Research Article

Formulation and Evaluation of Mouth Dissolving Strips incorporating *Opuntia dillenii*

G. Elakkiyamani[1]*, R. Shiyam Chandar[2], V. V. Dhayananthan[2], K.Nithish[2], K. Santhosh[2], M. Devendiran[2]
1. Assistant Professor, Department of Pharmaceutics; 2. Final Year-Bachelor of Pharmacy
PPG college of pharmacy, Viswapuram, Saravanampatti, Coimbatore, Tamil Nadu-641035, India.
***Corresponding author's E-mail:** sreeelakkiyamani202@gmail.com

Received: 03-01-2025; **Revised:** 26-04-2025; **Accepted:** 05-05-2025; **Published online:** 15-05-2025.

ABSTRACT

Mouth dissolving strips are an innovative oral dosage form that quickly disintegrates and dissolves in the mouth, allowing for rapid drug release and better absorption. These strips are especially useful for patients who struggle with swallowing tablets or capsules, such as elderly individuals and children. *Opuntia dillenii*, commonly known as prickly pear cactus, is a medicinal plant traditionally used for its anti-diabetic, anti-inflammatory, and antioxidant properties. Native to America and Mexico, it is rich in bioactive compounds like betalains, flavonoids, and polyphenols, which may help prevent various diseases and improve overall health. This study focuses on preparing mouth dissolving strips using *Opuntia dillenii* extract. HPMC is used as the polymer, glycerol as the plasticizer, mannitol as the sweetener, and citric acid as the saliva stimulant. The strips were tested for quality parameters such as folding endurance, weight uniformity, flexibility, disintegration time, and drug release. Results showed good pharmacological activity, particularly in managing blood sugar levels and inflammation.

Keywords: Mouth dissolving strips, *Opuntia dillenii*, Herbal formulation, Fast-dissolving films, Oral absorption.

INTRODUCTION

The oral route of drug administration is the most advantageous route due to ease of administration, non-invasiveness, adaptability, patient compliance and acceptability. Regarding the oral route of drug delivery many substitutes have been continuously presented using the latest new technologies for paediatric, geriatric, nausea and non-adherent patients.[1]

The main problem in the conventional oral dosage form such as tablets and capsules are the time taken for the onset of action which led to the development of the mouth-dissolving films (MDF), a new kind of solid oral dosage form. This dosage form disintegrates quickly in the mouth without the help of water for swallowing hence can be used by paediatric and geriatric patients who have difficulty in swallowing. Upon ingestion, saliva serves to rapidly disperse/dissolve the MDF. The saliva containing dissolved medicament is absorbed from mouth, pharynx, and esophagus bypassing the first pass metabolism. Due to this, bioavailability of drugs is significantly increased than those observed from conventional dosage forms.[2]

Advantages of mouth dissolving strips:

- It can be administered without the need for water.
- Rapid onset of action.
- Easy to handle and transport.
- Enhances bioavailability for specific active ingredients.
- Offers improved stability.
- Effectively masks unpleasant tastes.[3]

Disadvantages of oral thin films:

- The formulation should have good water solubility in saliva.
- Uniform drug distribution across the strips is challenging.
- High drug doses cannot be incorporated effectively.

Specialized packaging is required to ensure stability and safety.[4]

Ideal characteristics of MDS:

- The drug should have an acceptable and pleasant taste.
- It should have small molecular size and weight
- It should be water soluble and stable in saliva.
- They should be resistant to external factors such as humidity and temperature.
- They should efficiently penetrate the oral mucosa.[5]

Plant Profile:

Figure 1: *Opuntia dilleniii*

Opuntia dillenii, is commonly known as Prickly Pear, is a cactus species native to the America and Mexico. This succulent plant is taxonomically classified in Table 1

Table 1: Taxonomical classification of *Opuntia dillenii.*

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Caryophyllales
Family	Cactaceae
Genus	Opuntia
Species	*Opuntia dillenii*

The genus *Opuntia* has garnered extensive global research interest due to its potential in the prevention and management of chronic diseases. Additionally, *Opuntia* serves as a crucial fodder resource in arid and semi-arid regions. *Opuntia*-derived feed is a rich source of bioactive compounds, such as betalains, polyphenols, carotenoids, vitamin C, and minerals, known for their preventive properties against various diseases. These compounds exhibit significant physiological effects, including antioxidative, anticancer, and neuroprotective activities, effectively protecting cells from the harmful effects of free radicals through their inherent redox properties.[6]

Morphological Properties:

Opuntia dillenii is a perennial, xerophytic cactus with the following characteristics:

- Stem: Flattened, green, segmented (cladodes), covered with spines (glochids).
- Leaves: Small, conical, and fall off early (deciduous).
- Flowers: Large, yellow to orange-red, blooming on the margins of the cladodes.
- Fruits: Ovoid or pear-shaped, reddish-purple, covered with glochids, and edible.
- Roots: Fibrous and shallow, adapted for water absorption in arid conditions.[7]

Geographical Source:

Opuntia dillenii is native to tropical and subtropical regions worldwide. It is primarily found in:

- India: Tamil Nadu, Andhra Pradesh, Maharashtra, and Rajasthan.
- North America: Mexico and Southern United States (Florida, Texas).[8]

Materials:

Opuntia dillenii plant was identified and collected from the saravanampatti region and they were authenticated at Botanical Survey of India at Tamil Nadu Agricultural University at Coimbatore. The other excipients that were used like Hydroxy Propyl Methyl Cellulose (polymer), Mannitol (sweeting agent), Glycerol (plasticizer), Citric acid (saliva stimulating agent) was already present in the lab.

Table 2: List of materials used

S.NO	Name of the Material	Source
1	*Opentia dilllenii* extract	Natural Plant
2	HPMC	SDFCL d fine-chem limited
3	Citric acid	Isochem laboratories
4	Mannitol	Spectrum reagents
5	Glycerol	Spectrum reagents

Table 3: List of instruments used

S.No	Equipments /Instruments	Model/manufacture/ supplier
1	Electronic weighing balance	Scaletec
2	Magnetic stirrer	Remi 1mlh
3	Hot air oven	Rashimi scientific company
4	Vernier caliper	Accuplus steel
5	Dissolution apparatus	Kraftsman scientific

METHODOLOGY:

Extraction:

The plant was identified and collected using hand gloves and handled with care to avoid any injuries. It was then washed thoroughly with distilled water to remove dirt and impurities. To prevent injury, contamination, and irritation, the spiny outer layer and the upper layer of the cladodes were carefully removed. After this, the gel inside the cladode was scooped out, washed, and stored in a suitable container. The gel was then filtered using a muslin cloth to separate the liquid extract from the solid gel residues. A petri dish was smeared with glycerol, and the filtered gel was poured into it, followed by heating at 45°-50°C for 24 hours. After completing this process, the dried gel from the petri dish was collected and stored in a suitable container as the final herbal drug.

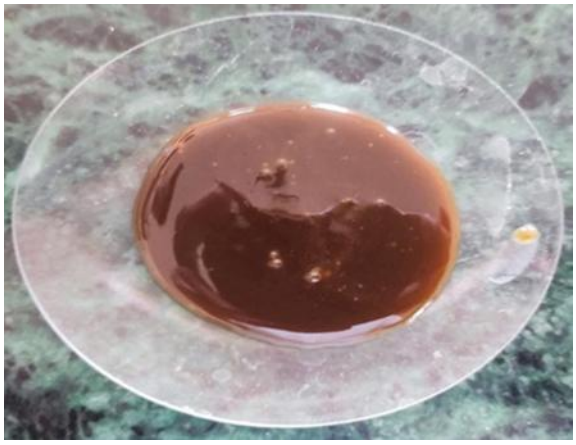

Figure 2: Extraction of *Opuntia dillenii* preparation of MDS:

Table 4: Composition of Formulation

Ingredients	F1(mg)	F2(mg)	F3(mg)
Herbal drug	40	80	500
HPMC	250	500	1000
Mannitol	20	40	40
Citric acid	20	40	40
Glycerol	0.10	0.20	0.20
Distilled water	10	20	20

Among the three formulations (F1, F2, and F3), **F3 was selected as the optimized formulation**.

- **F1**: Contained lower concentrations of the herbal drug and HPMC, leading to weak mechanical strength, slower disintegration, and inadequate drug release.
- **F2**: Showed better film-forming properties than F1 but exhibited **slower drug release and lower content of drug**.
- **F3**: Demonstrated the **best drug release profile**, faster disintegration, good mechanical strength, and uniformity, making it the most suitable formulation for mouth dissolving strips.

Solvent casting method:

The mouth dissolving strips were prepared by mixing 500 mg of herbal drug, 1000 mg of HPMC, 40 mg each of mannitol and citric acid, 0.10 ml of glycerol, and 20 ml of distilled water. This mixture was stirred at 1000-1200 rpm for 2 hours. The resulting solution was then poured into a glycerol-smeared Petri dish and allowed to dry for 16hrs, forming the strips.[9]

Figure 3: Mouth dissolving strips Evaluation Parameters:

1) Thickness: The thickness of strip was measured by vernier caliper at different locations. This is necessary to establish uniformity in the thickness of the film.

2) Weight Variation: The weight variation test is determined by measuring the weight of the individual film of 2cm x2cm area. Electronic weighing balance was used for the measurement of the weight. The weight of five films was determined.

3) Folding endurance: Folding endurance is determined by repeat folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is proportional to the folding endurance value.

4) Disintegration time: There is no official guidance available for mouth dissolving strips, this method may be used as a qualitative guideline for quality control test. By taking the 25ml of distilled water in 50 ml beaker and an individual film is dipped into that solution and disintegration time was recorded.[10]

5) In-vitro dissolution test: Standard official paddle and basket apparatus are used for conducting dissolution studies on films. Medium used is 6.7 PH phosphate buffer (900 ml).

Table 5: Drug Release Profile of Mouth Dissolving Strips Over Time

Time	Amount of drug released
0minutes	0.0270
5minutes	0.0372
10minutes	0.0409
15minutes	0.0498
20minutes	0.0579
25minutes	0.0688
30minutes	0.0734

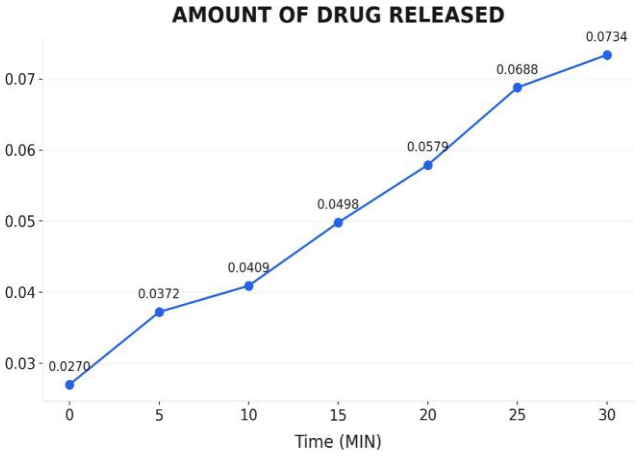

Figure 4: UV-Vis graph of drug release from mouth dissolving strips over time

Pharmacological Activity Test:

Anti-inflammatory Activity:

Albumin denaturation assay:

The albumin denaturation assay was performed as per the protocols presented by Bougandoura et al. (2016) with a slight modification. Various aliquots of sample were mixed with 3 ml of 5% aqueous bovine albumin. The reaction mixture was incubated for a period of 20 min at a temperature of 37°C and then heated for 20 min at 50°C. The test tubes were allowed to reach to the room temperature and then the OD values at 660 nm were noted.

Inhibition (%) = (Absorbance of Control – Absorbance of Sample) / (Absorbance of Sample) × 100

Heat-induced hemolysis assay:

RBC suspension at 10% v/v was made with normal saline using previously described procedures (Sakat et al., 2010). The heat-induced hemolysis assay was performed to find

out the anti-inflammatory activities of the sample, as per the protocols described by Obluchinskaya et al. (2022) with minor modifications. 3 ml of RBC solution was mixed with various concentrations of sample, followed by incubation for 30 min at 550C. The prepared reaction mixture was then centrifuged for 10 min and then the supernatant was collected. The OD values of the collected supernatant was determined at l=560 nm.

Inhibition (%) = (Absorbance of Control – Absorbance of Sample) / (Absorbance of Sample) × 100

Antihyperglycemia Activity:

Alpha Amylase Inhibition Assay

The alpha-amylase inhibitory activities of the sample were carried out according to the standard method (Nickavar, Yousefian, 2009). The starch solution (0.5% w/v) used as the substrate was prepared by boiling potato starch in distilled water for 15 min. The enzyme solution was prepared by dissolving 1mg of porcine pancreatic alpha amylase in 20 mM phosphate buffer (100 mL, pH 6.9). The sample solutions were prepared in DMSO (dimethyl sulfoxide) in different concentrations. The DNS solution (20 ml 96 mM 3,5-dinitrosalicylic acid, 12 g sodium potassium tartrate in 8 ml of 2 M NaOH and 12 ml deionized water) was used as the colouring reagent of reaction. Three sets of experiments were conducted for test, blank and control. A mixture of 1 ml of each of the test and enzyme solutions, in a test tube was incubated at 2 5°C for 30 min. Then, after taking out 1 ml from this mixture, 1 ml of the above mentioned starch solution was added and the mixture was incubated at 25 °C for 3 min. Finally, 1 ml of the DNS.

Table 6: Comparative Evaluation of Anti-Diabetic and Anti-inflammatory Activities

Concentration (µg/ml)	Albumin denaturation assay (Aspirin)		Heat-induced hemolysis assay (Aspirin)		Alpha Amylase Inhibition Assay (Acarbose)	
	Sample	Standard	Sample	Standard	Sample	Standard
25	0.024	6.00	2.12	9.57	0.13	14.98
50	0.49	13.05	6.29	16.72	5.39	29.04
75	1.23	19.48	14.11	24.82	11.88	36.92
100	4.60	23.97	22.30	37.34	13.08	45.12
250	10.48	35.09	27.39	49.77	19.42	60.79
500	28.59	50.16	32.26	53.71	25.13	76.13
750	36.68	69.64	44.36	77.98	32.97	81.58
1000	49.05	98.1398	54.29	84.63	39.12	98.24

The presence of anti-hyperglycemia and anti-inflammatory activity was found to be **positive** in the strips.

CONCLUSION

Mouth dissolving strips of *Opuntia dillenii* were successfully formulated and evaluated for anti-diabetic and anti-inflammatory activities. The formulation met pharmacopeial standards, showing uniformity, rapid disintegration, and effective drug release. Pharmacological tests confirmed significant enzyme inhibition and anti-inflammatory effects. The results suggests that the mouth dissolving strips that are made from the *opuntia dillenii* can be used as alternative to the conventional medicines. Further studies such as animal model and invivo trials are need to be done to confirm the safety and efficacy of this formulation.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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