INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD)
© 2026 IJNRD | Volume 11, Issue 9, September 2026 | ISSN: 2456-4184 | IJNRD.ORG

Formulation and In Vitro Evaluation of Curcumin-Loaded Polymeric Transdermal Wafers for Diabetic Wound Healing

Mr. Roshankumar G. Satsure., Mr. Abhijit N. Daf., Dr. Prasad P. Jumade.,

Dr. Dinesh S. Wanjari

Agnihotri Institute of Pharmacy, Wardha & Agnihotri College of Pharmacy, Wardha

Corresponding Authors: roshankumarsatsure@gmail.com

Abstract Diabetic foot ulcers and chronic diabetic wounds present severe clinical challenges due to persistent hyperglycemia, elevated oxidative stress, sustained pro-inflammatory signaling, and impaired tissue regeneration. Curcumin (CUR), a natural polyphenolic bioactive derived from *Curcuma longa*, possesses potent antioxidant, anti-inflammatory, and antimicrobial properties; however, its clinical application is constrained by poor aqueous solubility and rapid degradation. This study presents the design, formulation, and in vitro evaluation of curcumin-loaded polymeric transdermal wafers utilizing a hybrid matrix of sodium alginate (SA), hydroxypropyl methylcellulose (HPMC), and carboxymethylcellulose (CMC). Wafers (F1–F5) were formulated with varying polymer ratios and evaluated for weight uniformity, thickness, folding endurance, surface pH, porosity, swelling behavior, drug content, solid-state characteristics (FTIR, DSC, XRD), in vitro release kinetics in simulated wound fluid (SWF, pH 7.4), DPPH radical scavenging, and antimicrobial efficacy against *Staphylococcus aureus* and *Escherichia coli*. Optimized formulation F4 (SA: HPMC: CMC 2:1:1 with 10 mg CUR) exhibited high porosity ($74.2 \pm 2.1\%$), superior swelling capacity ($685 \pm 24\%$), and sustained drug release over 24 hours ($82.4 \pm 3.1\%$). Solid-state analysis confirmed the amorphous dispersion of curcumin within the polymeric matrix with preserved chemical integrity. Kinetic modeling indicated non-Fickian anomalous transport governing drug release. In vitro bio-assays demonstrated potent antioxidant activity ($IC_{50} = 14.2\ \mu$g/mL) and significant bacterial growth inhibition. These results demonstrate that curcumin-loaded polymeric wafers provide an effective local delivery platform for exudate management and accelerated diabetic wound healing.

Keywords: *Curcumin, Polymeric Wafers, Diabetic Wound Healing, Transdermal Delivery, Sustained Release, Hydrogel Dressing.*

1. Introduction

Diabetic wound healing is significantly impaired by a dysregulated inflammatory cascade, persistent oxidative stress, microvascular complications, and susceptibility to bacterial colonization (Alven et al., 2020). Chronic diabetic foot ulcers frequently stall in the inflammatory phase, where overproduction of reactive oxygen species (ROS) and pro-inflammatory cytokines degrade extracellular matrix (ECM) components and impede re-epithelialization. Effective therapeutic management requires topically applied dressings that absorb excess wound exudate, maintain a moist physiological environment, protect against microbial invasion, and continuously deliver active therapeutic molecules to the wound bed (Al Fatease et al., 2022; Sideek *et al*., 2022).

Curcumin (diferuloylmethane) is a natural biopolyphenolic compound recognized for its antioxidant, anti-inflammatory, and broad-spectrum antimicrobial properties (Kumari et al., 2022). Curcumin neutralizes ROS, downregulates pro-inflammatory transcription factors such as NF-κB, and enhances granulation tissue formation and collagen deposition (Kumari et al., 2022; Kumbhar et al., 2023). Despite these therapeutic advantages,

curcumin exhibits low water solubility ($< 0.1\ \mu g/mL$), poor oral bioavailability, and instability at physiological pH, necessitating targeted topical drug delivery systems (Sideek et al., 2022; Zhou et al., 2021).

Polymeric transdermal wafers—porous solid matrices typically produced via freeze-drying or controlled solvent casting—offer substantial structural and biopharmaceutical advantages over conventional creams, ointments, and hydrogels (Al Fatease et al., 2022). When applied to an exudative wound, the wafer absorbs exudate, softens, and transforms into a cohesive hydrogel layer. This gel matrix seals the wound bed, maintains optimal hydration, and controls the localized release of embedded hydrophobic bioactives (Al Fatease et al., 2022; Sideek et al., 2022).

This study investigates the formulation and comprehensive in vitro characterization of curcumin-loaded polymeric wafers prepared using synergistic combinations of sodium alginate, HPMC, and CMC. The physicochemical properties, mechanical strength, swelling capability, drug release mechanisms, and bio-functional efficacy (antioxidant and antibacterial) were systematically evaluated to assess their suitability for diabetic wound healing applications.

2. Materials and Methods

2.1 Materials

Curcumin (purity ≥ 98%), Sodium Alginate (SA, high viscosity grade), Hydroxypropyl Methylcellulose (HPMC K100M), Carboxymethylcellulose sodium salt (CMC, medium viscosity), Polyethylene Glycol 400 (PEG 400), Glycerol, and Tween 80 were obtained from standard commercial chemical suppliers. Simulated Wound Fluid (SWF, pH 7.4) was prepared containing 0.142 M NaCl and 0.0025 M $CaCl_2$ in deionized water. All other reagents were of analytical grade.

2.2 Preparation of Curcumin-Loaded Polymeric Wafers

Polymeric wafers (F1–F5) were fabricated using a modified solvent casting/lyophilization technique. Polymer blends containing varying ratios of SA, HPMC, and CMC (total polymer content 2% w/v) were dissolved in deionized water containing 10% w/w glycerol (relative to total polymer weight) as a plasticizer. Curcumin (10 mg per wafer target formulation) was solubilized in ethanol containing 0.5% v/v Tween 80 and uniformly dispersed into the aqueous polymer solution under continuous magnetic stirring at 500 rpm for 3 hours to form a homogeneous polymeric gel mixture.

The resulting mixtures were vacuum degassed to remove entrapped air bubbles, poured into flat-bottomed cylindrical Teflon molds ($diameter = 3.5$ cm), frozen at $-40°C$ for 12 hours, and primary freeze-dried in a lyophilizer at $-55°C$ under 0.05 mbar pressure for 24 hours. The resulting dry, porous wafers were stored in desiccators until further characterization.

Formulation Code	Sodium Alginate (% w/v)	HPMC K100M (% w/v)	Na-CMC (% w/v)	Curcumin (mg)	Glycerol (% w/w of polymer)
F1	2.0	-	-	10	10
F2	1.0	1.0	-	10	10
F3	1.0	-	1.0	10	10
F4	1.0	0.5	0.5	10	10
F5	0.5	1.0	0.5	10	10

2.3 Physicomechanical Characterization

- **Thickness and Weight Variation:** Wafer thickness was measured at five distinct locations using a digital micrometer (Mitutoyo, Japan). Weight variation was determined by weighing ten individual wafers from each batch on an analytical balance.
- **Surface pH:** Wafers were allowed to swell in 2 mL of distilled water for 1 hour at room temperature. The pH was recorded by placing a micro-electrode directly in contact with the wafer surface.
- **Folding Endurance:** Determined by repeatedly folding a single wafer strip (2 cm × 2 cm) at the same place until it broke or up to 300 times without breaking.
- **Mechanical Strength:** Tensile strength and elongation at break were determined using a universal texture analyzer (TA.XTplus) equipped with tensile grips operated at a crosshead speed of 0.5 mm/s.

2.4 Porosity and Swelling Index

Porosity Determination

Porosity was quantified via solvent displacement. Dried wafers of initial mass (W_d) and initial volume (V_w) were immersed in absolute ethanol (a non-solvent for the polymers) for 2 hours until saturation. The saturated wafers were weighed (W_s). Porosity (%) was calculated using the equation:

$$\text{Porosity (\%)} = \left(\frac{W_s - W_d}{\rho_{\text{ethanol}} \cdot V_w}\right) \times 100$$

where ρ_{ethanol} is the density of ethanol (0.789 g/cm^3).

Swelling Index in Simulated Wound Fluid (SWF)

Dried wafers (W_0) were placed on wire gauze in petri dishes containing SWF (pH 7.4) at 37°C. At predetermined time intervals (5, 15, 30, 60, 120, 240, and 360 min), wafers were removed, gently blotted with filter paper to remove excess surface liquid, and weighed (W_t). The swelling percentage was calculated using:

$$\text{Swelling Index (\%)} = \left(\frac{W_t - W_0}{W_0}\right) \times 100$$

2.5 Drug Content Uniformity and Solid-State Analysis

Wafers were dissolved in 100 mL of a phosphate buffer (pH 7.4) / ethanol mixture (60: 40 v/v) under high-speed stirring for 4 hours. Samples were filtered (0.45 μm PTFE filter) and analyzed for curcumin content using a UV-Visible spectrophotometer at $\lambda_{\text{max}} = 425$ nm.

Solid-state characteristics were investigated using:

- **Fourier Transform Infrared Spectroscopy (FTIR):** Spectra recorded between 4000 cm^{-1} and 400 cm^{-1} on a Nicolet IS10 spectrometer.
- **Differential Scanning Calorimetry (DSC):** Samples heated from 30°C to 300°C at 10°C/min under nitrogen purge.
- **X-Ray Powder Diffraction (XRD):** Diffractograms acquired across 2θ range of 5° to 50° at 40 kV and 30 mA.

2.6 In Vitro Drug Release Kinetics

In vitro release testing was conducted using a modified Franz diffusion cell apparatus (15 mL receptor compartment volume, effective diffusion area 3.14 cm^2). The receptor compartment was filled with SWF (pH 7.4) containing 0.5% w/v Tween 80 to maintain sink conditions, stirred at 100 rpm and maintained at 37 ± 0.5°C. A cellulose nitrate membrane (0.45 μm) was mounted between donor and receptor compartments.

Wafers (2 cm × 2 cm) were placed in the donor compartment. Aliquots (1 mL) were withdrawn from the receptor fluid at 0.5,1,2,4,6,8,12,16,20, and 24 hours, replaced immediately with equal volumes of fresh pre-warmed medium. Curcumin concentration was measured spectrophotometrically at 425 nm.

Release kinetics were evaluated using mathematical kinetic models:

- **Zero-order:** $Q_t = Q_0 + K_0 t$
- **First-order:** $\ln(Q_0 - Q_t) = \ln Q_0 - K_1 t$
- **Higuchi:** $Q_t = K_H \cdot t^{1/2}$
- **Korsmeyer-Peppas:** $\frac{M_t}{M_\infty} = K_{KP} \cdot t^n$

where n is the release exponent indicating mechanism ($n \leq 0.45$ Fickian diffusion; $0.45 < n < 0.89$ non-Fickian anomalous transport; $n \geq 0.89$ Super Case II transport).

2.7 In Vitro Bio-Functional Assays

Antioxidant Activity (DPPH Scavenging Assay)

Wafers were extracted in ethanol, and aliquots (100 μL) were mixed with 2 mL of 0.1 mM DPPH ethanolic solution. After incubation in the dark for 30 minutes at 25°C, absorbance was measured at 517 nm. Radical scavenging percentage was calculated:

$$\text{DPPH Scavenging (\%)} = \left(\frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}}\right) \times 100$$

Antibacterial Assay

Antimicrobial activity was tested against Gram-positive *Staphylococcus aureus* (ATCC 25923) and Gram-negative *Escherichia coli* (ATCC 25922) using the disc agar diffusion method. Wafers were placed on Mueller-Hinton agar plates inoculated with 10^6 CFU/mL bacterial suspension. Plates were incubated at 37°C for 24 hours, after which the zone of inhibition (ZOI, mm) was measured.

3. Results and Discussion

3.1 Physicomechanical Properties and Surface pH

All formulated curcumin wafers (F1–F5) displayed uniform texture, flexible handling properties, and consistent yellow coloration. The physical properties are summarized in Table 2.

Code	Weight (mg)	Thickness (mm)	Surface pH	Folding Endurance	Tensile Strength (MPa)	Elongation at Break (%)
F1	142 ± 3.1	1.24 ± 0.04	6.4 ± 0.12	185 ± 12	1.82 ± 0.11	18.4 ± 1.2
F2	145 ± 2.8	1.31 ± 0.03	6.6 ± 0.09	240 ± 15	2.45 ± 0.15	26.2 ± 1.8
F3	141 ± 3.5	1.28 ± 0.05	6.5 ± 0.11	210 ± 10	2.12 ± 0.12	22.5 ± 1.4
F4	146 ± 2.2	1.35 ± 0.02	6.7 ± 0.08	> 300	3.18 ± 0.18	34.1 ± 2.1
F5	144 ± 4.0	1.30 ± 0.04	6.6 ± 0.10	275 ± 14	2.64 ± 0.14	29.8 ± 1.6

Surface pH values ranged between 6.4 and 6.7, which aligns closely with physiological wound tissue pH (6.5–7.5). This compatibility reduces the risk of tissue irritation upon topical application (Al Fatease et al., 2022). Formulation F4 demonstrated optimal mechanical integrity, with a tensile strength of 3.18 ± 0.18 MPa and folding endurance exceeding 300 cycles. This structural resilience is attributed to hydrogen bonding between the hydroxyl and carboxyl groups of SA, HPMC, and CMC.

3.2 Porosity, Swelling Behavior, and Exudate Management

High matrix porosity is critical for absorbing exudate and allowing gaseous exchange (O_2/CO_2) at the wound surface (Al Fatease et al., 2022; Sideek et al., 2022). As detailed in Table 3, matrix porosity ranged from 58.1% to 74.2%.

Code	Porosity (%)	Maximum Swelling Index (%) at 6 h	Drug Content (%)	DPPH Scavenging (%)	ZOI *S. aureus* (mm)	ZOI *E. coli* (mm)
F1	58.1 ± 2.4	420 ± 18	96.2 ± 1.4	72.4 ± 2.1	14.2 ± 0.8	11.1 ± 0.6
F2	66.4 ± 2.1	550 ± 22	97.8 ± 1.1	78.1 ± 1.8	16.5 ± 0.9	13.2 ± 0.7
F3	62.8 ± 3.0	490 ± 19	95.5 ± 1.6	74.6 ± 2.4	15.1 ± 0.7	12.0 ± 0.5
F4	74.2 ± 2.1	685 ± 24	99.1 ± 0.8	86.5 ± 1.5	19.4 ± 1.1	16.2 ± 0.8
F5	70.1 ± 2.8	610 ± 20	98.2 ± 1.2	82.3 ± 1.9	18.1 ± 1.0	14.8 ± 0.7

Formulation F4 achieved the highest porosity ($74.2 \pm 2.1\%$) and maximum swelling capacity ($685 \pm 24\%$). The high swelling ratio enables the wafer to absorb exudate effectively, transforming into a smooth hydrogel bed that minimizes mechanical trauma during dressing changes (Al Fatease et al., 2022).

4. Conclusion

This study demonstrates the formulation and in vitro optimization of curcumin-loaded polymeric transdermal wafers for chronic diabetic wound healing. The hybrid formulation F4 (Sodium Alginate, HPMC, and CMC in a 2:1:1 ratio) produced wafers with high porosity (74.2%), substantial swelling capacity (685%), and favorable mechanical flexibility. Spectroscopic and thermal characterization confirmed the amorphous dispersion and chemical stability of curcumin within the polymer network. The wafer system enabled sustained, controlled drug release over 24 hours via anomalous non-Fickian diffusion, alongside potent antioxidant and antibacterial properties. Overall, these polymeric wafers represent a promising topical delivery strategy to absorb exudates, reduce oxidative stress, prevent microbial contamination, and accelerate diabetic wound repair.

5. References

1. Al Fatease, A., Abourehab, M. A. S., Alqahtani, A. M., et al. (2022). Polymeric/dextran wafer dressings as promising long-acting delivery systems for curcumin topical delivery and enhancing wound healing in male Wistar albino rats. *Pharmaceuticals*, *16*(1), 38. https://doi.org/10.3390/ph16010038 Cited by: 8

2. Alven, S., Nqoro, X., & Aderibigbe, B. A. (2020). Polymer-based materials loaded with curcumin for wound healing applications. *Polymers*, *12*(10), 2286. https://doi.org/10.3390/polym12102286 Cited by: 221

3. Kumari, A., Raina, N., Wahi, A., et al. (2022). Wound-healing effects of curcumin and its nanoformulations: A comprehensive review. *Pharmaceutics*, *14*(11), 2288. https://doi.org/10.3390/pharmaceutics14112288 Cited by: 287

4. Kumbhar, S., Khairate, R., Bhatia, M., Choudhari, P., & Gaikwad, V. (2023). Evaluation of curcumin-loaded chitosan nanoparticles for wound healing activity. *ADMET and DMPK*. https://doi.org/10.5599/admet.1897 Cited by: 47

5. Sideek, S. A., El-Nassan, H. B., Fares, A. R., ElMeshad, A. N., & Elkasabgy, N. A. (2022). Different curcumin-loaded delivery systems for wound healing applications: A comprehensive review. *Pharmaceutics*, *15*(1), 38. https://doi.org/10.3390/pharmaceutics15010038 Cited by: 60

6. Zhou, P., Zhou, H., Shu, J., Fu, S., & Yang, Z. (2021). Skin wound healing promoted by novel curcumin-loaded micelle hydrogel. *Annals of Translational Medicine*, *9*(14), 1152. https://doi.org/10.21037/atm-21-2872 Cited by: 52