To Formulate and Evaluate Transdermal Patches Containing Guava Leaf Essential Extracts as A Natural Antioxidant.

Nikita Vishnu Jaybhaye[1], Snehal dhewale[2], Rutuja Sanjay Ethape[3], Shriram Babasaheb Gande[4], Dr. D. K. Vir[5]
[1,2,3,4,5]*Shree Goraksh college of pharmacy and research centre*

Abstract—**Aim and Objective**

Aim: To formulate and evaluate transdermal patches containing guava leaf essential extracts as a natural antioxidant.

Objective:

1. **Extract and characterize the essential extract from P. guajava leaves, identifying its major phytochemical constituents.**
2. **Develop adhesive patch formulations incorporating guava leaf extract, optimizing composition and structure for stability and release.**
3. **Characterize the mechanical and physicochemical properties of the patches (e.g. adhesion, thickness, flexibility, and oil loading). To ensure peel ability and stability of patches under controlled storage condition.**

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 non-invasiveness, 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.

Psidium guajava L. (guava) is a tropical fruit tree long valued in traditional medicine. Native to Central America and widely cultivated in subtropical regions, guava has a rich ethnobotanical history. Various parts of the guava plant (leaves, bark, fruit) have been used for ailments such as stomach-ache, diarrhea, diabetes, and inflammation. In particular guava leaves are noted in folk medicine for treating the gastrointestinal disorders, fevers, menstrual pain, and hypertension. Guava leaves have also been documented to exhibit anti-inflammatory, antidiabetic, and analgesic effects in preclinical studies, supporting their traditional uses. These uses suggest that leaf extracts contain bioactive phytochemicals relevant to health.

Chemical Constituents in Guava: Guava leaves are rich in diverse phytochemicals. Chemicals analyses have identified polyphenols (phenolic acid and flavonoids), terpenoids (triterpenes, volatile terpenes), tannins and other constituents in guava leaf extracts. Quercetin and related flavonoids are among the major antioxidants present. Secondary metabolites such as ferulic, caffeic, and gallic acids, as well as flavonoids like quercetin and kaempferol, have been reported in guava leaves. These compounds confer strong antioxidant and free-radical scavenging properties to guava leaf preparations. In fact, the high total phenolic content of guava leaves is through underlie much of their pharmacological activity. Overall, the phytochemical profile of guava leaves (rich in flavonoids and other phenolics) makes them promising sources of natural antioxidants.

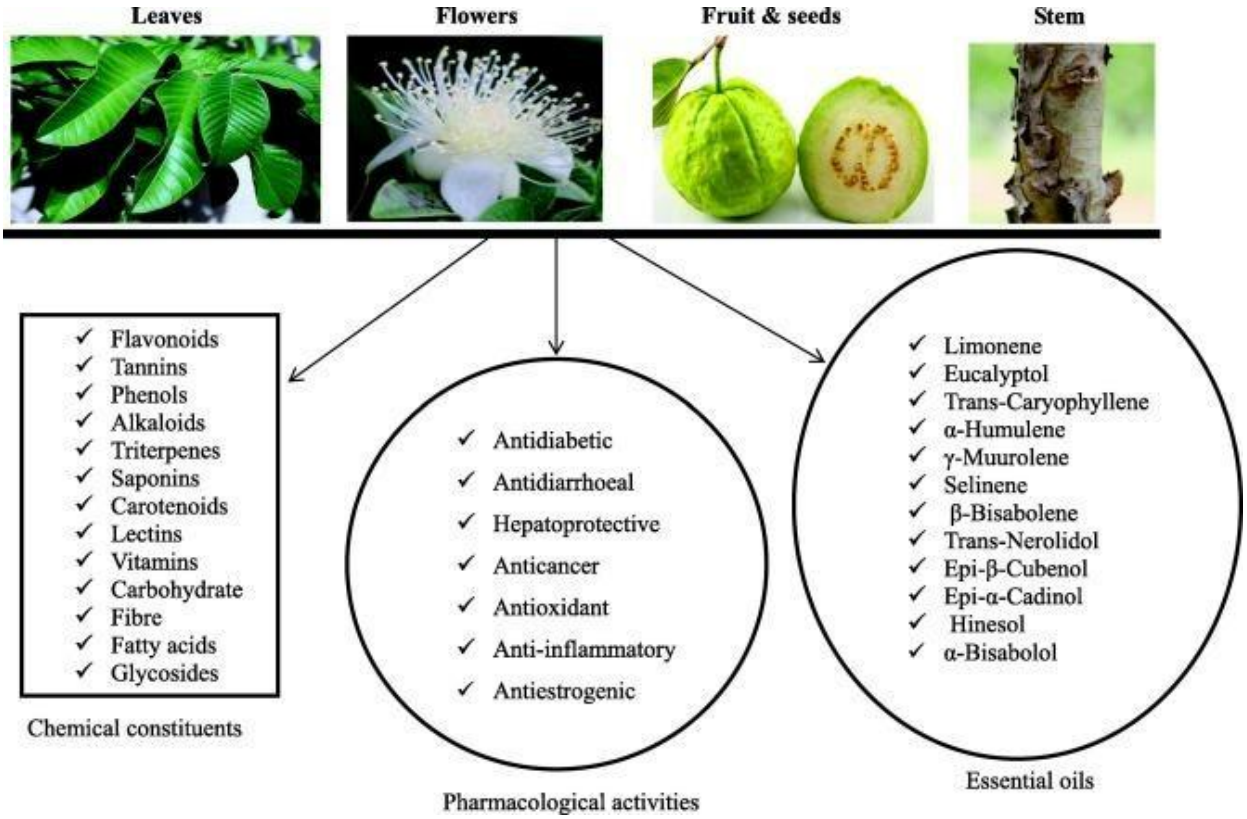
The essential oil extracted from guava leaves has also demonstrated potent antioxidant activity. Guava leaves essential oil (GLEO) contains volatile constituents such as 1,8-cineole a monoterpene oxide),

eugenol (a phenylpropene), and other terpenoid compounds. It also retains non-volatile polyphenolic and terpenoid constituents (e.g. flavonoids, tannins) that are not distilled but remain in extracts.

Experimental assay confirms that GLEO exhibits strong free-radical scavenging. The presence of multiple antioxidant compounds-flavonoids, tannins, phenols and terpenes "make it an excellent antioxidant". The oil components include limonene, alpha-pinene, beta-caryophyllene and other terpenes, as well as oxygenated terpenes, all of it contribute to its bioactivity. The essential oil of guava leaves is rich in flavonoids and terpenoids that confer significant antioxidant and therapeutic properties.

Fig. 1. Guava leaves

Many of the terpenes present in the guava leaves extract known to act as permeation enhancers for transdermal delivery. Natural terpenes (constituents of essential oils) can interact with fluidize the lipids of the stratum corneum, reducing skin barrier resistance and facilitating drug diffusion. Therefore, the cineole, pinene, and other terpenes in guava leaves may have the added benefits of increasing skin permeability, improving the delivery of co-administered antioxidants into the body. In this way guava leaf oil could play a dual role: providing antioxidant compounds and enhancing their transdermal uptake via its terpene content. These factors motivate the development of transdermal antioxidant patch based on guava leaf extract. The patch formulated could exploit the synergistic advantages of TDDS and the bioactivity of guava leaves constituents. Such a patch would deliver guava derived-antioxidants in a controlled manner, maintaining therapeutic levels of active compounds while avoiding oral metabolism or rapid clearance.



Fig, 2. Chemical constituents and pharmacological action

Mechanism of Action:

Table no. 1 Mechanism of Action

Compound	Type	Mech. Of Antioxidant Action	Effects
Limonene	Monoterpene	Scavenging free radicals by donating hydrogen atoms enhances activity of (superoxide dismutase) SOD and catalase	Reduces lipid peroxidation, inhibit oxidative stress pathways (e.g. p38MAPK)
Beta caryophyllene	Sesquiterpene	Activates CB2 receptors to regulate oxidative stress and inflammation-boost antioxidant enzymes	Decreases (reactive oxygen species) ROS generation protects tissues from oxidative injury
Terpineol	Monoterpenoid alcohol	Direct radical scavenging via hydroxyl group- inhibit pro-oxidant enzymes (e.g. COX-2)	Lowers (nitric oxide) NO and ROS levelssupports antioxidant enzyme expression

Pharmacological Properties:

1. Antioxidant Activity: Guava leaves extract 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 extract reduces inflammation by inhibiting cytokine production. Compounds like beta-caryophyllene interact with CB2 receptors, mimicking endocannabinoid action without psychoactive effects.
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. 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.

1.3 Advantages and Disadvantages

Advantages:

1 Natural source of antioxidant: Guava leaves extract contains flavonoids, terpenoids, tannins with potent antioxidant properties, beneficial for oxidative stress related disorders.

2 Dual functionality: The terpenes in guava extract 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 extract can minimize the need for synthetic excipients or enhancers, potentially improving biocompatibility and reducing side effects.

Disadvantages:

1 Volatility and stability issue: Essential oils are volatile and prone to degradation under heat, light, or oxygen, which may affect shelf life and efficacy.

2 Formulation challenges: Incorporating extract uniformity into polymeric patches and ensuring consistent drug loading and release can be technically challenging.

II. LITURATURE REVIEW

Year	Author / Study	Key Focus	Findings / Contribution	Relevance to Current Study
2013	Suthagar Pillai et al.	Antioxidant properties of guava leaves	Guava leaves show strong antioxidant activity due to rich phytochemicals	Supports use in anti-aging and skin formulations
2014	Bhutkar et al.	Mucoadhesive buccal patches (guava extract)	Successfully formulated herbal patches showing good drug delivery potential	Supports use of guava extract in patch systems
2018	K. Sridivya Goud	Guava leaf mucilage	Demonstrated natural mucoadhesive properties	Useful for bioadhesive patch formulation
2018	Sahu et al.	Transdermal patches with natural antioxidants	Highlighted importance of antioxidants in skin health	Supports antioxidant role in patches
2019	George & Suchithra	Plant-based bioadhesives	Natural mucilage useful in drug delivery and wound dressing	Supports use of natural polymers like guava mucilage
2020	Zhang & Michniak-Kohn	Flavosomes for transdermal delivery	Introduced deformable liposomes for flavonoid delivery	Relevant due to flavonoid content in guava leaves
2020	Kumar et al.	Herbal transdermal patches	Showed effectiveness in wound healing applications	Supports therapeutic potential of herbal patches
2023	Maroti M Jeurkar et al.	Phytochemistry of Psidium guajava	Detailed pharmacological and phytochemical properties	Supports scientific basis of guava leaves
2023	Won Fen Wong et al.	Advances in medical patches	Highlighted progress in transdermal drug delivery systems	Supports modern patch technology
2023	Priyanka Machigar et al.	Herbal hair oil (guava leaves)	Demonstrated formulation using guava leaves oil	Shows versatility of guava in formulations
2023	Tan Suwandecha et al.	Herbal transdermal patch (Crinum extract)	Showed good physical properties and drug release	Supports feasibility of herbal patches
2024	Yogiraj Prakash Tikande et al.	Guava leaf face serum	Demonstrated antioxidant, anti-aging & moisturizing effects	Supports cosmetic applications of guava extract

III. PLANT PROFILE

a. Psidium guajava L. (Guava)
Common name: Guava
Scientific name: Psidium guajava L.
Family: Myrtaceous
Origin: Tropical America (likely Southern Mexico and Central America)
Type: Tropical and subtropical fruit tree

b. 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.

c. 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.

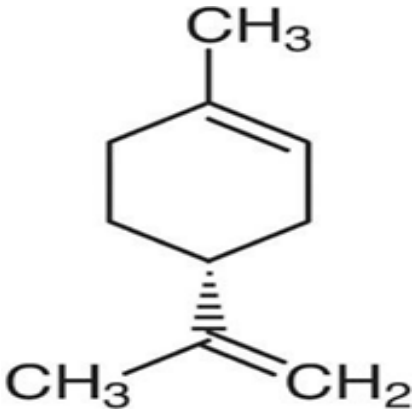
Fig. 3 Guava tree and Fruit

d. Taxonomical Classification:
Kingdom: plantae
Division: angiosperms
Class: eudicots
Order: Myrtales
Family: Myrtaceae
Genus: Psidium
Species: Psidium guajava L.

e. Common Vernacular Names:
English: Guava
Hindi: Amrood
Tamil: Koyya
Malayalam: Perakka Tagalog (Philippines): Bayabas f.
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 A
Minerals: potassium in the fruit pulp

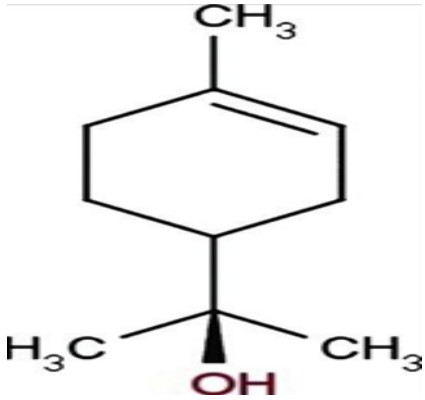
IV. DRUG PROFILE

A. Lionene



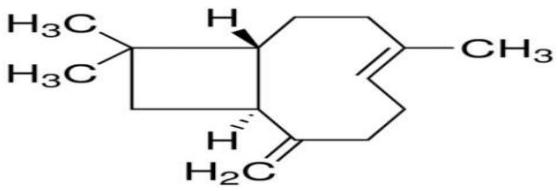
- Synonyms: Dipentene, p-mentha-1,8-dien
- Chemical name: 1-methyl-4-(1-methylethenyl) cyclohexane
- Chemical formula: $C_{10}H_{16}$
- Structure: monocyclic monoterpenes
- Molecular weight: 136.23g/mol
- Use: Antioxidant, Anti-inflammatory, Antimicrobial, Anticancer potential

B. Terpineol



- Synonyms: alpha-terpineol
- Chemical name: 2-(4-methyl-1-cyclohex-3-enyl) propan-2-ol
- 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 -Chemical name:(1R,4E,9S)-4,11,11-Trimethy-8-methylene-bicyclo [7.2.0] undec-4ene
- Chemical formula: $C_{15}H_{24}$
- Structure: Bicyclic sesquiterpene
- Molecular weight: 204.36 g/mol
- Use: Antioxidant, Anti-inflammatory, Antimicrobial, Anticancer potential



V. MATERIAL AND METHOD

Apparatus:
500 ml Round Bottom Flask, Digital Weighing Balance, Heating Mantle, Reflux Condenser, Hot Air Oven, magnetic stirrer, Desiccator.

Chemicals:
Guava Leaf extract, 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.

VI. DISSOLUTION EXTRACTION OF GUAVA LEAVES EXTRACT (MODIFIED METHOD)

Procedure:

1. Sample Preparation:

Collect fresh guava leaves, wash thoroughly with clean water to remove dirt and impurities. Dry the leaves in shade (to preserve phytoconstituents) for 2–3 days and grind them into a fine powder.

2. Weighing of Sample:

Weigh accurately about 10–15 g of powdered guava leaves.

3. Preparation of Solvent System:

Take a suitable solvent such as ethanol (70–96%) or hydroalcoholic solution in a beaker.

4. Dissolution Process:

Add the powdered drug into the solvent.
Place the mixture on a magnetic stirrer.
Stir continuously at 40–50°C for 2–4 hours to enhance dissolution of active constituents.
Ensure uniform mixing to allow maximum extraction of phytochemicals.

5. Filtration:

Filter the solution using Whatman filter paper or muslin cloth to remove insoluble plant residue.

6. Concentration of Extract:

Transfer the filtrate to a water bath.
Evaporate the solvent at controlled temperature (not exceeding 50°C) until a semi-solid extract is obtained.

7. Drying of Extract:

Dry the concentrated extract in a desiccator or vacuum oven to remove remaining solvent and obtain a stable dried extract.

8. Storage:

Store the final extract in an airtight container away from light and moisture for further formulation use.

Formulation Table 2. Formulation table

Sr. No.	Ingredients	Formulation F1	Formulation F2	Formulation F3
1	Guava leaves extract	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

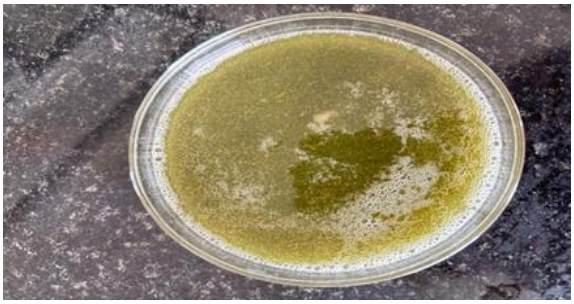


Figure 6: formulation of guava leaves extract

VII. FORMULATION OF PATCHES

Step-1: Prepare polymer base:

a. Dissolve 0.9 gm of polyviny alcohol in 15ml warm distilled water at (60^{o}C) 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 extract:

a. dissolve 1.8 ml guava leaves extract in 1.5 ml ethanol.
b. slowly add the extract solution into the polymer matrix while stirring cintinuously for 2030 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 (40^{o}C in oven) for 24-48 hours untill completely dried.

Step-5: Storage:

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

VIII. EVALUATION PARAMETERS:

1.Physical Appearance:
The patches were visually inspected for:
Colour
Transparency
Smoothness
Uniformity
Presence of air bubbles or cracks

- Importance: Ensures aesthetic acceptability and uniform formulation.

2. Thickness Uniformity:
Measured using a digital vernier caliper at different points.
Average thickness calculated.

- Importance: Ensures uniform drug distribution and controlled release.

3.Weight Uniformity:
Individually weigh 3–5 patches.
Calculate mean weight and standard deviation.

- Importance: Indicates uniformity in formulation and drug content.

4.Folding Endurance:
Patch repeatedly folded at the same point until it breaks.
Number of folds recorded.

- Importance: Indicates flexibility and mechanical strength.

1. Tensile Strength:
Determined using tensile testing apparatus.
Formula:

- Importance: Measures patch durability during handling.

2. Percentage Elongation:

- Importance: Indicates elasticity of patch.

3. Moisture Content:
Patch weighed initially.
Dried in desiccator containing calcium chloride.
Reweighed after 24 hours.

- Importance: Prevents microbial growth and improves stability.

4. Moisture Uptake:
Patch placed in a humid chamber (75% RH).
Weight gain measured.

- Importance: Indicates stability in humid conditions.

5. Drug Content Uniformity:
Patch dissolved in suitable solvent (ethanol/phosphate buffer).
Analyzed using UV spectrophotometer.

- Importance: Ensures uniform drug distribution.

6. Surface pH:
Patch placed in distilled water.
pH measured using pH meter.

- Importance: Should be skin-compatible (4.5–6.5).

7. Flatness Test:
Patch cut into strips.
Length measured before and after stretching.

- Importance: Ensures patch does not shrink.

8. Adhesion Test (Peel Strength):
Patch applied to a surface and peeled off.
Force required measured.

- Importance: Enses proper sticking ability on skin.

9. Water Vapor Transmission Rate (WVTR):
Patch placed over vial containing desiccant.
Weight gain measured over time.

- Importance: Indicates moisture permeability.

10. Skin Irritation Test:
Patch applied on animal/human skin.
Observed for redness, swelling, irritation.

- Importance: Confirms safety of formulation.

11. Dissolution Study:
Aim: To determine drug release from transdermal patches.

Membrane (cellophane) soaked overnight before use.

- Membrane fixed between donor and receptor compartment.

- Patch placed on membrane (drug side facing membrane).
- Receptor compartment filled with phosphate buffer (pH 7.4).
- Temperature maintained at 37°C with continuous stirring.
- Samples withdrawn at intervals (0, 1, 2, 4, 6, 8, 12, 24 hrs).
- Equal volume of fresh buffer added to maintain sink condition.
- Samples analyzed using UV spectrophotometer.
- Cumulative % drug release calculated.
- Graph plotted (Time vs % Drug Release).
- Result shows sustained drug release; F3 > F2 > F1.
- Confirms controlled and prolonged drug delivery.

IX. RESULT AND DISCUSSION:

There are three samples of the transdermal antioxidant patches are formulated by using the guava leaves extract, 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 is used as antioxidant activity.

Table 3. Result and Discussion

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)		

X. 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 avoids the first pass metabolism. The patches demonstrate the potential for skin related therapeutic use.

REFERANCE

[1] W. F. Wong, K. P. Ang, G. Sethi, and C. Y. Looi, "Recent advancement of medical patch for transdermal drug delivery."

[2] S. R. Fathima *et al.*, "Mucoadhesive buccal patches—A review."

[3] K. G. Bhutkar, "Formulation and evaluation of mucoadhesive herbal buccal patch of *Psidium guava* L.," *Journal of Current Pharma Research*, vol. 5, no. 1, p. 1372, 2014.

[4] M. Boddupalli, Z. N. Mohammed, R. A. Nath, and D. Banji, "Mucoadhesive drug delivery system: An overview," *Journal of Advanced Pharmaceutical Technology and Research*, vol. 1, no. 4, p. 381, 2010.

[5] Choudhary, G. Tiwari, M. Pandey, K. M. Kymonil, and S. A. Saraf, "Formulation and characterization of carvedilol buccal mucoadhesive patches," *International Journal of Research in Pharmaceutical Sciences*, vol. 1, no. 4, pp. 396–401, 2010.

[6] Figueiras, A. Vieira, S. Simões, and F. Veiga, "Mucoadhesive buccal systems as a novel strategy for anti-inflammatory drugs administration," *Anti-Inflammatory and Anti-Allergy Agents in Medicinal Chemistry*, vol. 10, no. 3, pp. 190–202, 2011.

[7] T. Suwandecha and P. Changklang, "Formulation development and characterization of a transdermal patch containing *Crinum asiaticum* leaves extract," *Journal of Applied Pharmaceutical Science*, vol. 13, no. 12, pp. 207–213, 2023.

[8] K. S. Goud, "Preparation and evaluation of mucilage from fresh leaves of *Psidium guajava*," *Research Journal of Pharmacy and Technology*, vol. 10, no. 3, pp. 125–132, 2018.

[9] S. Sahu *et al.*, "Development and evaluation of transdermal patches using natural antioxidants," *Journal of Drug Delivery and Therapeutics*, vol. 8, no. 4, pp. 105–112, 2018.

[10] S. Kumar *et al.*, "Formulation and evaluation of herbal transdermal patches for wound healing," *Journal of Pharmaceutical Sciences and Research*, vol. 12, no. 3, pp. 456–463, 2020.

[11] Y. Zhang and M. Michniak-Kohn, "Flavosomes for transdermal delivery of flavonoids," *Pharmaceutics*, vol. 12, no. 11, p. 1079, 2020.

[12] George and V. Suchithra, "Plant-derived bioadhesives for wound dressing and drug delivery systems," *Journal of Adhesion Science and Technology*, vol. 33, no. 14, pp. 1450–1465, 2019.

[13] "Natural compounds in transdermal delivery devices and wound dressing materials," *Journal of Controlled Release*, vol. 355, pp. 456–470, 2023.

[14] P. Patel *et al.*, "Formulation and evaluation of herbal transdermal patches for anti-inflammatory activity," *Journal of Pharmacy and Pharmacology*, vol. 71, no. 8, pp. 1110–1119, 2019.

[15] R. Sharma *et al.*, "Development and evaluation of transdermal patches containing natural antioxidants for skin health," *Journal of Cosmetics, Dermatological Sciences and Applications*, vol. 12, no. 2, pp. 145–153, 2022.

[16] Singh *et al.*, "Formulation and evaluation of mucoadhesive buccal patches using natural polymers," *Journal of Applied Polymer Science*, vol. 138, no. 15, p. 5035, 2021.

[17] R. Gupta *et al.*, "Herbal transdermal patches for wound healing: A review," *Journal of Ethnopharmacology*, vol. 253, p. 112642, 2020.

[18] N. Jain *et al.*, "Formulation and evaluation of transdermal patches containing herbal extracts," *Journal of Pharmaceutical Sciences and Research*, vol. 11, no. 2, pp. 234–241, 2019.

[19] Rajput *et al.*, "Development and evaluation of herbal transdermal patches for anti-aging activity," *Journal of Cosmetics, Dermatological Sciences and Applications*, vol. 12, no. 3, pp. 202–211, 2022.

[20] P. Yadav *et al.*, "Formulation and evaluation of mucoadhesive patches using natural polymers for buccal delivery," *Journal of Drug Delivery Science and Technology*, vol. 61, p. 102294, 2021.