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# Formulation and Evaluation of Anti-Acne Transdermal Patches Combining Kojic Acid and Niacinamide

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## Abstract

Acne is a chronic inflammatory condition of the pilosebaceous unit, featuring noninflammatory lesions (comedones) and inflammatory lesions (papules and pustules), often accompanied by seborrhea. Its severity ranges from mild comedonal acne to severe nodular forms, primarily affecting areas rich in hair follicles. Various factors, including medications, environmental influences, and hormonal changes, contribute to its development, complicating treatment which may involve topical, systemic, or surgical approaches. Kojic Acid, derived from fungi, inhibits melanin synthesis and possesses antioxidant, antibacterial, and anti-inflammatory properties. Niacinamide (vitamin B3) enhances skin barrier function and hydration, also exhibiting anti-inflammatory effects. Transdermal patches offer a non-invasive drug delivery method, bypassing first-pass metabolism and ensuring sustained release. Combining Kojic Acid and Niacinamide in such patches could enhance therapeutic efficacy while minimizing side effects and improving patient compliance. This study explores the formulation and evaluation of anti-acne transdermal patches using Kojic Acid and Niacinamide. The patches were prepared by blending Hydroxypropyl methylcellulose (HPMC) with glycerol, Kojic Acid, and Niacinamide, followed by the addition of propylene glycol and Tween 80, ensuring uniform dispersion. The mixture was poured into molds, dried, and evaluated for thickness, folding endurance, drug content, and in vitro drug release. The patches demonstrated uniform thickness, high folding endurance, and substantial drug content, particularly in formulation F7. In vitro diffusion studies confirmed effective drug release profiles, highlighting the potential of Kojic Acid and Niacinamide transdermal patches as a novel, patient-friendly treatment approach for acne management.

**Keywords:** Kojic Acid; Niacinamide; Anti-Acne; Transdermal; Transdermal Patch

## Abbreviations

BCS: Biopharmaceutical Classification System; RPM: Revolutions Per Minute; NCD: Niacinamide; HPMC: Hydroxypropyl Methylcellulose; NAD(H): Nicotinamide Adenine Dinucleotide; NADP(H): Nicotinamide Adenine Dinucleotide Phosphate.

## Introduction

Acne is a chronic inflammatory condition affecting the pilosebaceous unit, characterized by noninflammatory (open and closed comedones) and inflammatory lesions (papules and pustcionules), often accompanied by seborrhea [1]. It varies widely in severity from mild comedonal acne

to severe nodular cystic forms, typically appearing on areas rich in hair follicles like the face, neck, chest, and back. Acne's multifactorial causes include physiological factors, medications (e.g., corticosteroids, anticonvulsants), environmental influences (heat, humidity), and hormonal changes (pregnancy). Its complicate treatment, which may involve topical (retinoids, benzoyl peroxide), systemic (antibiotics, isotretinoin), or surgical approaches [2-4].

Kojic Acid, derived from fungi like Aspergillus, inhibits tyrosinase to reduce melanin synthesis. Discovered in 1907, it chelates copper at tyrosinase's active site and scavenges free radicals, contributing to its depigmenting, antioxidant, antibacterial, and anti-inflammatory properties. It is commonly used in cosmetics and combined with agents like arbutin. Kojic Acid is also used in the food industry to prevent browning. Despite extensive research, its exact mechanisms remain not fully understood [5].

Niacinamide, a form of vitamin B3, supports skin health as a precursor to NAD(H) and NADP(H) co-factors, essential for cellular metabolism. It aids in synthesizing ceramides and fatty acids, enhancing the skin barrier and reducing water loss. Niacinamide possesses anti-inflammatory properties that contribute to the improvement of rosacea and acne. By inhibiting the production of glycosaminoglycans, it reduces inflammation. Additionally, niacinamide fortifies the skin's protective barrier and enhances its hydration levels. Overall, niacinamide promotes healthy skin function and appearance through multiple mechanisms. Transdermal patches offer a non-invasive drug delivery route, bypassing first-pass metabolism and gastrointestinal degradation, ensuring sustained drug release and stable plasma concentrations. Integrating Kojic Acid and Niacinamide into such patches could optimize therapeutic efficacy while minimizing systemic side effects, enhancing patient compliance through prolonged, targeted treatment [6].

In conclusion, combining Kojic Acid and Niacinamide in a transdermal patch formulation represents a promising strategy for managing acne. This approach leverages their complementary mechanisms-depigmentation, anti-inflammatory, and barrier enhancement-to address the multifaceted nature of acne effectively. Such innovations highlight the potential of transdermal systems in dermatological therapy, offering a novel, patient-friendly treatment option.

## Materials and Methodology

### Materials

Kojic Acid was obtained from Sigma Enrich, Niacinamide from Himedia Laboratories Pvt. Ltd., HPMC polymer from Otto Chemie Pvt. Ltd., Glycerol (humectant) from S d fine-chem Limited, Mumbai, Tween 80 (humectant) from Himedia Laboratories Pvt. Ltd. and Propylene glycol from Loba Chemie Pvt. Ltd.

### Methodology

**Preparation of Patch:** The preparation of the transdermal patches followed a meticulous process starting with the homogeneous blending of Hydroxypropyl methylcellulose (HPMC) and glycerol. Subsequently, Kojic Acid and Niacinamide, previously dissolved in water, were added and thoroughly mixed to achieve even dispersion. Propylene glycol and Tween 80 were then sequentially incorporated into the mixture, with continuous stirring using a magnetic stirrer to ensure uniformity. Gradual addition of water adjusted the formulation's volume and maintained its consistency. Once a uniform mixture was attained, it was carefully poured into molds and left to evaporate at room temperature for 24 hours, promoting solidification. Noteworthy precautions were observed throughout the process due to Kojic Acid's photosensitivity. The entire procedure took place in a darkened environment using amber-colored equipment, and during drying, molds were shielded with aluminum foil to preserve the stability and efficacy of the active ingredients by minimizing exposure to light.

**Design of Anti-Acne Patch Formulation of Kojic Acid and Niacinamide:** Formulation of patches were casted using different concentration HPMC, Proylene glycol and glycerol.

| Materials | F1 | F2 | F3 | F4 | F5 | F6 | F7 |
|---|---|---|---|---|---|---|---|
| **Kojic Acid (mg)** | 250 | 250 | 250 | 250 | 250 | 250 | 250 |
| **Niacinamide (mg)** | 250 | 250 | 250 | 250 | 250 | 250 | 250 |
| **HPMC (mg)** | 142 | 142 | 142 | 150 | 150 | 150 | 157 |
| **Propylene glycol (ml)** | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| **Glycerol (ml)** | 0.4 | 0.7 | 1.05 | 0.45 | 0.7 | 1.05 | 0.45 |
| **Tween 80 (ml)** | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| **Water (ml)** | Q.s | Q.s | Q.s | Q.s | Q.s | Q.s | Q.s |

**Table 1:** Design of Anti-Acne Patch Formulation of Kojic Acid and Niacinamide.

**Preformulation Studies**

**Melting Point:** Melting point was carried out with thiele's tube.

**Wavelength Determination:**

**Preparation of Stock Solution of Kojic Acid in Buffer pH 6.8:** A stock solution of kojic acid was prepared by dissolving 100 mg of kojic acid in the required quantity of buffer (pH 6.8) in a 100 mL volumetric flask. The volume was then made up to 100 mL using the same buffer (Stock Solution A). From Stock Solution A, 1 mL was withdrawn and transferred to a 10 mL volumetric flask, and the volume was made up to 10 mL using the buffer (pH 6.8) to prepare Stock Solution B. From Stock Solution B, dilutions of 0.2 mL, 0.4 mL, 0.6 mL, 0.8 mL, and 1 mL were made, and the absorbance of these dilutions was measured at 216 nm [7].

**Preparation of Stock Solution of Niacinamide in Buffer pH 6.8:** A stock solution of niacinamide was prepared by dissolving 100 mg of niacinamide in the required quantity of buffer (pH 6.8) in a 100 mL volumetric flask. The volume was then made up to 100 mL using the same buffer (Stock Solution A). From Stock Solution A, 1 mL was withdrawn and transferred to a 10 mL volumetric flask, and the volume was made up to 10 mL using the buffer (pH 6.8) to prepare Stock Solution B. From Stock Solution B, dilutions of 0.2 mL, 0.4 mL, 0.6 mL, 0.8 mL, 1 mL, 1.2 mL, 1.4 mL, and 1.6 mL were made, and the absorbance of these dilutions was measured at 262 nm [8].

**Thickness:** The thickness of the patch was assessed using a vernier caliper at different points on each formulated patch. Three randomly selected patches from each formulation were used, and the average thickness of a single patch was determined [9].

**Folding Endurance:** Folding endurance is defined as the number of folds required to break any polymeric patch. This test was carried out to check the efficiency of the plasticizer and the strength of the patch. Folding endurance was determined by repeatedly folding the patch at the same location until it broke.

**Drug Content:** A particular patch was dissolved in 100 ml of solvent and shaken continuously until it was completely dissolved. After that, the drug content was determined spectrophotometrically [10].

***In Vitro* Diffusion Study:** The Franz diffusion cell was used to conduct in-vitro diffusion research. The prepared patch was placed on a cellophane membrane and set atop a Franz diffusion cell containing buffer 6.8. The entire assembly was fixed to a magnetic stirrer and swirled constantly at 50 rpm using magnetic beads to maintain the temperature at 32.05°C. Samples were taken at various times and analyzed spectrophotometrically for drug release [11].

## Results and Discussion

### Pre Formulation Studies

**Melting Point Determination**:

**Determination of Melting Point of Kojic Acid:** The melting point of Kojic Acid was found to be 152°C.

**Determination of Melting Point of Niacinamide:** The melting point of Niacinamide was found to be 128°C.

**Determination of Wavelength Maxima (λmax) of Kojic Acid:** The wavelength maxima (λmax) of Kojic Acid were found to be 216 nm.

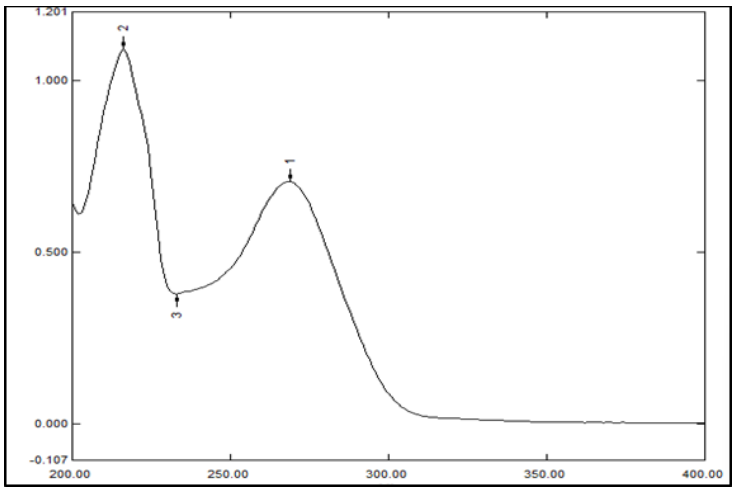


**Figure 1:** Wavelength maxima (λmax) of drug Kojic Acid.

| Concentration | Mean absorbance |
|---|---|
| 0 | 0 |
| 0.2 | 0.219 |
| 0.4 | 0.407 |
| 0.6 | 0.605 |
| 0.8 | 0.811 |
| 1 | 0.989 |

**Table 2:** Mean absorbance of Kojic Acid for different concentration.

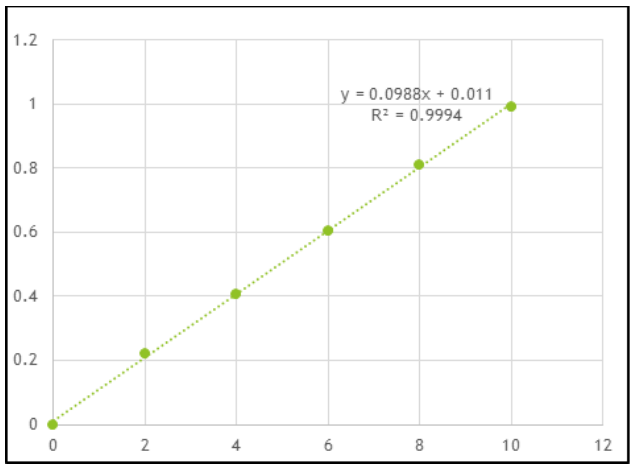


**Figure 2:** Graph showing Calibration curve for Kojic Acid.

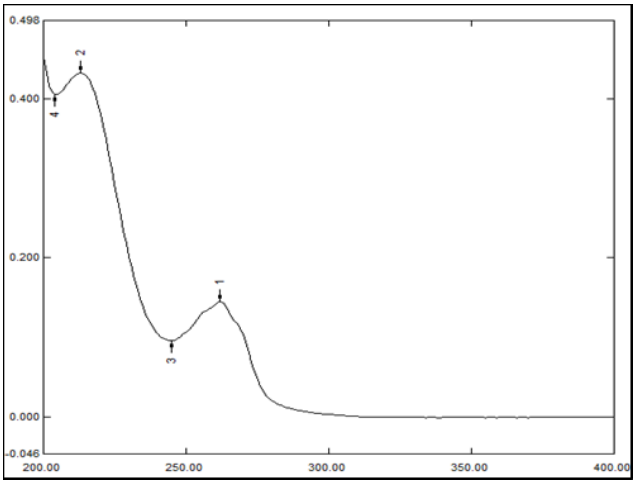


**Figure 3:** Wavelength maxima (λmax) of Niacinamide Calibration curve for Niacinamide.

| Concentration | Mean absorbance |
|---|---|
| 0 | 0 |
| 0.2 | 0.125 |
| 0.4 | 0.21 |
| 0.6 | 0.345 |
| 0.8 | 0.45 |
| 1 | 0.55 |
| 1.2 | 0.655 |
| 1.4 | 0.798 |
| 1.6 | 0.897 |

**Table 3:** Mean absorbance of Niacinamide for different concentration.

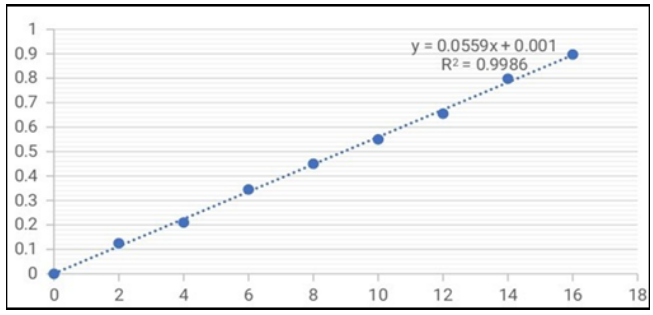


**Figure 4:** Graph showing calibration curve for Niacinamide.

## Result and Discussion of Evaluation Parameters of Patch

**Thickness:** The results given below in Table 4 showed that patches were uniform as it was evidenced by standard value which falls in the range of 0.01 for all factorial design patches.

| Formulation | Thickness(cm) |
|---|---|
| F1 | 0.01 |
| F2 | 0.01 |
| F3 | 0.01 |
| F4 | 0.01 |
| F5 | 0.01 |
| F6 | 0.01 |
| F7 | 0.01 |

**Table 4:** Thickness of Each Patch.

**Folding Endurance:** The results given below in Table 5 shows the folding endurance of each patch which was found to greater than 300 which proved that the prepared transdermal Patches were flexible enough, able to withstand mechanical pressure.

| Formulation | Folding endurance |
|---|---|
| F1 | 620 |
| F2 | 625 |
| F3 | 715 |
| F4 | 750 |
| F5 | 647 |
| F6 | 720 |
| F7 | 765 |

**Table 5:** Folding Endurance of Each Patch.

**Drug Content:** The results given below shows the drug content of Kojic Acid and Niacinamide in each patch. By optimization we can say that F7 has more percentage of drug content in both buffer and blank solution as compare to other formulation.

| Formulations | Drug content of Kojic Acid (%) | Drug content of Niacinamide (%) |
|---|---|---|
| F1 | 20.98 | 16.19 |
| F2 | 75.31 | 52.14 |
| F3 | 64.9 | 50.26 |
| F4 | 61.84 | 45.15 |
| F5 | 70.67 | 55.46 |
| F6 | 88.83 | 69.34 |
| F7 | 90.55 | 71.04 |

**Table 6:** Drug content of Kojic Acid and Niacinamide of each formulation done with 6.8 buffer solution.

| Formulations | Drug content of Kojic Acid (%) | Drug content of Niacinamide (%) |
|---|---|---|
| F1 | 57.42 | 46.25 |
| F2 | 31.11 | 27.97 |
| F3 | 21.34 | 20.36 |
| F4 | 52.39 | 26.01 |
| F5 | 44.66 | 37.91 |
| F6 | 50.55 | 43.19 |
| F7 | 95.33 | 77.66 |

**Table 7:** Drug content of Kojic Acid and Niacinamide of each formulation done with blank solution.

**(%) *In Vitro* Drug Release Profile:** The *in vitro* release of kojic acid and niacinamide was carried out, with kojic acid showing a 62.2% release and niacianamide showing a 48.06% release.

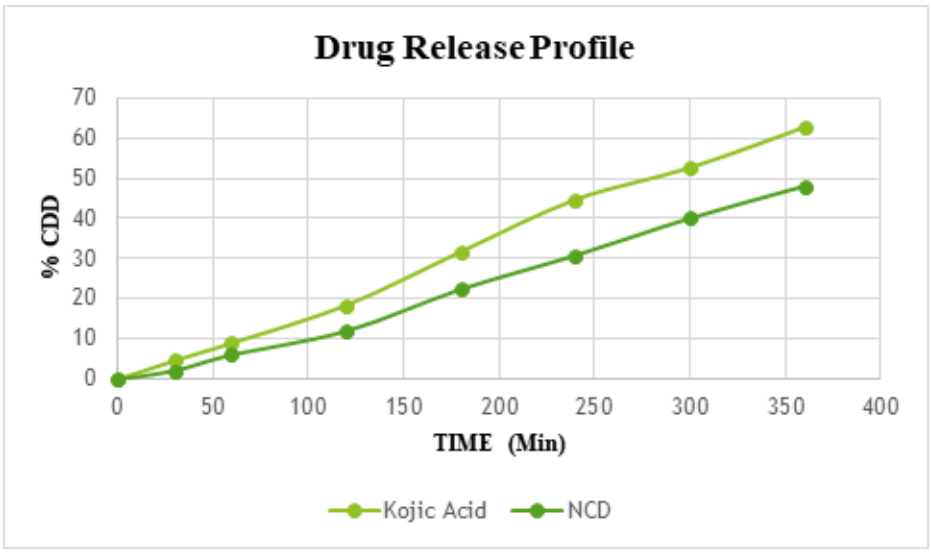


**Figure 5:** Graph showing drug release profile of Kojic Acid and Niacinamide.

## Conclusion

This study demonstrates that combining Kojic Acid and Niacinamide in transdermal patches offers a promising approach for managing acne. The formulation effectively utilizes the complementary properties of these agents-Kojic Acid's depigmenting and antioxidant effects, and Niacinamide's barrier-enhancing and anti-inflammatory benefits. The patches exhibited consistent quality, including uniform thickness and substantial drug content, with formulation F7 showing the most promising results. In vitro diffusion studies confirmed the patches' ability to release the drugs effectively, suggesting that this transdermal system can provide sustained therapeutic effects. This novel delivery method not only enhances drug efficacy but also reduces systemic side effects, potentially improving patient compliance and outcomes in acne treatment.

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