"Formulation and Evaluation of Dermal Patches Using Marigold Leaf Extract for Enhanced Wound Healing"

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Abstract
This study aims to develop a suitable dermal patch formulation that delivers the natural therapeutic agent, the plant extract of African marigold leaf, for minor wound treatment. Generally, minor wounds are treated with creams, ointments, or lotions. But a dermal patch has the advantage that it releases the drug for a longer duration in a controlled manner to the affected skin sites. Marigold leaf is selected for its antibacterial and tissue-regenerative effects during wound healing. Wound healing is a complex biological process. This process is very crucial in maintaining tissue integrity and preventing further complications. Traditional wound-healing dressings generally contain synthetic chemical agents that cause adverse effects, resistance, and are economically unsuitable. Further, synthetic chemical agents only prevent infection and help regenerate tissue naturally, whereas marigold leaf extract regenerates tissue and accelerates wound healing while limiting infections. Five dermal patches were formulated using various polymers by the solvent-casting technique, and Marigold leaf extract was incorporated at varying concentrations (0.3-3 ml) as a natural medicament, with polyethene glycol 400 as a plasticizer and ethanol as the solvent. The dermal patches were evaluated for their physicochemical properties and found to have consistent thickness, weight uniformity, and folding endurance. The antimicrobial activity of the dermal patch was evaluated against common wound pathogens. Two formulations were found to be effective. These two formulations were evaluated for wound-healing activity in an animal model, demonstrating accelerated wound healing and tissue regeneration compared with the control. This finding suggests that a Demal patch containing marigold leaf extract (Tagetes erecta) can be a potential natural antimicrobial and a suitable wound-healing delivery system for minor wound treatment, providing a safe and cost-effective alternative to chemical wound treatment.

Keywords: Marigold leaf extract, dermal patches, wound healing, antimicrobial activity, Tagetes erecta,
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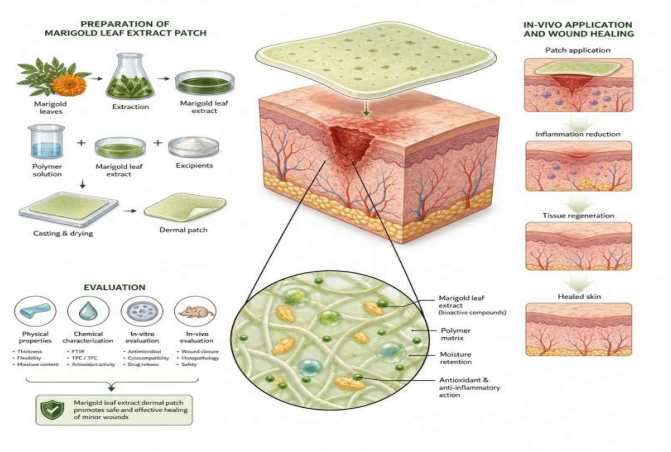
Graphical Abstract:-



Figure

1. Introduction

1.1 Overview of Dermal Delivery Systems

Dermal delivery systems have revolutionised the treatment of dermatological conditions. These systems deliver drugs directly to affected skin regions. It has a significant advancement over traditional topical formulations, providing controlled, sustained release of therapeutic agents with minimal systemic absorption. [1]Dermal patches are drug-containing adhesive devices with a specific surface area that deliver medicament to the skin surface at a predetermined rate. These innovative delivery systems also offer numerous advantages, such as reduced drug fluctuations, avoidance of first-pass metabolism, prevention of gastrointestinal incompatibility, and, most importantly, improved patient compliance through multiday therapeutic coverage and self-medication. [2]

For dermatological disorders in which the primary disease site is confined to the skin—including psoriasis, eczema, and microbial infections—targeted medication delivery via dermal patches helps reduce systemic absorption while maximising localised therapeutic effects.[1] The ability to deliver the medicament to specific disease locations in the skin while minimizing systemic absorption reduces associated systemic side effects.

1.2 Wound Healing: Biological Significance and Challenges

The wound-healing process is a complex biological response to tissue injury. This process involves a series of cellular and biochemical processes to restore tissue integrity and function. The healing process comprises blood clotting, inflammation, tissue regeneration, epithelialization, collagen production, and remodelling of injured tissue. To develop an effective drug delivery system, an understanding of these mechanisms is very much crucial. [3]

1.2.1 Stages of Wound Healing

The wound healing process progresses through three distinct stages

Inflammatory Stage: This stage occurs in the initial days after injury. The blood vessels narrow to reduce bleeding. The platelets form clots with thromboplastin. The debris and bacteria from the wound are removed by White blood cells, and the inflammatory response manifests as redness, heat, and swelling.[4]

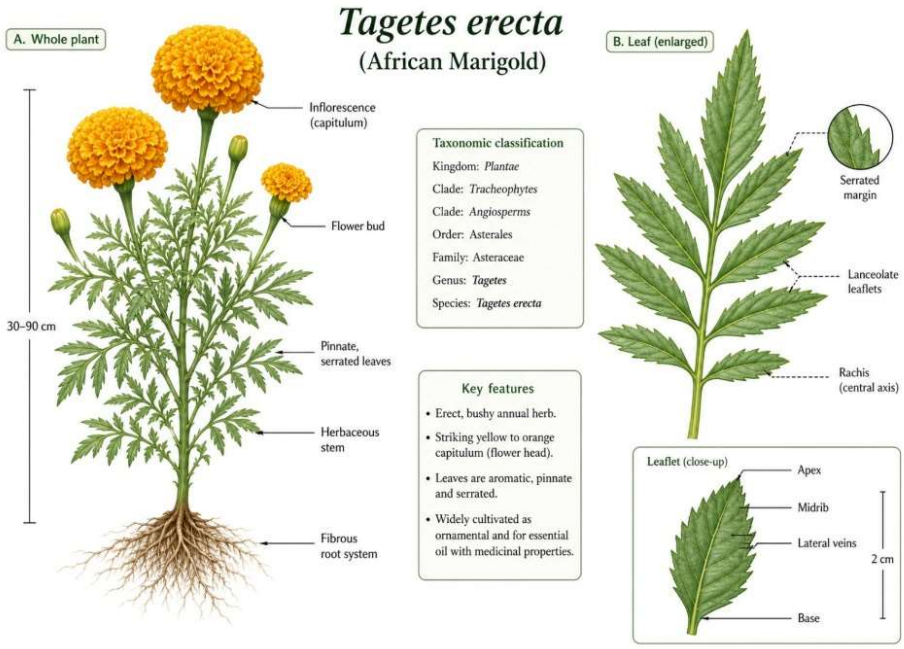
Proliferative Stage: This stage lasts approximately three weeks (potentially longer for severe wounds). Granulation tissue forms, and collagen is produced by specialised fibroblasts in this stage. New blood vessels appear. The wound gradually develops an epithelial layar.[5]

Maturation Stage: This stage lasts up to 2 years. This is the final phase, which involves remodelling the wound shape. At this stage, the surrounding tissues are strengthened through new collagen production. However, scar tissue strength reaches only approximately 80% of the original tissue strength.[5]

1.2.2 Wound Types and Classification

Based on the causative force, wounds can be classified as abrasions, lacerations, punctures, avulsions, crush wounds, burns, and ulcers. Each type has distinct healing challenges and requires different approaches for management.[6]

1.3 Challenges in Wound Healing



The wound -healing process is affected by multiple factors. This includes the following

Infections: Bacterial infections may complicate the natural wound-healing process. Infection causes swelling, redness, pain, and pus formation and risks systemic spread if untreated.

Chronic Diseases: Chronic diseases, such as diabetes, impair the wound-healing process by damaging blood vessels, reducing blood flow to the extremities, and compromising immune function. As obesity reduces blood circulation and increases inflammation, it affects wound healing. The natural wound healing process is also affected by autoimmune conditions.

Nutritional Deficiencies: The natural healing process is affected by inadequate intake of vitamins, proteins, and minerals.

Ageing: In old age, skin thins and the immune system weakens. This slows the wound-healing process.

Medications: Steroids and chemotherapy agents suppress immune function and hence affect the wound healing process.

Smoking and Stress: Nicotine reduces blood oxygen levels. Physical and emotional stress weakens immune responses. This also affects the natural healing process.[7]

1.4 Traditional Wound Healing Methods

For wound treatment, natural remedies have been used in traditional medicine for centuries. Turmeric is used as an anti-inflammatory and antibacterial agent, aloe vera is used for its soothing effects and skin repair, whereas honey is used for its natural antiseptic properties. Similarly, neem leaves are used in traditional medicine as antibacterials and antifungals. Coconut oil is used for its moisturising effect, garlic paste for its antibacterial effect, and plantain leaves for their soothing, antibacterial, and anti-inflammatory effects.[8]

1.5 Marigold (Tagetes erecta) as a Medicinal Plant

The Tagetes erecta plant leaf exhibits various pharmacological properties. This includes wound-healing, antibacterial, antifungal, antiepileptic, hepatoprotective, insecticidal, larvicidal, and antinociceptive activities. [9]

In Pharmaceutical applications, Marigold plant leaf extract is one of the most promising natural alternatives for wound healing. The marigold flowers and leaves are recognized for its anti-inflammatory, antipyretic, antibacterial, and antiepileptic properties in Ayurvedic and Unani traditional medicine systems.[10]

1.5.1 Plant Profile

Botanical Classification:

Botanical Name: Tagetes erecta L.

Common Names: African Marigold, Mexican Marigold

Subkingdom: Tracheobionta

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Asteridae

The plant is an annual herbaceous species normally reaching heights of 30-100 cm. It possesses fragrant, dark green, pinnately divided leaves and displays vibrant flower colours ranging from yellow and orange to red and mahogany. The flower heads contain numerous ray florets surrounding a central disc floret, creating a daisy-like appearance.[11]

1.5.2 Chemical Constituents

African marigold leaves contain the following bioactive compounds:
Flavonoids: These antioxidant-rich compounds—including patulin and quercetin—facilitate the extract's anti-inflammatory and wound-healing properties.
Triterpenes: Compounds such as taraxasterol and faradiol exhibit antibacterial and anti-inflammatory effects.

Carotenoids: Naturally occurring pigments, including zeaxanthin and lutein, provide antioxidant qualities that prevent cellular damage and protect against oxidative stress.

Phenolic Compounds: Chlorogenic acid and caffeic acid present in leaf extract have antioxidant and antimicrobial properties.

Essential Oils: These have antibacterial and fragrant properties. This also promotes tissue regeneration.[12]

1.5.3 Pharmacological Properties of Marigold Extract

The Anti-inflammatory properties, antimicrobial effects, Activation of collagen synthesis, and antioxidant properties of Marigold leaf extract have been established.

1.6.1. Need for the Study

Wound healing is a global healthcare challenge. Millions of people every year are affected by acute and chronic wounds. The limitations of conventional treatment include adverse effects and cytotoxicity associated with synthetic antimicrobial agents, which can hinder healing and lead to antibiotic resistance,especially with strains such as MRSA [13]. Chronic wounds impose substantial economic burdens due to prolonged care requirements. Effective wound healing is essential for preventing infection and further complications, as open wounds are vulnerable to bacteria that can cause severe infections. There is growing interest in natural alternatives, such as plant-derived antimicrobial agents. Because these agents not only demonstrate antibacterial properties but also support tissue repair. Dermal delivery systems offer an edge over traditional therapies by avoiding gastrointestinal absorption issues, enhancing patient compliance, and enabling easy discontinuation of therapy.[14]

1.6.2. Objectives of the Study

This study aims to investigate the wound-healing properties of a dermal patch containing marigold leaf extract. Specifically, the study investigates the efficiency of dermal patches containing marigold extract in promoting wound closure, antimicrobial effect, and tissue regeneration in minor wounds.

1.6.3. Significance of the Study

This study offers potential advantages over conventional wound dressings containing chemical antimicrobial agents. The study helps to identify a natural therapeutic agent and an effective delivery system for alternative medicine and natural wound care. This is to provide a cost-effective, side-effect-free therapeutic option. Marigold extract may offer sustained antimicrobial efficacy and reparative properties. It may be a superior alternative to synthetic agents for wound healing.

2. Materials and Methods

2.1 Materials and Excipients

The solvent-casting technique was used to prepare dermal patches. The following chemical excipients were utilised:

- Hydroxypropyl Methylcellulose (HPMC): A stable, safe, and non-irritating polymer used as a primary film-forming and matrix agent.
- Ethyl Cellulose (EC): A hydrophobic polymer used as a binder and film former, readily soluble in organic solvents like ethanol.
- Polyethene Glycol (PEG) 400: A clear, viscous liquid used primarily as a plasticiser to make the dermal patch flexible and to increase the solubility of the medication.
- Ethanol: Utilised as the primary organic solvent to dissolve the polymers and plant extract.

2.2 Methodology

2.2.1 Preparation of Marigold Leaf Extract

Marigold leaves were freshly harvested, washed, and dried. Extract preparation by maceration process in ethanol for 7-10 days. Then it was filtered and concentrated using a rotary evaporator. The concentrated extract was stored at 4°C in a refrigerator.

2.2.2 Formulation of Dermal Patches

Dermal patches were prepared by solvent casting using film-forming polymers. Hydroxypropyl methylcellulose (HPMC) and ethyl cellulose (EC) were accurately weighed and dispersed in ethanol. Polyethene glycol 400 was added as a plasticiser after the drug was properly dispersed in the polymeric solution. The solution was stirred using a magnetic stirrer. Then it was poured into glass Petri dishes. An inverted funnel was positioned above each dish to prevent rapid evaporation. The polymeric solution was allowed to dry for 24 hours at room temperature. [15]The ready-made patches were then separated and stored in self-sealing plastic envelopes.

Table 1: Composition of Dermal Patch of Marigold Leaf Extract

Ingredients	F1	F2	F3	F4	F5
Drug (ml)	0.3 ml	0.75 ml	1.5 ml	2.25 ml	3.0 ml
HPMC (mg)	400 mg	400 mg	400 mg	400 mg	400 mg
EC (mg)	100 mg	100 mg	100 mg	100 mg	100 mg
Polyethene Glycol (ml)	0.5 ml	0.5 ml	0.5 ml	0.5 ml	0.5 ml
Ethanol (ml)	10 ml	10 ml	10 ml	10 ml	10 ml

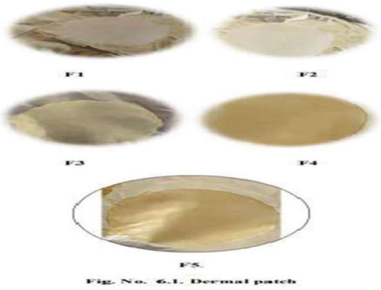


Fig. No. 6.1. Dermal patch

2.2.3 Evaluation Parameters:

Thickness Measurement: The thickness of dermal patches was measured using a digital vernier calliper at multiple locations along the film to ensure uniformity.[16]

Weight Uniformity: Ten randomly selected patches from each formulation were weighed separately. The average weight was then calculated. Individual patch weights were compared with the average weight to assess the acceptability of weight variation.[17]

Folding Endurance: Folding endurance was determined by repeatedly folding patches in the same area until breaking. The number of folds withstood without breaking was recorded as the folding endurance value.[18]

***Adhesive Studies*:** Dermal patch therapeutic effectiveness may be significantly affected by the contact quality between the skin and the patch. Pressure-sensitive adhesives (PSAs) were evaluated

for their ability to adhere to surfaces under light pressure.[19]

***Primary Skin Irritation Test*:** Conducted on the own skin using a 4.91 cm^2 circular patch, and it was monitored for irritation levels for each formulation.

[20]

***Antimicrobial Activity**:* An antimicrobial activity study was conducted against a common wound pathogenic bacterium. All formulations were evaluated against Staphylococcus aureus using the Disc Diffusion Method on Nutrient Agar. 60µl of inoculum was spread on the plates. [21]Sample dermal patches (F1-F5) and a double antibiotic control disc were placed on the agar and incubated at 37°C for 24 hours. The resulting zones of inhibition were measured.

In Vivo Wound Healing Activity: This study was conducted in Wistar rats. The rats were anaesthetised. Their dorsal hair was removed, and a full-thickness excision wound (10 mm^2) was created under sterile conditions. The wound was disinfected, and the marigold patches were applied[22]. To observe the healing process, the wound area was measured on days 3, 6, 9, 12, and 15 and compared with the control.

3. Results and Discussion

Using the solvent-casting technique, five dermal patch formulations were successfully developed at various concentrations of marigold leaf extract (0.3-3.0 ml). All formulations exhibit successful film formation with no visual defects or crystallization.

3.1. Physical Characterization

All five patch formulations successfully exhibited good structural integrity, flexibility, and physical stability. The variations in marigold extract concentration did not negatively affect the strength or uniformity of the patches.

Table 2: Physical Characterization of Dermal Patches *(Data expressed as mean value ± S.D)*

Formulations	Weight Uniformity (mg) (n=3)	Thickness (mm) (n=3)	Folding Endurance (n=5)
F1	401 ± 3.837	0.29 ± 0.0142	205 ± 1.26
F2	409 ± 1.919	0.35 ± 0.0142	208 ± 3.67
F3	417 ± 0.120	0.20 ± 0.0100	200 ± 3.67
F4	425 ± 1.910	0.37 ± 0.0100	210 ± 1.157
F5	436 ± 4.557	0.44 ± 0.0199	215 ± 3.566

*n=Number of randomly selected samples.

Physical characterization revealed that all formulations have consistent thickness measurements ranging from 0.29-0.44 mm, indicating uniform film formation. The weight of the patches (ranging from 401 mg to 436 mg) is within acceptable limits. The high folding endurance (200-215 folds) indicates that the patches possess high mechanical strength suitable for movement when applied to the skin.

3.2. Skin Irritation Test

Table 3: Primary Skin Irritation Test

Formulation	Day 1	Day 2	Day 3
F1	Negative	Negative	Negative
F2	Negative	Negative	Negative
F3	Negative	Negative	Negative
F4	Negative	Negative	Negative
F5	Negative	Negative	Negative

None of the tested formulations showed signs of erythema, oedema, or allergic reaction. This indicates that the marigold patch formulations are entirely safe and non-irritating for topical application.

5.3. Antimicrobial Activity

Table 4: Antimicrobial Activity against Staphylococcus aureus

Formulations	Observation	Result
C (Control)	Visible growth with zone of	Susceptible

	inhibition (17.5 mm)	
F1	Visible growth with no zone of inhibition	Resistant
F2	Visible growth with a very small zone of inhibition (14 mm)	Mildly Susceptible
F3	Visible growth with no zone of inhibition	Resistant
F4	Visible growth with no zone of inhibition	Resistant
F5	Visible growth with a very small zone of inhibition (12.75 mm)	Mildly Susceptible

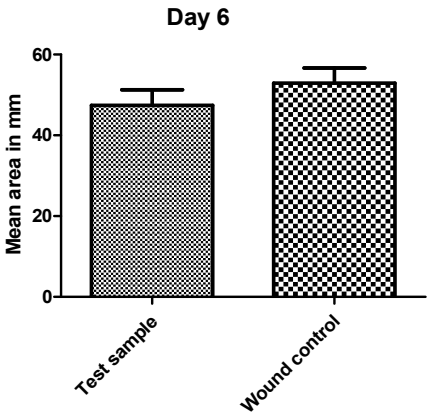
Formulations F2 and F5 exhibited distinct zones of inhibition against *Staphylococcus aureus* (14mm and 12.75mm, respectively). Formulations F1, F3, and F4 failed to produce a zone of inhibition. The active antimicrobial agents in F2 and F5 may exhibit optimised solubility and diffusion properties within those specific polymer ratios, allowing the bioactive compounds to diffuse into the culture medium effectively, whereas poor diffusion in the other samples prevented them from reaching bactericidal concentrations. Based on these results, only formulations F2 and F5 were selected for the *in vivo wound-healing* studies.

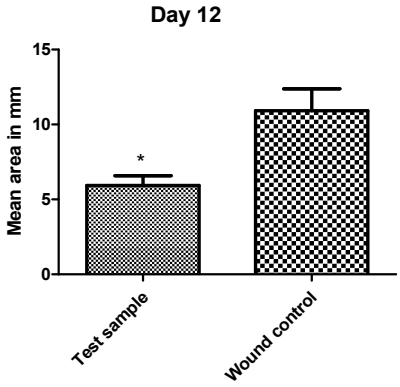
5.4. In-Vivo Wound Healing Activity The *in-vivo* excision wound model on Wistar rats were used for the study. A comparison of normal untreated wounds with wounds treated with patches F2 and F5 was conducted. On Day 3, minimal changes were noted across all groups. However, from Day 6 onward, the rats treated with the marigold patches showed vastly superior recovery rates. By Day 15, the treated wounds achieved near-complete healing, with the mean wound area of the test subjects reducing to an extraordinary 0.3 mm. The patches successfully accelerated tissue regeneration, wound contraction, and epithelialization compared to the control group.

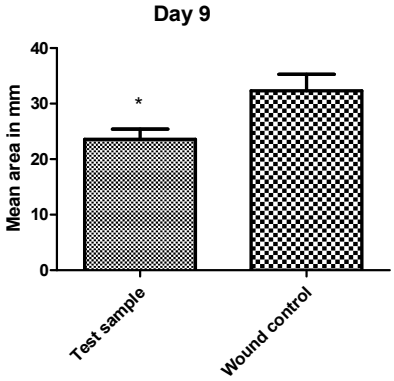
Table 6. wound area in (mm)

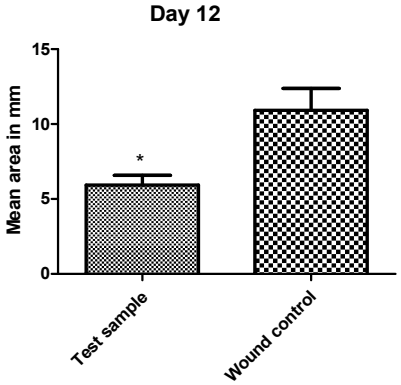
Sr. no.	Animal no	Day.0 F2	Day.0 F5	Mean	Day.6 F2	Day.6 F5	Mean	Day.9 F2	Day.9 F5	Mean	Day.12 F2	Day.12 F5	Mean	Day.15 F2	Day.15 F5	Mean
Dermal Patch	1	100	100	100	56	54	55	25	24	24.5	5	7	6.5	0.2	0.2	0.25
	2	100	100	100	30	20	25	12	18	15	6	5	5.5	0.3	0.3	0.25
	3	100	100	100	56	63	59.5	24	28	16	9	6	7.5	0.4	0.4	0.4
	Mean	100	100	100	47.3	47.3	46.5	20.3	23.5	21.8	6	6	6.5	0.3	0.3	0.3
Normal	14	100	100	100	72	72	72	25	20	22.5	12	8	10	5	7	6
	15	100	100	100	48	56	52	33	34	33.5	12	6	9	6	7	6.5
	116	100	100	100	81	45	63	38	36	37	6	6	6	7	7	7
	Mean	100	100	100	55	53	53.7	32	30	31	10	8.3	10.9	5	7	6.5

GRAPHS

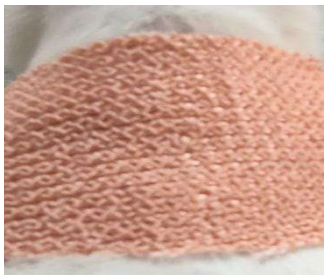






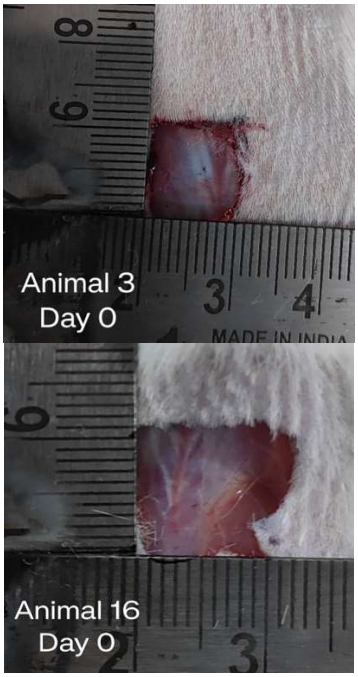


WOUND IMAGES

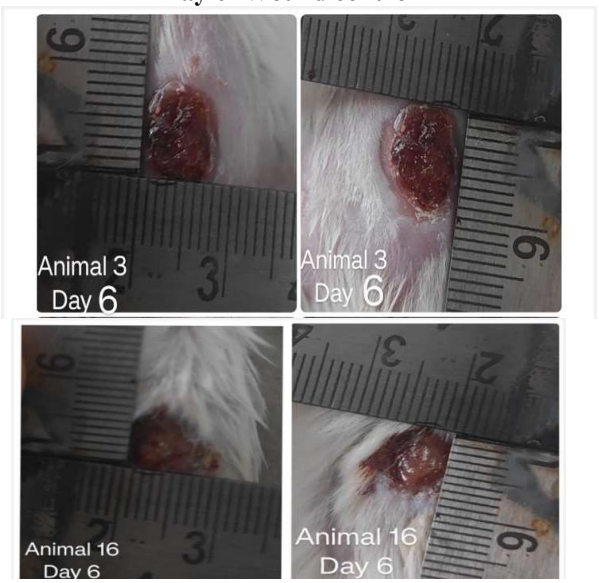


Wound creation, dressing and application of a patch

Day 0 – Test Sample
0 – Wound control

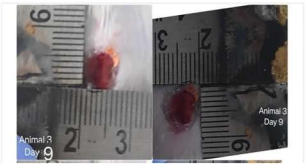


Day 6 – Treated
Day 6- Wound control

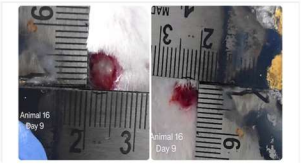


Day 3 Test sample
3 Wound control

Day 9- Test Sample

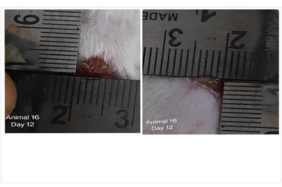


Day 9 Wound control



Day 12 – Test sample

Day 12-Wound control



Day 15 – Treated
15- Wound control

The treated wound areas were significantly smaller than those in the normal wound group. Plant extract in the dermal patch shows better recovery and activity than the control wound in normal animals. In this study, the plant extract-loaded dermal patch showed better activity than the control wounds in normal animals. On day 3, there was no change in both groups. However, an effect was observed from day 6 onward, and by day 15. The Complete healing was observed in the drug-treated group compared with the control group, as indicated by the graphical representation.

In vivo wound-healing studies showed that marigold extract-loaded dermal patches exhibited therapeutic efficacy. Wounds treated with marigold extract patches showed faster tissue regeneration and wound closure.

6. Conclusion

The present study demonstrated that both formulations, F2 and F5, exhibited excellent physicochemical properties, antimicrobial activity, and in vivo wound-healing activity.

This extensive study validates the efficacy of marigold leaf extract as a potent, natural wound-healing agent when formulated into a transdermal matrix patch. The developed patches not only exhibited physical stability and durability but also a continuous release profile. The wounds treated with the patches demonstrated accelerated tissue regeneration, significantly faster wound closure, and superior recovery compared to untreated controls in an *in vivo* animal testing model.

Furthermore, the extracts incorporated into the dermal patch are also effective against Staphylococcus aureus, a pathogen responsible for major wound infections

Natural marigold leaf extract provides a safer alternative to chemical-based wound dressings because of its reduced adverse effects and greater environmental friendliness. Formulation F5 is the recommended formulation for antimicrobial and wound-healing activity.

This study provides an effective natural treatment for minor wounds, using a plant extract in a dermal patch to accelerate healing, protect against infection, and offer a sustainable alternative to synthetic wound dressings.

7. FUTURE SCOPE OF STUDY

Despite encouraging animal testing results and the antimicrobial activity of the prepared dental patch, further clinical studies are necessary to confirm the efficacy and any adverse effects of the recommended patches in various human skin types and chronic minor wounds. Future research should focus on the release kinetics of medicament from the dermal patches to the wound bed.

8. ACKNOWLEDGEMENT

The authors wise to acknowledge to the

9. REFERENCES

[1] A. Metelitsa, I. Delorme, D. O'Sullivan, R. Zeinab, M. Legault, and M. Gooderham, "A Practical Guide to Advanced Topical Drug Delivery Systems in Dermatology.," *Skin therapy letter*, vol. 28, no. 5, Sept. 2023.

[2] C. Tiwari, M. Choudhary, P. Malik, P. K. Jaiswal, and R. Chauhan, "Transdermal Patch: A Novel Approach for Transdermal Drug Delivery," *J. Drug Delivery Ther.*, vol. 12, no. 6, pp. 179–188, Nov. 2022, doi: 10.22270/jddt.v12i6.5779.

[3] T. Velnar, T. Bailey, and V. Smrkolj, "The Wound Healing Process: An Overview of the Cellular and Molecular Mechanisms," *J Int Med Res*, vol. 37, no. 5, pp. 1528–1542, Oct. 2009, doi: 10.1177/147323000903700531.

[4] S. Engebretson, "Wound Healing." Wiley, pp. 14–17, Oct. 18, 2022. Doi: 10.1002/9781119793588.ch2.

[5] B. Praveen, "Wounds, tissue repair and scars," Crc, 2010, pp. 32–37. doi:10.1201/b13477-12.

[6] J. Pope, "Wound aetiology and classification," British Small Animal Veterinary Association, 2009, pp. 15–24. doi: 10.22233/9781905319558.2.

[7] H. A. Ahmed, N. K. Jawad, and J. I. A. Alrubaye, "Factors influencing wound healing after surgical procedures: A comprehensive clinical study," *Int. J. Case Rep. Surg.*, vol. 6, no. 2, pp. 122–125, July 2024, doi: 10.22271/27081494.2024.v6.i2c.123.

[8] N. Babu, A. Singh, and N. Navneet, "Traditional Herbs With Potential Wound Healing Properties," Igi Global, 2022, pp. 214–232. doi: 10.4018/978-1-6684-3546-5.ch012.

[9] "A REVIEW ON PHYTOCOMPOUNDS AND PHARMACOLOGICAL ACTIVITIES REPORTED FOR TAGETES ERECTA," *IJBPAS*, vol. 12, no. 12, Dec. 2023, doi: 10.31032/ijbpas/2023/12.12.7665.

[10] O. O. Maliuhina, H. P. Smoilovska, I. F. Bielenichev, O. V. Mazulin, and T. V. Khortetska, "Wound healing activity of the lipophilic extract of Tagetes erecta L.," *ZMJ*, vol. 0, no. 2, Apr. 2019, doi: 10.14739/2310-1210.2019.2.161510.

[11] J. Rojas-Sandoval, "Tagetes erecta (Mexican marigold).," Dec. 22, 2020, *Cabi*. doi: 10.1079/isc.52641.20203483362.

[12] H. Tenggono Son and D. Limanan, "Antioxidant Capacity Test, Total Phenolic, Total Alkaloid, and Toxicity of Marigold Flower (Tagetes Erecta L.)," *devotion*, vol. 4, no. 1, pp. 88–95, Jan. 2022, doi: 10.36418/dev.v4i1.352.

[13] P. M. Filius and I. C. Gyssens, "Impact of increasing antimicrobial resistance on wound management.," *American Journal of Clinical Dermatology*, vol. 3, no. 1, pp. 1–7, Jan. 2002, doi: 10.2165/00128071-200203010-00001.

[14] M. H. Hashempur *et al.*, "Topical Delivery Systems for Plant-Derived Antimicrobial Agents: A Review of Current Advances," *International Journal of Biomaterials*, vol. 2025, no. 11, p. 4251091, Jan. 2025, doi: 10.1155/ijbm/4251091.

[15] S. Keshari, A. Verma, and S. Pandey, "FORMULATION AND CHARACTERIZATION OF TRANSDERMAL PATCHES: A REVIEW," *IJPSM*, vol. 9, no. 5, pp. 83–90, May 2024, doi: 10.47760/ijpsm.2024.v09i05.009.

[16] T. A. Peterson, S. M. Wick, and C. Ko, "Design, Development, Manufacturing, and Testing of Transdermal Drug Delivery Systems," Crc, 2020, pp. 121–162. doi: 10.1201/9781315374215-4.

[17] V. N. Kushare, "Preparation of Transdermal Patch and Evaluation of Physical Parameters," *IJSRSET*, pp. 1–4, Dec. 2018, doi: 10.32628/ijsrset21841133.

[18] D. Committee, *Test Method for Folding Endurance of Paper by the M.I.T. Tester*, Dec. 18, 2008. doi: 10.1520/d2176.

[19] L. Wang, J. Ma, J. Li, L. Fang, and C. Liu, "Transdermal patch based on pressure-sensitive adhesive: the importance of adhesion for efficient drug delivery," *Expert Opinion on Drug Delivery*, vol. 22, no. 3, pp. 405–420, Feb. 2025, doi: 10.1080/17425247.2025.2460650.

[20] D. Basketter, G. Gilpin, M. Kuhn, D. Lawrence, F. Reynolds, and E. Whittle, "Patch tests versus use tests in skin irritation risk assessment.," *Contact Dermatitis*, vol. 39, no. 5, pp. 252–256, Nov. 1998, doi: 10.1111/j.1600-0536.1998.tb05919.x.

[21] G. Gito and E. Rochmawati, "Effectiveness of Modern Wound Dressing on the Growth of Staphylococcus Aureus Bacteria," *JK*, vol. 9, no. 2, p. 88, July 2018, doi: 10.22219/jk.v9i2.5160.

[22] G. E. Deligiannidou, K. Papadimitriou, E. Poulios, C. Kontogiorgis, S. K. Papadopoulou, and C. Giaginis, "An Update of Phytotherapeutic Advances of Marigold (Calendula officinalis L.) in Wound Healing," *Plants*, vol. 14, no. 22, p. 3497, Nov. 2025, doi: 10.3390/plants14223497.