

Formulation and Evaluation of Herbal Oral Film Containing Piper Betle Extract

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Abstract: Oral thin films containing Piper betle extract are showing promise as a herbal drug delivery system for oral healthcare. These fast-dissolving films improve the release and bioavailability of medicinal compounds without requiring water. Piper betle leaves contain bioactive compounds such as hydroxychavicol, inflammatory, and wound-healing properties. The films may help treat mouth ulcers, sore throats, bad breath, and gum infections. Polymers, plasticizers, sweeteners, and flavoring agents are frequently used in formulations to enhance film quality and patient acceptability. Thickness, tensile strength, folding endurance, disintegration time, and drug release are all measured to ensure effectiveness. Piper betle oral thin films show promise as a safe and convenient herbal oral healthcare solution.

Keywords: Piper betle extract, Oral thin film, Fast dissolving film, Herbal drug delivery system, Anti-inflammatory activity, Oral healthcare, Herbal formulation.

I. INTRODUCTION

Piper betle, commonly known as betel leaf or “paan,” is a medicinal climber widely used in traditional Indian medicine for treating pain, inflammation, oral infections, wounds, cough, asthma, rheumatism, and digestive disorders. Its leaves possess important biological activities such as antibacterial, antioxidant, antifungal, anti-inflammatory, analgesic, and wound-healing effects due to bioactive compounds like hydroxychavicol, eugenol, and chavicol.

Inflammation is a protective response of the body, but prolonged inflammation can lead to chronic diseases such as arthritis and oral mucosal disorders. Although conventional anti-inflammatory drugs like NSAIDs are effective, their long-term use may cause side effects including gastric irritation and ulcers. Therefore, herbal alternatives such as Piper betle are gaining importance because of their better safety profile.

Oral film drug delivery systems are a modern and effective approach for administering herbal extracts. These films rapidly dissolve in the mouth, improve patient compliance, bypass first-pass metabolism, and deliver the drug directly to the site of action. Hence, Piper betle-loaded oral films show promising potential for the treatment of localized inflammatory and oral conditions.



Fig. No. 01 Piper Betle Leaf



Constituents

Piper betle extract contains several phytochemicals, including hydroxychavicol, eugenol, and flavonoids. Hydroxychavicol is the main bioactive compound, known for its antimicrobial, antioxidant, and anti-inflammatory effects, which enhance the therapeutic efficacy of the extract in oral thin-film formulations.

Properties

Piper betle oral thin films are flexible, quick-dissolving formulations used for easy oral drug administration. They have antimicrobial, antioxidant, and anti-inflammatory properties, as well as good strength, elasticity, and a saliva-compatible pH, allowing for rapid action and patient comfort.

Herbal drugs

Piper betle extract is a key herbal ingredient that contains hydroxychavicol and eugenol. It has antimicrobial, analgesic, antioxidant, and healing properties that can help treat mouth ulcers, oral infections, inflammation, and bad breath.

Pharmacognosy

Piper betle is a medicinal plant high in flavonoids, tannins, alkaloids, saponins, and terpenes. These phytoconstituents have antimicrobial, anti-inflammatory, antioxidant, and wound healing properties.

Herbal Drug Promotion

Piper betle oral thin films are modern herbal formulations that dissolve quickly in the mouth, resulting in improved drug absorption and patient compliance, particularly in children and seniors.

Herbal Products and Quality Control

To ensure quality and effectiveness, the films are evaluated based on physical appearance, flexibility, pH, time disintegration, drug content, antimicrobial activity, and stability.

Current State of Herbal Drugs

Piper betle oral films provide rapid drug release, increased bioavailability, and convenient oral care. However, issues such as taste masking, stability, standardization, and regulatory approval persist.

Future Scenario for Herbal Medicines

Future developments may enhance the stability, safety, and efficacy of Piper betle oral films. Proper standardization and advanced drug delivery techniques can improve their therapeutic efficacy.

INTRODUCTION TO PIPER BETLE LEAVES

Botanical name: Piper betle Linn.

Synonyms: Chavica betle, Betel leaf, Betel vine, Paan leaf

Family: Piperaceae

Morphology:

Oral thin films are smooth, thin, flexible, uniform, and rapidly dissolve, with high mechanical strength and stability.

Habit:

Films may be transparent or pale green, with a mild herbal odor and a slightly strong taste.

Leaves:

The leaves contain hydroxychavicol, eugenol, flavonoids, tannins, and phenols, which have antimicrobial and antioxidant properties.

Leaf Size:

The leaves are medium to large, measuring 8-20 cm long and 5-15 cm wide; glossy; and heart shaped.

Cultivation:

The plant thrives in warm, humid climates with partial shade and propagates through stem cuttings.

Chemical constituents:

The primary constituents are hydroxychavicol, chavicol, chavibetol, eugenol, phenols, tannins, and terpenoids.



Medical uses:

Antimicrobial and anti-inflammatory properties make it useful for treating oral infections, ulcers, sore throats, bad breath, and wound healing.

Toxicity:

Therapeutic doses are safe, but higher concentrations can cause irritation or allergic reactions.

Research Needs:

More research is needed on formulation optimization, stability, safety, and clinical efficacy of oral thin films.

Kingdom Plantae

Kingdom	Plantae
Subkingdom	Tracheobionta (Vascular plants)
Superdivision	Spermatophyta (Seed plants)
Division	Magnoliophyta (Flowering plants / Angiosperms)
Class	Magnoliopsida (Dicotyledons)
Subclass	Magnoliidae
Order	Piperales
Family	Piperaceae
Genus	Piper
Species	Piper betle L.

Table No. 1: Scientific Classification of Piper betle L.

MEDICINAL PROPERTIES

Piper betle extract oral thin films have antimicrobial, anti-inflammatory, antioxidant, antiseptic, analgesic, and wound-healing properties thanks to compounds such as hydroxychavicol, eugenol, flavonoids, and tannins. They treat mouth infections, ulcers, sore throats, gum inflammation, and bad breath with rapid oral drug delivery.

Aim and Objective

Aim

To formulate and evaluate an oral thin film containing Piper betal extract for anti-inflammatory activity

Objective

- To prepare the extract of Piper betle leaves using a suitable extraction method.
- To create oral thin films with Piper betle extract using appropriate plasticizers and film- forming polymers.
- To assess the prepared oral films' physicochemical characteristics, such as drug content uniformity, thickness, weight variation, folding endurance, and surface pH.
- To determine the disintegration time and in vitro drug release profile of the formulated oral thin films.
- To evaluate the prepared formulations' in vitro anti-inflammatory activity using appropriate techniques like the protein denaturation assay.
- To contrast the optimized formulation's anti-inflammatory activity with that of a conventional anti-inflammatory medication.

REVIEW OF LITERATURE

1. Patel R. et al. (2018) Patel and colleagues created herbal oral thin films containing Piper betle leaf extract for antimicrobial activity in oral infections. The films were created by solvent casting with HPMC as the polymer. The study found that the film had good flexibility, disintegrated quickly, and effectively inhibited oral pathogens. The authors concluded that Piper betle extract can be effectively combined with oral films for local drug delivery.



2. Kumar S. et al. (2019). Kumar et al. examined fast-dissolving oral films containing herbal extracts, including Piper betle. The films demonstrated satisfactory tensile strength, folding endurance, and rapid dissolution within one minute. The presence of phenolic compounds such as hydroxychavicol and eugenol conferred significant antimicrobial activity against *Streptococcus mutans*.
3. Sharma P. et al. (2017) Sharma and colleagues looked at the antioxidant and anti-inflammatory properties of Piper betle extract in oral formulations. The prepared films demonstrated high free radical scavenging activity and increased stability. The authors proposed that herbal oral films could help with mouth ulcer management and oral care therapy.
4. Rao N. et al. (2020). Rao et al. created mucoadhesive oral thin films with Piper betle extract using sodium alginate and glycerin. The films showed uniform thickness, an acceptable surface pH, and rapid drug release. The study demonstrated Piper betle's suitability for treating microbial infections in the oral cavity.
5. Gupta A. et al. (2016) Gupta and co-authors investigated the phytochemical properties of Piper betle leaves and their use in oral drug delivery systems. The researchers discovered that the leaf extract contains flavonoids, tannins, alkaloids, and essential oils that have antimicrobial and wound-healing properties.
6. Mehta D. et al. (2021). Mehta et al. created fast-dissolving oral films of herbal extract using pullulan polymer. Films containing Piper betle extract disintegrated quickly and were more acceptable to patients. The study concluded that herbal films provide a convenient method of administration in the absence of water.
7. Singh V. et al. (2018) Singh and colleagues examined the antimicrobial activity of Piper betle leaf extract against oral microorganisms. The results revealed a strong inhibitory activity against *Candida albicans* and *Staphylococcus aureus*. The findings supported the use of Piper betle in oral healthcare formulations.
8. Joshi M. et al. (2022). Joshi et al. created herbal oral thin films with HPMC and PEG-400 as plasticizers. The prepared films exhibited smooth surface morphology, high folding endurance, and uniform drug distribution. The addition of Piper betle increased antimicrobial effectiveness and mouth freshness.
9. Verma K. et al. (2019) Verma and colleagues reviewed medicinal plants used in oral films and identified Piper betle as a key herb due to its antioxidant and antibacterial properties. The study emphasized its traditional use for oral hygiene and throat infections.
10. Desai H. et al. (2020) Desai et al. evaluated the physicochemical properties of herbal oral films containing Piper betle extract. The films demonstrated an acceptable pH, a rapid swelling index, and good drug content uniformity. The study found that buccal absorption improves bioavailability.
11. Chavan P. et al. (2021). Chavan and colleagues created oral dissolving films for mouth ulcer treatment using Piper betle extract. The formulation had anti-inflammatory properties and reduced irritation in the oral cavity. The films quickly dissolved and provided long-lasting local action.

MATERIALS AND METHODS

MATERIALS USED FOR THE STUDY

Sr. No.	Instrument	Manufacturer
1.	Digital Weighing Balance.	Sartorius
2.	Magnetic Stirrer	IKA
3.	pH Meter	Elico Limited.
4.	Hot Air Oven	Yamato Scientific
5.	Dissolution Test Apparatus	Labindia Instruments
6.	Ultrasonicator	PCI analytics
7.	Soxhlet extraction apparatus	Borosil
8.	Water Bath	Tanco

Table No. 2: List of Instruments



Sr. No	Ingredient	Common Manufacturers / Suppliers
1.	Sodium alginate	Merck KGaA, FMC Corporation, Kimica Corporation
2.	Piper betle extract	Natural Remedies Pvt. Ltd., Amsar Pvt. Ltd., Sami Labs Limited
3.	Propylene glycol	Dow Chemical Company, BASF SE
4.	Glycerin	Godrej Industries, KLK OLEO
5.	Citric acids	Jungbunzlauer, Cargill
6.	Sweetener (Glucose)	Roquette, Ingredion Incorporated
7.	Methyl paraben	Salicylates and Chemicals Pvt. Ltd., Merck KGaA
8.	Colour (Ambered)	Sensient Technologies, Roha Dyechem Pvt. Ltd.
9.	Distilled water	Laboratory purified water suppliers or in-house preparation

Table No. 3: List of Chemicals.

METHODS

PLANT COLLECTION AND AUTHENTICATION

Fresh Piper betle leaves were collected in Sangli District, Maharashtra, and authenticated by the Department of Botany, Padmabhushan Vasantraodada Patil Mahavidyalaya, Kavathemahankal- 416405. Shortly after collecting, the leaves were thoroughly washed with distilled water to remove dirt and impurities before being shade-dried at room temperature for several days. After drying completely, the leaves were ground into a coarse powder and stored in airtight plastic containers to be used later in the production of an oral film containing Piper betle extract

□ Extraction process

1. Fresh Piper betle leaves were collected and thoroughly cleaned with distilled water.
2. The leaves were shade-dried at room temperature until completely moisture-free.
3. Dried leaves were ground to a coarse powder.
4. 20 grams of powdered material were precisely weighed.
5. The powder was transferred to a clean conical flask.
6. Ethanol was used to fully immerse the powder.
7. The mixture was left for 48-72 hours, with occasional shaking (maceration).
8. The mixture was filtered through Whatman filter paper.
9. The filtrate was collected and concentrated.
10. The solvent was evaporated to produce a dried extract weighing 2.5 grams.
11. The extract was kept in an airtight container for future analysis.



Fig. No. 02 Soxhlet Extraction Apparatus



QUALITATIVE PHYTOCHEMICAL ANALYSIS

Preparation for test samples

The oral film containing Piper betle extract was dissolved in 5 mL distilled water and filtered through Whatman filter paper. The resulting filtrate was used for qualitative phytochemical analysis.

1. Alkaloids (Dragendorff Test):

About 2 mL of the extract was combined with Dragendorff's reagent. An orange to reddish-brown precipitate indicated the presence of alkaloids.

2. Flavonoids (the Shinoda Test):

To 2 mL of extract, magnesium turnings and a few drops of concentrated hydrochloric acid were added. Flavonoids were confirmed when they turned pink or crimson red.

3. Tannins (Test for Ferric Chloride)

The extract was treated with a 5% ferric chloride solution. The development of a dark green or bluish-black color indicated the presence of tannins.

4. Saponin (Foam Test):

The extract was vigorously shaken using distilled water. Saponins were confirmed by the formation of a stable foam that lasted several minutes.

5. Glycosides (the Keller-Killiani Test):

The extract was treated with glacial acetic acid, which contained ferric chloride, before being carefully added to concentrated sulfuric acid. The brown ring at the junction indicated glycosides.

6. Phenolic Compound:

The addition of ferric chloride solution to the extract resulted in a bluish-black coloration, indicating phenolic compounds.

7. Steroids (Salkowski test):

The extract was treated with chloroform and concentrated sulfuric acid. The formation of a reddish-brown ring confirmed the presence of steroids.

8. Terpenoids (Liebermann–Burchard Test):

The extract was treated with chloroform, acetic anhydride, and Concentrated sulfuric acid. Green coloration confirmed the presence of terpenoids.



Fig. No. 03 Phytochemical Tests



Sr. No.	Phytochemical Tests	Observation	Result
1.	Alkaloids Dragendorff's Test	Orange precipitate formation	Present (+).
2.	Flavonoids Shinoda Test	Pink/red coloration	Present (+).
3.	Tannins Ferric Chloride Test	Dark blue/green color.	Present (+).
4.	Saponins Foam Test.	Stable froth formation	Present(+).
5.	Glycosides Keller-Killiani Test.	Brown ring formation.	Present (+).
6.	Phenolic compounds. Ferric Chloride Test	Bluish-black coloration	Present (+).
7.	Steroids Salkowski Test	Reddish-brownring.	Present (+).
8.	Terpenoids Liebermann– Burchard test	Green coloration.	Present (+).

Table No.4: Phytochemical Tests

In vitro anti-inflammatory activity

In vitro anti-inflammatory activity by Protein Denaturation Method

The reaction mixture (10 mL) consisted of 0.4 mL of egg albumin (from fresh hen's egg), 5.6 mL of phosphate buffered saline (PBS, pH 6.4) and 100 µL of different concentration samples. Similar volume of double-distilled water served as control. Then the mixtures were incubated at (370c ±2) in a incubator for 15 min and then heated at 70oC for 5 min. After cooling, their absorbance was measured at 660 nm by using vehicles as blank. Diclofenac sodium at the concentration was used as reference drug and treated similarly for determination of absorbance. The percentage inhibition of protein denaturation was calculated by using the following formula,

$$\% \text{ Inhibition} = \frac{C - T}{C} \times 100$$

T = absorbance of test sample C = absorbance of control

Protein Denaturation Assay

Protein Denaturation Assay								
SR.NO.	Sample Code	Concentration (g/ml)	Absorbance at 660nm				% Inhibition	IC50 (µg/ml)
			Test 1	Test 2	Test 3	Mean		
1	Control	-	1.54	1.54	1.54	1.54	-	
2	Standard (Diclofenac Sodium)	20	1.40	1.37	1.39	1.32	16.98%	70.89
		40	1.11	1.19	1.15	1.15	25.32%	
		60	0.91	0.89	0.93	0.91	42.76%	
		80	0.67	0.65	0.63	0.65	59.11%	
		100	0.21	0.18	0.23	0.21	86.79%	
3	Piper betal	20	1.45	1.41	1.47	1.44	6.28%	99.13
		40	1.26	1.23	1.29	1.26	18.18%	
		60	1.05	1.01	1.08	1.04	32.46%	
		80	0.91	0.88	0.94	0.91	40.91%	
		100	0.75	0.78	0.74	0.76	50.87%	

Table No.5: Protein Denaturation Activity of Piper betle



Graphical Data:

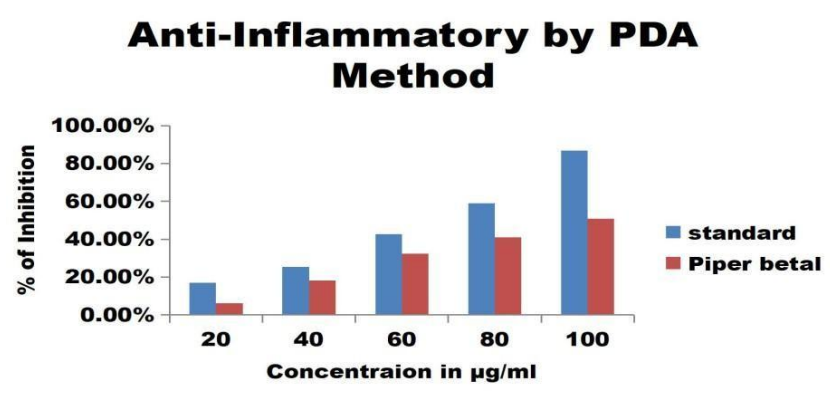


Fig. No.4: % Inhibition of Protein Denaturation by Piper betel

Images of the Activity:



Fig. No.5: Anti-inflammatory Activity of Piper betel by Protein Denaturation Method

Conclusion of the study:

The anti-inflammatory activity evaluated by the protein denaturation assay shows a clear concentration-dependent inhibition for both the standard and Piper betel extract. Protein Denaturation is a key mechanism associated with inflammation, and inhibition of this process indicates potential anti-inflammatory properties. In the present data, the standard exhibits strong inhibition, increasing from approximately 15–20% at 20 µg/mL to around 85–88% at 100

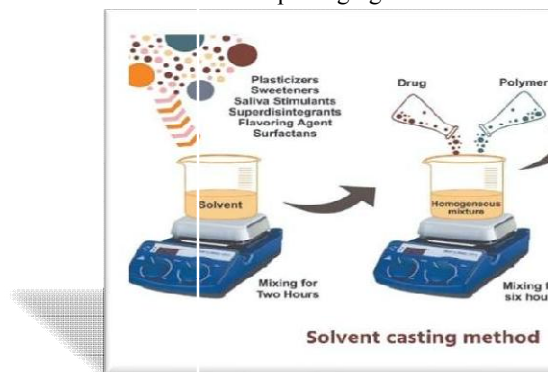


$\mu\text{g/mL}$, confirming its high efficacy. The Piper betel extract also demonstrates a steady increase in inhibition with rising concentration, starting from about 5–8% at 20 $\mu\text{g/mL}$ and reaching nearly 50% at 100 $\mu\text{g/mL}$. Although its activity is comparatively lower than the standard, the extract shows significant inhibition at higher concentrations, indicating moderate anti-inflammatory potential. Overall, the Results suggest that Piper betel possesses dose-dependent anti-inflammatory activity through stabilization of proteins and prevention of denaturation, supporting its potential use as a natural anti-inflammatory agent.

Preparation of oral film

• Solvent Casting Method

1. Preparing the Polymer Solution: Weigh the required amount of sodium alginate (a film-forming polymer). Dissolve it in a measured amount of distilled water while stirring continuously. Allow the solution to stand for 2-3 hours to remove any air bubbles and create a clear, viscous solution.
2. Making Piper betel extract solution: Take the appropriate amount of piper betel extract. Dissolve it in a small amount of appropriate solvent (distilled water or an ethanol-water mixture). Mix until a uniform solution is produced.
3. The incorporation of plasticizers and additives: To improve flexibility, add plasticizers such as propylene glycol and glycerin to the polymer solution. Mix in the citric acid (which stimulates the saliva). Add the sweetener (glucose) and methyl paraben (a preservative). Mix until the mixture is homogeneous.
4. Addition of Extract: Slowly incorporate the piper betel extract solution into the polymer mixture. Stir continuously to ensure that the drug is evenly distributed.
5. Deaeration: Allow the final solution to stand or use a mild vacuum to remove any trapped air bubbles.
6. Casting of Film: Pour the final solution into a level glass or Petri dish. Spread evenly to achieve a uniform thickness.
7. Drying: Dry the cast film at room temperature or in a hot air oven (40-45°C) until the solvent has evaporated completely.
8. Cut and Package: Carefully peel off the dried film. Cut into desired size strips (usually 2×2 cm). To keep moisture out, store in an airtight container or aluminum foil packaging.



Sr. No.	Ingredients	Batch A	I
1.	Sodium alginate	2 gm	2.5
2.	Piper betle extract	50 mg	75 r
3.	Glycerin	0.5 mL	0.75
4.	Propylene glycol	0.3 mL	0.5
5.	Citric acid	5 mg	10 r
6.	Methyl paraben	5 mg	5 m
7.	Sweetener (Glucose)	100 mg	100
8.	Colour (Ambered)	q.s.	q.s.
9.	Distilled water	up to 10 mL	up t

Table no. 6 Formulation Table

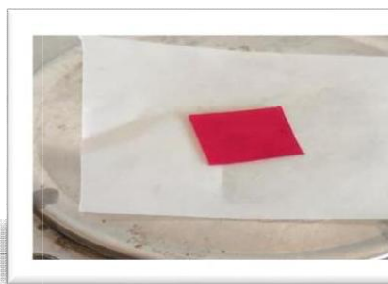


Fig.No.06 Oral Film of Piper Betle Evaluation Test for Oral Film

1. Physical appearance.

The prepared oral films were visually examined for color, transparency, smoothness, and surface texture.

2) Thickness

The film's thickness was measured at various points with a micrometer screw gauge, and the average value was calculated.



Fig.No.07 Thickness Test

3. Weight Variation.

Each film was weighed with an analytical balance, and the average weight and deviation were recorded





Fig.No.08 Weight Variation Test

4. Folding Endurance

A strip of film was repeatedly folded at the same spot until it broke. The number of folds required to break the film was referred to as folding endurance.

5. Surface pH.

The film's surface pH was determined by placing it in contact with distilled water and measuring it with a pH meter.



Fig.No.09 pH Test

6. Disintegration Time.

The time it took for the film to disintegrate completely in distilled water was recorded.



Fig.No.10 Disintegration Time Test

7. Drug Content Uniformity

A known amount of film was dissolved in a suitable solvent, and the concentration of Piper betle extract was determined using spectroscopy.



Evaluation Table

Sr. NO.	Parameter	Observation / Results
1.	Physical appearance.	Smooth, uniform greenish- brown film
2.	Thickness	1.14 mm
3.	Weight variation	0.43 g \pm 0.05 g
4.	Surface pH	6.19
5.	Disintegration Time	35 seconds

Batch	Appearance	Thickness (mm)	Weight Variation	PH	Disintegration Time (Sec)
A	Transparent	0.12 \pm 0.01	45 \pm 1.2	6.19	35 (sec)
B	Smooth	0.14 \pm 0.02	47 \pm 1.0	5.78	30 (sec)
C	Flexible	0.13 \pm 0.01	46 \pm 1.1	5.94	36 (sec)
D	Uniform	0.15 \pm 0.02	48 \pm 1.3	6.2	38 (sec)

Table no. 7: Organoleptic Evaluation of oral Film

RESULT & DISCUSSTION

Extraction and standardization

Sr. No.	Parameters	observation of leaves
1.	Color	Dark green
2.	Odor	Typical aromatic odor
3.	Taste	pungent and slightly bitter.
4.	Shape	Heart-shaped leaves
5.	Surface	Smooth and glossy.

Solvent extraction of air-dried plant material

Sr. No.	Extracts	Method	Nature of Extract	Colour	Plant Material (g)	Weight Of Dried Extract (g)	Yield (% w/w)
1.	Ethanol extract	Soxhlet method	Semi-solid	Greyish green	20 g	2.5 g	12.5 %

Summary & Conclusion Background:

Piper betle leaves have antimicrobial, antioxidant, and anti-inflammatory properties, which make them ideal for herbal oral drug delivery systems.

Objective:

Formulate and evaluate oral dissolving films containing Piper betle extract, as well as investigate their physicochemical properties and anti-inflammatory activity.

Methods:

Piper betle leaves were shade-dried, ground, and extracted with ethanol. The extract was incorporated into oral films with appropriate polymers and plasticizers. The films were assessed for thickness, weight variation, folding endurance, surface pH, disintegration time, and drug content.

Extract Preparation:

Maceration with ethanol extracted the powdered leaves, which were then filtered, concentrated, and stored for formulation.



Instrumental analysis:

The physicochemical parameters of the prepared films were examined, including thickness, weight uniformity, folding endurance, surface pH, disintegration time, and drug content uniformity.

Anti-inflammatory Activity:

The presence of flavonoids, tannins, and phenolic compounds in Piper betle extract resulted in good anti-inflammatory activity in the formulated films.

Results:

The oral films had satisfactory mechanical and physicochemical properties, including rapid disintegration and a near-neutral surface pH. Phytochemical screening confirmed the presence of active constituents, and the films showed promising anti-inflammatory properties.



Fig.No.11 Authentication Certificate



II. CONCLUSION

The study successfully formulated and evaluated herbal oral dissolving films containing an ethanolic extract of Piper betle leaves. Phytochemical analysis confirmed the presence of bioactive compounds such as alkaloids, flavonoids, tannins, phenolics, and essential oils responsible for antimicrobial, antioxidant, and anti-inflammatory activities. The prepared films showed satisfactory physicochemical properties, including uniform thickness, acceptable weight variation, good folding endurance, suitable surface pH, rapid disintegration, and uniform drug content. Phytochemical screening of the formulation verified the retention of active constituents in the films. The films also exhibited significant anti-inflammatory activity, suggesting potential use in oral ulcers, inflammation, and oral infections. Due to advantages such as easy administration, rapid action, improved patient compliance, precise dosing, and reduced first-pass metabolism, the developed Piper betle oral dissolving film may serve as a promising herbal drug delivery system for oral healthcare. Further stability and clinical studies are recommended for future therapeutic applications.

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