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Research paper

Formulation and Evaluation of Topical Dosage Forms Containing Niacinamide

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Abstract

This study focuses on the formulation and evaluation of a cream and gel containing niacinamide, a commonly used active ingredient in skincare. Niacinamide, a water-soluble form of vitamin B_3, is known for its ability to strengthen the skin barrier, reduce inflammation, and regulate sebum production. Two formulations were developed: a cream composed of cetyl stearyl alcohol, stearic acid, glycerol, isopropyl myristate, sucrose ester, propylene glycol, distilled water, and niacinamide, and a gel formulated with glycerol, carbopol, triethanolamine, distilled water, and niacinamide. The cream, an oil-in-water emulsion, was designed for rich, long-lasting moisturization, while the gel was intended as a lightweight, water-based alternative. Both formulations were analyzed for pH and texture to compare the physicochemical properties, dissolution *in vitro* Franz diffusion and potential toxicological properties to check skin compatibility with MTT assay. The results revealed distinct differences: the cream provided superior hydration and barrier repair, whereas the gel offered a non-greasy, refreshing texture more suitable for oily or combination skin types. These findings highlight the versatility of niacinamide in topical applications and establish a foundation for further research on its efficacy in different delivery systems.

1. Introduction

Niacinamide, the water-soluble form of vitamin B_3, has a long history in both nutrition and dermatology. Initially it was used in the early 20th century to prevent pellagra, and later gained prominence for its skin benefits, such as enhancing the epidermal barrier, increasing ceramide production, and reducing inflammation(1). By the 1980s, niacinamide become a key cosmetic ingredient due to its roles in improving hydration,

reducing hyperpigmentation, and combating oxidative stress,making it an essential component in modern skincare formulations[2]. Niacinamide provides a range of dermatological benefits, including improved hydration, oil control, acne reduction, and a more even skin tone. It minimizes hyperpigmentation by inhibiting melanosome transfer, regulates sebum production, supports collagen maintenance, and reduces fine lines and wrinkles. It is suitable for all skin types, and it can be used both day and night,offering antioxidant protection during the day and barrier repair overnight [3,4].

Emerging research explores niacinamide's use in post-inflammatory hyperpigmentation (PIH), wound healing, and chronic conditions such as eczema and atopic dermatitis[5–7]. Niacinamide relevance has grown in response to modern environmental stressors such as pollution and blue light exposure[8]. It supports skin resilience and is increasingly included in sustainable and eco-friendly skincare formulations. Combination therapies with ingredients like vitamin C, hyaluronic acid, zinc, and salicylic acid enhance its effects while minimizing irritation[9–11].

Nowadays, it is incorporated into various skincare products;moisturizers for hydration, serums for targeted treatment, sunscreens for enhanced UV protection, and cleansers or toners for balancing and soothing the skin[12,13]. Clinical research confirms niacinamide efficacy in conditions like acne, melasma, and photoaging, with 4% niacinamide shown to be comparable to hydroquinone in treating hyperpigmentation[4,14,15].

The primary aim of this study was to compare the physicochemical properties (pH, texture analysis), skin compatibility (MTT assay), and efficacy (in vitro Franz diffusion) of niacinamide-containing cream and gel formulations to understand which formulation is better for which type of skin.

2. Materials and methods

2.1 Materials

Niacinamide was obtained from Sigma-Aldrich (St. Louis, Missouri, USA). Cetyl stearyl alcohol, stearic acid, glycerol, isopropyl myristate and propylene glycol were ordered from VWR International (Debrecen, Hungary). Sucrose esters were kindly gifted by Sisterna (Roosendaalc, The Netherlands). HaCaT cells were supplied from Cell Lines Service (CLS, Heidelberg, Germany). MTT dye (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide), phosphate buffered saline (PBS) buffer solution, Dulbecco's Modified Eagle's Medium (DMEM), heat-inactivated fetal bovine serum

(FBS), L-glutamine, non-essential amino acids solution, and penicillin-streptomycin solution, were obtained from Sigma-Aldrich (St. Louis, Missouri, USA). TrypLE™ Express Enzyme (no phenol red) was ordered from Thermo Fisher Scientific (Waltham, Massachusetts, USA). Ninety-six-well cell plates and culturing flasks were obtained from VWR International (Debrecen, Hungary).

2.2 Methods

2.2.1 Formulation of niacinamide cream

Formulation of the niacinamide cream involves a controlled emulsifying process in which the oil and water phases are combined under specific conditions to ensure stability, homogeneity, and efficacy. A total of 100 g cream was prepared per dose, as follows. The oily phase consists of cetyl stearyl alcohol (4.6 g), stearic acid (10 g), glycerol (5 g), and isopropyl myristate (5 g). These ingredients are heated in a water bath at 60°C until completely melted. The aqueous phase is prepared separately and contains propylene glycol (5 g), sucrose ester (3 g), and distilled water (62.4 g). This mixture is also heated to the same temperature to ensure complete dissolution. Propylene glycol acts as a penetration enhancer, while sucrose ester functions as an emulsifier to stabilize the final formulation. The active ingredient, niacinamide (5 g), a water-soluble compound, is dissolved in the aqueous phase before emulsification. Once both phases reach the same temperature (60°C), the aqueous phase is gradually added to the oil phase in three portions with constant stirring. Then the formulation is allowed to cool to 25°C under continuous stirring to prevent clumping and obtain a uniform consistency.

2.2.2 Formulation of niacinamide gel

The formulation of niacinamide gel is a carefully controlled process designed to ensure stability, uniformity, and optimal performance for topical application. A total of 100 g of gel was prepared per dose, as follows. (73 g) of distilled water was accurately measured and transferred into a clean, sterile beaker. To this, (10 g) of glycerol was added. Following the incorporation of glycerol, (1 g) of Carbopol 974P was slowly dispersed into the aqueous phase under constant magnetic stirring at room temperature. Continuous stirring for 3–4 hours allows complete swelling and hydration of the polymer, resulting in a uniform andlump-free dispersion. Once the gelling agent was fully hydrated, a separate solution was prepared by mixing (10 g) of distilled water

with (1 g) of triethanolamine. The hydrated polymer mixture was continuously stirred to prevent localized gelation, while the triethanolamine solution was gradually incorporated to ensure even distribution and consistency throughout the formulation.

2.2.3 pH measurement

pH measurement was performed potentiometrically using a portable digital pH meter (Sension™1, Hach Company, USA). Five grams of cream/gel were added to 20 mL of pre-heated distilled water to 37 ± 2 °C and vigorously stirred on a magnetic stirrer for 1 minute. After cooling, the dispersion was filtered, and the pH of the filtrate was measured. The pH values of the formulations were analyzed in the results section to evaluate their skin compatibility.

2.2.4 Texture analysis

To obtain objective data on the mechanical properties of the formulations, a Brookfield CT3 Texture Analyzer was used under standardized conditions. A cylindrical probe was applied to measure firmness and spreadability by moving upward at a constant speed and pressing the sample to a specified depth. The resistance force exerted by the sample was recorded and analyzed to determine firmness in millinewtons (mN) and spreadability, ensuring that the formulations have optimal sensory characteristics.

2.2.5 *In vitro* Franz diffusion

An *in vitro* release test was conducted to evaluate the release profile of niacinamide from both the cream and gel formulations under controlled laboratory conditions. Franz diffusion is widely known as a standardized and reliable technique in pharmaceutical and cosmetic research[16]. The Franz diffusion chamber system consists of two compartments, a donor chamber and a receiver chamber, separated by a cellulose acetate membrane with a pore size of 0.5 µm. The receiver chamber was filled with a pH 5 buffer solution to simulate the natural acidity of the skin. To enhance membrane permeability, the cellulose acetate membrane was pre-soaked in isopropyl myristate, a neutral medium, for 30 minutes before use. This step imitates the lipid composition of the stratum corneum. A 300 mg sample of each formulation (cream or gel) was evenly applied to the membrane surface in the donor chamber. During the experiment, the receiver chamber was continuously stirred at 450 rpm using a magnetic stirrer to maintain uniform experimental conditions. The temperature was maintained at 32 °C

to replicate average skin temperature. Samples were collected from the receiver chamber at predetermined time intervals to monitor the release of niacinamide. The concentration of niacinamide in each sample was determined via a spectrophotometric method at 262 nm using a UV spectrophotometer (Shimadzu, Tokyo, Japan)[17].

2.2.6 HaCaT cell line passaging

Spontaneously transformed aneuploid immortal keratinocyte cell line from adult human skin was selected for MTT and permeability assays[18]. Cells were maintained by weekly passaging in a plastic cell culture flask in DMEM supplemented with 2 mM L-glutamine, 100 mg/L gentamycin and 10% heat inactivated fetal bovine serum. Cells were stored in 5% CO_2 cell incubator at 37°C.

2.2.7 MTT assay

Cell viability of HaCaT cells was evaluated by MTT assay. Cells were seeded at a density of 10^4 cells/well on flat bottom 96-well tissue culture plates and allowed to grow for 7 days. Before the MTT assay, cell culture medium was removed and cells were treated with the cream and gel formulations. Mitochondrial activity of viable cells was determined after 3-hours incubation with the MTT dye. The formed formazan crystal precipitate was dissolved in acidic isopropanol and absorbance was measured with FLUOstar OPTIMA Microplate Reader (BMG LABTECH, Offenburg, Germany) at 570 nm against a 690 nm reference. Cell viability was demonstrated as the percentage of the negative control, which was PBS. We used Triton-X 100 as a positive control.

3. Results

3.1 pH measurement

The pH values of niacinamide cream was(5.73) and niacinamide gel was (5.89), which both were within the skin-friendly range, meaning they will not cause skin irritation. ofskin. Results are summarized in **Table 1**.

Composition	pH
Niacinamide cream	5.73
Niacinamide gel	5.89

***Table 1**.:* pH of the formulated ointment and cream. The pH value of niacinamide cream was 5.73 and niacinamide gel was 5.89 which both were within the skin friendly range.

3.2 Texture analysis

Niacinamide cream had a higher compression force which indicated a firmer consistency, while niacinamide gel has a softer texture makeing it more suitable for lightweight application. Results are shown in **Figure** 1.

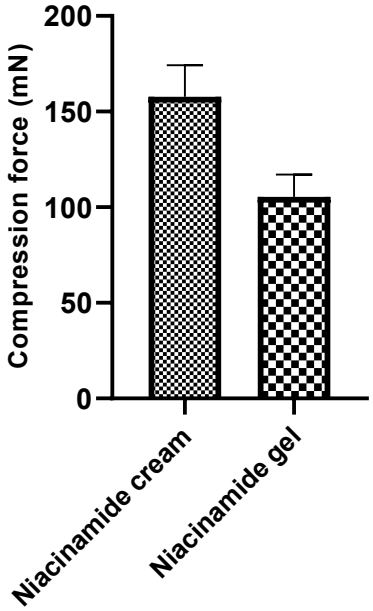

Figure 1*.:* Results of the texture analysis. Niacinamide cream showed a higher compression force, indicating a firmer consistency, whereas the niacinamide gel showed a softer texture, making it more suitable for lightweight application.

3.3 MTT assay

Both formulations maintained high HaCaT cell viability which confirms their biocompatibility, while the positive control (Triton X-100) significantly reduced cell survival. Results can be found in **Figure 2**.

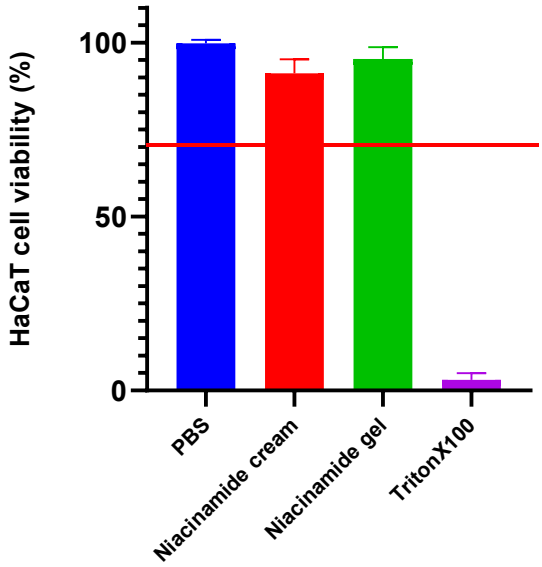

Figure 2.: Results of the MTT assay. Theformulations did not show substantial toxicity. Triton-X was used as a positive control, while PBS-treated group was the negative control. Each data point represents the mean ± SD, n = 10.

3.4 In vitro Franz diffusion

Niacinamide gel exhibited a higher diffusion rate than niacinamide cream, which indicates that the gel has a higher drug penetration due to its formulation. Results are summarized in **Figure 3**.

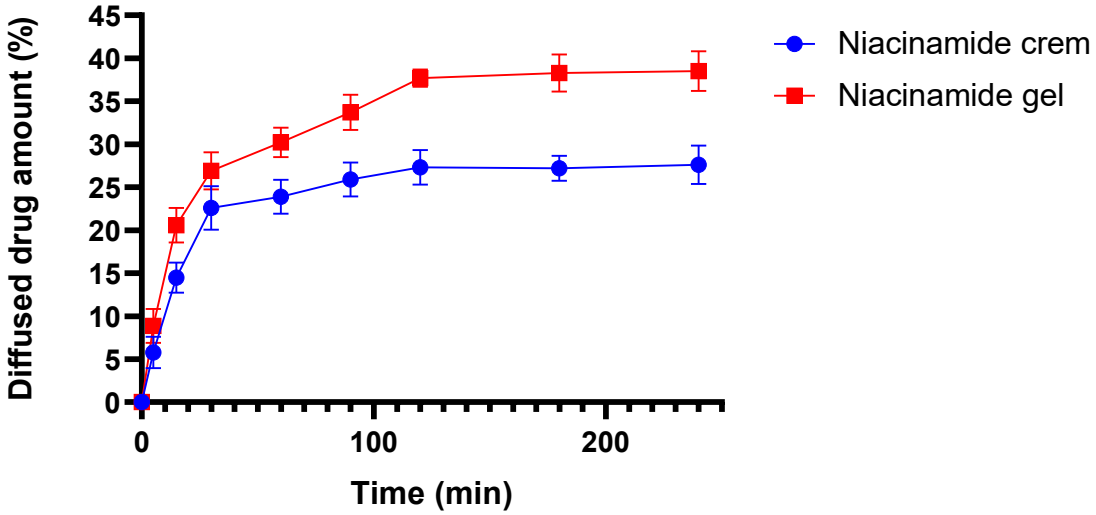

Figure 3.: Results of the in vitro Franz diffusion test. Release profiles of niacinamide across cellulose acetate membrane from the ointment and gel indicating that the gel has higher drug penetration.

4. Discussion

This research aimed to compare the physicochemical properties and performance of niacinamide-containing cream and gel formulations. Through a series of analytical evaluations, including pH measurement, texture analysis, and in vitro release studies, significant differences in formulation characteristics were identified. The results from the analysis of the niacinamide-containing cream and gel formulations provided valuable insights into their chemical properties and potential suitability for topical application. pH measurement is an important indicator for evaluating whether a skincare formulation is compatible with the skin. Human skin typically has a pH range of 4.5 to 5.5, and significant deviations from this range can cause irritation, dryness, or disruption of the skin barrier [19,20]. The pH values of both formulations were within the optimal range, indicating compatibility and a low risk of irritation or disruption to the skin microbiome. The slight pH difference between the two formulations is minimal and does not affect their dermatological compatibility, it may be attributed to variations in ingredient composition or concentration. Texture analysis is an essential test used to evaluate the physical properties of formulations, including firmness, spreadability, and elasticity, which directly influence product performance and user experience [21]. The texture of a skincare product plays a crucial role in its application characteristics and absorption rate. Texture analysis revealed that the cream showed higher compression force compared to the gel, suggesting a more viscous consistency that may provide a richer and more moisturizing application. In contrast, the gel demonstrated a lower compression force, indicating a lighter texture with greater spreadability and faster absorption. These characteristics align with the typical behavior of emulsions versus gel-based formulations. Consequently, the cream may be more suitable for individuals with dry skin due to its hydrating properties, while the gel formulation may be preferable for those with oily or acne-prone skin because of its lighter feel and quicker absorption. The MTT assay results showed that both formulations exhibite high cell viability comparable to the PBS control group, indicating that they are non-cytotoxic and safe for topical use. These results suggest that the ingredients, including niacinamide, do not induce cell damage at the tested concentrations. Results of the Franz diffusion test demonstrated that the gel formulation released a higher percentage of niacinamide over time compared to the cream. This suggests that the gel promotes enhanced drug diffusion and absorption due to its lower viscosity and reduced resistance to penetration. The faster release of niacinamide from the gel could be advantageous for conditions requiring rapid action, such as acne treatment. In contrast, the slower

release from the cream may support prolonged hydration and maintenance of the skin barrier over an extended period. Overall, our findings confirmed that both formulations have distinct advantages depending on the skin type and intended application.

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Data Availability Statement:

All measurement data are available at the corresponding author upon request.

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