Formulation and Evaluation of Moringa oleifera Leaf Extract Loaded Transdermal Patches with Antioxidant Activity for Rheumatoid Arthritis Management

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ABSTRACT

Introduction: TDDS are among the best ways to administer medications. through skin into blood circulation, with the advantages of fewer adverse drug effects in the gastrointestinal tract, improved bioavailability, sustained release and avoiding first-pass metabolism. *Moringa oleifera* is indigenous to the Indian subcontinent, having intense antioxidant and anti-inflammatory activities, studied for thousands of years in traditional medicine, and possessing high bitter and spicy compounds, including flavonoids, polyphenols, vitamins and minerals. It is being studied for RA (rheumatoid arthritis) treatment, which is an aggressive immune illness that progresses over time due to the destruction of the joints. **Aim and Objective:** To develop and evaluate the *M. oleifera* leaf extract-loaded transdermal patches and compare the physicochemical and antioxidant activities for RA management. **Materials and Methods**: *M. oleifera* leaves were collected, washed, shade-dried and powdered. The extracts were ready for aqueous extraction. The solution-used casting procedure was used to make a drug that used the film-forming polymer like HPMC K, glycerine gelatine as a secondary polymer and dimethyl sulfoxide (DMSO) as the permeation enhancer. Physiological properties have been assessed for solutions. And also various tests are carried out, like moisture absorption and pH, and the technique has been employed to determine antioxidant activity. **Results:** The prepared patches were smooth, flexible and uniform in appearance. All the formulations showed acceptable physicochemical properties. F3 showed the best antioxidant activity with an IC50 value of 62.2 ppm, followed by F2 (67.5 ppm) and F1 (72.5 ppm), indicating better free detoxification of charges. **Conclusion:** To possess the ability to select a formulation for the prevention of RA, an *M. oleifera* transdermal patch was successfully prepared; F3 had the best antioxidant activity.

KEY WORDS Transdermal Drug Delivery System (TDDS), *M. oleifera*, Rheumatoid Arthritis, Antioxidant Activity, Herbal Transdermal Patch.

INTRODUCTION

TDDS

One commonly used and efficient technique for delivering drugs is by way of this system. It has gained most of its popularity over other methods of delivery because of their efficiency, ease of use, and patient compliance (Evans, 2009). This is considered one of the cost-effective, safe, and practical means of delivering drugs. Designing a TDDS is primarily concerned with targeting specific sites of action and controlling the delivery of the drug at optimal therapeutic levels (Dyer, 2000). These are self-contained dosage forms that, when put on intact skin, work towards the controlled taking in medication present in the blood (Kokate *et al.,* 2008). A medicated adhesive, it operates on the epidermis. And releases a medication into the bloodstream at a controlled rate when put on intact skin is termed a transdermal patch or skin patch. While incorporating the drugs into TDDS patches, the aim is increasing penetration via the dermis while decreasing their retention and breakdown in the body (Akinyemi *et al*., 2021). Transdermal drug administration is a successful method of delivering drugs systemically and locally. A few benefits related to topical medication administration include painless, non-invasive, and convenient drug administration; protection from stomach acids; and sustained, consistent release of medication (Gupta, 2003).

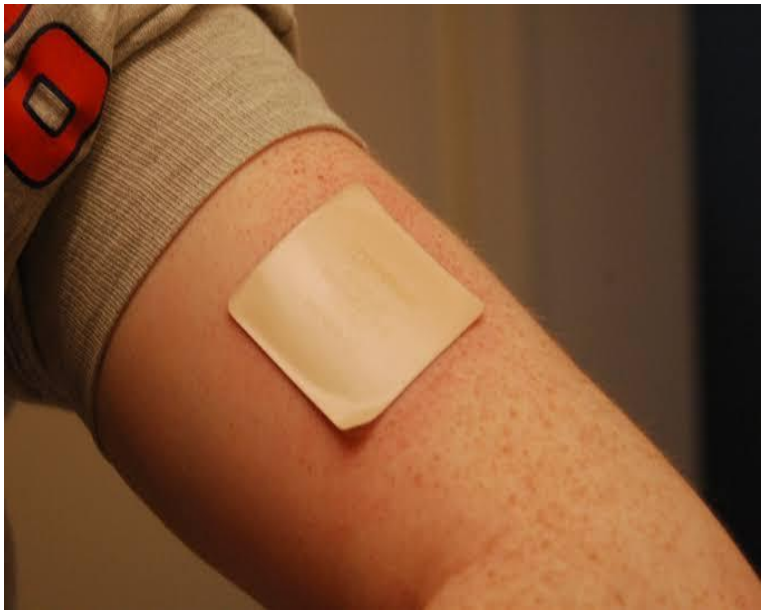

Fig. no. 1: Transdermal Patch (Mahato *et al*., 2025).

Merits

- TDDS enables a constant drug level in the bloodstream by providing continuous absorption of the medicine into skin .
- Since the drug is absorbed and not taken actively.
- By avoiding first-pass metabolism through the stomach, it is advantageous for patients having gastric disorders.
- TDDS maintains a steady-state plasma concentration of drug over time, like intravenous infusion.
- In case of an adverse effect, the patch can be easily taken off to avoid further drug absorption.
- The user-friendly design of TDDS provides an easy way for patients to administer the drug (Rashed *et al*., 2019).

Demerits

- Many hydrophilic drugs cannot readily via epidermis or only do so very slowly, and this can compromise their therapeutic effect.
- erythema, and edema may occur when using a transdermal patch.
- Epidermal role changes with Class, between individuals, and in different areas of the body (Ansel *et al*., 1995).

Primary Components Used in the Formulation

Backing Film: This is the first layer of the transdermal patch, intended as a protective layer for the medicament formulation once the patch is in use. It is often used as a printable surface for product instructions or directions on how to use the patch. In some cases, the backing supports keeping the medicament formulation in place thus, it becomes necessary to use a material of high toughness and strength.

Drug Formulation: The term refers to the active pharmaceutical ingredients within the patch that are gradually released into and absorbed by skin. Membrane: A membrane is employed for offering regulation of the frequency of emission from the medicament formulation and to allow controlled delivery to the skin.

Liner: This protective layer, which covers the adhesive side of the patch, is removed immediately before use. While this seems simple, the liner must also be easy to remove, become regulatory compliant, and be compatible with the drug formulation and adhesive.

Classification of Transdermal Patch

1. Rate Programmed Transdermal Patches
2. Physical Stimuli Activated Transdermal Patches

Rate Programmed Transdermal Patches (Prajapati *et al*., 2020).

Different type of Rate Programmed Transdermal Patch

Membrane Patch

Membrane thin films can contain many different materials. These include silicones, polyester elastomers, and high-density polythene. The covering is expected to be capable of preserving additional manufacturing ingredients, including enabling medication distribution & penetration enhancers if needed. Various materials are suitable to the drug reservoir; they can be simple arrangements such as mineral oil or more complex systems such as gels or aqueous alcohol solutions with or without co-solvent (Samuel *et al*., 2021).

Drug in Matrix

In this form of medication delivery, the drug is embedded in the polymeric matrix in a uniform manner prior to diffusion to the outermost exterior (Khandelwal *et al*. 2010). This matrix, acting as a drug reservoir, often consists of polyvinyl pyrrolidone. The molecules eventually make their way to the skin's surface by diffusing through the matrix.

Drug-in-Adhesive Matrix

In these simple systems, the patch is produced by placing a combination of an adhesive mixture containing both the medication and the enhancer onto a backing layer (e.g., polyester film).In these simple systems, the patch is produced by placing a combination of an adhesive mixture containing both the medication and the enhancer onto a backing layer (e.g., polyester film). (John, 2000).

Drug in Micro reservoir

This method creates a reservoir by suspending the medication in an aqueous solution of a water-soluble polymer.

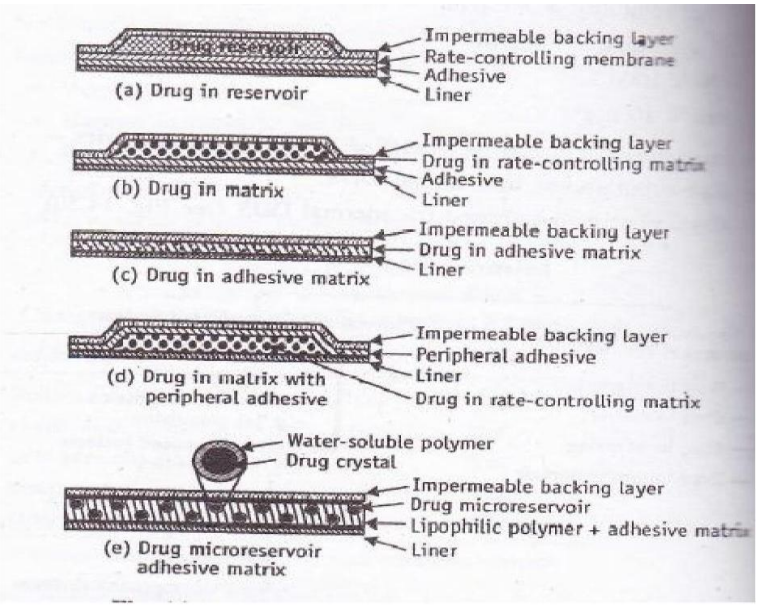

Fig. no. 2: Different type of Rate Programmed Transdermal Patch (Mahato *et al.*, 2025).

Physical Stimuli Activated Transdermal Patches

Drug delivery transdermally can be achieved not only with 'normal' transdermal patches but also with other methods. The system consists of a thin titanium screen with 200 μm-long micro-projections attached to the bottom side. When the system is pressed into the skin, superficial routes through the nerve free stratum corneum are created without damaging the dermal receptors because of the micro-projection length. For bolus administration, drugs can be coated directly on the micro-projections. This TDDS is capable of delivering biopharmaceuticals, low molecular weight substances, and vaccines.

Types of physical stimuli-activated systems:

1. Structured systems, such as microneedles
2. Systems depending on velocity, such as propulsion
3. Electrical systems, such as microneedles, Iontophoresis, fourth
5. Electrochemistry
6. The sonophoresis method
7. Waves produced by photomechanical

MOA of Transdermal Patches

It has various methods of applying the transdermal patch and transferring the active ingredient to circulate through the skin. The phases of medication distribution in a transdermal patch are listed below (Jesindha *et al*., 2020).

1. Medication is released from the vehicle.

2. Getting past the boundaries of the skin.

3. The pharmaceutical response being triggered.

Three essential components have to coexist for transdermal patches to be a successful treatment approach: the medicine, the vehicle, and the skin. In systems like TDDS, this uses a rate-controlling barrier to control percutaneous absorption; these parameters collectively affect the flow of drug molecules. To allow molecules to permeate towards the patch membrane, drug particles must first dissolve in the vehicle (More *et al*., 2013). While some medications penetrate deeper where they split into the viable epidermis, others can build up at a depot site. The partitioning coefficient for lipophilic compounds could be less favourable (i.e., smaller than 1). Enzymes in the epidermis may interact with receptors or metabolise the medication. Before the medication enters the capillary system, where it divides into the capillary wall and enters the bloodstream for systemic circulation, it may be redirected by additional depot sites and metabolic processes once it reaches the dermis. Non-steroidal anti-inflammatory medicines were demonstrated as beneficial when a fraction of medication reaches deeper muscle layers and deposits into subcutaneous fat, forming another depot. Tissue non-homogeneity, lymphatics, interstitial fluid, hair follicles, sweat glands, cell division, and the movement of cells across the skin are certain of the complicating elements. The healing process, medication formulation, and vehicle components. Sweat, sebum, cellular debris, and surface impurities are all carried by the vehicle ingredients when they enter the skin and alter the physicochemical characteristics of the dermis. Volatile solvents may evaporate and emulsions may degrade or invert when applied.

Skin

With its whole external surface, the human epidermis is its large organ. Additionally, this organ controls the amount of water discharged into the atmosphere and the temperature. The thickness of the dermal and epidermal layers affects skin thickness, which varies by body region. Due to its thick epidermis, the back has the thickest skin among these areas (Bonifant et al., 2019). The epidermis is vulnerable to some inflammatory and infectious diseases due to barrier role. Furthermore, cosmesis, sensory alterations, and wound healing are important surgical issues.

Organisation and Purpose

Epidermis

The accumulation contains aberrant, polyhedral cells with cytoplasmic approaches sometimes called spine that grow outward and use desmosomes to make contact with other cells. This layer allows for the identification of dendritic cells (Herskovitz *et al*., 2016). With three to five cellular layers, the stratum granulosum contains lamellar granules and diamond-shaped cells with keratohyalin. Keratin precursors detected in grains of a protein called agglomerate, cross-link. The glycoproteins secreted to the mobile surfaces are incorporated into the lamellar granules, which act as an adhesive to maintain cellular cohesion. The thicker skin of the arms and soles contains the stratum lucidum, which is composed of two to three cell layers. Eleidin, a modification made from keratohyalin, is part of this thin, clean layer. Keratin and dead keratinocytes, which are nucleate squamous cells that form appealing scales, constitute the outermost layer of cornea.

Dermis

The basement membrane serves as the connection between the dermis. The papillary and reticular connective tissue layers, which make up the epidermis, blend together without obvious boundaries. The basement membrane serves as the connection between the dermis. The papillary and reticular connective tissue layers, which make up the epidermis, blend together without obvious boundaries.

Hypodermis

The subcutaneous fascia, called the hypodermis, is located beneath the dermis. This layer, called the private skin layer, has blood arteries and adipose lobules and afferent neurones, as well as a small number of follicles and other dermatological extensions.

Functions

The skin many functions demonstrate its complexity and significance in maintaining normal health and fitness. Below is a discussion of these responsibilities.

Barrier characteristic

Some larger proteins form a strong working barrier, for example, cystatin, desmoplakin and filaggrin. The lipid envelope is a hydrophobic layer that is joined to the plasma membrane of the outer cell. Keratinocytes from the stratum spinosum produce keratohyalin granules, and lamellar bodies are formed in the Golgi complex, including glycosphingolipids, phospholipids and ceramides

Law of homeostasis

Skin and pores are important for water stability and metatarsus temperature. The exocrine functions of the pores and skin are to bring down the body temperature through sweating and to protect the skin by secreting sebum. Sebaceous glands and sweat are necessary for these functions. A person's skin evaluation is often an important part of their physical assessment(O connell *et al.,* 2015).

Rheumatoid arthritis

Arthritis is a disease which is characterised by pain and swelling of a joint or joints. The most common symptoms include joint pain and stiffness, which may increase in severity with age. The two predominant forms are osteoarthritis and rheumatoid arthritis. Osteoarthritis results from degeneration of the cartilage that sits between the ends of the bones in the joint and associated pain, oedema and joint movement problems. When osteoarthritis spirals out of control, the bones themselves may come into contact; osteoarthritis symptoms may develop into painful contact between bones. Conversely, rheumatoid arthritis is an autoimmune disease in which the immune system targets self-tissues and joints; the immune system can, over time, cause inflammation and pain to the joint and, in time, damage and deform the joint (Patel et *al.,* 2011). Causes of different types of arthritis can vary. Gout is caused by a build-up of uric acid, which produces crystals that form in the joint (Rajgor *et al*., 2023); other types of arthritis may be the result of other conditions such as psoriasis or lupus. Treatment can consist of painkillers and anti-inflammatory drugs, motion enhancers, lifestyle modifications and, in extreme cases, joint replacement surgery.

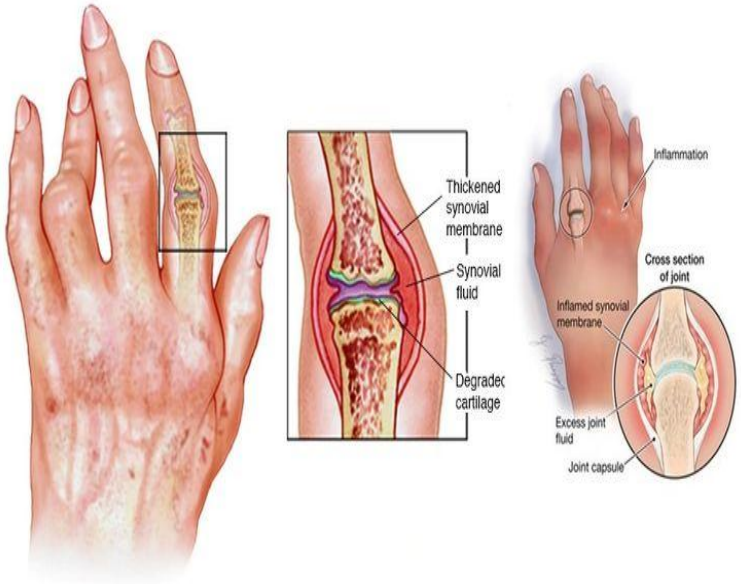

Fig. no. 3: Rheumatoid Arthritis in Joints.

Pathogenesis of Rheumatoid Arthritis

The body's own defenses attack the joints in rheumatoid arthritis (RA), a chronic immune mediated disorder. The results are oedema or swelling of the tissues cell lining the joint, and the increased destruction of the articular bone and cartilage. Immune proteins, such as Ig M, stimulate other defense agents that then promote or stimulate the inflammatory cycle by releasing signals such as TNF and IL-1. These are picked up by the defense cells around the joint, which then release mediators that enhance pain and warmth in the tissues and lead to destructive changes in the joint. Due to the joint type and the fact that joints in the hand and feet are more typically affected, the disease will generally progres. It appears that epigenetic processes such as DNA methylation, modifications to Histone proteins, and present in MicroRNA, enable the activation of inflammation and result in continuous production of inflammatory cytokines and auto reactive inducing self-antibodies. Continued activation of RANKL pathways activated the osteoclasts, resulting in breakdown of the osseous tissue, and continued apoptosis of the chondrocytes leads to loss of the cartilage scaffolding. This knowledge has underpinned the development of the disease modifying anti-rheumatic drugs (DMARDS) and Cytokine blocked therapies that target the TNF- α, IL-6 and Janus kinase (JAK) pathways. (Firestein, 2018).

Plant Profile

Table no. 1: Taxonomical classification (Stevens *et al.*, 2013)

Kingdom	Plantae
Sun kingdom	Tracheobionta
Super division	Spermatophyte
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Dilleniidae
Order	Capparales
Family	Moringaceae
Genus	Moringa
Species	Oleifera

Fig. no. 4: *M. oleifera* leaves (Rastogi *et al.*, 2012).

Phytochemical Constituents

Bioactive substances found in *M. oleifera* include:

Flavonoids: kaempferol, quercetin.

Phenolic acids: include caffeic acid and chlorogenic acid.

Isothiocyanates and glucosinolates: 4-(α-L-rhamnosyloxy) benzyl isothiocyanate.

Vitamins: vitamins A and C.

Minerals: iron, calcium, and potassium (Rastogi *et al*. 2012).

Cultivation

It thrives in warm, humid climates and on clay or clay-type soils with adequate water drainage. A seed must be slightly fresh in order to germinate successfully.. Stem cuttings, which range in length from 10 to 60 cm, are also best planted in the spring and summer (Patel *et al*., 2010).

MATERIALS AND METHOD

Collection, identification and authentication of plant material

The plant of *M. oleifera* was collected from Sangola region, Solapur District, Maharashtra, India, and was authenticated by Dr. Pawar R. G., Department of Botany, Sangola Mahavidyalaya, Sangola. Authentication certificate No. 2175/2025-26 dated 6 April 2026 was obtained from sangola Mahavidyalaya, Sangola.

Drugs and chemicals

All excipients i.e. hydroxypropyl methylcellulose (HPMC), polyethylene glycol 400 (PEG 400), glycerol, gelatin and dimethyl sulfoxide (DMSO) have been employed in the preparation

the active component used was *M. oleifera* leaf powder extract. All chemicals and reagent used were of analytical grade.

Instruments

The formulation and evaluation were performed using a various instruments ensure homogeneous mixing. Standard laboratory glassware such as beakers (50 and 100 ml), glass rods and measuring cylinders, Petri plate/Molds were used during the formulation process. The formulation was dried using a hot air oven (Sandeepthi *et al*., 2017).

Processing of plant materials

Standard scientific techniques were used in the laboratory in handling the plant material, the processes were performed carefully by using the appropriate methods as shown below: Sorting: Bruised, discoloured, leaving a small pile of fresh, green, healthy, undamaged, insect free leaves (Isitua *et al.,* 2015).

Extraction process

Solvent extraction process Water (aqueous) extraction: The extraction process is as follows: 500 g of A portion of crushed leaves had been immersed in 1.5 litres (hot) 60°C ionised water. Each extract was conditioned for 1 complete day, and then they were sifted in muslin wrapping and filtered through a Buchner funnel. They were then centrifuged at 6000 rpm and subsequently subjected to a freeze dryer to condense it. And store it in air tight container (Makanjuola *et al.,* 2013).

Table no. 2: Materials and Purpose

Sr. No.	Ingredients	Purpose
1	Hydroxypropyl Methyl cellulose (HPMC)	Film-forming polymer
2	PolyethyleneGlycol400 (PEG400)	Plasticizer
3	Glycerol	Plasticizer
4	Gelatin	Secondary polymer
5	Dimethyl Sulfoxide (DMSO)	Permeation enhancer/Solvent
6	*M. oleifera* leaf powder extract	Active ingredient
7	Distilled Water	Solvent

Methods

Hydroxypropyl methylcellulose together with gelatin were first dissolved in distilled water. The mix was kept stirring, on a magnetic stirrer until it became a clear and uniform polymer like solution. Then a plasticizer, for example polyethylene glycol 400 or simple glycerol was added to make it more flexible and to help the film forming ability of the final patch. This part was mixed well. Afterwards the *M. oleifera* extract was put into the solution, and then a permeation helper which used to help the active pass through the skin more easily. The whole blend was stirred thoroughly to make sure everything was spread evenly. That transfer into Petri dishes and spread out evenly to make a thin uniform layer. They were placed in a hot air oven and dried until completely dry. Once dry, the patches were carefully removed cut into the needed sizes, kept in suitable box to protect them from moisture and from contamination (Sandeepthi *et al*., 2017).

Table no. 3: Composition of formulation

Sr. No.	Ingredients	Formulation			Purpose
		F1	F2	F3	
1	*M. oleifera* leaf powder extract	0.5 gm	0.5 gm	0.5 gm	Active drug ingredient
2	PolyethyleneGlycol400 (PEG400)	0.08 gm	0.16 gm	0.32 gm	Plasticizer
3	Glycerol	0.12 gm	0.24 gm	0.48 gm	Plasticizer
4	Gelatin	0.08 gm	0.16 gm	0.32 gm	Secondary polymer
5	Dimethyl Sulfoxide (DMSO)	0.08 ml	0.16 ml	0.32 ml	Permeation enhancer/Solvent
6	Hydroxypropyl Methyl cellulose (HPMC)	0.8 gm	1.6 gm	3.2 gm	Film-forming Polymer
7	Distilled Water	08 ml	08 ml	08 ml	Solvent

EVALUATION TEST FOR TRANSDERMAL PATCHES

Organoleptic Characteristics

The patch piece appearance, its colour clarity flexibility and smoothness were looked at to decide the physical quality. A visual check was done to see if it was all the same and no bubbles or cracks and also the patch transparency was noted. Flexibility was tested by folding gently

the patch to make sure it did not break. Smoothness was felt by touch to confirm an even surface. A good patch should be all the same, smooth and able to bend.

Weight Uniformity

Three pieces were picked at random from every batch and weighed one by one on a properly calibrated analytical balance. Then the average mass of those pieces was worked out, and the calculate it for each set. Basically, this was done to judge how uniform the mass is, as well as how steady the casting method turns out to be. When the percentage deviation stays low Compared with mean, it suggests a fairly even spread of the matrix of polymer then the drug across the patches. Every measurement got repeated three times (Yadav *et al*., 2021).

Average Weight= $\frac{W1+W2+W3}{n}$

Where:

W1, W2, W3 = individual patch weights

N=Number of patches

% Deviation= Wi-Average Weight/ Average Weight × 100

Where:

W_1 = individual patch weight

Folding Endurance

Take a patch, fold it at the same place repeatedly until it breaks or cracks visibly. Count and record how many folds it takes to break. Carefully perform the test to keep uniformity of folding pressure. Repeat procedure on at least 3 patches of each formulation. Compute the average value of folding endurance. The test is indicative of the patch flexibility and mechanical strength.

Moisture content

Method: Weigh the prepared films one by one. Then they are left in a desiccator, a closed container filled with calcium chloride. Calcium chloride takes the moisture. The films were re-weighed after one day. This procedure is repeated until the weight stabilises. Finally, the films are analysed for percent moisture content using a formula.

% Moisture Content = [(Initial weight – Final weight) / Final weight] × 100

pH

A test solution prepared by dissolving a suitable quantity dist. Vehicle in patch taken. The solution was kept for proper removal . This solution was then determined by calibrated LT-5001 table top pH meter. The electrode was dipped into the solution and readings were taken.

This measurement was taken again for accuracy. This test confirms the patch is compatible with skin pH (Parveen *et al.,* 2025).

***In Vitro* Studies**

Antioxidant Activity

DPPH Method

Preparation of reagents DPPH (0.1 mM conc.) 1mL of DPPH has been combined using

pH 7.4 Tris HCL buffer. The solution collected in microwells at various concentrations (1 mL). Five hundred seventeen nm was used to quantify absorbency

with butylated hydroxytoluene as control. The eggs hatched in half an hour. Absorption was observed at 517 nm. As control, BHT was used (Yokozawa *et al.*, 1998).

The percentage of inhibition formula:

Inhibition (%) = [(Absorbance of control – Absorbance of test sample) / Absorbance of control] × 100

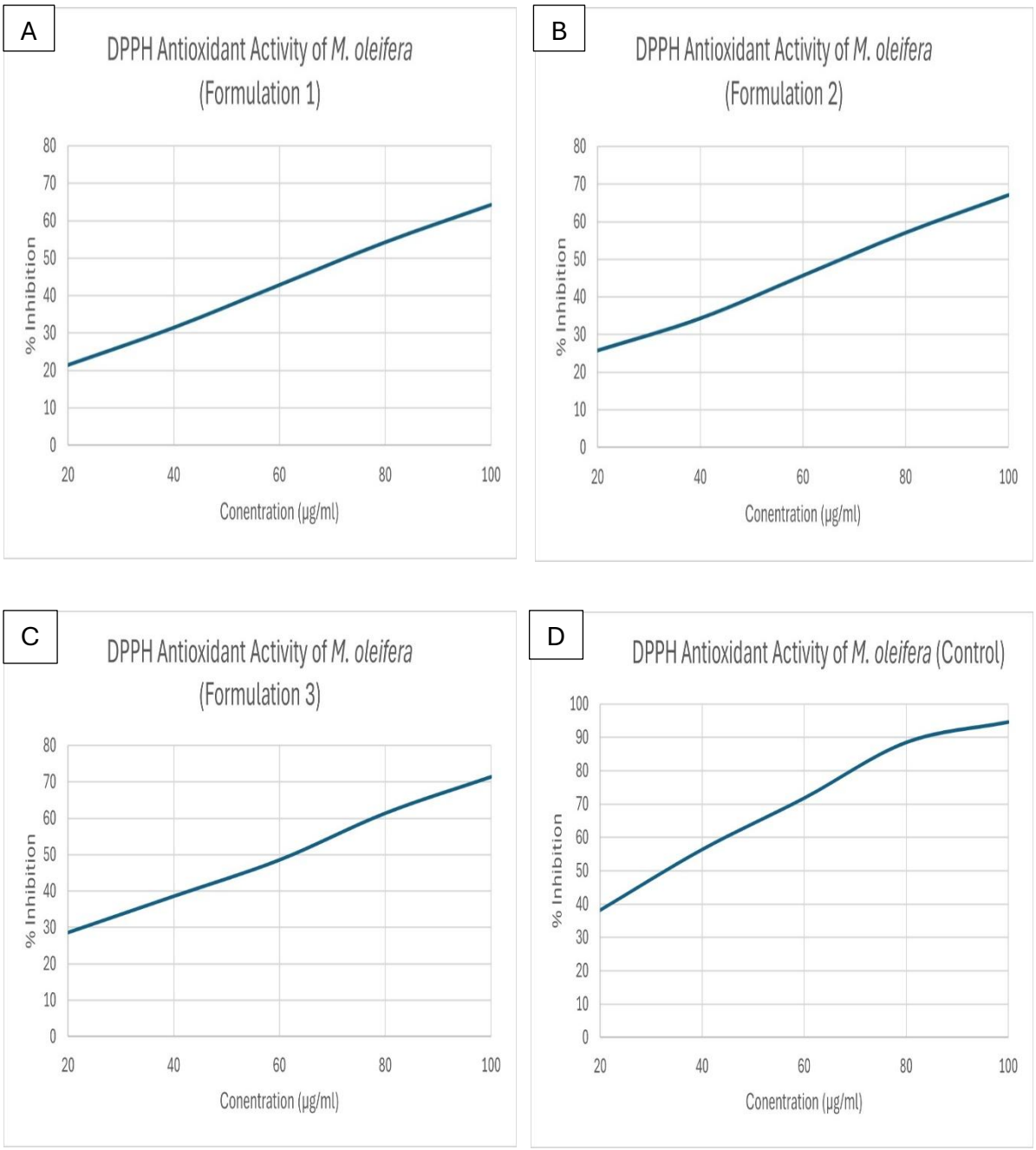

Fig. No. 9: DPPH Antioxidant Activity of *M. oleifera:* (A) Formulation 1; (B) Formulation 2; (c) Formulation 3; (D) Control at Different Concentrations.

RESULT AND DISCUSSION

Table no. 4: Result of evaluation

Sr. no.	Evaluation parameter	Result		
		F1	F2	F3
1	Organoleptic Characteristics	Smooth, Transparent	Smooth, Transparent	Smooth, Transparent
2	Weight Uniformity	1.69%	1.48%	0.21%
3	Folding Endurance	15 ± 2.60	12 ± 3.21	13 ± 2.50
4	% Moisture content	5.06%	5.00%	4.5%
5	pH	6.1	6.3	6

Formulation of *M. oleifera*

It made by taking the *M. oleifera* leaf extract and adding it into suitable polymers like hydroxypropyl methylcellulose (HPMC) and gelatin, then they used a solvent casting method [Table 3]. Those chosen polymers really helped with film formation, and also gave the patches decent mechanical strength too. For flexibility, and to avoid that brittle feel, polyethylene glycol (PEG 400) plus glycerol were included as plasticizers. Then dimethyl sulfoxide (DMSO) was added as a permeation enhancer so the drug could pass through the skin more easily. When the patches were finally prepared, they looked smooth flexible and transparent. The blend of polymers and plasticizers gave uniform films no obvious cracks and no trapped air bubbles. Overall, the formulation plan supported a good distribution of the extract inside the polymer network, which matters a lot for controlled release (Prajapati et al., 2020; Mahato *et al.,* 2025).

Evaluation of formulated transdermal patches

Physical appearance

A good transdermal patch should look uniform, feel smooth, and stay flexible enough so it can be placed easily and people can actually stick with it. In this work, the prepared patches from every formulation were checked by eye, focusing on color, clarity, smoothness, and flexibility. For all formulations (F1, F2, and F3), the patches appeared smooth, transparent.

Weight uniformity

Uniformity in mass, is an important parameter to make sure the drug really gets distributed in a steady way within transdermal patches. For the formulations F1, F2, and F3 the percentage weight variation was observed as 1.69%, 1.48%, and 0.21% respectively.

In general, F3 turned out with the smallest variation, which suggests better evenness in the polymer as well as in the drug dispersion(Yadav *et al.,* 2021).

Folding endurance

In this test a sort of idea about the mechanical strength and how flexible the patch really is. In the observation, formulation F1 seemed to perform the best, with folding endurance of 15 ± 2.60. Next came F3 at 13 ± 2.50 and then F2 at 12 ± 3.21. Overall, when folding endurance numbers are higher, it generally means the patch bends better and shows improved resistance to breakage. These findings imply that a proper or optimum concentration of the polymer along with the plasticizer plays a major role in boosting.

pH

The pH level of transdermal patches is, pretty much, a key point when you want to avoid skin irritation. In this study the pH of the formulations ended up sitting around 6.1–6.3. That is fairly near the normal skin pH level, so it suggests the formulated patches are safe(Parveen *et al.,* 2025).

% Moisture content

Moisture content kind keeping transdermal patches steady and still flexible. In this case, results are 5.06% for F1, 5.00% for F2, and 4.5% for F3. All the formulations keep a moderate moisture level, which in turn helps maintain flexibility while at the same time limiting microbial growth. Also, the lower moisture content in F3, like 4.5%, seems to point toward better stability than the other formulations.

Antioxidant activity (DPPH assay)

This activity formulated *M. oleifera* transdermal patches (F1, F2 and F3) was kind evaluated with the DPPH free radical scavenging method. This activity was written as IC_{50} values (ppm), meaning the amount needed to inhibit 50% of DPPH radicals. So yeah, when the IC_{50} number is lower, it usually signals a stronger antioxidant potential.

The IC_{50} values for each seen in Table 5. Formulation F1 showed an IC_{50} value of 72.5 ppm, while F2 was 67.5 ppm, and F3 came out at 62.2 ppm. Overall, between all the tested patches,

F3 had the lowest IC_{50} value, so it hints at the best antioxidant activity. After that, the order goes F2 then F1.

The better antioxidant activity for F3 could be linked to the more decent incorporation and uniform distribution of the *M. oleifera* extract inside the polymeric matrix, plus the increased level of supporting ingredients, like HPMC, PEG 400, and glycerol. These components may support drug liberation and make active phytoconstituents more available. In other words, the antioxidant effect is likely mainly guided by bioactive constituents such as flavonoids, phenolic acids, and vitamins found in *M. oleifera*. These molecules donate hydrogen atoms to neutralize the DPPH radicals, which then helps reduce oxidative stress(Yokozawa et al., 1998). Taken as a whole, all formulations displayed noticeable antioxidant activity, but F3 stands out as the most effective one, suggesting it might be useful for handling oxidative stress related conditions, for example rheumatoid arthritis.

Table no. 5: Antioxidant activity of formulations (IC_{50} values).

Sr. No.	Formulation	IC_{50} (PPM)	Category
1	F1	72.50 PPM	Moderate
2	F2	67.5 PPM	Good
3	F3	62.2 PPM	Strong

CONCLUSION

All the tested formulations, F1, F2 and F3, exhibited acceptable physicochemical properties like smooth surface, transparency, even thickness, acceptance and drug penetration. Parameters of evaluation like pH were well within the permissible range , displaying the known resonance of their stability and consistency of their physical state. The pH value of the formulations was in close proximity to that of normal skin, thus displaying a negligible chance of irritation of the skin upon topical application. Regarding the F3 formulation gave the best results and select this formulation as best. due to its highest physicochemical stability, least weight variation and excellent mechanical strength with optimum moisture content; thus, the shelf life would be high. The free radical scavenging activity of the formulations was computed by performing the DPPH free radical scavenging method. Formulation F3 was found to have the best antioxidant activity on the basis of the least IC50 value (62.2 ppm). The improved antioxidant activity of F3 is probably which contains vitamins, glucosinolates, etc. in the extract of *M. oleifera* along with their comparatively better sustained drug release features from the optimised matrix. This research that the incorporation of herbal extracts in transdermal systems enhances the activity

of herbal drugs. The antioxidant potential of *M. oleifera* indicates that the plant possesses therapeutic benefit in combating excess oxidants present in rheumatoid arthritis. In conclusion, the transdermal patches loaded with *M. oleifera* leaf which is cost-effective, non-invasive and efficient potential system for treatment of RA and all other free radical-mediated diseases and conditions.

FUTURE PROSPECTIVE

The formulated transdermal patch is promising for future treatment of rheumatoid arthritis, although the potential for clinical use and therapeutic effect needs to be established through further investigation. Future research should incorporate *in vivo* studies and clinical trials to study the safety, efficacy and pharmacokinetic parameters in human subjects. Hence, a comprehensive study of drug permeation and release rates, bioavailability and skin permeation rates needs to be carried out transdermal drug delivery. Advanced drug delivery techniques employing novel Nano carriers, microneedles, and vesicular systems should be developed to improve skin drug permeation. Bio adhesive, controlled-release patches with optimised polymer, plasticiser and permeation enhancer content should be formulated to enhance transdermal bioavailability and drug release behaviour. In addition, development and evaluation of the product are needed to identify other variations necessary to optimise product usage, and stability studies on the product under various test conditions must be performed to determine shelf life and storage conditions. Isolation and characterisation of active phytoconstituents responsible for the pharmacodynamic activity can help in developing more specific formulations. Toxicity and other safety tests for prolonged use were also necessary. Scale-up and production feasibility studies are needed to translate the study into commercial products. In conclusion, this formulation provides a non-invasive, convenient and sustained drug delivery system and has considerable value for future pharmaceutical and clinical implementation.

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