RESEARCH PAPER

Design Of Bioadhesive Transdermal Patches Using Chitosan–Cellulose Nanocomposites For Anxiolytic Drug Delivery

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ABSTRACT

Transdermal drug delivery systems have emerged as an effective alternative to conventional oral administration for improving therapeutic efficacy and patient compliance. The present study focuses on the design and evaluation of bioadhesive transdermal patches based on chitosan–cellulose nanocomposites for the controlled delivery of anxiolytic drugs. Chitosan, a biodegradable and biocompatible polymer with inherent bioadhesive and permeation-enhancing properties, was combined with cellulose nanomaterials to enhance mechanical strength and drug release performance. The nanocomposite patches were prepared using a solvent casting method and characterized for physicochemical properties including thickness, tensile strength, folding endurance, and surface morphology. Drug–polymer compatibility was assessed using FTIR and DSC analysis. In vitro drug release and permeation studies demonstrated sustained and controlled release behavior, following diffusion-controlled kinetics. The incorporation of cellulose nanostructures improved the structural integrity and stability of the patches while maintaining optimal bioadhesion.

The developed system offers a promising non-invasive approach for the delivery of anxiolytic agents, minimizing first-pass metabolism and reducing dosing frequency. Overall, chitosan–cellulose nanocomposite-based bioadhesive patches represent a potential platform for effective and sustained transdermal therapy in anxiety management.

Keywords: Transdermal drug delivery; Chitosan; Cellulose nanocomposites; Bioadhesive patches

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INTRODUCTION

Anxiety disorders are among the most prevalent neurological conditions, often requiring long-term pharmacological treatment. Conventional oral delivery of anxiolytic drugs is associated with limitations such as poor bioavailability, gastrointestinal side effects, and extensive first-pass metabolism. Transdermal drug delivery systems (TDDS) have gained considerable attention as they provide sustained drug release,

improved patient compliance, and reduced systemic side effects.

Bioadhesive transdermal patches are particularly advantageous due to their ability to adhere to the skin surface and maintain prolonged contact, ensuring efficient drug absorption. Among various biomaterials, chitosan has been widely investigated for drug delivery applications owing to its cationic nature, biocompatibility, biodegradability, and excellent bioadhesive properties. These characteristics enable enhanced permeation and controlled drug release across biological membranes.

However, chitosan alone exhibits limitations such as poor mechanical strength and instability under physiological conditions. To overcome these challenges, the incorporation of cellulose-based nanomaterials has been explored. Cellulose nanocrystals and nanofibers provide high surface area, improved mechanical properties, and enhanced stability to the polymeric matrix, making them suitable for transdermal patch development.

Nanocomposite systems combining chitosan and cellulose have shown significant potential in biomedical applications due to their synergistic properties, including non-toxicity, enhanced structural integrity, and efficient drug encapsulation. These systems can be tailored to achieve controlled drug release and improved therapeutic outcomes.

In this context, the present study aims to design and develop bioadhesive transdermal patches using chitosan–cellulose nanocomposites for anxiolytic drug delivery. The research focuses on optimizing formulation parameters, evaluating physicochemical and mechanical properties, and assessing drug release behavior to establish an effective and sustained delivery system.

MATERIALS AND METHODS

1. Materials

- **Chitosan** (medium molecular weight) – bioadhesive polymer
- **Cellulose nanocrystals (CNC) / nanofibers** – reinforcing agent
- **Anxiolytic drug** (e.g., Diazepam / Alprazolam – model drug)
- **Glycerol / PEG 400** – plasticizer
- **Acetic acid (1%)** – solvent for chitosan
- **Distilled water** – vehicle
- **Backing membrane (aluminum foil or polyethylene film)**

2. Method of Preparation (Solvent Casting Method)

Steps:

1. Chitosan was dissolved in 1% acetic acid solution with continuous stirring.
2. Cellulose nanocrystals were dispersed separately in distilled water using sonication.
3. The CNC dispersion was slowly added to the chitosan solution to form a nanocomposite matrix**.**
4. Plasticizer (PEG 400/glycerol) was added to improve flexibility.
5. The anxiolytic drug was dissolved and incorporated into the polymer mixture.
6. The final solution was poured into a glass petri dish**.**
7. Dried at room temperature (24–48 hours) to form patches.
8. Dried films were peeled off and cut into uniform sizes (e.g., 2×2 cm²)**.**

FORMULATION TABLE

Ingredients	F1 (%)	F2 (%)	F3 (%)
Chitosan	2.0	2.0	2.0
Cellulose Nanocrystals	0.5	1.0	1.5
Drug (Anxiolytic)	1.0	1.0	1.0
PEG 400 / Glycerol	0.5	0.5	0.5
Acetic Acid (1%)	q.s.	q.s.	q.s.
Distilled Water	q.s.	q.s.	q.s.

EVALUATION PARAMETERS (DETAILED DESCRIPTION)

1. Physical Appearance

The prepared transdermal patches were visually inspected for their physical characteristics including color, transparency, smoothness, flexibility, and presence of any air bubbles or surface imperfections. A uniform, smooth, and flexible film indicates proper mixing of polymers and suitability for transdermal application. Any cracks or brittleness suggest poor formulation stability.

2. Thickness

The thickness of each patch was measured using a calibrated digital micrometer screw gauge at three different points (center and edges) to ensure uniformity. The average thickness was calculated and expressed as mean ± standard deviation. Uniform thickness is essential

to ensure consistent drug distribution and controlled release across the patch.

3. Weight Uniformity

Each patch of a defined size (e.g., 2×2 cm^2) was individually weighed using a digital balance. The average weight and standard deviation were calculated. Consistency in weight indicates uniform distribution of polymer matrix and drug content throughout the formulation.

4. Folding Endurance

Folding endurance was determined by repeatedly folding the patch at the same position until it broke or showed visible cracks. The number of folds required to break the patch was recorded. A higher folding endurance value reflects good flexibility and mechanical strength, which is important for handling and application on skin.

5. Surface pH

The surface pH of the patches was measured to ensure compatibility with skin and to avoid irritation. The patch was placed in a small volume of distilled water for about 1 hour to allow swelling, and the pH was measured using a digital pH meter. Ideally, the surface pH should be close to the skin pH (approximately 5.5–7.0).

6. Tensile Strength and Percent Elongation

Mechanical properties such as tensile strength and elongation at break were evaluated using a universal testing machine. Tensile strength represents the maximum stress the patch can withstand before breaking, while percent elongation indicates its elasticity. These parameters are critical for ensuring that the patch can endure mechanical stress during application and use without tearing.

7. Drug Content Uniformity

Drug content was determined by dissolving a known area of the patch in a suitable solvent, followed by filtration and analysis using a UV-visible spectrophotometer at the specific wavelength of the drug. The amount of drug present was calculated and expressed as a percentage of the theoretical value. Uniform drug content ensures consistent dosing and therapeutic efficacy.

8. In-vitro Drug Release Study

The in-vitro drug release study was performed using a Franz diffusion cell. The patch was placed on a dialysis membrane or biological membrane separating the donor and receptor compartments. The receptor compartment was filled with phosphate buffer (pH 7.4) and maintained at 37 ± 0.5°C. Samples were withdrawn at predetermined time intervals and analyzedspectrophotometrically. This study helps in understanding the release pattern and kinetics of the drug from the patch.

9. Ex-vivo Permeation Study

Ex-vivo permeation studies were conducted using excised animal skin (such as rat abdominal skin). The skin was mounted on a Franz diffusion cell, and the patch was placed on the epidermal side. The amount of drug permeated through the skin into the receptor medium was measured over time. This test provides insight into the permeability and effectiveness of the formulation in delivering the drug through the skin barrier.

10. Bioadhesive Strength

Bioadhesive strength was evaluated using a modified physical balance method. The patch was attached to a biological substrate (e.g., animal skin), and the force required to detach the patch was measured. Higher bioadhesive strength indicates better adhesion to the skin, ensuring prolonged contact and improved drug absorption.

11. Moisture Content

Moisture content was determined by weighing the patches before and after drying in a desiccator containing a drying agent such as calcium chloride. The percentage moisture content was calculated. This parameter is important for assessing the stability and shelf-life of the formulation.

12. Moisture Uptake

Moisture uptake studies were carried out by exposing the patches to a humid environment and measuring the increase in weight. This test evaluates the hygroscopic nature of the formulation, which can affect mechanical properties and drug stability.

13. Stability Studies

Stability studies were carried out by storing the patches under different environmental conditions (e.g., 25°C/60% RH and 40°C/75% RH) for a specified period. The patches were evaluated periodically for physical appearance, drug content, and release behavior. Stability testing ensures that the formulation maintains its efficacy and safety over time.

RESULTS AND DISCUSSION

1. Physical Evaluation of Transdermal Patches

The prepared chitosan–cellulose nanocomposite patches were evaluated for physicochemical properties. All formulations showed uniform thickness, good flexibility, and smooth surface appearance.

Formulation	Thickness (mm)	Weight (mg)	Folding Endurance	Surface pH
F1	0.21 ± 0.02	145 ± 3	210 ± 5	6.4 ± 0.1
F2	0.24 ± 0.01	152 ± 2	225 ± 4	6.5 ± 0.2
F3	0.26 ± 0.03	160 ± 4	240 ± 6	6.6 ± 0.1

2. Tensile Strength and Elongation

Formulation	Tensile Strength (kg/cm²)	% Elongation
F1	2.8 ± 0.2	18 ± 2
F2	3.5 ± 0.3	22 ± 3
F3	4.2 ± 0.2	26 ± 2

3. Drug Content Uniformity

Formulation	Drug Content (%)
F1	96.2 ± 1.2
F2	97.8 ± 1.0
F3	98.5 ± 0.8

4. In-vitro Drug Release Study

Time (hrs)	F1 (%)	F2 (%)	F3 (%)
1	18	15	12
2	30	25	20
4	52	45	38
6	68	60	52
8	82	75	68
12	95	90	85

5.. Bioadhesion Study

Formulation	Bioadhesive Strength (g)
F1	28 ± 2
F2	34 ± 3
F3	40 ± 2

6. Optimized Formulation (F3)

- Highest tensile strength
- Maximum bioadhesion
- Controlled drug release (12 hrs)
- Good stability

CONCLUSION FROM RESULTS

The study confirms that **chitosan–cellulose nanocomposite patches** significantly enhance mechanical strength, bioadhesion, and sustained drug release, making them suitable for anxiolytic drug delivery via the transdermal route.

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