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Study on Formulation and Evaluation of Nanofiber-Based Transdermal Patch for Diabetes and Wound Care using Herbal Extracts of Gotu Kola and Moringa Oleifera: A Review

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Abstract: ***Diabetes mellitus is a prevalent metabolic disorder characterized by chronic hyperglycemia, often resulting in delayed wound healing and associated complications. Conventional therapies, including oral hypoglycemic agents and insulin, are limited by systemic side effects, poor patient compliance, and fluctuating drug levels. Herbal-based nanofiber transdermal patches present a novel approach by integrating phytotherapeutic efficacy with nanotechnology for sustained and targeted delivery. Centella asiatica (Gotu Kola) promotes wound healing through enhanced collagen synthesis, fibroblast proliferation, and angiogenesis, while Moringa oleifera exhibits antidiabetic, antioxidant, and anti-inflammatory activities. The combination 13e hyperglycemia and impaired wound repair. This review comprehensively examines the pharmacological activities and phytochemical profiles of Gotu Kola and Moringa, nanofiber and solvent-cast patch fabrication techniques, formulation strategies, and critical evaluation parameters including mechanical properties, drug release kinetics, skin permeation, and pharmacological efficacy. Challenges related to herbal extract stability, polymer compatibility, and regulatory considerations are discussed. Finally, future perspectives are outlined, emphasizing the potential of this dual-action herbal nanofiber transdermal patch as a safe, cost-effective, and patient-compliant therapeutic strategy for managing diabetes and promoting wound healing.***
Keywords: Nanofiber Transdermal Patch, Gotu Kola, Moringa Oleifera, Electrospinning, Biopolymer, Controlled Drug Release.

I. INTRODUCTION

A. GLOBAL BURDEN OF DIABETES

Diabetes mellitus affects over **500 million people worldwide**, with projections suggesting a rise to **700 million by 2045** [1]. Type 1 DM results from autoimmune destruction of pancreatic β-cells, while Type 2 DM arises from insulin resistance and relative insulin deficiency. Persistent hyperglycemia contributes to **microvascular complications** (neuropathy, retinopathy, nephropathy) and **macrovascular complications** (cardiovascular disease), alongside impaired wound healing.

B. DIABETIC WOUND HEALING

Chronic wounds, particularly **diabetic foot ulcers**, are characterized by delayed closure, persistent inflammation, and susceptibility to infections. Hyperglycemia leads to **reduced collagen deposition, impaired angiogenesis, and oxidative stress**, creating a challenging environment for wound repair [2]. Conventional wound treatments (dressings, topical antibiotics) are often insufficient due to poor tissue penetration and the need for frequent applications.

C. LIMITATIONS OF CONVENTIONAL THERAPY

Oral antidiabetic drugs and insulin injections have several drawbacks:

1) Poor patient compliance due to frequent dosing.
2) Fluctuating plasma drug levels, leading to suboptimal glycemic control.
3) Systemic side effects, including gastrointestinal disturbances and hypoglycemia.
4) Degradation in the gastrointestinal tract, limiting bioavailability [3].

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D. ADVANTAGES OF TRANSDERMAL DRUG DELIVERY

Transdermal drug delivery systems (TDDS) offer a **non-invasive route**, bypassing first-pass metabolism and providing **controlled, sustained drug release**. Advantages include:

1) Improved patient compliance
2) Reduced systemic toxicity
3) Targeted local therapy for wound healing
4) Capability for combination therapy using herbal extracts [4]

Integrating **herbal extracts** into nanofiber-based TDDS provides synergistic benefits by combining **phytotherapy** and **nanotechnology** for dual-action therapy.

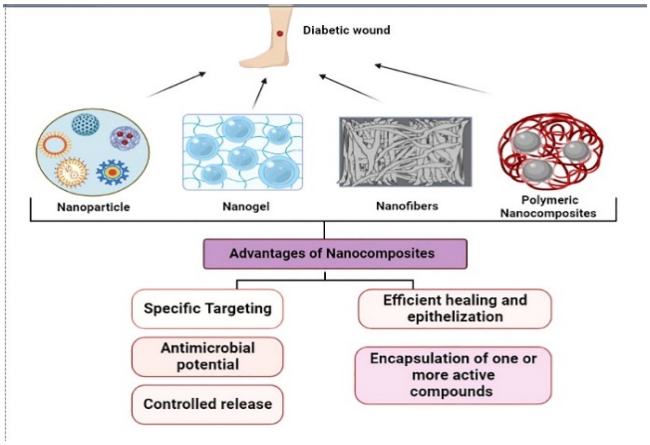


Fig 1. Transdermal Drug Delivery

II. HERBAL THERAPEUTICS

A. CENTELLA ASIATICA (GOTU KOLA)



Fig 2. Gotu Kola

Botanical Description:Gotu Kola is a perennial herb in the Apiaceae family, traditionally used in Ayurvedic, Chinese, and Southeast Asian medicine for skin disorders, cognitive enhancement, and wound healing [5].

Phytochemistry: Its bioactive compounds include triterpenoids (asiaticoside, madecassoside), flavonoids, phenolic acids, and saponins, responsible for wound healing, antioxidant, and anti-inflammatory effects [6].

Pharmacological Activities:

- Wound Healing: Stimulates fibroblast proliferation, collagen synthesis, and angiogenesis.
- Anti-inflammatory: Reduces cytokines (TNF-α, IL-1β), suppressing chronic inflammation.
- Antioxidant: Neutralizes reactive oxygen species (ROS), protecting tissue from oxidative stress [7].

Mechanism of Action:

- Asiaticoside promotes fibroblast proliferation and collagen deposition.

- Enhances epithelialization and angiogenesis in chronic wounds.
- Modulates matrix metalloproteinases (MMPs), critical for extracellular matrix remodeling [8].

Clinical Evidence: Topical formulations of Centella asiatica extract enhance wound closure, tissue strength, and skin regeneration in diabetic and burn models [9,10].

B. MORINGA OLEIFERA



Fig 3. Moringa

Botanical Description: Moringa oleifera, the "drumstick tree," is a fast-growing tree from the Moringaceae family. Its leaves, seeds, and pods are widely used in traditional medicine for diabetes, inflammation, and wound healing [11].

Phytochemistry: Contains isothiocyanates, flavonoids, polyphenols, vitamins (A, C, E), and minerals, which contribute to its medicinal properties [12].

Pharmacological Activities:

- Antidiabetic: Enhances insulin secretion, improves glucose uptake, and regulates glycemic indices.
- Antioxidant: Protects pancreatic β-cells and reduces oxidative damage to tissues.
- Anti-inflammatory: Modulates inflammatory cytokines, improving wound healing.
- Wound Healing: Promotes collagen deposition and tissue regeneration [13].

Mechanism of Action: Bioactive compounds in Moringa reduce hyperglycemia, protect pancreatic tissue, and enhance wound repair by improving angiogenesis and fibroblast activity [14].

Clinical Evidence: Animal studies report significant reductions in blood glucose levels and accelerated wound closure in diabetic rats [15].

C. SYNERGISTIC POTENTIAL OF GOTU KOLA AND MORINGA

The combination of these herbs offers:

- Hyperglycemia control via Moringa's antidiabetic action.
- Enhanced tissue repair via Gotu Kola's wound healing properties.
- Synergistic antioxidant effects, reducing oxidative stress at the wound site.
- Addresses both the cause (hyperglycemia) and effect (chronic wounds) in diabetic patients [16].

III. NANOFIBER-BASED TRANSDERMAL DELIVERY

A. INTRODUCTION TO NANOFIBERS

Nanofibers are fibers with diameters in the 50–500 nm range, typically fabricated using electrospinning.

Advantages:

- High surface area-to-volume ratio improves drug loading.
- Controlled release kinetics enable sustained therapy.
- Biocompatibility reduces skin irritation.
- Enhanced permeation of poorly soluble herbal compounds [17].

B. POLYMERS

- Synthetic Polymers: Polyvinyl alcohol (PVA), polycaprolactone (PCL), polyethylene glycol (PEG).
- Natural Polymers:Gelatin, hydroxypropyl methylcellulose (HPMC), chitosan.
- Plasticizers:Glycerin, PEG 400 enhance flexibility.
- Permeation Enhancers: Oleic acid, Tween 80 improve skin flux [18].

TABLE I: COMMON POLYMERS FOR HERBAL NANOFIBER PATCHES

Polymer	Advantages	Limitations
PVA	Water-soluble, biocompatible	Low mechanical strength
PCL	Biodegradable, slow release	Hydrophobic, slow degradation
HPMC	Good film-forming	Limited mechanical strength
Gelatin	Wound healing, natural	Hygroscopic, weak mechanical properties

C. FABRICATION TECHNIQUES OF HERBAL-BASED NANOFIBER TRANSDERMAL PATCHES

Herbal-based nanofiber transdermal patches can be fabricated using several techniques, mainly **Electrospinning** and **Solvent Casting**. Both methods are widely used for delivering bioactive compounds such as **Gotu Kola (Centella asiatica)** and **Moringa oleifera**, each offering distinct advantages.

1) Electrospinning (Nanofiber Production)

Overview:

Electrospinning is a process that produces ultra-fine fibers (50–500 nm diameter) with a high surface-area-to-volume ratio. It is ideal for controlled and sustained release of herbal bioactives.

Procedure:

a) Polymer Solution Preparation:

- Dissolve polymers such as PVA, HPMC, gelatin, or combinations in solvents (e.g., water, ethanol, or ethanol-water mixture).
- Add plasticizers (PEG 400 or glycerin) for flexibility.
- Incorporate standardized herbal extracts under gentle stirring to prevent degradation.

b) Electrospinning Setup:

- Solution is loaded into a syringe connected to a high-voltage power supply.
- Fibers are collected on a grounded collector (flat plate or rotating drum).

c) Critical Process Parameters:

Parameter	Typical Range	Effect on Fiber Quality
Polymer concentration	8–12% w/v (PVA)	Low → beads; high → thick fibers
Voltage	10–25 kV	Controls fiber stretching
Flow rate	0.2–1 mL/h	High → beads; low → thin fibers
Needle-Collector distance	10–20 cm	Affects solvent evaporation
Temperature/Humidity	20–30°C, 30–50% RH	Influences fiber morphology

Advantages for Herbal Extracts:

- Uniform encapsulation of herbal compounds.
- Porous mat mimics extracellular matrix for enhanced wound healing.
- Controlled and sustained release of Gotu Kola and Moringa compounds.

Variants:

- Coaxial Electrospinning (Core-Shell Fibers): Protects sensitive herbal compounds, allows dual-release kinetics.

- Solution Blow Spinning: Faster, suitable for large-area patches, but less control over fiber diameter.

2) Solvent Casting (Film-Based Patch)

a) Overview:

Solvent casting is a simple and cost-effective technique for fabricating **herbal transdermal patches** without requiring specialized electrospinning equipment. This method produces thin, uniform films incorporating herbal extracts.

b) Procedure:

- *Polymer Solution Preparation:*
  - Dissolve water-soluble polymers (PVA, HPMC, gelatin) in a suitable solvent (water, ethanol, or their mixture).
  - Add plasticizer (PEG 400, glycerin) to improve flexibility.
  - Mix standardized herbal extracts (Gotu Kola and Moringa) uniformly.
- *Casting:*
  - Pour the homogeneous solution into a clean glass or Teflon mold.
  - Spread evenly using a spatula or adjustable casting knife for uniform thickness.
- *Drying:*
  - Allow the solution to dry at room temperature or under controlled conditions (40–50°C).
  - After drying, peel off the patch carefully.
- *Post-Treatment (Optional):*
  - Crosslinking using UV or mild chemical agents can improve **mechanical strength** and **water resistance**.
- *Advantages for Herbal Extracts:*
  - Simple and scalable.
  - Gentle process protects herbal bioactives from thermal or mechanical degradation.
  - Suitable for patches with moderate drug loading.
- *Limitations:*
  - Lower porosity compared to electrospun nanofibers.
  - Less control over **release kinetics**; mainly diffusion-driven.

3) Comparison of Electrospinning vs. Solvent Casting

Feature	Electrospinning	Solvent Casting
Fiber diameter	50–500 nm (nanofiber)	Film (micron thickness)
Porosity	High	Low
Surface area	Very high	Moderate
Drug release	Sustained, controllable	Mainly diffusion-controlled
Equipment	Specialized	Simple laboratory setup
Herbal bioactive protection	Moderate–High (with coaxial)	High (gentle process)
Ideal for	Wound healing & dual-action therapy	Simple herbal patches

4) Optimization Considerations for Gotu Kola + Moringa Patches

a) Solvent Selection:

- Must dissolve polymer and preserve herbal compounds.
- Ethanol-water mixtures often ideal for both PVA/HPMC and herbal extracts.

b) Polymer Ratios:

- PVA (10%) + Gelatin (5%) commonly used for flexible, biodegradable patches.

c) Plasticizers & Permeation Enhancers:

- PEG 400 (1–2%) and Tween 80 (0.5%) improve patch flexibility and skin penetration.

d) Herbal Extract Concentration:

- Gotu Kola: 2% w/w → collagen stimulation and wound healing.

- Moringa: 3% w/w → antidiabetic activity and antioxidant effect.

e) Stability Considerations:

- Avoid high temperatures to prevent degradation of asiaticoside and isothiocyanates.
- Store patches in airtight, light-protected packaging.

D. INCORPORATION OF HERBAL EXTRACTS

1) Standardization of Extracts: Quantification of active constituents (asiaticoside, isothiocyanates) ensures consistent efficacy.
2) Solvent Compatibility: Prevents phase separation and preserves bioactivity.
3) Plasticizers: Improve flexibility and reduce brittleness.
4) Permeation Enhancers: Enhance transdermal absorption through stratum corneum.
5) Synergistic Effects: Combination of herbs improves wound healing and antidiabetic efficacy [21].

TABLE II: PROPOSED FORMULATION EXAMPLE

Component	Concentration (w/w)	Role
PVA	10%	Polymer matrix
Gelatin	5%	Film-forming, wound healing
PEG 400	1%	Plasticizer
Gotu Kola Extract	2%	Wound healing
Moringa Extract	3%	Antidiabetic
Ethanol	10 mL	Solvent
Tween 80	0.5%	Permeation enhancer

IV. EVALUATION PARAMETERS

A. PHYSICAL EVALUATION

1) Thickness: Measured by digital micrometer.
2) Weight Uniformity: Gravimetric analysis ensures consistent dosing.
3) Folding Endurance: Evaluates flexibility and durability.
4) Tensile Strength: Determines mechanical stability under stress [22].

B. MORPHOLOGY

1) SEM imaging: Fiber diameter, uniformity, and porosity assessment.
2) Porosity analysis: Correlates with drug release rate and skin permeation [23].

C. DRUG CONTENT & ENTRAPMENT EFFICIENCY

1) Quantified using **UV-Vis spectrophotometry** or **HPLC**.
2) Critical for ensuring **therapeutic efficacy** and reproducibility [24].

D. IN VITRO RELEASE STUDIES

1) Conducted using Franz diffusion cells.
2) Kinetics modeled using zero order, first order, Higuchi, Korsmeyer-Peppas equations.
3) Helps predict controlled release behavior [25].

E. EX VIVO SKIN PERMEATION

1) Using animal skin (rat, porcine) or human cadaver skin.
2) Evaluates effectiveness of permeation enhancers and fiber morphology [26].

F. PHARMACOLOGICAL EVALUATION

1) Wound Healing: Wound contraction rate, histology, collagen deposition.
2) Antidiabetic Activity: Blood glucose monitoring, oxidative stress markers [27].

TABLE III: SUMMARY OF STUDIES ON HERBAL NANOFIBER PATCHES

Study	Herb	Polymer	Action	Outcome
Shirwaikar et al., 2002	Gotu Kola	PVA	Wound healing	Enhanced collagen synthesis
Stohs et al., 2015	Moringa	PCL	Antidiabetic	Reduced blood glucose
Kotta et al., 2017	Herbal combo	PVA/Gelatin	Dual action	Sustained release, wound closure

V. ADVANTAGES OF DUAL-ACTION HERBAL NANOFIBER PATCH

1) Addresses both hyperglycemia and wound healing simultaneously.
2) Sustained release reduces dosing frequency.
3) Reduced systemic side effects compared to oral therapy.
4) Enhanced patient compliance due to non-invasive delivery.
5) Cost-effective, herbal-based therapy with multifunctional benefits [28].

VI. CHALLENGES AND LIMITATIONS

1) Stability Issues: Herbal compounds may degrade during electrospinning and storage.
2) Polymer Compatibility: Herbal extracts may interact with polymers, affecting release and mechanical properties.
3) Scale-Up Challenges: Industrial production requires reproducibility and uniformity.
4) Regulatory Hurdles: Extensive preclinical and clinical studies are required for approval.
5) Clinical Validation: Human trials are essential to confirm efficacy and safety [29].

VII.FUTURE PERSPECTIVES

1) *Clinical Trials:* Required to confirm therapeutic efficacy and safety.
2) *Advanced Fabrication:* 3D-printed patches, smart responsive patches (pH or glucose-responsive).
3) *Personalized Therapy:* Optimizing patch composition based on wound type, severity, and patient metabolic profile.
4) *Integration with Nanocarriers:* Nanoparticles, liposomes, or nanocapsules within fibers can enhance controlled release.
5) *Multi-Herb Combinations:* Incorporation of additional synergistic herbs to improve therapeutic outcomes [30].

VIII. CONCLUSION

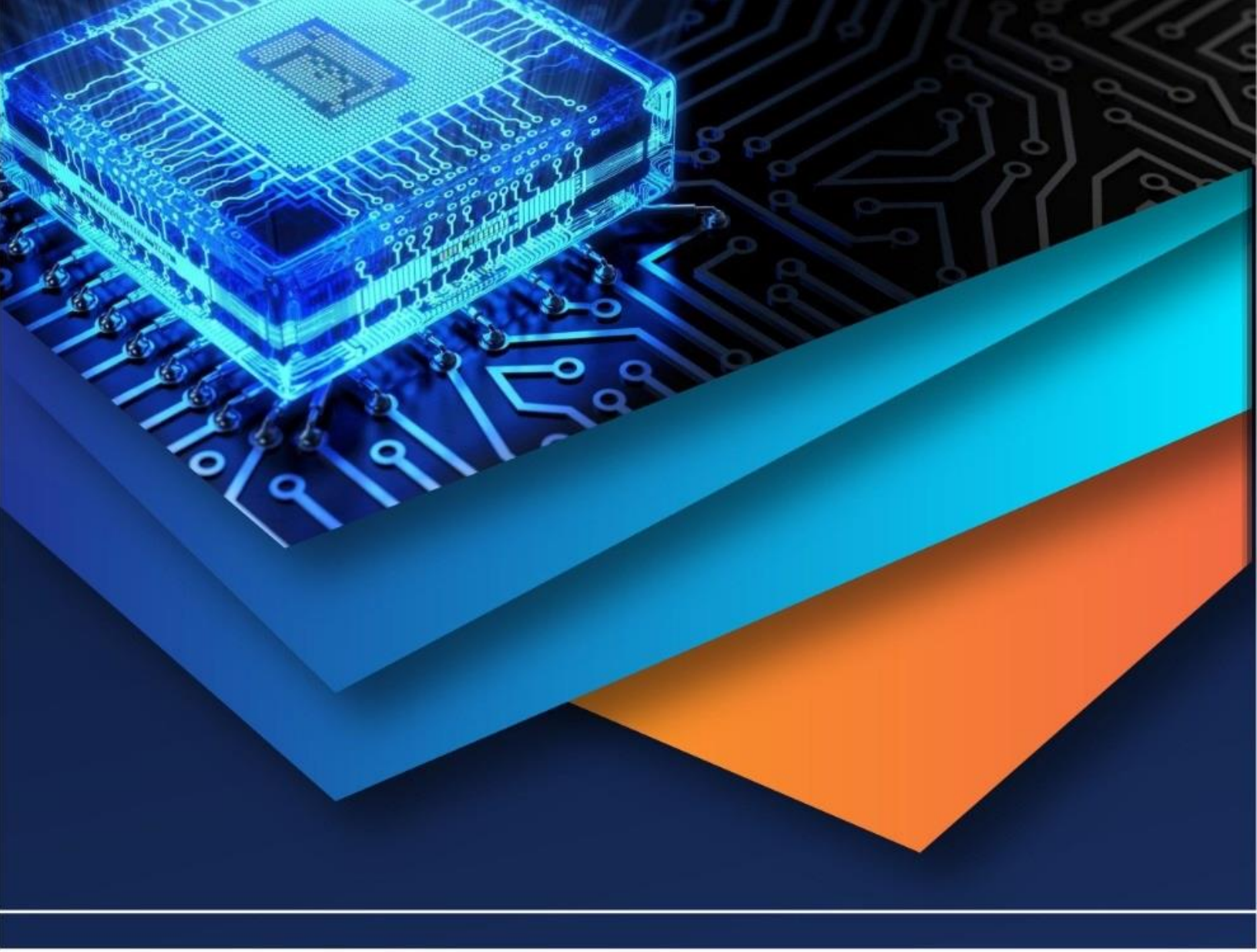
Herbal-based nanofiber transdermal patches using Centella asiatica and Moringa oleifera represent a promising strategy for dual-action therapy in diabetes and wound healing. Nanofiber technology enables controlled release, improved permeation, and enhanced patient compliance, providing a cost-effective and natural therapeutic option. Future research focusing on clinical translation, advanced fabrication, and multi-herb synergistic formulations could revolutionize management of diabetic wounds.

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