



“FORMULATION AND EVALUATION OF HYDROGEL BEAD SERUM FOR SKIN HYDRATION AND ACNE TREATMENT”

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ABSTRACT :

Acne vulgaris is a chronic inflammatory disease of the sebaceous follicles that requires long-term treatment with topical drugs, the frequent use of which leads to various side effects, including dermatitis and xerosis of the skin. The purpose of this study was to develop and investigate a serum containing niacinamide and hyaluronic acid in the form of hydrogel beads for prolonged release of the active ingredients and improved moisturizing properties. The hydrogel beads were obtained by ionotropic gelation of sodium alginate using calcium chloride solution as a crosslinking agent according to the egg-box mechanism.

Keywords: Hydrogel beads, niacinamide, hyaluronic acid, ionotropic gelation, sodium alginate, acne vulgaris, controlled release.

1. INTRODUCTION

Acne vulgaris is one of the most common skin disorders caused by acne's chronic, inflammatory and stressful nature. Treatment of acne has always been based on topical agents that reduce sebum production, inflammation, and bacteria proliferation. Niacinamide and hyaluronic acid being two of the major skincare ingredients these days. Niacinamide is a biologically active and stable form of vitamin B3, which is known for its ability to improve sebum production, reduce inflammation, and enhance the skin barrier function, while hyaluronic acid has powerful moisture-retaining properties, thus solving the problem of dryness – another side effect of the traditional acne treatment. Nevertheless, both ingredients compete with some formulation challenges. Niacinamide has the requirement of certain conditions in terms of pH and temperature so that it does not lose its effectiveness, whereas hyaluronic acid needs a proper matrix to enable delivery of this extremely hydrophilic substance into the skin. As a result of this, modern technologies are being introduced to address the drawbacks of these ingredients and improve their bioavailability. So the hydrogel beads have been established for this purpose. Hydrogel beads are small polymeric nanoparticles for controlled release of drug.

1.1 Hydrogel Bead-Based Delivery System:

Hydrogel beads serve as an ideal carrier for niacinamide and hyaluronic acid due to their ability to:

- Enhance stability by protecting the active ingredients from environmental degradation.
- Allow controlled and sustained release, ensuring prolonged therapeutic effects at the site of application.
- skin penetration will be improved
- and localized controlled delivery, enhance the efficacy.
- Reduce potential skin irritation by regulating the release of active ingredients over time.

In this study, ionotropic gelation was used as the method for hydrogel bead preparation. Sodium alginate, derived from brown algae, is a non-toxic linear polysaccharide widely used in medical applications including drug delivery systems, wound dressing, and tissue engineering, with gelation achieved through the interaction between its guluronate residues and multivalent cations such as calcium. Calcium chloride was used as the cross-linking agent to form stable beads. Such hydrogel beads have shown great potential as drug delivery systems, and this method is widely employed in pharmaceutical and cosmetic formulations due to its biodegradable, biocompatible, and non-toxic nature.

1.2 Hyaluronic Acid as an Additional Active Ingredient:

Apart from niacinamide, the serum contains hyaluronic acid as an additional active ingredient for its excellent moisturizing and emollient properties. Hyaluronic acid is present in the dermis and epidermis of the skin in high concentrations. In the former layer, it ensures skin resilience and fluid retention, and in the latter, it is involved in the homeostasis of the epidermis and normal structure of the stratum corneum. The acid's ability to control sebum production and normalization of the function of the sebaceous glands has also been proven. Moreover, hyaluronic acid reduces oiliness of the skin, preventing the formation of comedones and blackheads and treating their early signs. Finally, the anti-inflammatory and hydrating effects of this ingredient are beneficial for sensitive and acne-prone skin because it is tolerated well by the skin and reduces roughness, irritation, and redness. Thus, combining hyaluronic acid with niacinamide in hydrogel beads is a great solution for treating oily and acne-prone skin.

1.3 Formulation of Hydrogel Bead-Based Serum:

After successful preparation of niacinamide and hyaluronic acid-loaded hydrogel beads, they were incorporated into a serum base to develop a stable and effective topical formulation. The serum was designed to provide:

- Enhanced hydration and skin compatibility using a lightweight, water-based gel matrix suited for water-soluble actives.
- Improved texture and spreadability, ensuring smooth and rapid absorption into the skin.
- Controlled release of niacinamide and hyaluronic acid from the hydrogel beads, preventing premature degradation and maximizing sustained therapeutic benefit at the target site.
- Non-comedogenic, lightweight delivery suitable for acne-prone and sensitive skin, avoiding the heaviness typically associated with conventional creams.

2. OBJECTIVES OF THE STUDY

The primary objective of this research is to develop and characterize a niacinamide and hyaluronic acid-loaded hydrogel bead serum for acne treatment, focusing on the following aspects:

- Preparation of hydrogel beads using the ionotropic gelation method and evaluation of drug entrapment efficiency.
- Incorporation of hydrogel beads into a stable serum base with optimal physicochemical properties.
- Characterization of the serum, including bead particle size, pH, viscosity, spread ability, stability, and irritancy testing.
- Assessment of the formulation's in-vitro drug release and release kinetics, providing sustained delivery and enhanced skin benefits for acne management.

3. SCOPE OF THE STUDY

This research contributes to the growing field of advanced cosmeceutical drug delivery systems, offering a novel approach for the topical delivery of niacinamide and hyaluronic acid in acne management. The study aims to demonstrate that hydrogel bead technology can significantly enhance the stability, controlled release, and skin compatibility of anti-acne serums compared to conventional formulations. By optimizing polymer and cross-linker concentrations, the study seeks to establish a formulation that balances efficacy with minimal skin irritation, addressing a key limitation of existing topical acne treatments. The findings may serve as a foundation for further advancements in polymer-based topical delivery systems and open new possibilities for controlled-release cosmeceutical and pharmaceutical formulations targeting acne and other dermatological conditions.

4. MATERIALS AND METHODS

4.1 Materials:

Niacinamide was used as an active ingredient in our formulation. Niacinamide (Pharmaceutical grade) was purchased online. Hyaluronic acid (low molecular weight, cosmetic grade) was purchased from a online. Sodium alginate was used as a polymer, and calcium chloride was used as a cross-linking agent for the preparation of hydrogel beads. The chemicals used to prepare the serum base formulation were purchased from isochem and molychem Chemicals Pvt. Ltd. Gelling agents and other excipients were procured from standard pharmaceutical suppliers.

Test	Observation	Inference
Colour	White to off-white powder	Niacinamide present
Odour	Odourless /faint characteristic odour	Niacinamide present
Solubility	Freely soluble in water	Niacinamide present

Table 1: Preliminary identification tests for Niacinamide

Test	Observation	Inference
Colour	White to off-white powder	Hyaluronic acid present
Odour	Odourless	Hyaluronic acid present
Solubility	Soluble in water, forms viscous solution	Hyaluronic acid present

Table 2: Preliminary identification tests for Hyaluronic acid

5. METHODOLOGY

5.1 Preliminary Identification Tests:

Preliminary identification tests for niacinamide and hyaluronic acid were carried out to confirm the identity and purity of the raw materials prior to formulation, following standard organoleptic and solubility-based screening procedures. Each sample was assessed for colour, odour, and solubility behaviour in water and organic solvents, consistent with routine pharmacopoeial identification approaches used for active ingredient verification.

6. FORMULATION

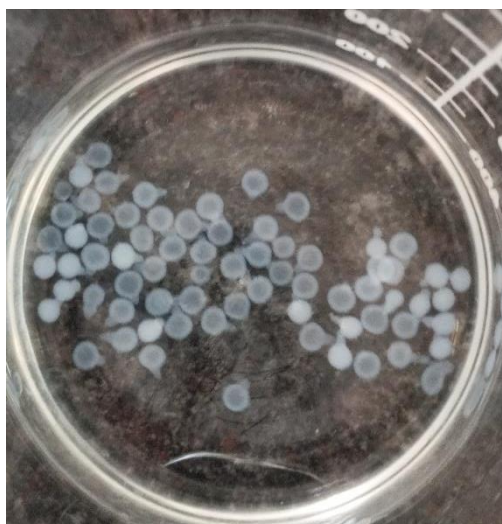
6.1 Preparation of Hydrogel Beads:

Hydrogel beads were formed by the ionotropic gelation method, where sodium alginate was used as the polymer and calcium chloride as the cross-linking agent. 50 ml of 2–4% w/v sodium alginate solution was prepared. Niacinamide and hyaluronic acid, in the required quantities, were then added to the prepared sodium alginate solution and mixed by mechanical stirrer until a homogeneous, bubble-free dispersion was obtained. The obtained dispersion was extruded dropwise into 100 ml of calcium chloride solution (10% w/v) with the help of a syringe (22 G needle) while stirring on a magnetic stirrer. The resulting hydrogel beads were left to harden and cross-link for a defined period, then filtered and given a water wash to remove unreacted calcium chloride before being air-dried.

6.2 Formulation of Hydrogel bead:

S.NO	COMPOSITION	F1	F2	F3
1.	Sodium alginate	2g	4g	1.5g
2.	Calcium chloride	5g	10g	2g
3.	Niacinamide	1.5g	2g	1g
4.	Hyaluronic acid	1g	1.5g	0.5g
5.	Glycerine	3ml	4ml	2ml
6.	Distilled water	100ml	100ml	100ml

Table 3: Formulation of Hydrogel bead



Figures 1: Hydrogel bead

6.3 Ingredients and its functions:

S.NO	INGREDIENT	CATEGORY	FUNCTION
1.	Sodium Alginate	Natural polymer / Gelling agent	Forms hydrogel beads
2.	Calcium Chloride	Crosslinking agent	Provides Ca ²⁺ ions
3.	Distilled Water	Solvent/Vehicle	Base medium
4.	Glycerine	Humectant	Retains moisture
5.	Hyaluronic Acid	Biopolymer	Deep hydration
6.	Niacinamide	Vitamin B3	Brightens & controls oil
7.	Sodium benzoate	Preservative	Prevents contamination
8.	Fragrance	Sensory agent	Adds pleasant smell

Table 4: Ingredients and its functions

6.4 Procedure for Serum Base:

A certain amount of gel-forming substance (carbomer/sodium carbomer) was taken and mixed with distilled water until a viscous mixture was formed. The mixture was left to swell, and then it was neutralized to the required pH (5.0-6.0) with a triethanolamine solution or another suitable pH regulator while stirring until a viscous gel of the desired consistency was obtained. The gel was then mixed with humectants, chelating agents, and preservatives until a homogeneous serum base was obtained.

6.5 Procedure for the Incorporation of Niacinamide and Hyaluronic Acid Loaded Hydrogel Beads into the Serum Base:

Free (unencapsulated) hyaluronic acid solution was added to the serum base with stirring to improve the hydrating and viscosity-increasing properties of the base. The mixture was left to swell at room temperature to form a uniform gel. The required amount of niacinamide and hyaluronic acid loaded hydrogel beads was introduced into the serum base with stirring to minimize damage to the hydrogel structure. A few drops of a suitable preservative/fragrance-free stabilizer were added as required.

6.6 Formulation of Hydrogel bead serum:

S.NO	COMPOSITION	F1	F2	F3
1.	Sodium alginate	2g	4g	1.5g
2.	Calcium chloride	5g	10g	2g
3.	Niacinamide	1.5g	2g	1g
4.	Hyaluronic acid	1g	1.5g	0.5g
5.	Glycerine	3ml	4ml	2ml
6.	Sodium benzoate	1g	1g	1g
7.	Carbomer	0.5g	1g	1.5g
8.	Triethanolamine	Q.s	Q.s	Q.s
9.	Distilled water	100ml	100ml	100ml
10.	Fragrance	0.2ml	0.2ml	0.2ml

Table 5: Formulation of Hydrogel bead serum

7. EVALUATION

7.1 Evaluation of Hydrogel beads:

7.2 Particle size analysis:

Stero zoom microscopy method was used for the determination of the particle size and morphology of the chamomile microsphere.

7.3 Entrapment efficiency:

50 mg of microsphere were appropriately weighed and crushed, then crushed microspheres are transferred into beaker containing 100 ml phosphate buffer pH 6.8. It was stirred by magnetic stirrer for few minutes. Then 1ml of sample was withdrawn and make up to 10ml using a phosphate buffer pH 6.8. Absorbance was taken at 210 nm, and the concentration was calculated.

% entrapment efficiency (practical drug content/theoretical drug content) 100

7.4 Evaluation of Hydrogel beads Serum:

7.5 Physical appearance:

The physical appearance such as, color, odour, state and texture of the formulated microsphere loaded Hydrogel beads serum were evaluated.

7.6 Determination of pH:

The pH measurement was conducted by utilizing a digital pH meter. Firstly, calibrate the pH meter by using different buffer solutions 4, 7, and 9. Then pH of then formulated serum was measured by using pH meter.

7.7 Spreadability:

Spreadability was determined by placing a required amount of sample between the glass slides, then apply a definite amount of weight on a glass slides for a definite. The spreadability was calculated by the following formula,

$$S=MXL/T$$

$$\text{Spreadability (S)} = \frac{\text{weight tide to upper slide (W)} \times \text{length of the glass slide (L)}}{\text{Time taken to separate (T)}}$$

Time taken to separate (T)

7.8 Viscosity:

Viscosity of serum was done by using Brooke field viscometer at the temperature of 25°C. Using LV spindle #7 at 1000 rpm.

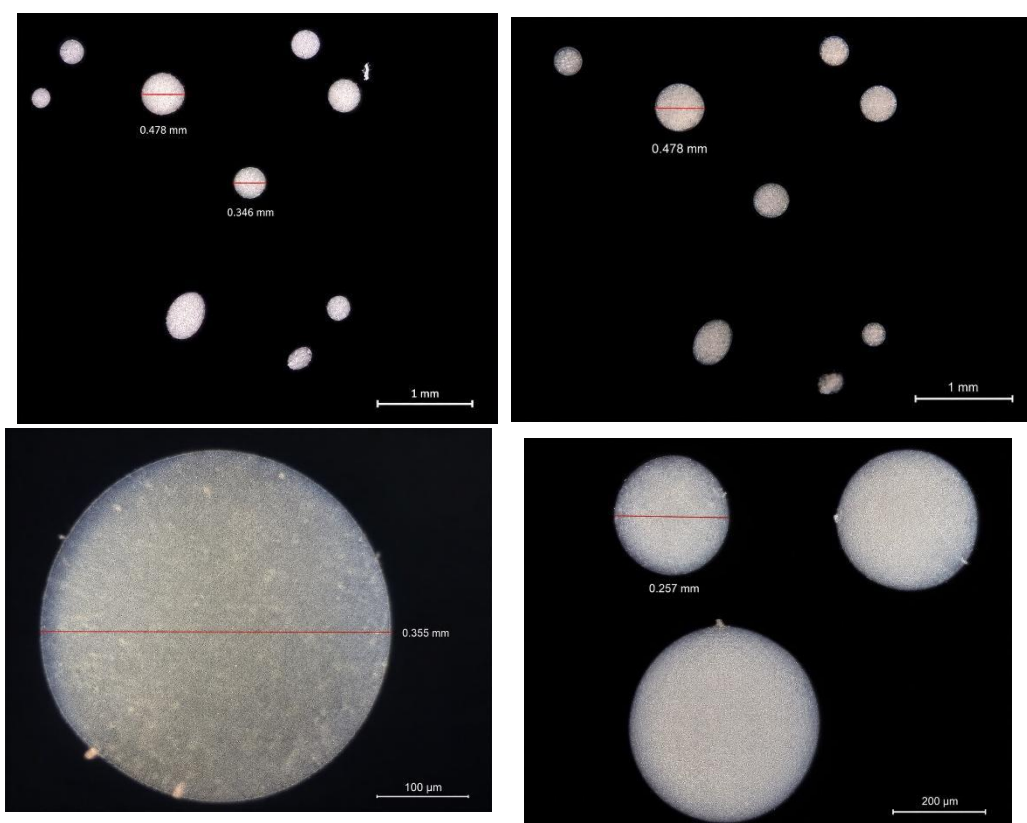
7.9 Phase separation:

The prepared Hydrogel beads serum was transferred in a suitable wide mouth container. Set aside for the oil phase and aqueous phase separation were visualizing after 24hrs.

8. RESULT AND DISCUSSION

8.1 Particle size analysis:

The Particle size was found within the desired range 271 µm to 473 µm.



Figures 2: Particle size analysis

8.2 Determination of pH:

The pH of our formulated Hydrogel beads loaded face serum falls with the ideal pH range of the face serum i.e., 5.5-6.5. The F2 formulation shows desired pH (5.92) when compared to F1 & F3.

S.NO	Formulation	pH
1.	F1	6.59

2.	F2	5.92
3.	F3	5.62

Table 6: Determination of pH

8.3 Entrapment efficiency:

The entrapment efficiency of the Hydrogel beads formulations was found to be in the range of 74.6% to 89.43%. From the obtained entrapment efficiency results, maximum entrapment efficiency was found in F2. i.e., amount of polymer increases entrapment efficiency of drug within the Hydrogel beads also increases.

S.NO	ENTRAPMENT EFFICIENCY
F1	74.6%
F2	89.43%
F3	78.37%

Table 7: Entrapment efficiency

8.4 Physical appearance:

The Hydrogel beads loaded face serum was found to be milky white in color with a pleasant odour and having a smooth texture when applied to the skin. Observations were shown in the below table.

CHARACTERISTICS	F1	F2	F3
Colour	White	White	White
Odour	Pleasant	Pleasant	Pleasant
State	Semi solid	Semi solid	Semi solid
Texture	Smooth	Smooth	Smooth

Table 8: Physical appearance

8.5 Spreadability:

The spreadability of the formulated Hydrogel beads loaded face serum was found to be,

S.NO	Formulation	Spreadability
1.	F1	5.5cm
2.	F2	6cm
3.	F3	5cm

Table 9: Spreadability

8.6 Viscosity:

The viscosity of the formulated Hydrogel beads loaded face serum was found to be,

S.NO	Formulation	Viscosity (Cps)
1.	F1	5670
2.	F2	7589
3.	F3	8769

Table 10: Viscosity

9. CONCLUSION

The present study successfully formulated and characterized a niacinamide and hyaluronic acid-loaded hydrogel bead serum for acne treatment using ionotropic gelation as the encapsulation technique. The use of sodium alginate as a polymer and calcium chloride as a cross-linking agent resulted in stable hydrogel beads that effectively entrapped niacinamide, enhancing its stability, controlled release, and skin bioavailability. The incorporation of hyaluronic acid further enriched the formulation by providing intense hydration, barrier-repair support, and additional skin-soothing properties, addressing the dryness commonly associated with conventional acne treatments. The formulated serum demonstrated favourable physicochemical characteristics, including optimal pH, spreadability, viscosity, and non-irritancy, making it suitable for acne-prone and sensitive skin types. Overall, this study highlights the potential of hydrogel bead technology in cosmeceutical and pharmaceutical formulations, offering an innovative approach to delivering active ingredients in a sustained and effective manner. Future research could explore long-term stability, in-vivo skin penetration studies, and clinical acceptability trials to further validate the commercial viability of this formulation. Future studies can also focus on enhancing bead stability and controlled release for prolonged therapeutic benefit. In-vivo and clinical evaluations will help confirm safety, efficacy, and consumer acceptability. Expanding this formulation approach into other topical products like creams and lotions can further increase its commercial potential.

Three formulations of niacinamide and hyaluronic acid-loaded hydrogel bead serum were prepared.

Selection of the best formulation was based on the evaluation parameters.

Comparing the three formulations, F2 gave better results in terms of entrapment efficiency and controlled drug release.

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Disclosure of conflict of interest:

There is no conflict of interest.

Author contribution:

Rahul P, Rathinam A, Rathinapriya M, Revathi S, had principal responsibility for the conception, design of the study and drafting of manuscript. Mr. S. Mohan Kumar was responsible for the revision of the manuscript for important intellectual content, Mr. S. Mohan Kumar, Dr. J. Karthi, Dr. S. Swarnalatha contributed towards reviewing of the literature. All authors agreed on the final version of manuscript.

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