Formulation and Evaluation of Transdermal Antioxidant Patches from Guava Leaves Extract

Shubhangi K. Kute [1], Amanpreet Kaur Dumda [2]
[1] *Student, Yashodeep Institute of Pharmacy, Chh. Sambhajinagar*
[2] *Principal, Yashodeep Institute of Pharmacy, Chh. Sambhajinagar*

Abstract- Transdermal patches are non-invasive method of drug administration. It is adhesive patch designed to deliver a specific dose of medication through the skin and into the bloodstream throughout the body. Transdermal drug delivery has several advantages over other routes of administration, for instance, it is less invasive, patient friendly, and has ability to bypass first pass metabolism and the destructive acidic medium. Transdermal drug delivery system offers a promising route for administering therapeutic agents, especially those with antioxidant properties, due to their ability to bypass first-pass metabolism and provide controlled drug release. This study focuses on formulation and evaluation of transdermal patches incorporating guava *(Psidium guajava L.)* leaf essential oil, which is rich in antioxidants such as flavonoids and terpenoids. The patches were prepared using the solvent casting method with hydroxypropyl methylcellulose (HPMC) as the film forming polymer and glycerin as a plasticizer. The formulated patches were subjected to physicochemical evaluations including thickness, tensile strength, moisture content, folding endurance, and drug content uniformity. Antioxidant activity was assessed using the DPPH Radical scavenging assay, while in vitro drug release and ex vivo skin permeation studies were conducted using Franz diffusion cells and excised rat skin, respectively. In conclusion, guava leaves oil based transdermal patches exhibit promising characteristics for delivering the antioxidant compounds and have a potential application in the prevention and management of oxidative stress-related condition. Future work will focus on in vivo testing of efficacy and safety to validate potential.

Keywords- Guava leaf oil, transdermal patches, antioxidant activity, Psidium guajava, solvent casting, in vitro release, skin permeation, DPPH assay, natural antioxidants, herbal drug delivery.

I. I INTRODUCTION

Transdermal drug delivery system (TDDS) offers a non- invasive alternative to oral or injectable routes by administering drugs through the skin into the bloodstream. Such patches can provide controlled, sustained release of active compounds over extend period (hours to days). Importantly, transdermal delivery bypasses the gastrointestinal tract and first-pass hepatic metabolism, avoiding drug degradation in the stomach or liver and improving systemic bioavailability. This route is especially patient-friendly: patches are painless, convenient for self-administration, improve compliance, particularly for chronic therapies. Collectively, these features noninvasiveness, steady dosing, avoidance of first-pass effects, and ease of use make TDDS an attractive platform for delivering a wide range of pharmaceuticals (e.g. hormones, pain medications, nicotine) and bio actives.

Oxidative stress, driven by an excess of reactive oxygen species (ROS) underlines the pathology of many chronic conditions (e.g. cardiovascular disease, diabetes, neurodegenerative disorders, and certain skin diseases) antioxidants are molecules that can neutralize ROS and mitigate oxidative damage, and thus are of great interest for disease prevention and therapy. However, conventional antioxidant therapy (oral supplementations or creams) often suffers from poor control over delivery, low bioavailability, and unwanted systemic distribution. For example, oral antioxidants may be degraded in the guts and metabolized before reaching target tissues, while repeated topical of application may cause non-specific exposure or allergic reaction. A patch can provide localized and sustained release of antioxidant compounds directly into the systemic circulation or skin avoiding gastrointestinal loss and improving patient adherence. Thus, developing the TDDS for antioxidants can potentially enhance therapeutic efficacy in managing oxidative stress-related conditions.

Benefits of Guava Leaves Extract:

1. Natural source of antioxidant: Guava leaves oil contains flavonoids, terpenoids, tannins with potent antioxidant properties, beneficial for oxidative stress related disorders.
2. Dual functionality: The terpenes in guava oil not only offer therapeutic benefits but also act as natural permeation enhancers, improving skin penetration of activities.
3. Broad pharmacological activity: In addition to antioxidant effects, guava leaf compounds have documented anti- inflammatory, antimicrobial and analgesic properties.
4. Low cost and abundant availability: As guava us widely cultivated, its leaves offer an inexpensive, renewable source of bioactive material for pharmaceutical applications.
5. Reduce synthetic additives: Using natural oils can minimize the need for synthetic excipients or enhancers, potentially improving biocompatibility and reducing side effects.
Pharmacological Properties:
1. Antioxidant Activity: Guava leaves oil rich in flavonoids, terpenes (like limonene and beta-caryophyllene), and phenolic compounds. These neutralize the free radicals, protecting skin cells from oxidative stress and aging.
2. Anti-inflammatory: Guava leaf oil reduces inflammation by inhibiting cytokine production. Compounds like beta- caryophyllene interact with CB2 receptors, mimicking endocannabinoid action without psychoactive effects

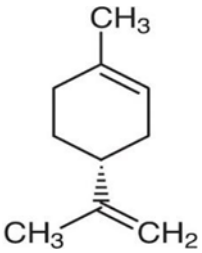
PLANT PROFILE
1. GUAVA LEAVES

Psidium guajava L. (Guava)
Common name: Guava
Scientific name: Psidium guajava L. Family: Myrtaceae
Origin: Tropical America (likely Southern Mexico and Central America)
Type: Tropical and subtropical fruit tree
Botanical description: Psidium guajava is a small, evergreen tree or shrub, topically reaching heights of 3-10 meters. If features a rigid, woody stem with light to reddish-brown bark that is smooth and exfoliate in flakes. The leaves are simple, opposite, ovate to elliptic, measuring 9-12 cm in length and 4.5- 7 cm in width, with prominent veins and a pubescent underside. Flowers are white, fragrant and bisexual, usually appearing singly or in clusters of 2-3 in leaf axils. The fruit is many- seeded berry, globose to pyriform, with a fleshy pericarp and a sweet or mildly acidic pulp that varies in color from white to pink or red, depending on the cultivar.
3. Antimicrobial and Antifungal: Exhibits activity against Staphylococcus aureus, E. coli, Candida spp., etc. helps in wound healing and infection prevention when applied topically.
4. Analgesic: Terpenes such as alpha terpinol and limonene have mild analgesic effects. Useful in localized pain relief when delivered transdermally.
5. Wound Healing: Promotes collagen synthesis and accelerates epithelial regeneration. Beneficial when patches are applied to damaged or sensitive skin.
6. Antispasmodic and Antipyretic: Traditionally used to treat gastrointestinal discomfort and fevers. These systemic effects are not the primary focus on a transdermal patch but may support overall therapeutic use.

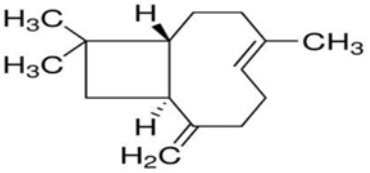
Habitat and Distribution: Native to tropical America, P. guajava is now widely cultivated in tropical and subtropical regions worldwide, including India, southeast Asia, Africa, and Latin America.
Taxonomical Classification:
Kingdom: planta Division: angiosperms Class: eudicots
Order: Myrtales Family: Myrtaceae Genus: Psidium
Species: Psidium guajava L.
Common Vernacular Names:
English: Guava Hindi: Amrood Tamil: Koyya
Malayalam: Perakka
Tagalog (Philippines): Bayabas
Phytochemical constituents:
Flavonoids: Quercetin, kaempferol, guaijaverin, rutin
Phenolic acids: Gallic acid, protocatechuic acid
Tannins: Ellagitannins
Essential oil: limonene, beta-caryophyllene, 1,8-cineole
Vitamins: High level of Vitamin C (ascorbic acid),

Vitamin Minerals: potassium in the fruit pulp

DRUG PROFILE:
A. Lionene
Synonyms: Dipentene, p-mentha-1,8- dien
Chemical name: 1-methyl-4-(1-methylethenyl) cyclohexane
Chemical formula: $C_{10}H_{16}$



Apparatus:

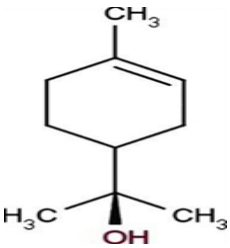


II. MATERIAL AND METHOD

Structure: monocyclic monoterpenes Molecular weight: 136.23g/mol
Use: Antioxidant, Anti-inflammatory, Antimicrobial, Anticancer potential

B. Terpineol
Synonyms: alpha-terpineol
Chemical name: 2-(4-methyl-1-cyclohex- 3-enyl)propan-2-ol
500 ml Soxhlet-Extraction Apparatus, 500 ml Round Bottom Flask, Digital Weighing Balance, Heating Mantle, Reflux Condenser, Hot Air Oven, magnetic stirrer, Desiccator.
Chemicals:
Guava Leaf Oil, Hydroxypropyl Methylcellulose (HPMC) Polyvinyl alcohol (PVA), Glycerin, Propylene Glycol 400, Ethanol (96%), Distilled Water, Chloroform or Ethanol, D- limonene, Oleic Acid.
Sample Preparation:
The guava leaves are collected from the guava tree, and washed it by clean water properly then shed dried oven dried it for 2-3 days and then powdered it and then stored it for further processes.

Chemical formula: $C_{10}H_{18}O$



Structure: alpha-terpineol Molecular weight: 154.25 g/mol
Use: Sedative and Anticonvulsant, Skin Permeation Enhancer

C. Beta-caryophyllene
Synonyms:(1R,9S)-4,11,11-Trimethyl-8-methylene-bicyclo[7.2.0]undec-4-ene
Chemicalname:(1R,4E,9S)-4,11,11-Trimethy-8-methylene- bicyclo[7.2.0]undec-4-ene
Chemical formula: $C_{15}H_{24}$ Structure: Bicyclic sesquiterpene Molecular weight: 204.36 g/mol
Use: Antioxidant, Anti-inflammatory, Antimicrobial, Anticancer potential.

Soxhlet Extraction of the Guava Leaves Oil Procedure:
1. Sample Preparation: Collect fresh guava leaves, wash thoroughly, and air-dry in shade to retain bioactive compounds. Grind the dried leaves into the fine powder.
2. Weigh and Load Sample: Weigh about 10-15 gm of the powdered leaves. Place the powder in thimble or folded filter paper, and insert into the Soxhlet extractor.
3. Add Solvent: Fill the round bottom flask with a suitable solvent (e.g. ethanol). Connect the Soxhlet extractor to the flask and condenser.
4. Start Extraction: Heat the solvent using heating mantle. The solvent evaporates, condenses in the condenser and drips into the thimble containing guava leaf powder. Once the extractor chamber fills to the siphon point, it drains back into the flask. Repeat this cycle 4-8 hours.
5. Solvent Recovery: after extraction, concentrate the extract by removing the solvent using the rotary evaporator.
6. Drying the Extract: Dry the obtained extract/oil under the reduced pressure in a desiccator.

2. SOXHLET EXTRACTION

4. Development: place the spotted TLC plate in a chamber saturated with your selected mobile phase. Then allow the solvent to rise about ¾ the way up the plate. Remove and mark the solvent front.

5. Drying: air dry or use the warm air source to dry the plate completely.

6. Visualization: spray with vanillin-sulfuric acid and gently heat for 2-5 minutes for color development.

7. Observation: the Rf value calculated for each spot

Rf = distance traveled by the solvent front

Distance travelled by the compound

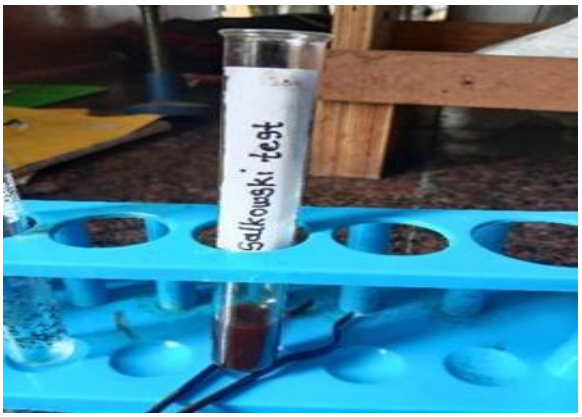
Compare the Rf value with standard Rf value to identify the component. Matching Rf value indicates the presence of essential oils.

Phytochemical Screening 0f guava leaves oil:

1) Salkowski Test:

1. The organic compound to be tested is taken in test tube.
2. Add 2 ml of chloroform in it.
3. then add the 3ml of concentrated H_2SO_4.
4. If reddish- brown color indicates the presence of beta- caryophyllene.

3. SALKOWSKI TEST



Thin Layer Chromatography (TLC):

5. Preparation of Mobile phase: Toluene:ethyl acetate (93:7)
6. Sample preparation: dilute guava leaf oil in a volatile solvent (e.g. ethanol or hexane) in 1:10 ratio.
7. Plate spotting: use the capillary tube to spot the sample 1 cm above the bottom edge of the TLC plate.
8. TLC TEST

Formulation of Patches:-

Step-1: Prepare polymer base:

a. Dissolve 0.9 gm of polyviny alcohol in 15ml warm distilled water at (60ºC) stir umtill clear.

b. Dissolve 1.8 gm HPMC in 10 ml distlled water at room temprature (stir well untill swell)

c. Mix above both solutions and allow to cool.

Step-2: Add plasticizer:

a. Add 0.6 ml glycerol or propylene glycol to the combined polymer mixture and stirr for 15 min. for even distribution.

Step-3: incorporate guava leaves oil:

a. dissolve 1.8 ml guava leaves oil in 1.5 ml ethanol.

b. slowly add the oil solution into the polymer matrix while stirring cintinuously for 20-30 minutes.

Step-4: Casting the film:

a. Poor the final homogenous mixture into the leveled petri dish or or flat mold.

b. let it dry at room temprature (40ºC in oven) for 24-48 hours untill completely dried.

Step-5: Storage :

a. Store alright container or lmaminate into a backing membrane.

NOTE: Follow the Table of Ingredients

Sr. No.	Ingredients	Formulation F1	Formulation F2	Formulation F3
1	Guava leaves oil	1.8 ml	2 ml	2.5 ml
2	HPMC	1.8 gm	1.5 gm	2 gm
3	Polyvinyl alcohol	0.9 gm	1 gm	1 gm
4	Glycerol/ propylene glycol	0.6 ml	0.8 ml	1 ml
5	Ethanol	1.5 ml	1.8 ml	2 ml
6	Distilled water	30 ml	30 ml	30 ml
7	Oleic acid (optional)	0.3 ml	0.3 ml	0.3 ml

9. MATERIAL OF PATCHES 6. PATCHES

Evaluation Parameters:

The following parameters are checked to evaluate the antioxidant patches.

1. Weight Uniformity: Assuring the uniform drug or consistent drug distribution.

2. Moisture Content: Low moisture content prevents the microbial growth and enhance the shelf life of the drug.

3. Folding Endurance: number of times patch can be folded at the same place.

4. Tensile Strength and Elongation: Measure the mechanical strength and flexibility of the patch.

5. Drug content Uniformity: Assures the drug is evenly distributed in the patch.

6. pH of Patch: It is compatible with the skin (Typically pH 4.5-6.5).

Formulation	pH
F1	4.3
F2	5.4
F3	6.5

7. Skin Irritation Test: Ensure the formulation does not cause any irritation or allergic reaction.

10.SKIN IRRITATION TEST

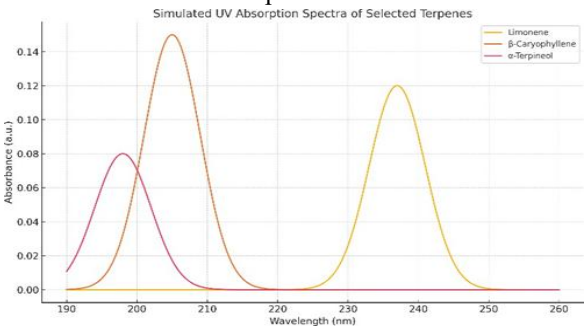
8. UV Analysis of Patch: Measure the absorbance of light.

Drug	Standard Absorbance
Limonene	214-220nm
Beta-Caryophyllene	200-205nm
Terpineol	220-230nm

9. Result:

Sr. No	Compound	Wavelength (nm)	Absorbance
1	Limonene	240nm	0.08
2	Terpineol	198nm	0.16
3	Beta-Caryophyllene	203nm	0.12

10. UV Spectra of the Formulation



III. RESULT AND DISCUSSION

There are three samples of the transdermal antioxidant patches are formulated by using the guava leaves

extract (oil), hydroxypropyl methylcellulose (HPMC) as the film forming polymer, polyvinyl alcohol (PVA) for the flexibility and propylene glycol as the plasticizer. The formulation is resulted as the flexible, smooth, jelly like and transparent. The guava leaves extract (oil) is used as antioxidant activity.

Formulation			
	F1	F2	F3
Appearance	Smooth, transparent, uniform		
Weight variation	Within acceptable limits		
Tensile strength	Moderate easy to peel		
Folds	Flexible		
pH	4.3-6.5 (skin compatible)		

IV.CONCLUSION

This study depicted that these prepared new formulations are very good therapeutic composition for the antioxidant activity. The patches showed the good physical characteristics such as flexibility, uniform thickness and the compatible with the skin pH. The transdermal route offers the sustained drug delivery and avoid the first pass metabolism. The patches demonstrate the potential for skin related therapeutic use.

REFERENCE

[1] Recent Advancement of Medical Patch for Transdermal Drug Delivery Won Fen Wong 1, Kuan Ping Ang 2, Gautam Sethi 3, Chung Yeng Looi 4.

[2] Fathima, S.R., Kumar, S.N., Rao, B.N., Ruksana, S., Harish, P., Joy, S., Divya, S. and Ayesha, S. Mucoadhesive Buccal Patches-A Review.

[3] Bhutkar, K.G. Formulation and evaluation of mucoadhesive herbal buccal patch of Psidium Guava L. Journal of Current Pharma Research. 2014; 5(1): 1372.

[4] Boddupalli, B.M., Mohammed, Z.N., Nath, R.A. and Banji, D.Mucoadhesive drug delivery system: An overview. Journal of Advanced Pharmaceutical Technology and Research. 2010; 1(4): 381.

[5] Choudhary, A., Tiwari, G., Pandey, M., Kymonil, K.M. and Saraf, S.A. Formulation and characterization of carvedilol buccal mucoadhesive patches. Int. J. Res. Pharm. Sci. 2010; 1(4): .396-401.

[6] Figueiras, A., Vieira, A., Simões, S. and Veiga, F. Mucoadhesive buccal systems as a novel strategy for anti- inflammatory drugs administration. Anti-Inflammatory and Anti-Allergy Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Inflammatory and Anti- Allergy Agents). 2011; 10(3): .190-202.

[7] Figueiras, A., Vieira, A., Simões, S. and Veiga, F. Mucoadhesive buccal systems as a novel strategy for anti- inflammatory drugs administration. Anti-Inflammatory and Anti-Allergy Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Inflammatory and Anti- Allergy Agents). 2011; 10(3): .190-202.

[8] Tan Suwandecha and Papassara Changklang (2023): "Formulation development and characterization of a transdermal patch containing Crinum asiaticum leaves extract" Journal of Applied Pharmaceutical Science, 13(12), 207-213.

[9] K. Sridivya Goud (2018): "Preparation and Evaluation of Mucilage from Fresh Leaves of Psidium guajava" Research Journal of Pharmacy and Technology, 10(3), 125-132.

[10] Bhutkar et al. (2014): "Formulation and Evaluation of Mucoadhesive Herbal Buccal Patch of Psidium Guava L." Journal of Current Pharma Research, 5(1), 1372.

[11] Sahu et al. (2018): "Development and Evaluation of Transdermal Patches Using Natural Antioxidants" Journal of Drug Delivery and Therapeutics, 8(4), 105-112.

[12] Kumar et al. (2020): "Formulation and Evaluation of Herbal Transdermal Patches for Wound Healing" Journal of Pharmaceutical Sciences and Research, 12(3), 456-463.

[13] Zhang and Michniak-Kohn (2020): "Flavosomes for Transdermal Delivery of Flavonoids" Pharmaceutics, 12(11), 1079.

[14] George and Suchithra (2019): "Plant-Derived Bioadhesives for Wound Dressing and Drug Delivery Systems" Journal of Adhesion Science and Technology, 33(14), 1450- 1465.

[15] Various Researchers (2023): "Natural Compounds in Transdermal Delivery Devices and Wound Dressing Materials" Journal of Controlled Release, 355, 456-470.

[16] Patel et al. (2019): "Formulation and Evaluation of Herbal Transdermal Patches for Anti-Inflammatory Activity" Journal of Pharmacy and Pharmacology, 71(8), 1110-1119.

[17] Sharma et al. (2022): "Development and Evaluation of Transdermal Patches Containing Natural Antioxidants for Skin Health" Journal of Cosmetics, Dermatological Sciences and Applications, 12(2), 145-153.
[18] Singh et al. (2021): "Formulation and Evaluation of Mucoadhesive Buccal Patches Using Natural Polymers" Journal of Applied Polymer Science, 138(15), 5035.
[19] Gupta et al. (2020): "Herbal Transdermal Patches for Wound Healing: A Review" Journal of Ethnopharmacology, 253, 112642.
[20] Jain et al. (2019): "Formulation and Evaluation of Transdermal Patches Containing Herbal Extracts" Journal of Pharmaceutical Sciences and Research, 11(2), 234-241.
[21] Rajput et al. (2022): "Development and Evaluation of Herbal Transdermal Patches for Anti-Aging Activity" Journal of Cosmetics, Dermatological Sciences and Applications, 12(3), 202-211.