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THE ROLE OF HERBAL DRUG-LOADED BUCCAL FILMS IN THE MANAGEMENT OF DIABETES MELLITUS

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ABSTRACT

Diabetes mellitus is a long-term metabolic disease characterised by high blood sugar levels and related health problems. Conventional oral antidiabetic drugs often face limitations such as poor absorption, liver metabolism, and reduced patient compliance. To overcome these issues, buccal drug delivery has gained attention because it allows drugs to be absorbed directly through the lining of the mouth, bypassing liver metabolism and improving therapeutic effectiveness. In recent years, herbal medicines have become popular as supportive treatments for diabetes due to their safety and multiple biological benefits. Flavonoids, a major group of plant-based compounds found in fruits and vegetables, show strong antidiabetic activity. They help control blood glucose by improving insulin sensitivity, reducing oxidative stress, lowering inflammation, and regulating glucose absorption. However, flavonoids often have low solubility and bioavailability, which limits their effectiveness. Advanced drug-delivery systems such as nanoparticles and mucoadhesive formulations help improve their stability and absorption. Buccal films are thin polymeric dosage forms designed to deliver drugs through the buccal mucosa for both local and systemic action. They improve drug absorption, allow controlled release, and enhance patient convenience. Buccal films are mainly classified as mucoadhesive, fast-dissolving, and bilayered films. Mucoadhesive films remain attached to the mucosa for longer periods, while fast-dissolving films release the drug quickly in saliva. Bilayered films provide directional drug release toward the mucosa. Suitable polymers, plasticizers, and permeation enhancers are selected to ensure flexibility, adhesion, and effective drug release. Different preparation methods such as solvent casting, hot-melt extrusion, and solid dispersion techniques are used. Evaluation tests ensure film quality, safety, stability, and drug release behaviour. Overall, flavonoid-loaded buccal films offer improved bioavailability, sustained drug release, and better patient compliance, making them a promising and patient-friendly approach for diabetes management.

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INTRODUCTION

Diabetes mellitus is a long-term metabolic disorder characterised by persistently high blood glucose levels due to inadequate insulin secretion, impaired insulin action, or both. Although a wide range of synthetic antidiabetic drugs is currently available, their long-term use is often associated with undesirable side effects, reduced effectiveness, and issues related to patient compliance. These limitations have encouraged researchers to investigate alternative treatment approaches. In this context, medicinal plants have gained considerable attention due to their better safety profile, cost-effectiveness, and ability to act on different mechanisms involved in glucose regulation. One useful approach that has recently gained interest is the use of buccal films. These are thin and flexible dosage forms that are placed on the inner lining of the cheek, where they adhere and release the active drug directly into systemic circulation. Since this route avoids the gastrointestinal tract and first-pass hepatic metabolism, it can provide a faster onset of action and improved bioavailability. When herbal antidiabetic agents such as Gymnema sylvestre**,** Momordica charantia**, or** Trigonella foenum-graecum are incorporated into these films, they can offer sustained glucose-lowering effects with a reduced the risk of systemic side effects. Overall, herbal drug-loaded buccal films represent a simple and patient-friendly approach for diabetes management, combining the benefits of herbal therapy with modern drug-delivery methods to support more effective and personalised treatment[(1)].

Overview of Diabetes Mellitus: Diabetes mellitus is one of the most common non-communicable diseases across the worldwide and remains a major cause of illness and early death. This is mainly due to its long-term complications, which commonly affect the

cardiovascular, renal, nervous, and ocular systems. From a biological point of view, diabetes is associated with disturbances in glucose, lipid, and protein metabolism, leading to overall metabolic imbalance and increased oxidative stress. According to reports from the International Diabetes Federation, approximately 537 million adults were living with diabetes in 2021, and this number is expected to rise to nearly 783 million by 2045, highlighting the increasing global burden of the disease (IDF, 2023)[2]. Diabetes mellitus is generally classified into three major types: type 1 diabetes mellitus, type 2 diabetes mellitus, and gestational diabetes mellitus. Type 1 diabetes is an autoimmune disorder in which pancreatic β-cells are gradually damaged, resulting in an absolute deficiency of insulin. On the other hand, type 2 diabetes makes up about 90–95% of total cases and is mainly associated with insulin resistance along with decreased the insulin release. The development and progression of type 2 diabetes are strongly influenced by lifestyle-related factors such as obesity, poor dietary habits, physical inactivity, and genetic risk. Gestational diabetes develops during pregnancy and is known to higher risk of future metabolic problems in both the mother and the child[3]. Persistent hyperglycaemia in diabetes leads to increase in the production of reactive oxygen species (ROS) and advanced glycation end products (AGEs). These factors play an important role in the development of diabetic complications by causing oxidative stress and long-term inflammation, which finally leads to tissue damage. Although commonly used antidiabetic treatments, including insulin and oral hypoglycaemic agents, are clinically effective, their long-term use is often affected by side effects, poor patient compliance, and the gradual loss of pancreatic β-cell function. Consequently, there is increasing interest in complementary and alternative treatment strategies that involve natural bioactive compounds along with advanced drug-delivery approaches aimed at improving therapeutic efficiency while minimizing systemic side effects. Overall, diabetes mellitus remains a complex metabolic disorder that demands long-term and multifaceted management. Current research focusing on polymer-based drug-delivery systems, phytomedicine, and nanotechnology reflects a shift toward more patient-centred and innovative therapeutic strategies beyond conventional pharmacotherapy[4]. The classification and etiology of diabetes mellitus along with its characteristics has been shown in figure 1.

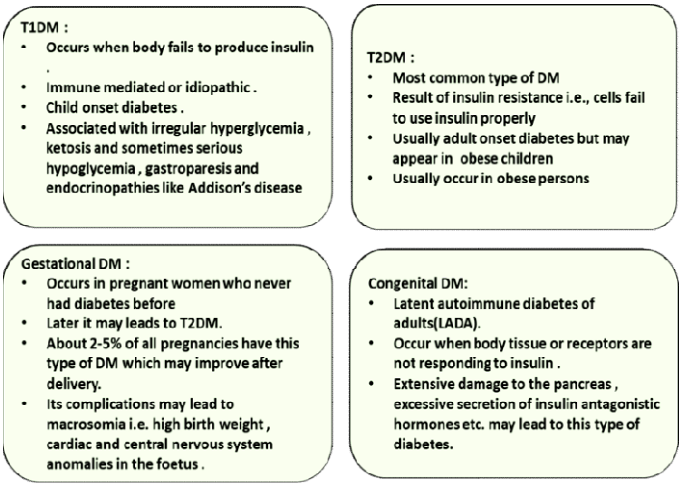

Figure 1. Classification of Diabetes Mellitus based on etiology and clinical characteristics

Pathophysiology of Diabetes Mellitus: The maintenance of blood glucose levels in the human body depends on the combined action of different hormones. Among these, insulin and glucagon play an important role in maintaining the glucose balance. Under normal physiological conditions, a rise in blood glucose levels, such as after food intake, stimulates the pancreatic β-cells to release insulin into the blood stream.

Insulin helps to regulate the blood glucose level by the two primary mechanisms:

- First, insulin helps to decrease the glucose release into the liver by slowing down processes such as glycogen breakdown and the production new glucose from non-carbohydrate sources.
- Second, it promotes the uptake and use of glucose by body tissues, especially the liver, skeletal muscles, and fat tissue. This helps in energy storage and helps reduce the high blood glucose levels[5].

Limitations of Conventional Antidiabetic Therapies: Several limitations like pharmacokinetic, pharmacodynamics and poor patient compliance etc. that is faced by diabetic patients with conventional therapy is being elaborated below in Figure no. 2.

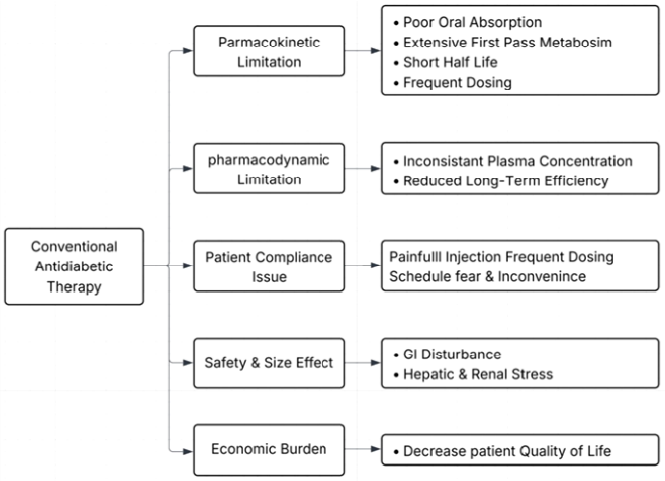

Figure 2. Limitations associated with conventional antidiabetic therapy

Rationale for Herbal Drug Delivery by Buccal Films: Herbal formulations often face problems such as poor oral bioavailability, breakdown in the digestive system, and irregular absorption. Buccal films provide a useful alternative by allowing the active compounds to be absorbed directly through the lining of the mouth, bypassing the first-pass metabolism and improving their availability in the bloodstream. Their thin and mucoadhesive design keeps the films closely attached to the mucosa, which supports sustained and controlled release of the herbal actives[6]. This method not only Improve the effectiveness of herbal compounds that are otherwise unstable, but it also improves patient compliance, as the films are easy to use and allows faster onset of action. Additionally, delivering drugs through the buccal route helps protect sensitive plant-based molecules from breakdown by enzymes or acidic conditions in the digestive system, ensuring improved stability and consistent result. Overall, buccal films represent a simple and patient-friendly approach to deliver herbal drugs with enhanced absorption, improved pharmacokinetics, and improved therapeutic outcomes[7].

Buccal Drug Delivery System: The buccal drug delivery system works by administering therapeutic agents through the inner lining of the cheek, where the drugs can pass through the buccal epithelium and enter systemic circulation. The buccal mucosa is rich in blood vessels and relatively permeable, which make it suitable for both local and systemic drug delivery. Unlike conventional oral administration, which exposes drugs to digestive enzymes and extensive first-pass metabolism in the liver, buccal delivery allows the drug to directly reach the bloodstream, thereby, improving bioavailability and therapeutic effectiveness. This route generally uses mucoadhesive dosage forms such as films, patches, tablets, or gels that stick to the inner cheek surface. Buccal films, in particular, are becoming increasingly popular due to their flexibility, rapid hydration, and controlled drug release for a longer period of time. They are especially useful for delivering biologically unstable molecules—like peptides, proteins, and herbal phytochemicals—that would otherwise degrade in the gastrointestinal tract[8].

Advantages of Buccal Route in Diabetes Management

- Easy administration and handling lead to improved patient compliance.
- Designed for placement on the buccal or oral mucosa, offering convenient drug delivery.
- Suitable for a wide range of therapeutic agents.
- Enhanced bioavailability of drugs due to avoidance of first-pass metabolism.
- Small size and thin structure improve patient comfort and acceptability.
- Rapid dissolution without the need for water, beneficial for patients with dysphagia or physical limitations.
- Large surface area promotes rapid wetting, disintegration, and dissolution in the oral cavity.
- Enables both local and systemic drug delivery.
- Faster onset of action compared to conventional oral dosage forms.
- Improved dosing accuracy and uniformity compared to liquid formulations.
- Reduction in drug dose and side effects due to bypassing hepatic metabolism.
- Better stability and durability compared to other fast-dissolving oral dosage forms[9]

Challenges and Considerations in Buccal Formulation

- Limited Permeability of Buccal Epithelium
- Restricted Surface Area for Drug Absorption
- Salivary Washout and Reduced Residence Time
- Taste, Irritation, and Patient Acceptability Issues
- Formulation Stability in Moist Oral Environment
- Need for Safe and Effective Permeation Enhancers
- Challenges in Achieving Sustained Adhesion
- Potential Impact of Mucosal Turnover on Drug Delivery

Herbal treatment available for diabetes: Herbal therapies are increasingly being studied as complementary strategies for managing diabetes, mainly due to their safety and multiple beneficial biological effect. Among plant-based compounds, flavonoids—including flavones, flavanols, flavanones, flavonols, isoflavones, and anthocyanin's—play an important role. These polyphenol compounds, commonly found in fruits and vegetables, are known to have antidiabetic, antioxidant, and anti-inflammatory properties[10]. Flavonoids help in controlling blood glucose level by improving insulin sensitivity, reducing oxidative stress, and regulating glucose absorption and its metabolism. Their therapeutic potential has been shown through many in vitro and in vivo studies.

Table 1. Antidiabetic herbs used in the management of Diabetes Mellitus

Herb (Scientific Name)	Primary Antidiabetic Mechanisms	Active Constituent	Common Dosage Forms	Buccal Delivery Suitability	References
Gymnema sylvestre	↓Intestinal glucose absorption; ↑insulin secretion; β-cell stimulation	Gymnemic acids	Capsules, tablets, extracts, powders	Moderate – suitable after extraction and molecular size reduction	(12)
Momordica charantia	Insulin-mimetic effect; ↑ glucose uptake; ↓ gluconeogenesis	Charantin, polypeptide-P	Juice, capsules, dried fruit extract	Low–Moderate – peptides may need enhancers for permeability	(13)
Trigonella foenum-graecum	Slows carbohydrate absorption; ↑ insulin sensitivity	Diosgenin, trigonelline	Seeds, powders, capsules	Moderate – saponins can be used in films after purification	(14)
Pterocarpus marsupium	β-cell regeneration; antioxidant activity	Pterostilbene, epicatechin	Bark extract, capsules	Moderate – effective in polyphenolic extract form	(15)
Cinnamomum verum	↑ Insulin receptor signalling; ↓ fasting glucose	Cinnamaldehyde, cinnamic acid	Powder, capsules, essential oil	High – essential oils suitable for buccal gels/films	(16)
Aloe barbadensis	Improves glucose tolerance; antioxidant action	Aloin, polysaccharides	Gel, juice, capsules	Low – polysaccharides too large; limited permeability	(17)
Ocimum sanctum	Modulates insulin release and lipid metabolism	Eugenol, ursolic acid	Leaves, extracts, capsules	High – volatile actives compatible with buccal films	(18)
Syzygium cumini	Inhibits α-amylase; protects pancreatic β-cells	Jamboline, ellagic acid	Seeds/extract capsules	Moderate – alkaloid fraction suitable for buccal loading	(19)
Tinospora cordifolia	Regulates glucose metabolism; anti-inflammatory	Tinosporaside, berberine	Tablets, extracts, decoctions	Moderate – berberine suitable but needs permeation enhancers	(20)
Salacia reticulata	Potent α-glucosidase inhibition	Salacinol, kotalanol	Capsules, extracts	Low to Moderate effective but large constituents	(21)

Table 2. Synergistic Herbal Combinations for Diabetes Management

Herbal Combination	Rationale for Synergy	Primary Mechanistic Actions	Major Phytochemicals Involved	Expected Therapeutic Outcome	References
Gymnema sylvestre + Momordica charantia	Complementary insulin tropic& insulin-mimetic actions	↑ Insulin secretion, ↑ GLUT-4 translocation, ↓ intestinal glucose uptake	Gymnemic acids, polypeptide-P, charantin	Improved glycaemic control & enhanced peripheral glucose utilization	(22)
Pterocarpus marsupium + Syzygium cumini	Antioxidant reinforcement + β-cell regeneration	↑ β-cell mass, ↓ oxidative stress, ↓ lipid peroxidation	Pterostilbene, epicatechin, jamboline, ellagic acid	Long-term stabilization of fasting & postprandial glucose	(24)
Tinospora cordifolia + Ocimum sanctum	Anti-inflammatory + metabolic modulation	↓ TNF-α & IL-6, ↑ insulin sensitivity, ↓ oxidative damage	Tinosporaside, berberine, eugenol, ursolic acid	Improved insulin action in inflammatory/metabolic stress conditions	(26)
Cinnamomum verum + Trigonella foenum-graecum	Enhanced insulin signalling + improved glucose tolerance	↑ Insulin receptor phosphorylation, ↓ gluconeogenesis	Cinnamaldehyde, diosgenin	Better fasting glucose & reduced insulin resistance	(28)
Momordica charantia + Syzygium cumini	Amplified antioxidant + glucose uptake pathways	↑ AMPK activation, ↓ ROS, ↑ cellular glucose uptake	Charantin, polypeptide-P, jamboline	Stronger glucose-lowering and antioxidant profile	(30)

While synthetic antidiabetic drugs are still commonly used, their side effects and long-term limitations have increased interest in flavonoid-based herbal medicine. In recent years, advances in drug-delivery technologies—such as nanoparticles, solid lipid carriers, mucoadhesive formulations, and buccal films—have further improved the bioavailability and effectiveness of flavonoids, making them promising option for diabetes therapy [11].

Commonly Used Medicinal Herbs in Diabetes Management with Mechanism, Dosage Forms, and Buccal Suitability: This table provides an overview of commonly used herbal plants in diabetes management, describing their mechanism of action, traditional and modern dosage forms, and their suitability for incorporation into Buccal drug delivery system.

Evidence-Based Synergistic Herbal Combinations: The table mentioned below emphasizes on several herbal combinations along with their rationale for synergy as well as their mechanism and the phytochemicals involved with expected outcomes which has been reported previously are being mentioned in Table 2.

Buccal Films: Formulation and Design: Buccal films are specially designed mucoadhesive formulations that deliver therapeutic agents through the lining of the mouth, allowing the drug to enter the bloodstream while bypassing first-pass metabolism in the liver. These films are particularly useful for different types of drugs, including herbal antidiabetic compounds, as they can improve bioavailability, support better patient compliance, and provide controlled and prolonged drug release[32]. Selecting suitable film-forming polymers is an important step in designing buccal films. Commonly used polymers, such as hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA), provide good mechanical strength and flexibility while remaining compatible with the mucosal tissue. To make the films more durable and easier to handle, plasticizers like PEG 400 are often added to reduce film brittleness. Additionally, permeation enhancers—such as bile salts, fatty acids, or chitosan derivatives—play an important role in helping less-permeable or large herbal molecules cross the buccal epithelium effectively[33]. When formulating herbal antidiabetic compounds, it is also important to consider stability and solubility challenges. Many phytochemicals are likely to degrade or have poor water solubility. To overcome this, techniques such as encapsulating the active compounds in nanoparticles—for example, lipid-based carriers combined with cyclodextrins—can be highly effective. These strategies not only help stabilize the herbal molecules but also improve their absorption and systemic bioavailability[34].

Types of Buccal Films (Mucoadhesive, Fast-Dissolving, Bilayered): Buccal films are thin polymer-based formulations designed to deliver active pharmaceutical ingredients through the lining of the mouth, allowing both local and systemic effects while bypassing first-pass metabolism in the liver. Recent studies have classified buccal films into three main types based on their design and functional properties: mucoadhesive, fast-dissolving, and bilayered.

Mucoadhesive Buccal Films: Mucoadhesive films are designed to stick to the buccal mucosa for longer periods and which allows the drug to be released in a controlled and sustained manner. These films commonly use mucoadhesive polymers such as HPMC, chitosan, and sodium alginate, which provide strong adhesion through hydrogen bonding, electrostatic interactions, and interlocking between the polymer chains. Plasticizers like PEG 400 and glycerol are also include to provide flexibility without affecting adhesion. Proper optimisation of these formulations can significantly improve the drug's residence time on the mucosa and improve its bioavailability[35].

Fast Dissolving Buccal Films: Fast-dissolving films are designed to dissolve rapidly in saliva—usually within seconds to a few minutes—releasing the drug for rapid absorption. These films commonly use hydrophilic polymers, such as low-molecular-weight HPMC or PVA, along with super disintegrants or saliva-soluble excipients to enhance dissolution. Their rapid onset of action and ease of use make them particularly suitable for acute treatments, patients who have difficulty in swallowing, or situations where rapid systemic exposure is required[36].

Bilayer (Multilayer) Buccal Film : Bilayered films are made up of two or more distinct layers, generally combining a mucoadhesive layer containing the active ingredient with a backing layer that directs the drug release toward the mucosa. The backing layer, commonly made from water-insoluble polymers, helps prevent the loss of the drug due to saliva, enhances patient comfort by masking bitter and unpleasant tastes, and prevents early removal of the film. This design not only enhances the stability of the film but also regulates the drug release rate and minimises the drug wastage, which is particularly useful for bitter or low-dose drugs.

Polymers and Excipients Used : The performance of buccal films mainly depends on the selection of polymers and excipients, which affects their mechanical strength, mucoadhesion, and drug-release characteristics. Various excipients are used in buccal film formulations, each having a specific role. Some commonly used polymers and their roles are summarised in table 3[37].

Table 3. Polymers and excipients along with their function

Polymer / Excipient	Role in Buccal Films	Functional Outcome / Effect in Formulation
HPMC (Hydroxypropyl Methylcellulose)	Film-forming polymer; provides structural integrity	Smooth flexible films, controlled drug release, good mucoadhesion, excellent swelling behaviour
PVA (Polyvinyl Alcohol)	Synthetic film-former with good mechanical strength	Produces strong, elastic films with rapid hydration; improves fold ability and handling
Chitosan	Natural cationic polymer; mucoadhesive and permeation enhancer	Enhances mucosal adhesion, increases drug permeation, provides controlled release; bio adhesive interactions with mucin
Sodium Alginate	Anionic polymer used for mucoadhesion and gel formation	Enhances swelling, improves drug dispersion, provides moderate sustained release
Carbopol / Carbomer	Strong mucoadhesive polymer	High adhesion strength, controlled release; increases residence time on mucosa
PEG 400 (Plasticizer)	Improves flexibility and reduces brittleness	Enhances film elasticity, reduces cracking, improves patient comfort
Glycerol (Plasticizer)	Softener for natural and synthetic polymers	Increases flexibility, reduces dryness, improves mechanical durability
PVP (Polyvinylpyrrolidone)	Film former + solubility enhancer	Improves drug dispersion, increases dissolution rate for poorly soluble drugs
Xanthan Gum	Natural polymer used for viscosity and mucoadhesion	Enhances stickiness and swelling; supports sustained drug release
β-Cyclodextrin (Complexing Agent)	Solubility enhancer for herbal/flavonoid compounds	Improves stability and solubility of phytoconstituents; enhances permeation
Citric Acid (Saliva stimulant / pH modifier)	Adjusts pH and aids disintegration	Improves taste, enhances dissolution rate, stabilizes pH-sensitive drugs
Bile Salts (Permeation Enhancers)	Enhances trans buccal absorption	Increases membrane fluidity and improves transport of poorly permeable molecules
Lecithin / Phospholipids	Natural surfactants; used in lipid-based films	Improve solubility of hydrophobic herbal drugs; can enhance penetration

Herbal Drug Incorporation Techniques: The incorporation of herbal drugs into buccal films involves a systemic formulation approach to ensure stability, uniformity and effective drug delivery. Proper selection and standardization of herbal extracts are essential to achieve consistent therapeutic activity. Since many herbal compounds have poor solubility and stability, various enhancement techniques such as cyclodextrin complexion, nanotechnology-based loading, and co-solvent systems are used to improve their performance. These optimized herbal actives are then incorporated into suitable polymer matrices using appropriate plasticizers to obtain flexible and uniform films. The prepared films undergo controlled casting, drying, cutting, packaging, and quality evaluation to ensure safety, efficacy, and patient acceptability. The overall process involved in herbal drug incorporation into buccal films is illustrated in Figure 3.

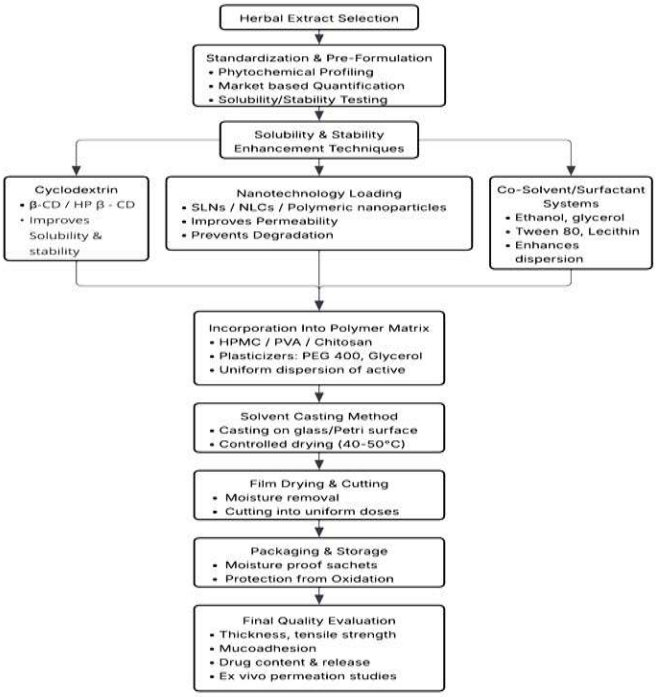

Figure 3. Schematic illustration of the formulation process for herbal buccal films

Various Methods of preparation of buccal drug delivery system
Buccal film formulation is mainly prepared by following methods:

Solvent Casting Method: Solvent casting is one of the most widely used methods for preparing buccal films. In this approach, the chosen polymer is first dissolved in distilled water to create a uniform solution. The active drug is then added to this polymer solution, followed by a suitable plasticizer to enhance the flexibility of the resulting film[38]. The mixture is stirred well and poured into petri dishes, which are then placed in a hot-air oven at around 40 °C to dry slowly. Once the films are completely dried, they are carefully removed, stored in a desiccator for 24 hours, and finally cut into the desired sizes to produce uniform dosage units[39].

Steps involved:

- **Step 1:** Preparation of polymeric casting solution
- **Step 2:** Adjustment or dilution of the solution
- **Step 3:** Pouring or spreading the required volume into the casting mold
- **Step 4:** Drying the cast film
- **Step 5:** Cutting the dried film into units containing the required drug dose

Hot Melt Extrusion Method: Hot melt extrusion is a solvent-free method in which the drug and excipients are blended and heated until they melt into a homogenous mixture. This molten mass is then pushed through an extruder die to form films, granules, or other solid shapes. The process is especially suitable for transdermal and trans mucosal drug delivery systems because it allows uniform dispersion of ingredients and avoids solvent-related issues[40].

Steps involved

- **Step 1:** Blending the drug with solid excipients
- **Step 2:** Melting the mixture in a heated extruder
- **Step 3:** Shaping the molten mass into a film using the die

Direct Milling Method: The direct milling method does not use any solvents. In this approach, the drug and excipients are combined directly through dry milling, grinding, or kneading. The resulting cohesive mass is then rolled onto a non-stick surface to reach the desired thickness. This method is often preferred because it eliminates the risk of residual solvents and avoids solvent-related toxicity or environmental issue[41].

Semisolid Casting Method: The semisolid casting technique is especially useful for formulations involving acid-insoluble polymers. In this method, a solution of a water-soluble polymer is first prepared and then combined with a separately prepared solution of an acid-insoluble polymer, which is dissolved in sodium or ammonium hydroxide. A plasticizer is added to create a gel-like mass, with its properties depending on the type and concentration of the plasticizer used. This gel is then cast onto rollers or drums under controlled temperature to form films or ribbons. Typically, the ratio of acid-insoluble polymer to film-forming polymer is kept around 1:4, producing films with a thickness ranging from 0.015 to 0.05 inches[42].

Solid Dispersion Extrusion: Solid dispersion extrusion is an advanced formulation technique focused on improving the solubility, dissolution rate, and overall bioavailability of drugs with poor water solubility. In this method, the active pharmaceutical ingredient (API) is evenly dispersed within an inert, hydrophilic polymer carrier in its solid state, making the drug more soluble and easier for absorption. The process generally starts by dissolving the drug in a suitable solvent to form a uniform solution, which is then mixed into molten polyethylene glycol (PEG) at temperatures below 70 °C. Unlike other methods, the solvent is intentionally retained to help form a homogeneous drug–polymer mixture. PEG is commonly used as the carrier because of its strong solubilizing ability, safety profile, and capacity to form hydrogen bonds with drug molecules, promoting the formation of amorphous structures that enhance solubility. After thorough mixing, the molten drug–polymer mass is extruded through a die to produce thin films, resulting in solid dispersion-based buccal films[43].

Challenges Developing and Considerations in Buccal Management

Mucoadhesion: Strong and lasting mucoadhesion to the buccal mucosa is crucial for keeping the film in place long enough to allow controlled drug release and efficient absorption. This property is particularly important for buccal films used in diabetes management, where maintaining consistent therapeutic levels is essential. Researchers have explored a variety of polymer systems and formulation strategies to enhance mucoadhesive strength and increase the residence time of the films on the mucosal surface[44].

Drug Stability: It is important to ensure that a drug remains stable within the buccal film during storage and normal handling, as instability can directly affect its therapeutic effectiveness. Any stability issues may reduce the drug's bioavailability and overall performance[45].

Biocompatibility and Safety Considerations

Irritation and Allergen: Buccal films need to be designed to prevent irritation or allergic reactions on the oral mucosa. Selecting safe and biocompatible polymers and excipients is especially important when the product is intended for long-term use[46].

Toxicity and Metabolism: Comprehensive safety evaluations—including both in vitro and in vivo toxicity testing—are needed to understand how the drug behaves metabolically when delivered through the buccal route[47].

Systemic Absorption: Evaluating the potential for a drug to enter systemic circulation through the buccal mucosa is important. Any unintended systemic absorption could cause side effects, making careful assessment essential[48].

Pharmacotechnical Evaluation of Buccal Films: Pharmacotechnical evaluation plays a key role in assessing the quality and safety of buccal film formulations. Important physical tests—such as measuring thickness, weight uniformity, surface characteristics, and moisture content—help ensure structural stability. Mechanical properties, including tensile strength, folding endurance, and elongation at break, are evaluated to confirm that the films can withstand normal handling. Mucoadhesive strength and swelling index are assessed to predict how well the film will stay on the buccal mucosa and how it will release the drug. Drug content uniformity and in vitro dissolution studies provide information on accurate dosing and release patterns, while ex vivo permeation studies estimate the potential for systemic absorption. Together, these assessments ensure mechanical reliability, compatibility with oral tissues, and effective drug delivery[49]. This section will discuss the various methods used to evaluate the performance of buccal film formulation, such as evaluating their mechanical characteristics, drug release behaviour, mucoadhesive properties, in vitro drug permeation, stability, and in vivo pharmacokinetic performance.

Film Weight and Thickness: The weight of each 1 × 1 cm² film was measured using a digital balance, and the average weight was calculated. The thickness of the films was recorded at several points using a Vernier caliper, and an average value was determined for each film[50].

Folding Endurance: Folding endurance of the films was evaluated by repeatedly folding each film at the same spot until it either broke or reached a maximum of 300 folds. The total number of folds the film could withstand without breaking was recorded as its folding endurance. The average value was calculated from three separate measurements.

Mucoadhesive Strength: The mucoadhesive properties of the films were tested using a 3% (w/v) mucin solution and a mucoadhesion testing apparatus based on the double beam balance principle. Ten microliters of the mucin solution were placed on each of two coverslips. The reverse sides of the coverslips were fixed to the upper and lower arms of the balance using double-sided tape. A 1 × 1 cm² film was attached to the lower coverslip. Contact between the film and the upper coverslip was established by removing a 5 g weight from the balance's right pan, allowing the surfaces to adhere for three minutes. Additional weight was then gradually added to the right pan until the film detached from the upper coverslip. The extra weight required for detachment (total weight minus 5 g) was recorded as the mucoadhesive strength in grams. The mean value from three trials was calculated to determine the maximum adhesive force[51].

Swelling Index: The films were placed in phosphate buffer (pH 6.8) for 8 hours to allow swelling, after first recording their initial weights. At specific time intervals, each film was removed from the buffer, gently blotted with filter paper to remove excess moisture, and the increase in weight was measured to determine the extent of swelling[52].

Surface pH: To assess the potential for mucosal irritation, the surface pH of the prepared buccal films was measured. Each film was allowed to swell in 5 mL of pH 6.8 distilled water in small beakers. The pH of the surrounding solution was then recorded using a pH electrode in contact with the swollen film. The average pH was calculated from three separate measurements[53].

Thickness: The thickness of ten randomly selected films from each formulation batch was measured using a Vernier calliper.

Weight Variation: The weight of three randomly selected films from each formulation batch was measured using an electronic balance.

Tensile Strength: A 2 × 2 cm² film strip, free of air bubbles or other visible defects, was placed between two clamps set 3 cm apart. To prevent the film from being cut by the clamp grooves, cardboard was attached to the clamp surfaces with double-sided tape. Weights were then gradually added to the pan attached to the lower clamp until the film broke, and the force required was recorded to determine its tensile strength[54].

$$\text{Tensile Strength (TS)} = \frac{\text{Force at break (F)}}{\text{Cross-sectional area (A)}}$$

Stability Study: A stability study was conducted at 40 °C and 75% relative humidity according to ICH guidelines. Each film was individually packaged using aluminium foil, plastic tape, and butter paper. After one month, the films were examined for any changes in appearance, drug content, and in vitro drug release[55].

Evaluation of Mucoadhesion In Vitro/Ex Vivo: Mucoadhesion is an important property for dosage forms that need to stick to mucosal surfaces, especially for formulations designed to provide sustained drug release. Strong mucoadhesive strength and sufficient retention time are crucial to ensure that the drug is released over an extended period. Although several in vitro methods have been developed to assess mucoadhesion, only a few are suitable for evaluating mucoadhesive films. Techniques such as atomic force microscopy and rheological assessments are generally applied to semi-solid preparations[56].

Challenges and Future Perspectives: Although buccal film formulations show great potential, several challenges still need to be addressed. This section focuses on issues related to manufacturing scalability and regulatory considerations. It also explores future commercial prospects, including opportunities for personalised medicine, combination therapies, and overall market viability[57].

CONCLUSION

Herbal drug-loaded buccal films offer a novel and patient-friendly strategy for diabetes management, effectively addressing the limitations of conventional therapies while harnessing the therapeutic potential of medicinal plants. By enhancing bioavailability, enabling controlled drug release, and supporting patient adherence, these systems represent a promising approach for integrative antidiabetic care. Ongoing research focused on formulation optimization, standardization of phytochemicals, and clinical validation will be critical to advance these films toward routine clinical application and ensure their long-term effectiveness and safety.

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