



EMERGING ROLE OF QUERCETIN AND IMMORTELE ESSENTIAL OIL EMULGEL IN DIABETIC WOUND CARE: A COMPREHENSIVE REVIEW

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Article Received on 27 March 2026,
Article Revised on 16 April 2026,
Article Published on 01 May 2026,

<https://doi.org/10.5281/zenodo.19874183>

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How To Cite This Article: Prof. Sorate Rushikesh Chandrakant^{*1}, Mr. Parab Dattaram Ashok¹, Ms. More Vedantika Vinod¹, Mr. Zore Dattaprasad Baburav¹, Ms. Kumbhar Riya Rajendra¹, Dr. Ubale Amol Tanaji¹. (2026). Emerging Role of Quercetin and Immortelle Essential Oil Emulgel In Diabetic Wound Care: A Comprehensive Review. World Journal of Pharmacy and Pharmaceutical Sciences, 15(5), 19–37.

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ABSTRACT

Diabetic wounds are characterized by prolonged inflammation, excessive oxidative stress, microbial infection and impaired tissue regeneration which significantly delay the healing process. This review focuses on the design, development and characterization of an emulgel formulation incorporating Quercetin and essential oil derived from *Helichrysum italicum* (immortelle). Quercetin which is potent flavonoid exhibits strong antioxidant and reactive oxygen species scavenging properties, thereby reducing oxidative damage at wound site. Immortelle essential oil contributes antimicrobial and anti-inflammatory effects and has been reported to inhibit matrix metalloproteinases which helps to preserve extracellular matrix integrity and promote tissue repair. The emulgel system combines the advantages of both emulsions and gels, offering improved drug solubilization, enhanced skin penetration and better patient compliance. Key formulation parameters such as selection of oil phase, surfactant system and gelling agent were

critically evaluated to obtain a stable and effective formulation. Characterization techniques including physicochemical evaluation, spreadability, viscosity, drug release, antimicrobial studies and hydrogen peroxide scavenging assay are discussed. The synergistic action of quercetin and immortelle essential oil within an emulgel matrix presents a promising topical

approach for improving diabetic wound healing outcomes. This review highlights the potential of combining natural bioactives in advanced delivery systems for enhanced therapeutic efficacy.

KEYWORDS: Quercetin, Immortelle Essential Oil, Diabetic Wound Healing, Emulgel, Antioxidant Activity, Matrix Metalloproteinase Inhibition.

INTRODUCTION

1.1 Complication and Socioeconomic Burden of Diabetic Wounds

Diabetic wounds constitute one of the most severe and debilitating complications associated with diabetes mellitus and arise primarily due to chronic hyperglycemia and impaired peripheral circulation. These wounds predominantly affect lower extremities and exhibit a prolonged inflammatory phase that disrupts the normal physiological process of wound healing. Sustained infiltration of inflammatory cells in diabetic wounds leads to excessive generation of Reactive Oxygen Species (ROS) and matrix metalloproteinases (MMPs) resulting in persistent oxidative stress. This pathological environment causes degradation of extracellular matrix, reduced angiogenesis and diminished availability of essential growth factors thereby delaying or completely arresting the healing process.



Fig No I Diabetic Foot Ulcer^[1]



Fig No II Diabetic Foot Ulcer^[2]

The condition is further aggravated by diabetic peripheral neuropathy which reduces protective pain sensation and delays wound recognition. Consequently, minor injuries may progress into chronic, non-healing foot ulcers, tissue necrosis and in advanced stages to gangrene. These complications significantly increase the risk of lower limb amputation and severely compromise patient mobility, independence and quality of life. Recurrent ulceration,

prolonged hospitalization and increased susceptibility to infection further contribute to physical disability and psychological distress among affected individuals.

In addition to clinical implications, diabetic wounds impose a substantial socioeconomic burden on healthcare systems worldwide. Diabetic foot ulcers account for approximately 24.7% of total diabetes related healthcare expenditure, with annual cost estimated at nearly 11 billion USD in United States and 460 million GBP in United Kingdom. These expenditures include costs related to long term wound care, surgical interventions, advanced therapeutic modalities and loss of productivity. The increasing global prevalence of diabetes further exacerbates this economic burden particularly in developing countries.

Therefore, effective and comprehensive wound management strategies are essential to prevent severe complications such as recurrent ulceration, infection, gangrene and limb amputation. The significant clinical and economic impact of diabetic wounds highlights the urgent need for innovative therapeutic approaches that can target the underlying pathophysiological mechanisms and improve healing outcomes.^[3]

1.2 Phases of Wound Healing

A wound is generally defined as disruption in the normal anatomical and cellular continuity of tissue including the skin, mucous membrane or underlying organs resulting from physical, chemical, thermal or mechanical injury. Restoration of tissue integrity following injury occurs through wound healing which is a highly dynamic, complex and tightly regulated biological process involving coordinated cellular responses and molecular signalling pathways.

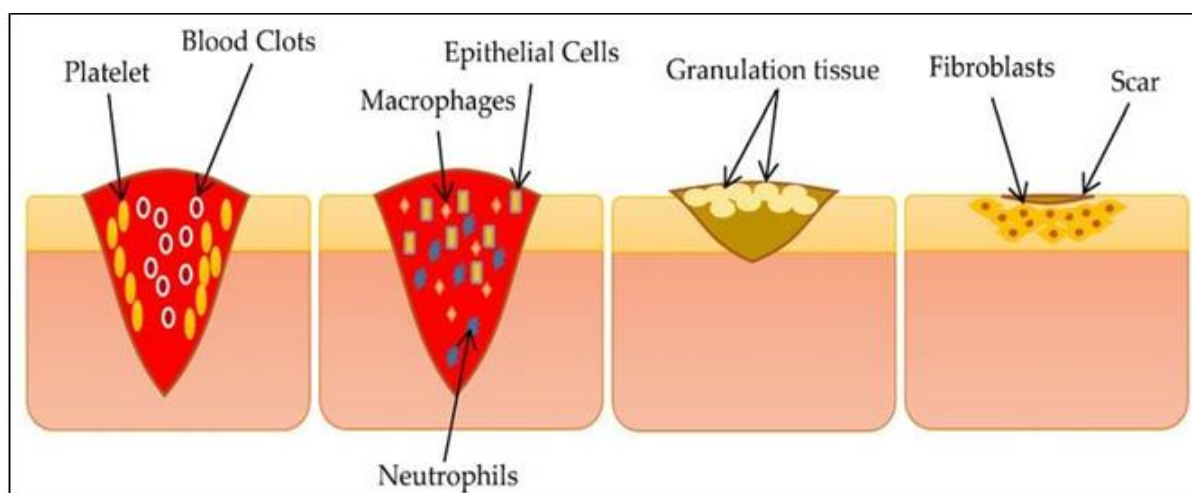


Fig. No. III Phases of wound healing^[4]

Wound healing proceeds through a series of overlapping and interdependent phases, each characterized by specific cellular activities and biochemical events. These phases are classically categorized as hemostasis, inflammation, proliferation and remodeling. Rather than occurring in isolation, these phases overlap temporally and spatially to ensure effective tissue repair and functional recovery.^[5]

Table No 1: Phases of wound healing.

Hemostasis	The hemostasis phase begins immediately after injury and involves vasoconstriction and platelet aggregation leading to clot formation that prevents excessive blood loss and provides a provisional extracellular matrix for cell migration.
Inflammatory Phase	This is followed by the inflammatory phase , during which neutrophils and macrophages infiltrate the wound site to remove debris, bacteria and necrotic tissue while releasing cytokines and growth factors essential for subsequent healing events.
Proliferative Phase	The proliferative phase is characterized by fibroblast proliferation, collagen synthesis, angiogenesis and re-epithelization leading to formation of granulation tissue and partial restoration of tissue structure.
Remodeling or Maturation Phase	Finally, the remodeling or maturation phase involves collagen reorganization, replacement of type III collagen with type I collagen and gradual strengthening of the repaired tissue resulting in scar formation and restoration of tensile strength.

Wound healing depends on precise regulation and timely progression of these phases. Any disruption or prolongation of specific phase (particularly inflammation) can impair healing and contribute to the development of chronic non-healing wounds as commonly observed in diabetic conditions.

1.3 Pathophysiology of Diabetic Wounds

Diabetic wound healing is profoundly impaired due to a combination of metabolic, vascular, inflammatory and neuropathic abnormalities associated with chronic hyperglycemia. Unlike normal wound healing which progresses through orderly and overlapping phases, diabetic wounds remain trapped in prolonged inflammatory state leading to delayed tissue repair and chronic ulcer formation.

Persistent hyperglycemia results in excessive formation of advanced glycation end products (AGEs) which alter cellular signaling. AGEs interact with their Receptors (RAGE) activating intracellular pathway that promote oxidative stress and sustained inflammation.

This condition leads to overproduction of reactive oxygen species (ROS) which damages cellular components, inhibits fibroblast function and reduces keratinocyte migration essential for re-epithelization. Impaired angiogenesis is another hallmark of diabetic wounds. Reduced expression of vascular endothelial growth factor (VEGF) and endothelial dysfunction limit new blood vessel formation resulting in decreased oxygen and nutrient supply to the wound site. Hypoxia further aggravates inflammation and suppresses collagen synthesis preventing granulation tissue formation.

Diabetic neuropathy contributes significantly to wound chronicity by reducing pain sensation and delaying wound recognition. Loss of protective sensation allows repeated mechanical stress while autonomic neuropathy impairs sweat gland function leading to dry and fissured skin that is more susceptible to injury and infection.

Additionally, an imbalance between matrix metalloproteinases (MMPs) and tissue inhibitors causes excessive degradation of extracellular matrix components. Simultaneously, reduced levels of growth factors such as platelet derived growth factor (PDGF) and transforming growth factor- β (TGF- β) impair fibroblast proliferation and collagen deposition. The combined effect of these pathological mechanisms results in delayed wound closure, recurrent ulceration and increased risk of infection and amputation.^[6]

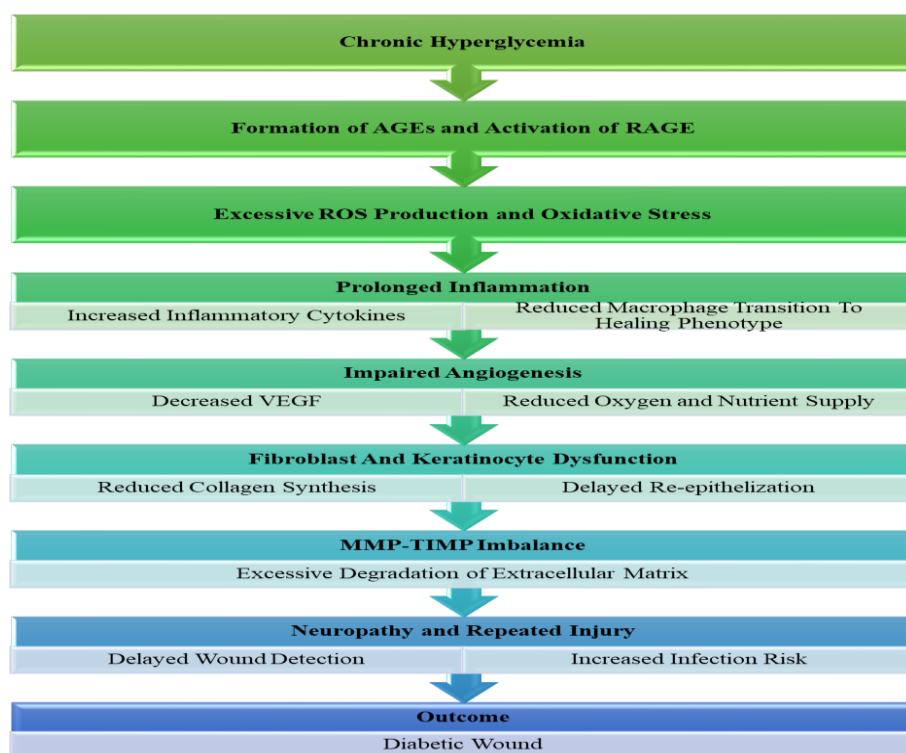


Fig. No. V Pathophysiology of Diabetic Wounds^[7]

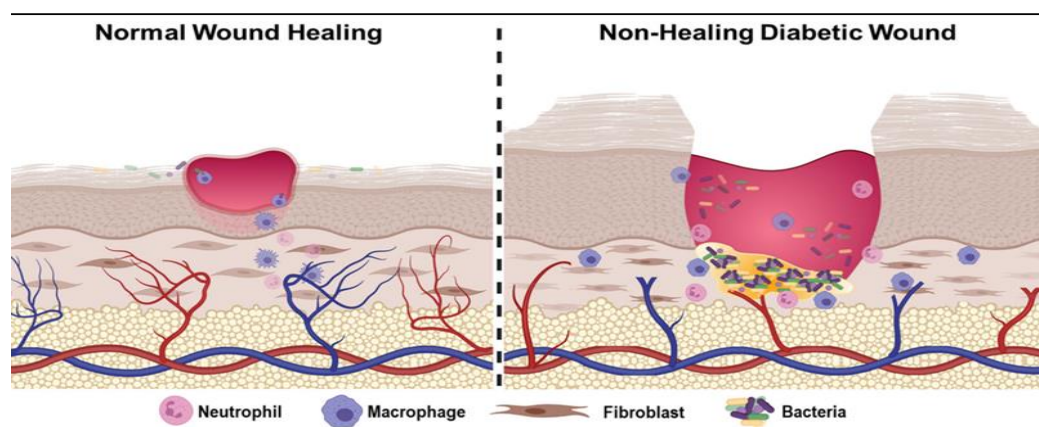


Fig. No. VI Pathophysiology of Diabetic Wounds.^[8]

1.4 Current Therapies in Diabetic Wound Management.^[9]

Diabetic wounds are now managed using a comprehensive approach that includes prevention, accurate diagnosis, medical management, surgical intervention, and complementary therapies.

1.4.1 Diabetic Wound Diagnosis

- Clinical assessment focuses on vascular health, infection symptoms and wound features.
- Imaging such as MRI or X-rays can measure tissue damage and diagnose illnesses like osteomyelitis.
- Tissue or bone cultures are favoured over surface swabs for identifying bacteria that cause infections.
- To examine total limb health, neuropathy and peripheral artery disease are assessed clinically.

1.4.2 Preventive Care

- Patient education includes information on risk factors, diabetes management and correct foot care techniques
- Podiatric care includes regular inspection and screening of feet.
- Offloading devices and customized footwear can help to avoid pressure ulcers and facilitate recovery.
- Early management of fungal infections and pre-ulcerative signs to prevent progression towards chronic wound.
- Incorporation of proper footwear as well as feet and ankles exercises to maintain mobility can reduce potential risks of ulcer formation.

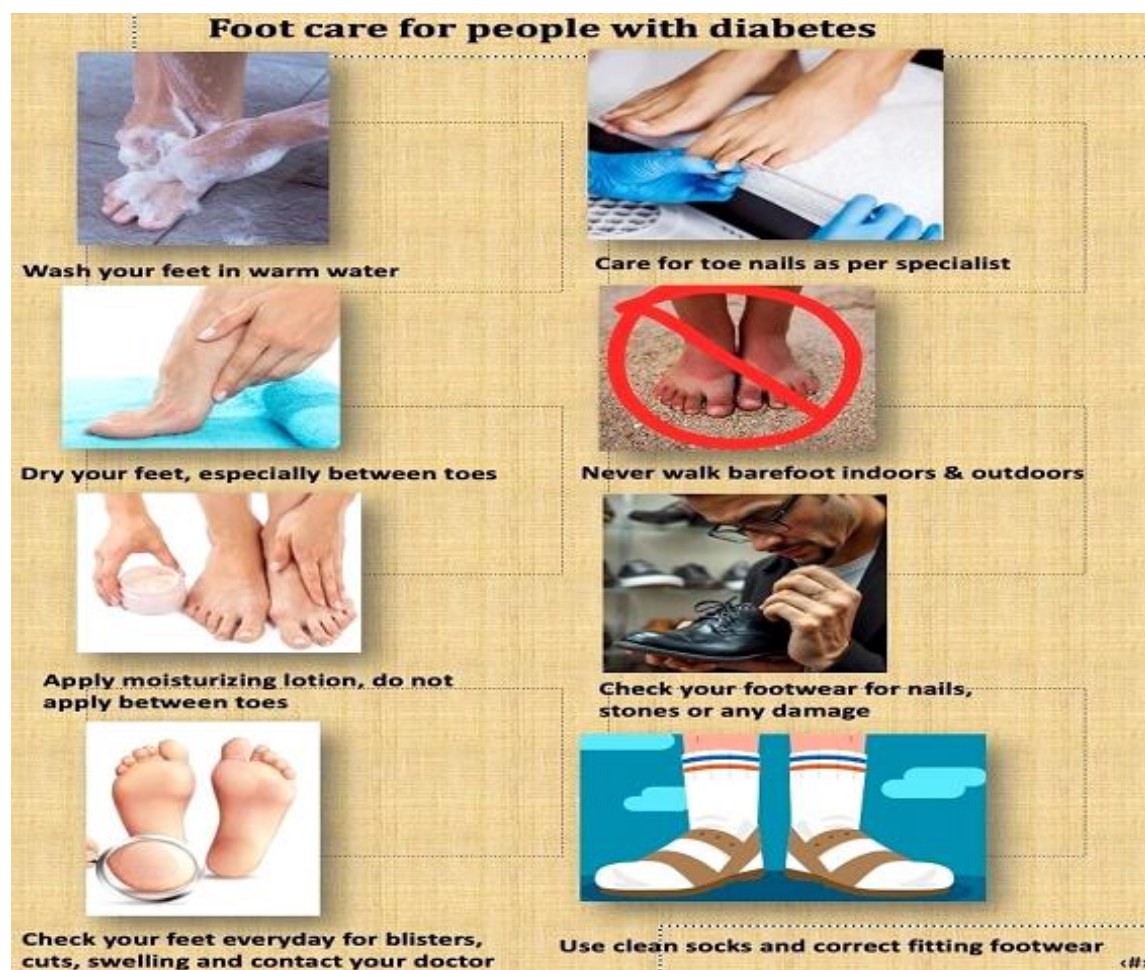


Fig. No. VII Foot care for people with diabetes.^[10]

1.4.3 Treatments

A. Medical Management

1. Blood Glucose Control

Multidisciplinary management by endocrinologists and primary care physicians optimizes glycemic control and improves healing results.

2. Infection Control

- Infection control involves administering antibiotics based on wound culture results and infection severity.
- Systemic antibiotics are often given for one to two weeks in mild to severe illnesses.
- Antibiotic selection should take into account of both patient's condition and pathogenic organisms.
- To avoid resistance and harmful consequences, antibiotics should not be used in clinically uninfected ulcers.

3. Topical Wound Care

Topical wound care involves using dressings that are appropriate for wound type such as moisture-retentive, antimicrobial or sophisticated choices like collagen and hyaluronic acid.

4. Debridement

It is used to remove bioburden, promote granulation tissue development and remove necrotic tissue to promote wound healing.



Fig. No. VIII Debridement of Diabetic Wound.^[11]

B. Surgical Procedures

- Early surgical debridement removes necrotic or contaminated tissue in moderate to severe infections, increasing infection management and recovery.
- To treat osteomyelitis, resection of the diseased bone and long-term antibiotic treatment are commonly used.
- Critical limb ischemia requires revascularization treatments like bypass surgery or angioplasty to restore blood flow.
- Amputation is the final option when limb salvage is not possible due to irreversible tissue damage or systemic danger.

C. Adjunctive Therapies in Diabetic Wound Management

1) Negative Pressure Wound Therapy (NPWT)^[12]

NPWT uses a sealed dressing attached to a vacuum pump to impart regulated negative pressure to the wound. By boosting blood flow, decreasing edema, eliminating exudate and promoting the formation of granulation tissue which aids in the healing of wounds.

Drawbacks

- The risk of infection remains if necrotic tissue is not fully debrided prior to application.
- Patients on anticoagulants or with exposed blood arteries may be at risk for bleeding.
- Close monitoring is required to detect problems such as discomfort, ischemia and device malfunction.
- Contraindications include wounds with untreated infection, necrosis or exposed organs or veins

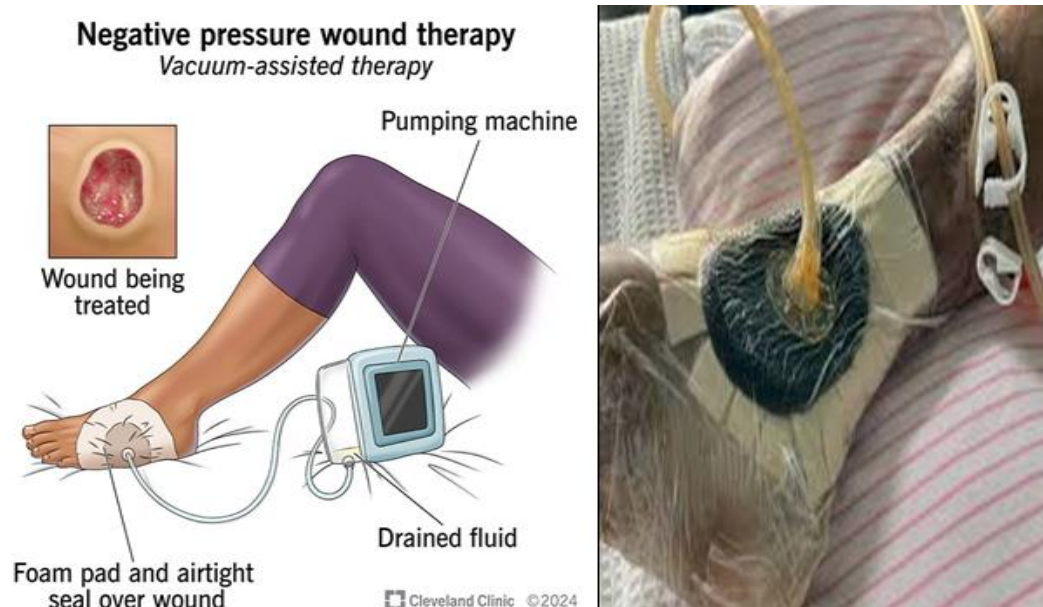


Fig. No. IX Negative Pressure Wound Therapy (NPWT).^[13]

2) Hyperbaric Oxygen Therapy (HBOT)^[14]

In HBOT, patients breathe 100% oxygen at elevated atmospheric pressure in a pressurized chamber. This greatly boosts oxygen delivery to hypoxic areas, leading to angiogenesis, bacterial death and improved cellular metabolism which are essential for tissue healing.

Drawbacks

- Therapy sessions are time consuming and expensive, with limited availability.
- Untreated pneumothorax and certain respiratory diseases are contraindicated.
- Common side effects include middle ear barotrauma, sinus pain, temporary vision abnormalities and claustrophobia.
- Rare but serious hazards include oxygen toxicity, convulsions, pulmonary problems, hypoglycemia in diabetics and accelerated cataract progress.



Fig. No. X Hyperbaric Oxygen Therapy (HBOT).^[15]

1.5 Emulgel^[16]

Emulgel is a novel topical drug delivery technology that combines the features of emulsions and gels to efficiently delivers hydrophilic and lipophilic drugs. The biphasic system optimizes drug release and enhances skin penetration. The gel base provides a non-greasy, smooth texture that enhances patient compliance. Emulgels have excellent physical and chemical stability, high drug loading capacity and bioadhesive characteristics that extend contact time with the skin surface. They are cost-effective, versatile and particularly beneficial in dermatology for administering anti-inflammatory, analgesic and wound-healing agents. Emulgels overcome drawbacks of traditional topical formulations such as poor spreadability and greasiness leading to improved therapeutic efficacy.

1.5.1 Advantages of Emulgel

Facilitates the incorporation and effective topical delivery of both hydrophobic and hydrophilic drugs through its biphasic composition.

- Exhibits a non-greasy, non-sticky character with excellent spreadability and thus providing superior patient acceptability and compliance.
- Prolongs residence time at the application site due to inherent bioadhesive properties.
- Allows for easy removal from the skin without causing staining or irritation.
- Demonstrates robust chemical and physical stability resulting in extended product shelf-life.
- Offers a cost-effective and simple formulation process suitable for scale up.

REVIEW OF INGREDIENTS

Quercetin

- 1) **Molecular formula:** $C_{15}H_{10}O_7$
- 2) **Structural formula:**
- 3) **IUPAC name:** 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy chromen-4-one
- 4) **Molecular weight:** 302.238 g/mole
- 5) **Category:** Antioxidant
- 6) **BCS Class:** II
- 7) **Physical state and appearance:** Yellowish crystalline powder
- 8) **Odour:** Odourless
- 9) **Taste:** Bitter
- 10) **Colour:** Yellow
- 11) **Melting point:** 316 °C
- 12) **Solubility:** Poorly soluble in water, freely soluble in ethanol, methanol and acetone.
- 13) **Storage:** Store in tightly closed container, in cool and well-ventilated places.
- 14) **Mechanism**

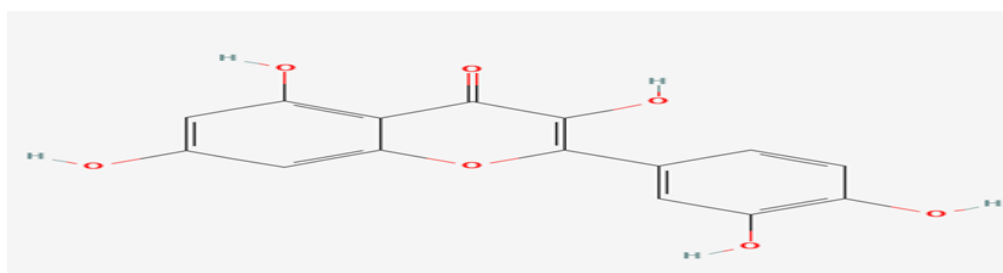


Fig. No. XI Structure of Quercetin.^[17]

Quercetin promotes diabetic wound healing by blocking the NF- κ B pathway and lowering pro-inflammatory cytokines (TNF- α , IL-1 β , and IL-6) to reduce chronic inflammation. Its powerful antioxidant effect involves scavenging reactive oxygen species (ROS) and increasing endogenous antioxidant enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase, thereby reducing oxidative tissue damage. Quercetin promotes collagen synthesis and extracellular matrix deposition through the TGF- β 1/Smad signalling pathway, which is crucial for tissue repair. It promotes angiogenesis by increasing VEGF and endothelial nitric oxide synthase (eNOS), which improves blood flow and oxygenation. Furthermore, quercetin converts macrophages from the pro-inflammatory M1 to the pro-healing M2 phenotype which promotes inflammation resolution and tissue regeneration.^[18]

Immortelle Essential Oil

- 1) **Biological Source:** Immortelle essential oil is extracted from the flowering tops of *Helichrysum italicum*, a plant endemic to the Mediterranean region (including Italy, Corsica, North Africa, and the Adriatic coast).
- 2) **Chemical composition:** The oil contains bioactive terpenes and sesquiterpenes. Compounds found in neryl acetate include α -pinene, γ -curcumene, α -cedrene, limonene, β -caryophyllene and linalool with variations depending on plant age, geographic origin, and extraction process.
- 3) **Pharmacological Effects:** Anti-inflammatory: Reduces pro-inflammatory mediators prostaglandin E2 (PGE2) and nitric oxide (NO) by inhibiting cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS).

Antioxidant: Prevents tissue damage by scavenging free radicals and blocking oxidative stress pathways.

Antimicrobial: Effective against Gram-positive bacteria, it breaks down bacterial cell walls and prevents the formation of biofilms, lowering the risk of wound infection.

Wound healing: Increases keratinocyte migration and proliferation through MAPK/ERK and EGFR signalling pathways, promoting re-epithelialization; stimulates collagen synthesis and extracellular matrix remodelling by regulating matrix metalloproteinases (MMPs) activity.

- 4) **Therapeutic Uses:** Immortelle essential oil is applied topically to formulations for antiaging, skin regeneration, wound healing, and inflammation reduction. Its skin-soothing and regenerative qualities make it valuable in dermatological and cosmetic applications.
- 5) **Safety and storage:** To protect the oil's chemical integrity, store it in amber glass bottles away from heat and sunshine. It is usually considered safe for topical application, but should be used with caution because to the potential skin sensitization in some persons.^[19]

Formulation Approach and Scientific Approach

Diabetic wounds are characterized by prolonged inflammation, microbial infection, oxidative stress and overexpression of matrix metalloproteinases (MMPs), which delay the normal

wound healing process. Therefore, an effective topical formulation should address multiple pathological mechanism simultaneously. The present study focuses on developing a topical emulgel containing a quercetin and β -Cyclodextrin inclusion complex and immortelle essential oil to enhance wound healing.

Quercetin is a natural flavonoid known for its strong antioxidant and reactive oxygen species (ROS) scavenging activity which helps reduce oxidative damage in chronic wounds and supports cellular regeneration. However, its poor aqueous solubility limits its therapeutic potential. To overcome this limitation, quercetin is complexed with β -Cyclodextrin which improves its solubility and stability by forming an inclusion complex. This enhances the availability of quercetin at the wound site and promotes effective antioxidant activity.

The formulation also incorporates essential oil derived from *Helichrysum italicum* (immortelle) which possesses antimicrobial and wound healing properties. The bioactive constituents of immortelle oil are reported to inhibit matrix metalloproteinases enzymes that degrade extracellular matrix components and delay tissue repair in diabetic wounds. By inhibiting MMP activity, immortelle oil helps protect the structural integrity of the epithelial tissue and creates favourable conditions for tissue repair and regeneration.

The combination of quercetin and immortelle oil is expected to provide a synergistic therapeutic effect where quercetin acts as an antioxidant by scavenging ROS while immortelle oil contributes antimicrobial and enzyme-inhibiting activities. To deliver both components effectively, an emulgel system is selected as the dosage form.

Table No 2: Formulation composition of quercetin and immortelle essential oil emulgel.

Sr No	Ingredient	% W/W	Amount for 100 gm. (gm.)	Amount for 30gm (gm.)	Role
1.	Quercetin (API)- β Cyclodextrin complex	0.95	0.95	0.285	Active flavonoid
2.	Immortelle essential oil	1	1	0.3	Active wound healing oil
3.	Liquid paraffin	7.5	7.5	2.25	Oil phase
4.	Span80	2	2	0.6	Lipophilic Surfactant
5.	Tween80	4	4	1.2	Hydrophilic surfactant
6.	Carbopol 934	1	1	0.3	Gelling agent
7.	Propylene glycol	5	5	1.5	Humectant
8.	Triethanolamine	q. s	q.s	q.s	pH adjustment

9.	Methyl paraben	0.01	0.01	0.003	Preservative
10.	Distilled water	Up to 100	Up to 100	Up to 30	Aqueous Phase

Table No 3: Formulation approach and scientific approach.

Challenge	Description	Solution/ Approach
Poor aqueous solubility of Quercetin	Quercetin is hydrophobic, leading to low dissolution and poor bioavailability	Inclusion complexation with β -Cyclodextrin improves solubility by entrapping drug in hydrophilic cavity
Low skin penetration	Quercetin has limited permeability across stratum corneum	Quercetin- β -Cyclodextrin complex + emulgel enhances partitioning and permeation
Oxidative stress in diabetic wounds	High ROS delays healing and damages tissue	Quercetin acts as antioxidant and ROS scavenger
Excess MMP activity	Matrix degradation delays tissue repair	Immortelle oil inhibits MMPs and preserves ECM
Microbial infection	Wounds prone to bacterial contamination	Immortelle oil provides antimicrobial action
Poor drug stability	Quercetin is sensitive to oxidation	Cyclodextrin protects drug from degradation
Need for sustained release	Rapid drug release reduces effectiveness	Controlled release improves therapeutic action
Poor patient compliance	Ointments are greasy and less acceptable	Emulgel provides non-greasy, easily spreadable formulation
Phase separation in emulsion	Instability reduces effectiveness	Proper surfactant system stabilizes emulsion
Limited residence time on skin	Drug may be removed easily	Gel base improves adhesion and retention

EVALUATION PARAMETERS

Comprehensive evaluation of the formulated quercetin and immortelle essential oil emulgel intended for diabetic wound healing is crucial to ensure its quality, safety, and therapeutic effectiveness. A range of standardized physicochemical, microbiological, and analytical assessments were performed in compliance with international pharmacopeial and regulatory standards to confirm the formulation's appropriateness for clinical use.^[20,21]

Table No 4: Evaluation parameters and acceptance criteria.

Parameter	Objective	Method/Instrument	Acceptance Criteria
Organoleptic Characteristics	Assess colour, texture, and appearance for consumer acceptability	Visual and sensory evaluation	Smooth, homogeneous, yellowish gel with characteristic soothing odour
pH Measurement	Ensure skin compatibility and formulation stability	Digital pH meter (1 g dispersion in 10 ml distilled water)	6.0 – 7.0 (compatible with skin pH)
Viscosity	Evaluate	Brookfield viscometer	5,000 – 50,000 cps

	spreadability, consistency, and stability		consistent with topical gel standards
Spreadability	Determine ease of application on skin surface	Parallel plate method ($S = M \times L / T$)	≥ 5 g·cm/sec; uniform and smooth spreading
Swelling Index	Assess hydration capacity and polymer network strength	Immersion method in 0.1N NaOH; % increase in weight recorded	Stable swelling index $\leq 200\%$ without disintegration
Centrifugation Test	Check physical stability and phase separation tendency	Centrifugation at 3000 rpm for 30 min	No phase separation or creaming observed
Globule Size and Distribution	Determine droplet uniformity and stability of emulsion phase	Optical microscopy with image analysis software	Mean globule size $< 10 \mu\text{m}$, narrow size distribution
Drug Content Uniformity	Assess homogeneity of drug distribution	UV–Visible spectrophotometer/HP LC	95–105% of labelled quercetin content
<i>In Vitro</i> Diffusion Study	Evaluate drug release through semi-permeable membrane	Franz diffusion cell at 37°C using phosphate buffer (pH 7.4)	Sustained release up to 8 h with controlled kinetics
Antimicrobial Activity	Determine synergistic effect of quercetin and immortelle oil	Agar well diffusion against wound pathogens (e.g. <i>S. aureus</i> , <i>P. aeruginosa</i>)	Zone of inhibition $\geq$ that of standard antibiotic cream
Hydrogen Peroxide Radical Scavenging Activity	Evaluate antioxidant potential relevant to wound healing	Phosphate buffer– H_2O_2 assay, absorbance at 230 nm	$\geq 70\%$ scavenging at equivalent concentration
Stability Studies	Determine physicochemical stability under accelerated and long-term conditions	ICH guidelines (Q1A(R2)) at $25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH and $40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH	No significant phase separation, colour change, or drug degradation over 3 months
Patch Test (Primary Skin Irritation)	Evaluate dermal safety before clinical use	Draize patch test on albino rats/rabbits	No erythema or edema after 24 hours

NEED AND OBJECTIVES

Need

The need for the design, development and characterization of a quercetin and immortelle essential oil emulgel for the treatment of diabetic wounds arises from several important considerations

1. To address chronic diabetic wounds failing due to persistent inflammation, oxidative stress, and infections

2. To overcome quercetin solubility limitations (BCS II) through Cyclodextrin complexation
3. To deliver immortelle oil effectively with stable biphasic emulgel system
4. To provide superior efficacy over conventional treatments (Silver sulfadiazine, iodine)
5. To enable multi-target therapy simultaneously reducing ROS, MMPs, infection, enhancing angiogenesis
6. To improve patient compliance through non-greasy, spreadable topical formulation
7. To offer cost-effective natural alternative to expensive advanced wound therapies
8. To fill literature gap: first quercetin-immortelle emulgel combination

Objectives

1. To develop an emulgel formulation incorporating quercetin and immortelle essential oil suitable for topical application on diabetic wounds.
2. To characterize the optimized emulgel for physicochemical properties.
3. To evaluate antimicrobial activity of the formulated quercetin and immortelle essential oil emulgel against common diabetic wound pathogens such as *Staphylococcus aureus* and *Escherichia coli*, etc.
4. To compare the antioxidant efficacy of the emulgel with standard antioxidant compounds such as ascorbic acid supporting its role in reducing oxidative stress in diabetic wounds.

CONCLUSION

Diabetic wounds are complex and slow-healing due to persistent oxidative stress, inflammation, microbial infection and excessive degradation of the extracellular matrix. This review emphasizes a rational formulation approach using a topical emulgel containing a Quercetin- β -Cyclodextrin inclusion complex along with essential oil from *Helichrysum italicum* (immortelle). Complexation with β -Cyclodextrin effectively enhances the solubility, stability and bioavailability of quercetin enabling better therapeutic performance at the wound site. Quercetin contributes strong antioxidant and anti-inflammatory actions helping to neutralize reactive oxygen species and support tissue repair. Simultaneously, immortelle essential oil provides antimicrobial activity and modulates matrix metalloproteinases, thereby preserving extracellular matrix integrity and promoting regeneration. The emulgel system serves as an efficient delivery platform by combining the advantages of emulsions and gels leading to improved drug solubilization, enhanced skin permeation, controlled release and better patient compliance due to its non-greasy nature. Proper optimization of formulation parameters ensures stability, spreadability and sustained therapeutic action. Overall, this

synergistic approach offers a promising and innovative strategy for diabetic wound management. Further *in vitro*, *in vivo* and clinical studies are necessary to confirm its efficacy and translate it into practical therapeutic application.

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to Mr. Rushikesh Chandrakant Sorate for his valuable guidance, continuous support and insightful suggestions throughout the preparation of this review article.

We are also thankful to Vijayrao Naik College of Pharmacy for providing the necessary academic environment, facilities and resources that contributed to the successful completion of this work.

CONFLICT OF INTEREST: None.

FINANCIAL SUPPORT: None.

ETHICS STATEMENT: None.

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