation:



Fig.16: Day 1 Observation



Fig.17: Day 7 Observation



Fig.18: Day 15 Observation

Table 4: Accelerated stability study observation table.

Sr. No.	Parameter	Observation
1	Appearance change	No change observed
2	Colour change	No change observed
3	Clarity change	No change observed
4	Homogeneity change	No change observed
5	Odour change	No change observed
6	pH change	No change observed
7	Viscosity change	No change observed
8	Spreadability change	No change observed

7. **Identity of salicylic acid by TLC.** The gel was compared with a pure salicylic acid reference on the same plate, and Rf was calculated as the distance travelled by the spot divided by the distance travelled by the solvent front.

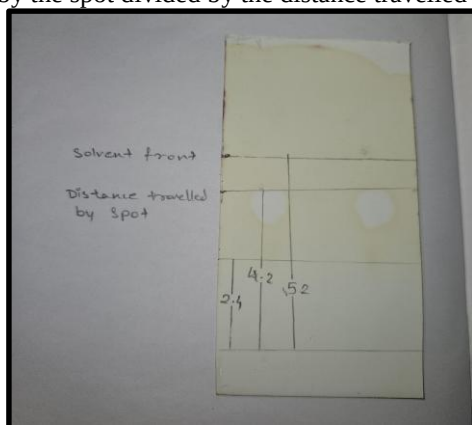


Fig. 19: Result for identification of the presence of salicylic acid

RESULT

The skin crack repair and peeling gel solution is prepared in the form of phase-wise dissolution, which was evaluated for organoleptic, physicochemical, and safety attributes.

The gel is smooth and has a homogeneous mass, showing that the carbomer was properly swollen and neutralized, and the polymers are homogeneously mixed. The product is observed to be transparent with no particles or air gaps observed, which indicates that active

substances are fully incorporated into the formulation and allows the elimination of bubbles during deaeration. Furthermore, the product spreads easily on the surface without leaving visible traces when removed, signifying that it has a good topical performance. In general, the obtained results demonstrated that a uniform gel with desirable organoleptic properties was prepared, fulfilling the objective of the study.

The pH of the gel was found to be in the acceptable range for topical use, as it was neither acidic nor alkaline, which may irritate the skin. Thus, the gel is properly neutralized, meeting the corresponding process objective. In addition, the spreadability tests showed that the gel was easily spread with minimal effort and did not leave any uneven spots after removal.

This indicates that the gelling and film-forming agents were dosed appropriately to provide satisfactory spreading and coating properties, meeting the corresponding objective. Concerning the physicochemical properties, the density of the preparation was found to be consistent with the expected value for an aqueous solution with the addition of humectants, polymers, and active ingredients.

This result proves that the gel has an optimum consistency, which can be manufactured consistently, thus fulfilling the corresponding objective. In addition, the patch test did not show signs of irritation, redness, itching, burning, or inflammation after the application of the gel, implying that the skin tolerates the product well. Thus, the safety evaluation was found to be in concordance with the expectations, thus meeting the corresponding objective.

DISCUSSION

The gel was prepared successfully via the stage-wise dissolution method. The division of the process into four stages contributed to obtaining the mixture with the desired working characteristics due to the convenience of the introduction of each polymer and active ingredient in the form suitable for dissolution or incorporation: melting PVA, hydrating carbomer before neutralization, mixing water-soluble humectants with PVP, and pre-dissolving salicylic acid in propylene glycol and adding it in a thin stream. The final product is a clear solution without lumps and bubbles, meaning that the hydration, neutralization, and de-aeration processes occurred properly. The determined pH of 5.78 was slightly higher than the healthy pH of the skin of approximately 4.7, but it was within normal limits for topical preparations and sufficient for the action of an acidic agent, salicylic acid. For reference, the pH was measured in the 1:10 aqueous dispersion; therefore, the value should not be compared directly with the gel composition.

The specific gravity of the gel is 1.12, which is expected for an aqueous solution with incorporated humectants, polymers, and active ingredients. It confirms the preparation consistency and can be used for further batch control analyses since the value is in the expected range. Besides, the gel's easy spreading properties ensure its uniform distribution over the skin area, which enhances the controlled release of active substances.

No irritation symptoms were detected in the patch test, which is a positive result given that the preparation contains urea and salicylic acid, both of which are known to cause dose-dependent irritation manifestations. The result, nevertheless, should be considered preliminary because the test was performed on an uncharacterized sample (the number of subjects and inclusion/exclusion criteria were not specified). Therefore, no conclusions can be drawn on the relationship between the test duration and the development of cumulative irritation or allergic reactions.

The TLC analysis confirmed the presence of salicylic acid in the composition and the absence of degradation products, as no additional spots were detected in the sample. However, no quantitative information was obtained, as TLC is a qualitative technique. In particular, the amount of acid and its concentration in the gel layer or the amount introduced into the skin were not determined.

The developed formulation is consistent with previously described clinical cases using combined urea-salicylic acid preparations for the treatment of hyperkeratotic skin conditions. However, instead of a traditional cream-gel consistency, a peel-off gel was selected as the delivery system. Its selection was dictated by the choice of the PVA-PVP polymer system, which allows the preparation of film-forming systems. The removal of the polymer film from the skin surface is facilitated by the addition of propylene glycol and PVP.

FUTURE PROSPECTS

1. The present study has demonstrated a stable, cosmetically acceptable, and skin-compatible gel-solution for the management of dry and fissured skin, but there are several avenues open for extending and strengthening this work.
2. A direct instrumental or subjective evaluation of the formulation's moisturizing and skin-conditioning performance should be undertaken in future work. For example, it would be interesting to undertake a corneometric assay of stratum corneum hydration prior to and following application, assessment of transepidermal water loss, and a structured subjective scoring of softness and dryness by volunteers over a defined application schedule.
3. Total viable microbial count should be supplemented with recorded observations across the different storage intervals, as well as being critical to determining the formulation shelf life; these are essential to assessing the formulation's ongoing safety.
4. Future work could extend the present work to a repeated or longer-duration patch test across a larger volunteer panel, which would provide a more robust indication of cumulative irritation potential across different skin types, particularly pertinent to a product intended for regular, ongoing use on cracked and already-compromised skin.
5. A formal assessment of the formulation's peeling and exfoliating efficacy on actual dry, rough, or fissured skin would also be a valuable extension of this work, given that the present study confirmed the chemical presence and integrity of salicylic acid through thin-layer chromatography but did not directly measure its clinical or cosmetic exfoliating effect on skin.
6. Future studies could also examine the optimization of the individual ingredient concentrations, particularly the relative proportions of urea and salicylic acid, through a systematic formulation design, in order to identify the combination that best balances hydrating, conditioning, and peeling effects while minimizing irritation potential, building on the single formulation

evaluated in the present study. Future studies could also examine the optimization of the individual ingredient concentrations, particularly the relative proportions of urea and salicylic acid, through a systematic formulation design, in order to identify the combination that best balances hydrating, conditioning, and peeling effects while minimizing irritation potential, building on the single formulation evaluated in the present study.

7. Finally, with a more complete set of efficacy, stability, and safety data in hand, the formulation could be considered for comparative evaluation against existing marketed moisturizing and keratolytic products for dry and fissured skin, which would help establish its relative performance and potential viability as a cosmetically elegant alternative to conventional heavy creams and ointments, as proposed in the rationale for this. Keratolytic products for dry and fissured skin, which would help establish its relative performance and potential viability as a cosmetically elegant alternative to conventional heavy creams and ointments, as proposed in the rationale for this.

CONCLUSION

A transparent, easily spreadable carbomer-based gel-solution that incorporates urea, salicylic acid, PVA, and PVP was successfully prepared through a reproducible phase-wise preparation method. The resulting preparation demonstrated a skin-compatible pH of 5.78, a specific gravity of 1.12, the absence of visible instability after 15 days, the lack of irritation on a preliminary patch test, and retained salicylic acid on TLC. The obtained results justify the formulation's potential as a cosmetically appealing cream for the management of dry and fissured skin through multiple routes of investigation. Instrumental evaluation of hydration and exfoliation, quantitative stability analysis, microbial limit and preservative-efficacy testing, optimization of the ratio of urea to salicylic acid, and a large-scale patch-test panel are required before efficacy or safety can be claimed.

REFERENCES

1. Arif, T. (2015). Salicylic acid as a peeling agent: A comprehensive review. *Clinical, Cosmetic, and Investigational Dermatology*, 8, 455-461. <https://doi.org/10.2147/CCID.S84765>
2. Kornhauser, A., Coelho, S. G., & Hearing, V. J. (2010). Applications of hydroxy acids: Classification, mechanisms, and photoactivity. *Clinical, Cosmetic, and Investigational Dermatology*, 3, 135-142. <https://doi.org/10.2147/CCID.S9042>
3. Lambers, H., Piessens, S., Bloem, A., Pronk, H., & Finkel, P. (2006). Natural skin surface pH is, on average, below 5, which is beneficial for its resident flora. *International Journal of Cosmetic Science*, 28(5), 359-370. <https://doi.org/10.1111/j.1467-2494.2006.00344.x>
4. Pan, P., Svirskis, D., Waterhouse, G. I. N., & Wu, Z. (2023). Hydroxypropyl methylcellulose bioadhesive hydrogels for topical application and sustained drug release: The effect of polyvinylpyrrolidone on the physicommechanical properties of hydrogel. *Pharmaceutics*, 15(9), 2360. <https://doi.org/10.3390/pharmaceutics15092360>
5. Piquero-Casals, J., Morgado-Carrasco, D., Granger, C., Trullàs, C., Jesús-Silva, A., & Krutmann, J. (2021). Urea in dermatology: A review of its emollient, moisturizing, keratolytic, skin barrier enhancing and antimicrobial properties. *Dermatology and Therapy*, 11(6), 1905-1915. <https://doi.org/10.1007/s13555-021-00611-y>
6. Proksch, E., & Lachapelle, J. M. (2005). The management of dry skin with topical emollients-recent perspectives. *Journal der Deutschen Dermatologischen Gesellschaft*, 3(10), 768-774.
7. Rawlings, A. V., & Harding, C. R. (2004). Moisturization and skin barrier function. *Dermatologic Therapy*, 17(S1), 43-48. <https://doi.org/10.1111/j.1396-0296.2004.04S1005.x>
8. Rowe, R. C., Sheskey, P. J., & Quinn, M. E. (2009). *Handbook of pharmaceutical excipients* (6th ed.). Pharmaceutical Press.
9. Bercea, M. (2024). Recent advances in poly (vinyl alcohol)-based hydrogels. *Polymers*, 16(14), Article 2021. <https://doi.org/10.3390/polym16142021>
10. Celleno, L. (2018). Topical urea in skincare: A review. *Dermatologic Therapy*, 31(6), Article e12690. <https://doi.org/10.1111/dth.12690>
11. Dréno, B., Zuberbier, T., Gelmetti, C., Gontijo, G., & Marinovich, M. (2019). Safety review of phenoxyethanol when used as a preservative in cosmetics. *Journal of the European Academy of Dermatology and Venereology*, 33(Suppl. 7), 15-24. <https://doi.org/10.1111/jdv.15944>
12. Fiume, M. M., Bergfeld, W. F., Belsito, D. V., Hill, R. A., Klaassen, C. D., Liebler, D., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., & Andersen, F. A. (2012). Safety assessment of propylene glycol, tripropylene glycol, and PPGs as used in cosmetics. *International Journal of Toxicology*, 31(5 Suppl.), 245S-260S.
13. Fluhr, J. W., Darlenski, R., & Surber, C. (2008). Glycerol and the skin: Holistic approach to its origin and functions. *British Journal of Dermatology*, 159(1), 23-34. <https://doi.org/10.1111/j.1365-2133.2008.08643.x>
14. Islam, M. T., Rodríguez-Hornedo, N., Ciotti, S., & Ackermann, C. (2004). Rheological characterization of topical carbomer gels neutralized to different pH. *Pharmaceutical Research*, 21(7), 1192-1199.
15. Kurakula, M., & Rao, G. S. N. K. (2020). Pharmaceutical assessment of polyvinylpyrrolidone (PVP): As an excipient from conventional to controlled delivery systems with a spotlight on COVID-19 inhibition. *Journal of Drug Delivery Science and Technology*, 60, Article 102046. <https://doi.org/10.1016/j.jddst.2020.102046>
16. Lanigan, R. S., & Yamarik, T. A. (2002). Final report on the safety assessment of EDTA, calcium disodium EDTA, diammonium EDTA, dipotassium EDTA, disodium EDTA, TEA-EDTA, tetrasodium EDTA, tripotassium EDTA, trisodium EDTA, HEDTA, and trisodium HEDTA. *International Journal of Toxicology*, 21(Suppl. 2), 95-142. <https://doi.org/10.1080/10915810290096522>
17. Piquero-Casals, J., Morgado-Carrasco, D., Granger, C., Trullàs, C., Jesús-Silva, A., & Krutmann, J. (2021). Urea in

- dermatology: A review of its emollient, moisturizing, keratolytic, skin barrier enhancing and antimicrobial properties. *Dermatology and Therapy*, 11(6), 1905–1915. <https://doi.org/10.1007/s13555-021-00611-y>
18. Varges, P. R., Costa, C. M., Fonseca, B. S., Naccache, M. F., & de Souza Mendes, P. R. (2019). Rheological characterization of Carbopol® dispersions in water and in water/glycerol solutions. *Fluids*, 4(1), Article 3. <https://doi.org/10.3390/fluids4010003>
 19. Verdier-Sévrain, S., & Bonté, F. (2007). Skin hydration: A review on its molecular mechanisms. *Journal of Cosmetic Dermatology*, 6(2), 75–82.
 20. Williams, A. C., & Barry, B. W. (2004). Penetration enhancers. *Advanced Drug Delivery Reviews*, 56(5), 603–618. <https://doi.org/10.1016/j.addr.2003.10.025>
 21. Coutanceau, C., Carballido, F., & Le Maître, M. (2008). Clinical evaluation of the efficacy and the tolerance of a cream gel with 30% urea, 2% salicylic acid, and 1% lactic acid versus vehicle in subjects with localized hyperkeratosis. *Journal of the American Academy of Dermatology*, 58(2, Suppl. 2), AB129.
 22. Dall'Oglio, F., Tedeschi, A., Verzi, A. E., Lacarrubba, F., & Micali, G. (2020). Clinical evidence of urea at medium concentration. *International Journal of Clinical Practice*, 74(11), e13815. <https://doi.org/10.1111/ijcp.13815>
 23. Kamoun, E. A., Chen, X., Mohy Eldin, M. S., & Kenawy, E.-R. S. (2015). Crosslinked poly (vinyl alcohol) hydrogels for wound dressing applications: A review of remarkably blended polymers. *Arabian Journal of Chemistry*, 8(1), 1–14. <https://doi.org/10.1016/j.arabjc.2014.07.005>
 24. Aulton, M. E., & Taylor, K. M. G. (Eds.). (2018). *Aulton's pharmaceuticals: The design and manufacture of medicines* (5th ed.). Elsevier.
 25. Khar, R. K., Vyas, S. P., Ahmad, F. J., & Jain, G. K. (Eds.). (2013). *Lachman/Lieberman's the theory and practice of industrial pharmacy* (4th ed.). CBS Publishers & Distributors.
 26. Sinko, P. J. (Ed.). (2011). *Martin's physical pharmacy and pharmaceutical sciences* (6th ed.). Lippincott Williams & Wilkins.
 27. Allen, L. V., Jr. (2016). *The art, science, and technology of pharmaceutical compounding* (5th ed.). American Pharmacists Association.
 28. Prestes, P. S., Oliveira, M. M. M., & Leonardi, G. R. (2013). Randomized clinical efficacy of superficial peeling with 85% lactic acid versus 70% glycolic acid. *Anais Brasileiros de Dermatologia*, 88(6), 900–905. <https://doi.org/10.1590/abd1806-4841.20131888>
 29. Dębowska, R. M., Kaszuba, A., Michalak, I., Dzwigałowska, A., Cieścińska, C., Jakimiuk, E., Zielińska, J., & Kaszuba, A. (2015). Evaluation of the efficacy and tolerability of mandelic acid-containing cosmetic formulations for acne skin care. *Przegląd Dermatologiczny (Dermatology Review)*, 102(4), 316–321. <https://doi.org/10.5114/dr.2015.5400> (Dermatology Review), 102(4), 316–321. <https://doi.org/10.5114/dr.2015.5400>
 30. Venetikidou, M., Lykartsis, E., Adamantidi, T., Prokopiou, V., Ofrydopoulou, A., Letsiou, S., & Tsoupras, A. (2025). Proteolytic enzyme activities of bromelain, ficin, and papain from fruit by-products and potential applications in sustainable and functional cosmetics for skincare. *Applied Sciences*, 15(5), 2637. <https://doi.org/10.3390/app15052637>
 31. Sinko, P. J. (Ed.). (2011). *Martin's physical pharmacy and pharmaceutical sciences* (6th ed.). Lippincott Williams & Wilkins.
 32. Sethi, P. D. (2007). *High-performance thin-layer chromatography: Quantitative analysis of pharmaceutical formulations*. CBS Publishers & Distributors.
 33. Cosmetic Ingredient Review. (2013). *Safety assessment of triethanolamine and related compounds as used in cosmetics*. Cosmetic Ingredient Review.

Copyright & License:

© Authors retain the copyright of this article. This work is published under the Creative Commons Attribution 4.0 International License (CC BY 4.0), permitting unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.