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Sumatriptan Succinate for Migraine Management: An Overview of Mucoadhesive Buccal Drug Delivery Approaches

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Abstract: Migraine is a common neurological disorder that significantly affects quality of life. Sumatriptan succinate a selective 5-hydroxytryptamine (5-HT1B/1D) receptor agonist, is widely used for the acute treatment of migraine; however, its oral administration is limited by low bioavailability and extensive first-pass metabolism. Mucoadhesive buccal drug delivery systems have emerged as a promising alternative due to their ability to enhance drug absorption, bypass hepatic metabolism, and improve therapeutic efficacy.

This review comprehensively examines the role of mucoadhesive buccal drug delivery systems as a promising platform for the administration of sumatriptan succinate. Emphasis is placed on the formulation and evaluation of buccal films, immediate- and sustained-release delivery approaches, drug loading considerations, and their therapeutic implications in migraine management. In addition, current advancements, existing challenges, and future prospects in buccal delivery of sumatriptan succinate are discussed.

Index Terms - Sumatriptan Succinate, Migraine, Mucoadhesive Drug Delivery System, Buccal Film, Immediate Release, Sustained Release.

1. Introduction

Migraine is a common, chronic, and disabling neurological disorder involving recurrent moderate to severe headache attacks associated with nausea, vomiting, photophobia, and phonophobia. It affects over one billion people worldwide and remains one of the leading causes of disability, especially in people under 50. **(1)**

It imposes a significant personal, social, and economic burden and seriously affects the quality of life and daily productivity. Migraine is a recurrent headache disorder with variable degrees of neurological dysfunction and sensory disturbances. Clinically, migraine attacks are usually episodic and last 4-72 hours if left untreated. Other common symptoms include nausea, vomiting, and sensitivity to light, sound, or movement, adding to the migraine-associated disability. **(1)**

Approximately 91% of men and 96% of women suffer from headaches, with 6% of men and 18% of women experiencing migraines (one-year prevalence). The migraine disorder is more common in adults in their 20s and early 30s from lower socioeconomic backgrounds. They have a higher prevalence of distress and anxiety symptoms, respectively. **(2)**

Several formulations and therapeutic agents are available for the treatment of migraine, including analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), gepants, ditans, ergot derivatives, and triptans. Among these, triptans are considered the first-line specific therapy for the acute management of moderate to severe migraine. Sumatriptan succinate, the first clinically approved triptan, remains one of the most widely prescribed antimigraine agents owing to its rapid onset of action and proven efficacy.
Sumatriptan was the first triptan introduced for the treatment of migraine and continues to be one of the most widely prescribed antimigraine agents worldwide. Sumatriptan succinate, a selective 5-hydroxytryptamine (5-HT1B/1D) receptor agonist, exerts its therapeutic effect by constricting dilated cranial blood vessels and inhibiting the release of pro-inflammatory neuropeptides involved in migraine pathogenesis. The Molecular Structure of Sumatriptan Succinate was shown in **figure 1.**

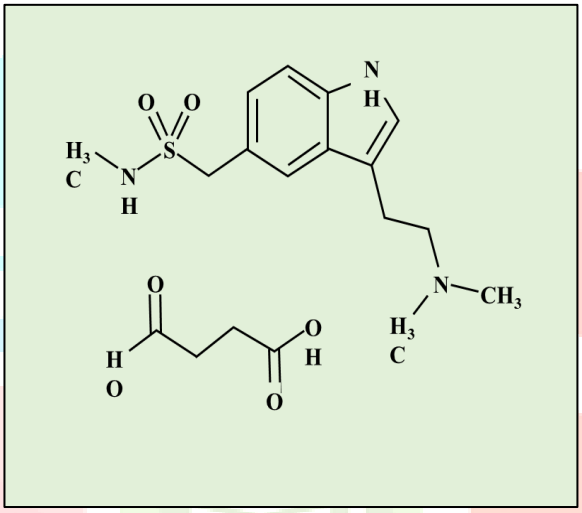

Figure 1: Molecular Structure of Sumatriptan Succinate

Sumatriptan Succinate (SS) is the succinate salt version of sumatriptan, the succinate salt is preferred in pharmaceutical formulations because it has higher water solubility and stability than the free base form while preserving the same pharmacological activity.
The Sumatriptan Succinate improved:

- Water Solubility
- Stability
- Manufacturing Process
- Drug Dissolution rate

The pharmacological activity stays unchanged because, after delivery, the salt dissociates and releases the active moiety, Sumatriptan. **(3)**

2. Approved Dose Strengths of Sumatriptan Succinate

To meet different patient needs and clinical situations, Sumatriptan Succinate has been developed in multiple dosage forms and administered through various routes, including oral, subcutaneous, intranasal, rectal, and transdermal delivery systems. These formulations are designed to provide rapid pain relief while improving patient convenience and therapeutic outcomes. Several dosage strengths have been evaluated in clinical studies; however, only specific strengths have received regulatory approval for clinical use. The currently approved dosage strengths are summarized in **Table 1.**

Route of Administration	Dosage Form	Dose Strength
Oral	Tablet	25 mg, 50 mg, 100 mg
Subcutaneous	Injection	4mg, 6mg
Intranasal	Nasal Spray	5 mg,10 mg, 20 mg
Intranasal	Nasal Powder	22 mg
Transdermal	Iontophoretic patch	6.5 mg

Table 1: Approved Dose Strengths of Sumatriptan Succinate

Among the various dosage forms, the oral tablet is the most widely prescribed and commercially available formulation of sumatriptan succinate for the treatment of migraine.**(4)**

3. Limitation of Oral Dosage Form of Sumatriptan Succinate

Despite its clinical effectiveness, oral administration of sumatriptan succinate is associated with several limitations. The limitations are: -

- **Low oral bioavailability (approximately 14 - 15%)** – Due to extensive first-pass hepatic metabolism.
- **Incomplete gastrointestinal absorption,** resulting in reduced systemic drug availability.
- **Delayed onset of action,** with therapeutic relief generally beginning about 30 minutes after oral administration, which may be insufficient for patients requiring rapid relief.
- **Migraine-associated nausea and vomiting** can make swallowing tablets difficult and may further compromise treatment effectiveness.
- **Short elimination half-life (approximately 2 hours),** which may contribute to headache recurrence and the need for repeat dosing.

These factors may reduce therapeutic efficacy and delay the onset of action, particularly during acute migraine attacks where rapid symptom relief is desired. **(5) (6)**

4. Strategies to Overcome the Limitations of Oral Sumatriptan Succinate

To overcome these limitations, alternative drug delivery approaches have been extensively investigated. Among them, mucoadhesive buccal drug delivery systems have attracted considerable attention because they bypass hepatic first-pass metabolism, improve drug bioavailability, provide rapid systemic absorption, and enhance patient compliance. Furthermore, buccal administration offers ease of application, non-invasive delivery, and the potential for both immediate and sustained drug release **(7)**

The capacity of mucoadhesive drug delivery systems (MDDS) to stick to the mucus layer covering different mucosal surfaces has drawn a lot of interest in pharmaceutical research. By extending the dosage form's residence time at the administration site, these devices improve drug absorption and therapeutic efficacy by enabling close contact with the underlying mucosal barrier. For both local and systemic medication delivery, mucoadhesive formulations have been successfully created for oral, buccal, nasal, rectal, and vaginal routes.

Strong mucoadhesive qualities, regulated drug release, sufficient drug loading capacity, patient acceptance, and non-irritating mucosal tissue are all desirable characteristics of a mucoadhesive dosage form. Mucoadhesive drug delivery systems improve bioavailability and therapeutic performance by maintaining the dosage form at the site of absorption in addition to offering prolonged drug release as compared to traditional sustained-release systems. **(8)**

5. Mechanism of Mucoadhesive Drug Delivery System

The mechanism of mucoadhesion occurs in two sequential stages: the Contact Stage and the Consolidation Stage.

1. Contact Stage

During the initial stage, the mucoadhesive dosage form comes into contact with the mucosal surface. The formulation spreads and hydrates in the presence of moisture, allowing intimate contact with the mucus layer and initiating adhesion.

2. Consolidation Stage

Following contact, the hydrated mucoadhesive polymer becomes flexible and interacts with mucin glycoproteins through interpenetration of polymer and mucin chains. The adhesive bond is strengthened by the formation of weak intermolecular interactions, primarily hydrogen bonds and van der Waals forces. According to the diffusion theory, effective mucoadhesion depends on the extent of polymer chain penetration into the mucus layer, whereas the dehydration theory suggests that adhesion is promoted by the removal of water from the mucus-polymer interface, resulting in stronger adhesive interactions.

These two stages collectively prolong the residence time of the dosage form on the mucosal surface, enhance drug absorption, and improve therapeutic efficacy**(8)**

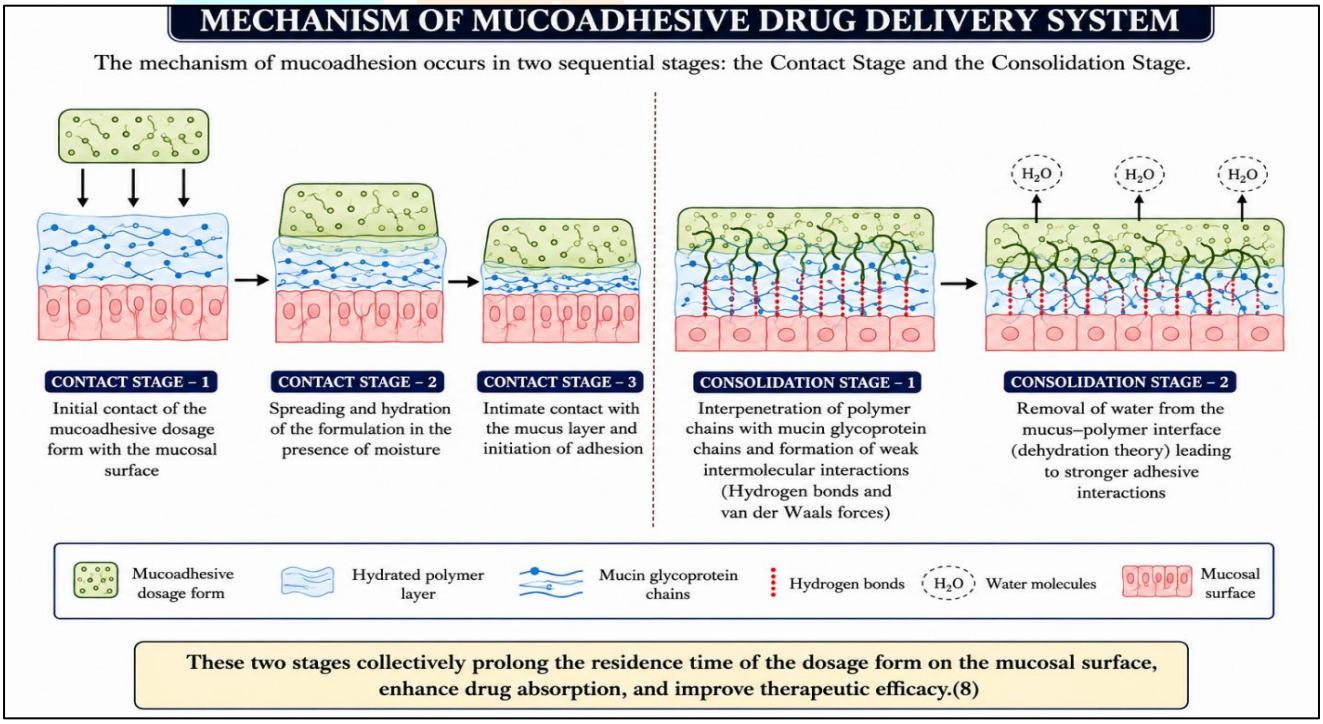

Figure 2: Process of the Contact Stage and the Consolidation Stage.

6. Mucoadhesive Buccal film

Mucoadhesive buccal films are thin, flexible polymeric dosage forms designed to adhere to the buccal mucosa and release drugs either locally or directly into the systemic circulation. These films combine the advantages of buccal drug delivery with mucoadhesive polymers, allowing prolonged residence at the site of application and improved drug absorption. Buccal administration bypasses hepatic first-pass metabolism and gastrointestinal degradation, thereby enhancing the bioavailability of drugs with poor oral absorption while providing rapid onset of action and improved patient compliance. Owing to their ease of administration, comfort, and suitability for pediatric, geriatric, and dysphagic patients, mucoadhesive buccal films have emerged as a promising platform for both immediate- and controlled-release drug delivery. Recent advances in polymer science and formulation technologies have further expanded their potential for the delivery of a wide range of therapeutic agents. **(9)**

7. Classification of Buccal Films

Buccal films can be classified based on several parameters:

a) Based on Number of Layers

- **Single-layered Films:** Drug is dispersed throughout the film.
- **Bilayered Films:** One layer contains the drug, while the other acts as a backing layer to prevent drug loss or secrete second drug in it.
- **Multilayered Films:** Designed to improve mechanical properties and release profiles.

b) Based on Release Profile

- **Immediate Release:** IR buccal films are thin, flexible polymeric membranes designed for rapid disintegration (typically within minutes) and quick drug dissolution upon contact with buccal mucosa, enabling fast absorption into systemic circulation while bypassing hepatic first-pass metabolism.
- **Sustained Release:** SR refers to drug delivery systems designed to release medication over an extended period at a predetermined rate, typically following first-order kinetics where release slows as drug concentration decreases, aiming to prolong therapeutic effect, reduce dosing frequency, and maintain plasma levels longer than immediate-release forms.
- **Controlled Release:** CR involves engineered systems that deliver drug at a constant, predictable zero-order rate independent of remaining concentration, using mechanisms like matrices, osmotic pumps, or coatings to achieve uniform plasma levels with minimal fluctuations over 8-24 hours. **(10)**

8. Immediate Release buccal film of Sumatriptan Succinate

Immediate-release (IR) buccal films of sumatriptan succinate are designed to provide rapid drug release and absorption through the buccal mucosa, enabling a faster onset of therapeutic action during acute migraine attacks.

The films Can be formulated using fast-hydrating, hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) like E 5 and E15, polyvinylpyrrolidone (PVP k 30), or Tween 80 and Polyxemer together with plasticizers and super - disintegrants to promote rapid hydration and dissolution upon contact with saliva.

Following application to the buccal mucosa, the drug is released within a short period of approx. 15 – 30 min and diffuses across the mucosal membrane directly into the systemic circulation, thereby bypassing hepatic first-pass metabolism and minimizing gastrointestinal degradation. This route has the potential to improve the bioavailability of sumatriptan succinate compared with conventional oral tablets while offering quicker pain relief, which is essential for the effective management of acute migraine episodes. Furthermore, immediate-release buccal films are particularly advantageous for patients experiencing migraine-associated nausea, vomiting, or dysphagia, as they eliminate the need for swallowing and improve treatment adherence.**(11)**

9. Advantages

- Rapid onset of action.
- Quick drug release.
- Bypasses first-pass metabolism.
- Improves bioavailability.
- Avoids gastrointestinal degradation.
- Suitable for acute migraine attacks.
- Easy administration without water.

- Beneficial for patients with nausea or dysphagia.
- Improves patient compliance.

10. Sustained-Release Buccal Film of Sumatriptan Succinate

Sustained-release (SR) buccal films of sumatriptan succinate are designed to provide controlled and prolonged drug release through the buccal mucosa, maintaining therapeutic drug concentrations over an extended period and reducing the frequency of administration.

The films can be formulated using mucoadhesive, swellable polymers such as hydroxypropyl methylcellulose (HPMC K4M or HPMC K100M), Carbopol 934P, ethyl cellulose, and polyvinylpyrrolidone (PVP K30), together with suitable plasticizers such as PEG 400. These polymers hydrate upon contact with saliva, forming a gel layer that regulates drug diffusion and prolongs residence time on the buccal mucosa.

Following application to the buccal mucosa, the film adheres firmly to the mucosal surface and gradually releases sumatriptan succinate upto 4 – 6 hrs. The released drug diffuses across the buccal membrane directly into the systemic circulation, bypassing hepatic first-pass metabolism and minimizing gastrointestinal degradation. This sustained delivery approach helps maintain consistent plasma drug concentrations, potentially reducing fluctuations associated with conventional oral dosage forms and improving therapeutic efficacy. Sustained-release buccal films may also reduce the need for repeated dosing, enhance patient compliance, and provide prolonged migraine relief, making them a promising alternative for patients who require extended symptom control following an acute migraine attack.**(12)**

11. Advantages

- Prolonged drug release.
- Maintains therapeutic drug levels.
- Reduces dosing frequency.
- Minimizes plasma concentration fluctuations.
- Prolongs buccal residence time.
- Enhances therapeutic efficacy.
- Bypasses first-pass metabolism.
- Improves patient compliance.
- Reduces migraine recurrence.

12. Bilayer Buccal Film of Sumatriptan Succinate

On combining both the layers, Bilayer buccal films of sumatriptan succinate are an advanced mucoadhesive drug delivery system that integrates an immediate-release (IR) layer with a sustained-release (SR) layer within a single dosage form. This biphasic design aims to provide rapid relief from acute migraine attacks through the immediate-release layer while maintaining therapeutic drug concentrations over an extended period through the sustained-release layer. Such a dual-release approach combines the advantages of both release profiles, improving overall therapeutic efficacy and patient convenience.

The immediate-release layer is typically formulated using fast-hydrating hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC E5 or HPMC E15) and polyvinylpyrrolidone (PVP K30), together with plasticizers (e.g., PEG 400), surfactants (e.g., Poloxamer 407 or Tween 80), and super - disintegrants to facilitate rapid hydration and drug release. In contrast, the sustained-release layer is commonly prepared using swellable and mucoadhesive polymers such as HPMC K4M or HPMC

K100M, Carbopol 934P, and ethyl cellulose, which hydrate to form a gel matrix that regulates drug diffusion and prolongs residence time on the buccal mucosa.

Upon application to the buccal mucosa, the immediate-release layer rapidly dissolves, releasing an initial dose of sumatriptan succinate to achieve a fast onset of action. Simultaneously, the sustained-release layer remains adhered to the buccal mucosa and gradually releases the remaining drug over several hours. The drug absorbed through the buccal membrane enters the systemic circulation directly, bypassing hepatic first-pass metabolism and minimizing gastrointestinal degradation. Consequently, bilayer buccal films have the potential to improve the bioavailability of sumatriptan succinate, provide rapid and prolonged migraine relief, reduce plasma concentration fluctuations, decrease dosing frequency, and enhance patient compliance. Therefore, bilayer buccal films represent a promising strategy for the effective management of migraine by combining immediate symptom relief with sustained therapeutic action in a single dosage form.

13. Advantages

- Combines rapid and sustained drug release.
- Provides biphasic drug delivery.
- Ensures immediate and prolonged migraine relief.
- Improves bioavailability.
- Bypasses first-pass metabolism.
- Reduces dosing frequency.
- Maintains consistent plasma drug levels.
- Enhances patient compliance.
- Improves overall therapeutic efficacy.
- Reduces recurrence of migraine symptoms.

14. Difference between Immediate Release, Sustained Release and Bilayer Buccal Film

Parameter	Immediate – Release Buccal Film	Sustained – Release buccal film	Bilayer Buccal Film
Purpose	Rapid drug Release	Prolonged Drug Release	Combined Rapid and Prolonged Drug Release
Drug Release	Immediate	Controlled	Biphasic (I. R. – S. R.)
Onset of Action	Fast	Slow	Fast initially, followed by sustained action
Main Polymers	HPMC E5/E15, PVP K30	HPMC K4M/K100M, Carbopol 934P, Ethyl Cellulose	Combination of IR and SR polymers
Best Application	Acute conditions requiring immediate action	Chronic or prolonged therapy	Conditions requiring both immediate and sustained drug delivery (e.g., migraine)

Table 2: Difference between Immediate Release, Sustained Release and Bilayer Buccal Film

16. Common Excipient and Polymers Used in Buccal film

Various polymers and excipients are used in the formulation of immediate-release (IR) and sustained-release (SR) buccal films to achieve the desired film characteristics and drug release profile. Each excipient performs a specific function, such as film formation, mucoadhesion, plasticization, controlled drug release, or enhancement of drug stability and patient acceptability. The commonly used polymers and excipients along with their primary roles are summarized in the following table.**(13)**

Excipients	Type	Primary Role
HPMC E5	Immediate Release polymer	Film Former
HPMCE15	Immediate Release polymer	Film Former
HPMC K4M	Sustained Release Polymer	Release retardant
HPMC K100M	Sustained Release Polymer	Release retardant
Carbapol 934 P	Mucoadhesive polymer	Mucoadhesion
Ethyl Cellulose	Hydrophobic polymer	Release Barrier
PVP K 30	Hydrophobic polymer	Film Former
Sodium CMC	Mucoadhesive polymer	Mucoadhesion
PEG 400	Plasticizer	Flexibility
Glycerol	Plasticizer	Flexibility
Propylene Glycol	Plasticizer	Flexibility
Tween 80	Surfactant	Wetting Agent
Poloxamer 407	Surfactant	Solubilizer
Mannitol	Filler	Bulking Agent
Aspartame	Sweetener	Taste Masking
Sucralose	Sweetener	Taste Masking
Sodium Saccharin	Sweetener	Taste Masking
Croscarmellose Sodium	Super disintegrant	Rapid Disintegration
Ethanol	Solvent	Polymer Dissolution
Water	Solvent	Polymer Dissolution

Tablet 3: Common Excipient and Polymers Used in Buccal film

15. Preparation of Bilayer Buccal Film

Several techniques have been employed for the preparation of buccal films, including solvent casting, hot-melt extrusion, semisolid casting, solid dispersion extrusion, rolling, and electrospinning. Among these, the solvent casting method is the most widely used at the laboratory scale because it is simple, cost-effective, reproducible, and capable of producing thin films with uniform thickness and drug distribution. Owing to these advantages, solvent casting is the preferred method for the preparation of bilayer buccal films.

In the solvent casting method, the immediate-release (IR) layer and sustained-release (SR) layer are prepared separately. Initially, the IR layer is prepared by dissolving the required fast-hydrating polymers, drug, plasticizer, surfactant, and other excipients shown in **table 3** in a suitable solvent system under continuous stirring until a homogeneous solution is obtained. The solution is then cast into a Petri dish or casting plate and allowed to dry partially.

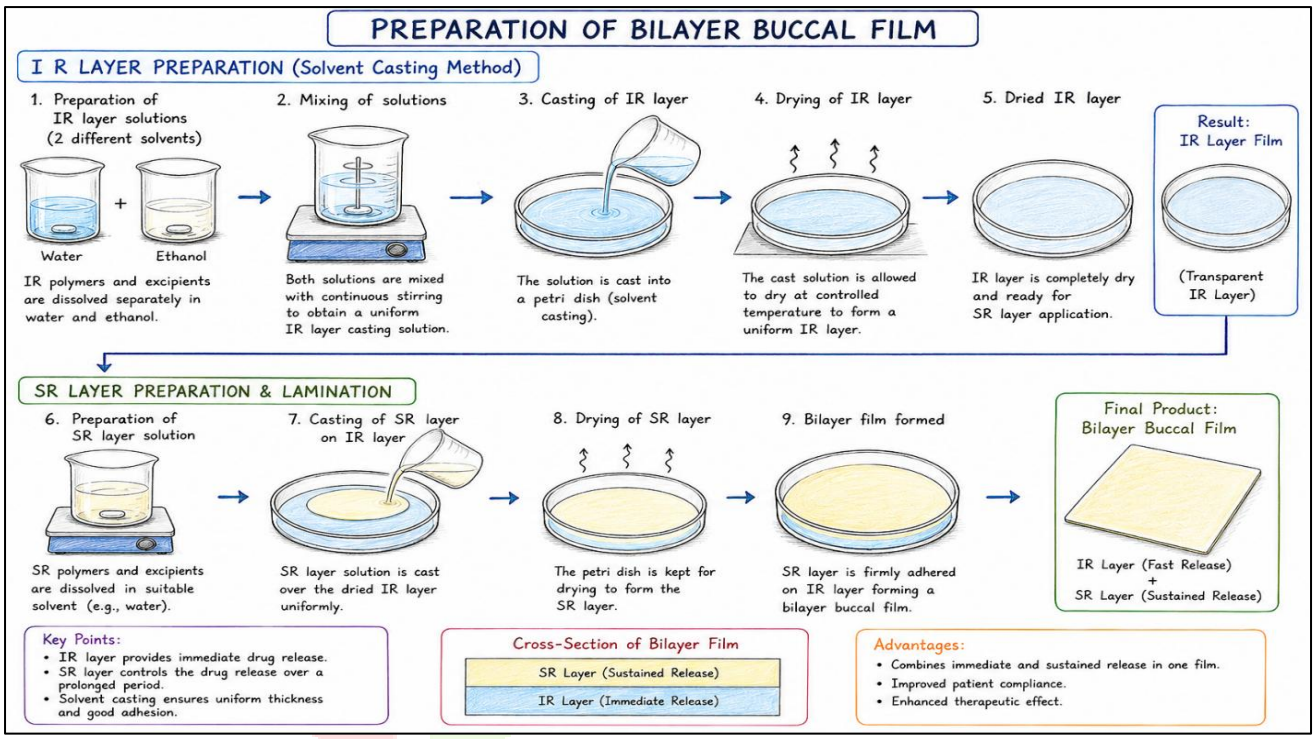

Figure 3: Preparation of Bilayer Buccal film

Separately, the SR layer is prepared by dissolving the required mucoadhesive and release-retarding polymers together with the drug, plasticizer, and other excipients shown in **table 3** in an appropriate solvent. The resulting homogeneous solution is carefully poured over the partially dried IR layer and spread uniformly to obtain a bilayer structure. The combined film is then dried completely under controlled conditions, peeled carefully from the casting surface, cut into the desired dimensions to obtain the required dose, and stored in airtight containers or aluminum foil until further evaluation.

16. Future Prospective of Buccal Film of Sumatriptan Succinate

- Development of bilayer buccal films for combined immediate- and sustained-release drug delivery.
- Exploration of novel mucoadhesive polymers to enhance residence time and drug absorption.
- Incorporation of nanocarriers (e.g., nanoparticles and nanofibers) to improve buccal permeation and bioavailability.
- Development of unidirectional buccal films with backing layers to minimize drug loss into saliva.
- Integration of permeation enhancers to increase transmucosal drug transport.

- Optimization of formulation using Quality by Design (QbD) and Design of Experiments (DoE) approaches.
- Evaluation of long-term stability and large-scale manufacturing techniques for commercial production.
- Conducting in vivo pharmacokinetic and clinical studies to establish safety and therapeutic efficacy.
- Development of patient-friendly formulations with improved taste masking and flexibility.
- Investigation of personalized buccal films with dose customization using advanced manufacturing technologies such as 3D printing.
- Exploration of combination buccal films for the simultaneous delivery of sumatriptan succinate with complementary anti-migraine agents.
- Commercial translation of buccal films as a non-invasive alternative to oral tablets and injectable formulations for migraine management.

17. Conclusion

Migraine remains one of the most prevalent and disabling neurological disorders worldwide, requiring therapeutic strategies that provide rapid and effective symptom relief. Although sumatriptan succinate is the first-line therapy for the acute treatment of migraine, its oral administration is limited by low bioavailability, extensive first-pass metabolism, gastrointestinal degradation, and the need for repeated dosing. Mucoadhesive buccal drug delivery systems have emerged as a promising alternative by enabling direct drug absorption through the buccal mucosa, thereby improving bioavailability, reducing gastrointestinal limitations, and enhancing patient compliance.

Among the various buccal dosage forms, bilayer buccal films integrating immediate-release and sustained-release layers represent a particularly attractive approach. Such systems provide rapid onset of action through the immediate-release layer while maintaining prolonged therapeutic drug levels through the sustained-release layer, resulting in improved therapeutic efficacy and reduced dosing frequency. Advances in polymer selection, formulation strategies, and manufacturing techniques have further expanded the potential of bilayer buccal films for migraine management.

Overall, the available literature suggests that mucoadhesive bilayer buccal films of sumatriptan succinate have considerable potential as a non-invasive and patient-friendly drug delivery system. However, further in vivo pharmacokinetic studies, clinical trials, long-term stability investigations, and large-scale manufacturing studies are required to facilitate their successful translation from laboratory research to commercial clinical application.

18. Reference

1. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020 Oct;396(10258):1204–22. doi:10.1016/S0140-6736(20)30925-9

2. Gupta J, Gaurkar SS. Migraine: An Underestimated Neurological Condition Affecting Billions. Cureus. 2022 Aug 24. doi:10.7759/cureus.28347

3. Moskowitz MA, Cutrer FM. Sumatriptan: A Receptor-Targeted Treatment for Migraine. Annu Rev Med. 1993 Feb;44(1):145–54. doi:10.1146/annurev.me.44.020193.001045

4. Derry CJ, Derry S, Moore RA. Sumatriptan (all routes of administration) for acute migraine attacks in adults - overview of Cochrane reviews. Cochrane Database of Systematic Reviews. 2014 May 27;2019(5). doi:10.1002/14651858.CD009108.pub2

5. Shivanand K, Raju S, Nizamuddin S, Jayakar B. In vivo bioavailability studies of sumatriptan succinate buccal tablets. Daru. 2011;19(3):224–30. PubMed PMID: 22615661.

6. Paczkowska M, Mizera M, Sałat K, Furgała A, Popik P, Knapik-Kowalczuk J, et al. Enhanced pharmacological efficacy of sumatriptan due to modification of its physicochemical properties by inclusion in selected cyclodextrins. Sci Rep. 2018 Nov 1;8(1):16184. doi:10.1038/s41598-018-34554-w

7. Shidhaye SS, Saindane NS, Sutar S, Kadam V. Mucoadhesive Bilayered Patches for Administration of Sumatriptan Succinate. AAPS PharmSciTech. 2008 Sep 5;9(3):909–16. doi:10.1208/s12249-008-9125-x

8. Boddupalli B, Mohammed ZulkarNK, Nath R, Banji D. Mucoadhesive drug delivery system: An overview. J Adv Pharm Technol Res. 2010;1(4):381. doi:10.4103/0110-5558.76436

9. Salehi S, Boddohi S. New formulation and approach for mucoadhesive buccal film of rizatriptan benzoate. Prog Biomater. 2017 Dec 6;6(4):175–87. doi:10.1007/s40204-017-0077-7

10. Alves TFR, Rios AC, da Silva Pontes K, Portella DL, Aranha N, Severino P, et al. Bilayer Mucoadhesive Buccal Film for Mucosal Ulcers Treatment: Development, Characterization, and Single Study Case. Pharmaceutics. 2020 Jul 11;12(7):657. doi:10.3390/pharmaceutics12070657

11. Salawi A, Tabassum N, Zaman M, Khan MA, Siddique W, Alshamrani M, et al. Design and Evaluation of Instant Release Buccal Films of Empagliflozin: A Statistical Approach. ACS Omega. 2025 Jun 10;10(22):23492–503. doi:10.1021/acsomega.5c02082

12. Shipp L, Liu F, Kerai-Varsani L, Okwuosa TC. Buccal films: A review of therapeutic opportunities, formulations & relevant evaluation approaches. Journal of Controlled Release. 2022 Dec;352:1071–92. doi:10.1016/j.jconrel.2022.10.058

13. Morales JO, McConville JT. Manufacture and characterization of mucoadhesive buccal films. European Journal of Pharmaceutics and Biopharmaceutics. 2011 Feb;77(2):187–99. doi:10.1016/j.ejpb.2010.11.023