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FORMULATION AND POTENTIAL APPLICATIONS OF AMLA (PHYLLANTHUS EMBLICA L.) MUCOADHESIVE ORAL GEL: PHYTOCHEMISTRY, DRUG DELIVERY, CHALLENGES AND FUTURE PERSPECTIVES

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Abstract

Phyllanthus emblica L., commonly known as amla or Indian gooseberry, is a medicinal plant rich in bioactive constituents, including polyphenols, tannins, and flavonoids. These constituents have been investigated for their antioxidant, anti-inflammatory, and antimicrobial properties, suggesting potential applications in oral healthcare. However, conventional herbal preparations may have limited contact time with oral mucosal tissues due to continuous salivary secretion. Mucoadhesive oral gels offer a promising approach by adhering to the oral mucosa and potentially prolonging local drug residence time. This review explores the phytochemical composition and reports pharmacological activities of amla, emphasizing its potential applications in oral healthcare. It also discusses the principles of mucoadhesion, commonly used polymers, formulation strategies, and evaluation parameters, including pH, viscosity, spreadability, mucoadhesive strength, stability, and in vitro drug release. Furthermore, challenges related to extract standardization, formulation optimization, mucosal safety, and therapeutic efficacy are highlighted. The incorporation of amla extract into a mucoadhesive oral gel represents a potential approach to developing an herbal oral-care formulation. Nevertheless, systematic formulation studies and appropriate experimental and clinical investigations are necessary to establish its safety, effectiveness, and suitability for oral applications.

Keywords

Phyllanthus emblica, Amla, bio adhesive polymer, mucoadhesive gel, herbal formulation, drug delivery.

Introduction

According to believe in ancient Indian mythology, Phyllanthus emblica L. is the first tree to be created in the universe.[3] India is among the tropical and subtropical nations that have traditionally grown Phyllanthus emblica L. (amla), a medicinal plant in Phyllanthaceae family.[1] It is also named as amla or Indian gooseberry.[3] The species is native to India and grows in Pakistan, Uzbekistan, Sri Lanka, Southeast Asia, China, and Malaysia.[3]

Amla exhibits a number of biological properties, such as antioxidant, anti-cancer, anti-diabetic, anti-inflammatory, anti-microbial treatment of stomach disorders, adaptogenic, rejuvenating, and fostering health and longevity.[1] Similarly, it has the application as immunomodulatory, antipyretic, analgesic, cytoprotective, antitussive, and lowering cholesterol level.[3] Additionally, it has a wealth of nutrients, including phenolic acids, alkaloids, carbs, vitamin C, and amino acids.[1] It has it's beneficial role in cancer, diabetes, liver treatment, heart trouble, ulcer, anaemia, and various other diseases.[3] In addition, it is useful in memory enhancing, ophthalmic disorders, and lowering cholesterol level.[3]

All parts of amla, particularly fruit, have been studied and reported to possess a variety of pharmacological activities in prevention and treatment of diseases.[1] The properties of the fruit of P. emblica have been extensively studied, and its beneficial effects are proven.[4] Presence of microbial contaminants may affect efficacy and stability of the active compounds.[3] Presence of pathogenic microorganisms in plant materials can precariously affect human health.[3]

The ethanolic extract of amla branch and its fraction exhibit the potent cytotoxicity against cancerous cells, including human leukaemia (HL-60) and human hepatocellular carcinoma (SMMC-7721) cells.[1]

Mucoadhesive Drug Delivery Systems (MDDS), as an innovative approach, have gained attention with their promising benefits like increased solubility, improved absorption, targeted-controlled drug delivery, enhanced oral bioavailability and therapeutic efficacy of the product.[5] Moreover, MDDS decreases the dosing frequency, ultimately lowers the product cost, and reduces unwanted side effects.[5]

Ex-vivo Mucoadhesive Drug Delivery System: Mucoadhesive Drug Delivery System utilizes mucoadhesion to enhance drug effectiveness by increasing their bioavailability, stability, and retention time in mucosal surfaces.[2]

Recurrent ulcers in the throat and oral cavity are a hallmark of aphthous stomatitis, often known as mouth ulcer, an inflammatory disorder involving the oral mucosa.[1] Oral ulcers or recurrent aphthous stomatitis is one of the most common oral diseases affecting about 25% of the population.[4] Currently, anaesthetic gels, creams, oxygenating agents, dissolvable and non-dissolvable patches, film-forming gels, and mouth rinses are the available treatment.[4]

In recent times, the plant-based natural products are in higher demand for containing the pharmacologically active constituents and having strong therapeutic potential.[5] Although the world has shifted towards synthetic chemistry, natural products are playing an important role due to their varied biological activities and unique behaviour by which they interact with their biological targets.[5] Natural products often face challenges in terms of their pharmacokinetic behaviour, such as their poor aqueous solubility, instability, impaired absorption, and poor permeability that ultimately leads to poor bioavailability of these compounds.[5]

Among the various routes of drug delivery, the oral route is perhaps the one mostly preferred by patients and clinicians.[6] Among the various transmucosal routes, buccal mucosa has an excellent accessibility, an expanse of smooth muscle and relatively immobile mucosa, hence suitable for administration of controlled release dosage forms.[6] Buccal drug delivery has a high patient acceptability compared to other non-oral transmucosal routes of drug administration.[6] The total surface area of the membranes of the oral cavity available for drug absorption is 170 cm^2 of which ~50 cm^2 represents non-keratinized tissues, including the buccal membrane.[6] Continuous secretion of saliva (0.5-2 L/day) leads to subsequent dilution of the drug.[6]

Advantages:

1. Enhanced drug bioavailability and efficacy at the target site.
2. Bypass first-pass metabolism, increasing drug availability.
3. Non-invasive administration without injection or invasive procedures.[2]

Disadvantages:

1. Potential irritation or allergic reactions at the site of application.
2. Possible discomfort or inconvenience during application or administration.[2]

Botanical Profile of Amla

Amla, commonly known as Indian gooseberry, is an important medicinal plant widely used in traditional Ayurvedic medicine. Its fruits are rich in polyphenols, tannins, and other bioactive constituents, making it an important subject of pharmacognostic and pharmaceutical research. [1, 2, 20, 21]



Fig 1: Phyllanthus emblica

Table: 1 Taxonomical classification [1, 2, 20, 21]

Taxonomic rank	Classification
Kingdom	Plantae
Clade	Angiosperms
Clade	Eudicots
Order	Malpighiales
Family	Phyllanthaceae
Genus	Phyllanthus
Species	Phyllanthus emblica L.
Synonym	Emblica officinalis Gaertn

Common names [1, 2, 20, 21]
English: Indian gooseberry
Hindi: Amla
Marathi: आवळा (Awala)
Sanskrit: Amalaki

Botanical characteristics [1, 2, 20, 21]

Habit: A small to medium-sized, deciduous tree, generally reaching about 8–18 m in height.
Root: Well-developed root system with a strong main root.
Stem and bark: Bark is generally greyish brown, sometimes exfoliating in thin flakes.
Leaves: Simple, small, oblong, and closely arranged along slender branchlets, giving a pinnate appearance.
Flowers: Small, greenish-yellow flowers, usually borne in clusters.
Fruit: Nearly spherical, fleshy, pale green to yellowish-green when mature, with six faint vertical furrows.
Seed: The fruit contains a hard, six-celled stone enclosing seeds.

Geographical distribution [1, 2, 20, 21]

Amla is native to tropical and subtropical regions of Asia and is widely cultivated in India. It grows in various soil types and is commonly found in dry deciduous forests, gardens, and agricultural plantations.

Part used [1, 2, 3, 4]

The fruit is the principal medicinal part used in traditional preparations and pharmaceutical research. Leaves, bark, roots, and seeds have also been investigated for different applications.

Major Phytochemical Constituents [2, 12]

The fruit contains several classes of bioactive compounds:
Polyphenols: Gallic acid and ellagic acid.
Hydrolysable tannins: Emblicanin A and Emblicanin B, among other tannins.
Flavonoids: Quercetin and related compounds.
Organic acids: Various naturally occurring organic acids.
Vitamin C: Present in variable amounts depending on cultivar, maturity, processing, and analytical method.

Medicinal Importance [2, 23]

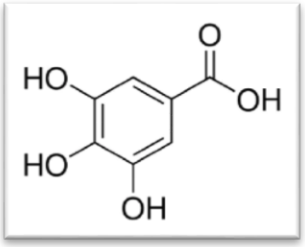
Amla has a long history of use in Ayurveda. Research has investigated its antioxidant, anti-inflammatory, and antimicrobial properties. However, the strength of evidence varies by activity, extract, and experimental model.

Phytochemistry of Amla

Table: 2 Major phytochemical constituents [1, 2, 3, 4, 20, 21]

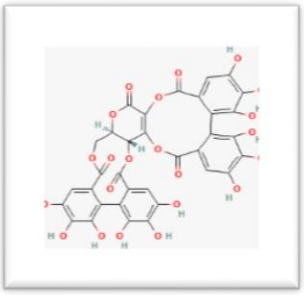
Phytochemical Class	Important Examples
Hydrolysable tannins	Emblicanin A, Emblicanin B, chebulagic acid, corilagin, geraniin
Phenolic acids	Gallic acid, ellagic acid, caffeic acid, chlorogenic acid, vanillin acid
Flavonoids	Quercetin, rutin, kaempferol
Vitamins	Vitamin C, other vitamins have also been reported
Organic acids	Malic acid and other organic acids
Alkaloids	Phyllantine and phyllantidine have been reported
Amino acids	Glutamic acid, proline, alanine and others
Lipids and fatty acids	Linoleic acid, oleic acid, palmitic acid and stearic acid

Important phytochemicals and their significance



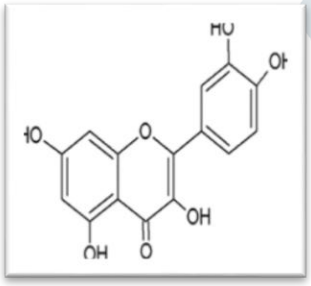
Gallic acid [1, 2, 4, 20, 21]

A phenolic acid reported in Amla. It exhibits antioxidant activity in experimental systems and can be used as a marker compound in phytochemical analysis.



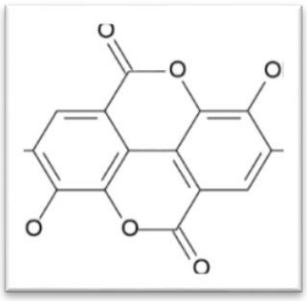
Emblicanin A and Emblicanin B [1, 2, 20, 21]

Hydrolysable tannins associated with the antioxidant properties reported in Amla fruit extracts.



Quercetin [1, 2, 20, 21]

A flavonoid with antioxidant and anti-inflammatory effects reported in experimental research.



Ellagic acid [1, 2, 4, 20, 21]

A polyphenolic compound associated with antioxidant activity and reported in Amla fruit and other plant parts.

Pharmacological Properties of Amla

Major Pharmacological Activities

1. Antioxidant activity

Amla contains polyphenols, tannins, and other antioxidant constituents that can scavenge free radicals and reduce oxidative damage in experimental models. This activity is commonly associated with gallic acid, ellagic acid, and related compounds. [1, 2, 3, 4, 20, 21]

2. Anti-inflammatory activity

Amla extracts have demonstrated effects on inflammatory mediators in laboratory and animal studies. Some research suggests modulation of nitric oxide and cyclooxygenase-related pathways. [1, 2, 3, 4, 20, 21]

3. Antimicrobial activity

Different Amla extracts have shown inhibitory effects against certain bacteria and other microorganisms in laboratory tests. Activity depends on the extract, concentration, and microorganism tested. [3, 20, 21]

4. Hepatoprotective activity

Experimental studies suggest that Amla extracts may protect liver tissue against certain forms of chemical-induced oxidative injury. Clinical effectiveness for liver diseases is not established by these findings alone. [3, 20, 21]

5. Antidiabetic activity

Amla has been investigated for effects on glucose metabolism, insulin-related responses, and oxidative stress. Some human studies are available, but the evidence is not sufficient to treat it as a replacement for diabetes medication. [3, 20, 21]

6. Immunomodulatory activity

Certain studies suggest that Amla extracts may influence immune responses. The effects depend on the preparation and experimental conditions, and their clinical significance requires further investigation. [3, 20, 21]

7. Cardioprotective and hypolipidemic activity

Research has examined possible effects on lipid profiles, oxidative stress, and cardiovascular risk markers. These findings do not establish that Amla prevents or treats cardiovascular disease. [1, 2, 3, 4, 20, 21]

8. Wound-healing activity

Preliminary experimental evidence suggests potential roles in tissue repair and protection against oxidative stress. The effectiveness of a particular topical or oral formulation must be tested separately. [1, 2, 3, 4, 20, 21]

Table: 3 Other reported pharmacological properties [4, 11, 12]

Activity	Reported research interest
Analgesic	Potential reduction of pain responses in experimental models
Anti -pyretic	Potential reduction of fever in experimental models
Gastroprotective	Protection against certain forms of gastric injury
Neuroprotective	Effects on oxidative stress and neuronal injury in experimental models
Anticancer	Effects on cancer cell growth and related pathways in preclinical research
Antimutagenic	Potential reduction of certain mutagenic effects in experimental tests
Anti-aging	Investigated effects on oxidative stress and skin related parameters

Relevance to proposed Amla Mucoadhesive Oral Gel

For your review paper, the most relevant properties to discuss are:

- Antioxidant activity: provides a rationale for studying local delivery of Amla phytochemicals.
- Antimicrobial activity: supports investigating whether the finished gel inhibits selected oral microorganisms.
- Anti-inflammatory activity: provides a basis for further research into potential local oral applications.
- Wound-healing potential: may justify future studies involving oral mucosal repair, subject to appropriate safety and efficacy testing.

Oral Mucosa and Drug Delivery

The oral mucosa is the moist membrane lining the oral cavity. It protects the underlying tissues and provides a route for delivering drugs locally or, in selected cases, through the mucosa into systemic circulation. Oral Mucosal Drug Delivery has gained importance because of its accessibility and potential to prolong drug contact with the site of application using mucoadhesive formulations.

Structure of the oral mucosa [5, 16, 19]

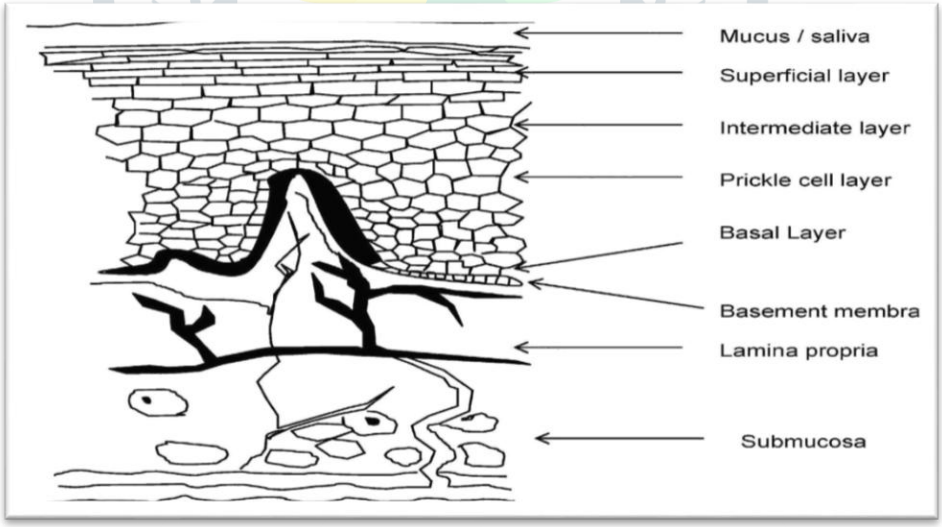


Fig: Structure of oral mucosa

The oral mucosa consists of three principal structural components:

1. Epithelium: The outer protective layer made of stratified squamous epithelial cells. It acts as a barrier against microorganisms, chemicals, and physical injury. [5, 16, 19]
2. Basement membrane: A thin supporting interface that connects the epithelium with the underlying connective tissue. [5, 16, 19]
3. Lamina propria and underlying submucosa: Connective tissues that provide structural support, blood vessels, nerves, and other supporting elements. The submucosa varies by anatomical site. [5, 16, 19]

The epithelium may be keratinized or non-keratinized, depending on the location in the mouth. These differences influence the permeability of drugs across the mucosa. [5, 16, 19]

Types of oral mucosa

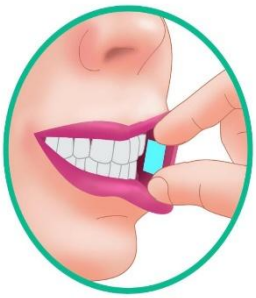
The buccal mucosa lining the inner cheek is particularly useful for mucoadhesive formulations because it is accessible and relatively suitable for retaining dosage forms. [5, 16, 17, 19]

Table: 4 Types of oral mucusa

Type	Location	Main function
Masticatory mucosa	Gingiva and hard palate	Resists friction and chewing forces
Lining mucosa	Cheeks, lips, floor of mouth, soft palate, and ventral surface of tongue	Provides flexibility and protection
Specialized mucosa	Mainly the upper surface of the tongue	Contains papillae and taste buds

Oral Mucosal Drug Delivery

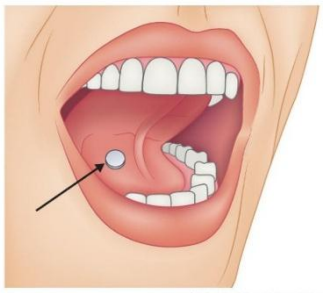
Oral Mucosal Drug Delivery is the administration of a drug through the mucous membranes of the oral cavity. It is broadly divided into two categories.



A. Buccal drug delivery [5, 16, 17, 19]

The drug is applied to the inner cheek. Mucoadhesive gels, tablets, patches, and films can be designed to remain at this site for prolonged periods.

Applications: Local treatment or systemic delivery, depending on the drug and formulation.



B. Sublingual drug delivery [5, 16, 17, 19]

The drug is placed beneath the tongue, where the mucosa permits relatively rapid absorption of suitable drugs.

Applications: Rapid systemic delivery of certain medicines, such as nitro-glycerine.

Mechanism of drug absorption [5, 7, 16, 17]

Drugs can cross the oral mucosa mainly through two pathways:

- Transcellular pathway: The drug passes through epithelial cells. This pathway often favours compounds that can partition into cell membranes.
- Paracellular pathway: The drug passes between adjacent epithelial cells. This pathway is influenced by the structure and permeability of the spaces between cells.

The extent of absorption depends on molecular size, solubility, ionization, concentration, formulation properties, and the permeability of the mucosal site.

Advantages of Oral Mucosal Drug Delivery [5, 6, 7, 8, 16, 17]

- Easy access and convenient application.
- Possibility of delivering drugs directly to a local site.
- Avoidance of gastrointestinal degradation for drugs absorbed directly through the mucosa.
- Potential avoidance of hepatic first-pass metabolism for drugs absorbed into systemic circulation through suitable oral mucosal routes.
- Potential for controlled release and prolonged residence using mucoadhesive polymers.
- Formulations can often be removed if necessary.

Limitations of Oral Mucosal Drug Delivery [5, 6, 7, 8, 16, 17]

- Continuous salivary secretion can dilute the formulation.
- Swallowing and tongue movements can remove the dosage form.
- The available surface area for absorption is limited.
- The mucosal barrier restricts the absorption of many drugs.
- Taste, irritation, and patient acceptability may affect use.
- Drug absorption varies with formulation characteristics and the site of application.

Important research parameters include:

- Mucosal compatibility and formulation pH.
- Mucoadhesive strength and residence time.
- Viscosity and spreadability.
- Release of selected Amla marker compounds.
- Stability and microbial quality.

- Appropriate safety and biological testing for the intended application.

Mucoadhesive Drug Delivery Systems (MDDS) [6, 7, 8, 9, 18]

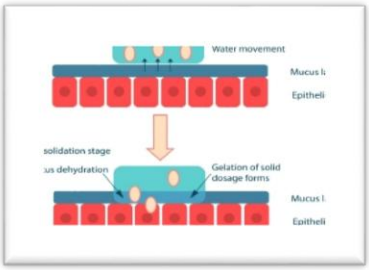
Mucoadhesive Drug Delivery Systems are pharmaceutical formulations designed to adhere to the mucus layer or mucosal surface of the body, thereby prolonging the residence time of a drug at the application site. These systems can improve local drug availability and, in suitable formulations, facilitate drug absorption across mucosal tissues.

Mucoadhesive systems are used in buccal, nasal, ocular, vaginal, gastrointestinal, and other mucosal drug delivery applications.

Principle of mucoadhesion

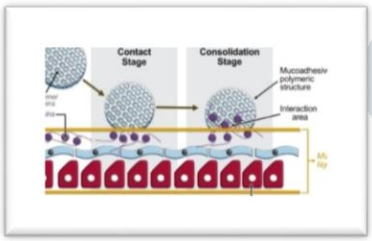
Mucoadhesion generally involves two interacting surfaces: the mucoadhesive polymer and the mucus-covered biological tissue. [6, 18]

The process can be explained in three stages: [6, 18]



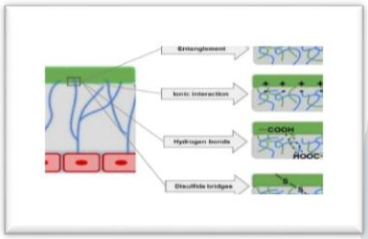
Stage 1: Contact

The formulation meets the mucosal surface and spreads over it.



Stage 2: Hydration and interpenetration

The polymer absorbs water, swells, and may interpenetrate with mucus glycoprotein chains.



Stage 3: Adhesion

Intermolecular interactions help maintain attachment, potentially prolonging drug release and local contact

Table: 5 Theories of Mucoadhesion

Six major theories are commonly described in pharmaceutical literature. [6, 7, 8, 9, 18]

Theory	Explanation
Wetting theory	Adhesion depends on the ability of a formulation to spread and make intimate contact with the mucosal surface.
Diffusion theory	Polymer chains interpenetrate with mucin chains, forming an adhesive interface.
Adsorption theory	Adhesion results from interfacial interactions, including hydrogen bonding, van der Waals forces, and hydrophobic interactions.
Electronic theory	Electron transfer between surfaces produces an interfacial electrical double layer that contributes to adhesion.
Fracture theory	Adhesion is evaluated by measuring the force or stress needed to separate the formulation from the mucosal surface.
Mechanical theory	The formulation enters irregularities on the tissue surface, producing mechanical interlocking.

Types of mucoadhesive drug delivery systems [7, 8, 9, 13, 14, 17, 18]

1. Tablets: Solid dosage forms that adhere to the mucosa and release the drug over time.
2. Films and patches: Thin dosage forms designed for localized retention and drug release.
3. Gels: Semisolid formulations that spread over the mucosal surface and may provide prolonged local contact.
4. Microspheres and nanoparticles: Particulate carriers that can be designed to interact with mucus and modify drug release.
5. Pastes: Semisolid preparations used when a thicker formulation is desirable for localized application.

Advantages [6, 7, 8, 9, 13, 14, 18]

- Prolongs the residence time of a dosage form at the application site.
- May improve local drug availability.
- Can support sustained or controlled drug release.

- May reduce the need for frequent application, depending on the formulation.
- Allows localized drug delivery.
- Certain oral mucosal formulations can provide systemic delivery and avoid gastrointestinal degradation and hepatic first-pass metabolism.

Limitations [6, 7, 8, 9, 13, 14, 18]

- Saliva and mucus turnover can remove the formulation.
- Food intake, speaking, swallowing, and mouth movements can affect retention.
- Excessive adhesion may cause discomfort or make removal difficult.
- Polymer properties and environmental pH can affect performance.
- Some drugs have poor mucosal permeability.
- Taste, irritation, stability, and patient acceptability can limit use.

Factors affecting mucoadhesion [6, 7, 8, 9, 13, 14, 18]

The main factors include:

1. Polymer properties: Molecular weight, concentration, chain flexibility, and functional groups.
2. Hydration: Insufficient hydration can limit chain mobility, while excessive hydration may weaken the adhesive structure.
3. pH: Influences polymer ionization and interactions with mucin.
4. Contact time and pressure: Adequate contact supports formation of an adhesive interface.
5. Mucosal condition: Mucus thickness, tissue characteristics, and surface moisture influence adhesion.
6. Formulation properties: Viscosity, spreadability, and excipient compatibility affect performance.

Mucoadhesive Polymers Used in Oral Gels

- Mucoadhesive polymers are natural, semisynthetic, or synthetic substances that help an oral gel adhere to the mucus layer or mucosal surface of the mouth. They can increase formulation residence time, improve local contact, and influence viscosity and drug release. [6, 7, 8, 9, 13, 14, 18]

Best polymers for your Amla oral gel [9, 13, 14, 18]

1. Carbopol 934P or 940

A strong candidate when high viscosity and mucoadhesion are desired. The formulation's pH, neutralization, and oral mucosal compatibility must be optimized.

2. HPMC

Useful for improving gel consistency, water retention, and release characteristics. It can be evaluated alone or in combination with Carbopol.

3. Chitosan

A promising natural-derived option with mucoadhesive properties. Its solubility, compatibility with the Amla extract, and performance at the intended pH need to be evaluated.

4. Sodium CMC

A useful alternative for thickening and adhesion, particularly if you want to investigate a cellulose-based gel.

Formulation Development of Amla Mucoadhesive Oral Gel

Formulation development of an Amla (Phyllanthus emblica L.) mucoadhesive oral gel involves incorporating standardized Amla fruit extract into a suitable gel base containing mucoadhesive polymers and other pharmaceutical excipients. The objective is to develop a formulation that spreads easily over the oral mucosa, remains at the application site for an adequate period, and maintains acceptable stability and mucosal compatibility. [2, 9, 13, 14, 23]

Selection and preparation of Amla extract [1, 2, 3, 4, 20, 21, 23]

Fresh, authenticated Amla fruits should be selected as the starting material. The fruits are cleaned, dried using a suitable method, and processed into powder before extraction.

Important considerations include:

- Authentication: Confirm the botanical identity of the plant material.
- Extraction: Select a suitable solvent and extraction procedure based on the target phytochemicals.
- Concentration: Remove the extraction solvent under appropriate conditions.
- Standardization: Characterize the extract and, where feasible, quantify marker compounds such as gallic acid.
- Quality assessment: Evaluate extract yield, phytochemical profile, microbial quality, and relevant contaminants.

Preparation method [9, 13, 14, 18]

A conventional aqueous gel may be prepared using the following general procedure:

- Prepare the polymer base. Disperse the selected polymer in the appropriate vehicle using a validated mixing procedure.
- Allow hydration. Give the polymer sufficient time to hydrate and develop its intended consistency.
- Prepare the extract phase. Dissolve or disperse the standardized Amla extract in a compatible vehicle.
- Incorporate the extract. Add it gradually to the polymer base while mixing to obtain a uniform dispersion.
- Add the remaining excipients. Incorporate the selected humectant, sweetener, and other necessary ingredients.
- Adjust pH and final batch mass using suitable materials, minimize air entrapment, and allow the gel to equilibrate.
- Package and evaluate. Transfer the preparation into a suitable, well-closed container and evaluate its quality and stability.

Evaluation Parameters for Amla Mucoadhesive Oral Gel

The evaluation of an Amla (Phyllanthus emblica L.) mucoadhesive oral gel is performed to assess its physicochemical properties, uniformity, mucoadhesive performance, release characteristics, stability, and safety for oral mucosal application.

1.Physical appearance and homogeneity [9, 13, 14, 24]

Purpose: To assess the overall quality and uniformity of the gel.

Method:

- Observe the colour, odour, and physical appearance.
- Examine for lumps, visible particles, phase separation, or air bubbles.
- Spread a small amount on a glass slide to check uniformity.

Expected result: A uniform gel without visible lumps or phase separation.

2. pH determination [9, 13, 14, 24]

Purpose: To assess whether the formulation is suitable for contact with the oral mucosa.

Method:

1. Calibrate a digital pH meter using suitable standard buffers.
2. Measure the pH of the gel directly using a suitable electrode or use a defined dispersion method if required by the method.
3. Record the result and repeat measurements as appropriate.

Interpretation: The target pH should be justified by the polymer system, extract stability, and oral mucosal compatibility. A pH near neutrality is often considered during development, but there is no single universal pH acceptance limit for every oral gel.

3. Viscosity determination [9, 13, 14, 18]

Purpose: To determine the resistance of the gel to flow and its consistency during application.

Method:

1. Place an appropriate quantity of gel in a viscometer container.
2. Measure viscosity using a suitable rotational viscometer or rheometer.
3. Record the spindle, speed, temperature, and measured viscosity.

Expected result: Suitable viscosity that allows application while supporting mucosal retention.

4. Spreadability test [9, 13, 14]

Purpose: To determine how easily the gel spreads over the application surface.

Method:

1. Place a specified quantity of gel between two glass slides.
2. Apply a defined load for a specified period.
3. Measure the spreading diameter or the time required for spreading, according to the selected method.

Interpretation: The gel should spread adequately without becoming excessively runny.

5.Extrudability test [9, 13, 14]

Purpose: To assess the ease of dispensing the gel from its container.

Method:

1. Fill the gel into a suitable collapsible tube.
2. Apply a defined force under controlled conditions.
3. Measure the quantity of gel extruded.

Interpretation: The gel should be easily dispensable while retaining sufficient consistency during storage.

6. Mucoadhesive strength [6, 9, 13, 14, 18]

Purpose: To measure the force required to detach the gel from a mucosal surface.

Method:

1. Mount a suitable mucosal tissue or validated mucosal model on the test apparatus.
2. Apply a measured quantity of gel to the surface.
3. Bring the surfaces into contact under defined force and contact time.
4. Measure the force required for detachment using a suitable texture analyser or modified balance method.

Interpretation: Greater detachment force generally indicates stronger adhesion under the specified test conditions, but excessively strong adhesion is not necessarily desirable.

7. Mucoadhesive residence time [6, 7, 8, 9, 13, 14]

Purpose: To estimate how long the gel remains attached to the mucosal surface.

Method:

1. Attach a suitable mucosal tissue sample to an appropriate test apparatus.
2. Apply the gel and expose it to a defined medium, such as simulated saliva.
3. Maintain controlled temperature and flow or agitation conditions.
4. Record the time until the gel detaches or is substantially removed.

Interpretation: Longer residence time may support prolonged local contact. Results depend on the test model and conditions.

8. Drug content or marker-compound assay [2, 20, 21, 23]

Purpose: To determine the amount and uniformity of selected Amla constituents in the gel.

Method:

1. Weigh a known quantity of gel.
2. Extract the selected marker compound using a validated analytical procedure.
3. Analyse, it uses a suitable method, such as HPLC or another validated assay.
4. Calculate the marker content and compare it with the established formulation target.

Important: For an herbal extract, measuring a suitable marker compound, such as gallic acid, may be more informative than referring to the result as conventional drug content.

9. In-vitro release study [9, 13, 14, 18]

Purpose: To investigate the release of selected Amla constituents from the gel.

Method:

1. Select a suitable release apparatus and membrane, if required.
2. Place a measured quantity of gel in the donor compartment.
3. Use an appropriate release medium under controlled temperature and agitation.
4. Collect samples at predefined intervals and replace the withdrawn volume where applicable.
5. Analyse the samples using a validated method and calculate the cumulative amount released.

Interpretation: The results indicate the release profile of the selected marker compound or compounds. They do not, by themselves, establish absorption through oral mucosa or therapeutic efficacy.

10. Swelling and erosion studies [9, 13, 14, 18]

Purpose: To assess changes in gel mass or structure during exposure to an aqueous medium.

Method: Weigh a defined quantity of gel or a prepared gel specimen, expose it to a specified medium for predetermined intervals, and measure changes in mass and physical integrity using a consistent protocol.

Interpretation: These results can help explain gel hydration, structural stability, and possible release behaviour.

11. Microbial quality testing [23, 24]

Purpose: To determine whether the formulation meets appropriate microbiological quality requirements.

Method: Test the formulation using suitable microbiological procedures for total microbial counts and specified microorganisms, as applicable to the product category and intended use.

Preservative effectiveness should also be evaluated when a preservative is included and required.

12. Stability studies [2, 23, 24]

Purpose: To determine whether the gel maintains acceptable quality during storage.

Method:

- Store samples under defined conditions appropriate to the product and study protocol.
- Examine them at predetermined intervals.
- Evaluate appearance, pH, viscosity, phase separation, marker-compound content, and microbial quality as appropriate.

Interpretation: Stability results help establish suitable packaging and storage conditions and support determination of shelf life.

13. Mucosal compatibility and irritation testing [11, 12, 16]

Purpose: To assess whether the formulation causes irritation or damage to oral mucosal tissue.

Method: Use an appropriate validated in-vitro tissue model or other ethically approved method suitable for the intended product. Clinical evaluation, if subsequently justified, requires the relevant ethical and regulatory approvals.

Interpretation: Acceptable physical properties alone do not demonstrate mucosal safety.

Marketed Preparations and Existing Research on Amla Mucoadhesive Oral Gel

1. Marketed preparations: products containing Amla and existing mucoadhesive oral gels containing other active ingredients.[8]
2. Existing research: scientific studies on Amla's phytochemicals, oral-health activities, and mucoadhesive drug delivery systems.[21]

Table: 6 Marketed preparations

The following examples help establish the current product landscape. Formulations and availability can change, so confirm the latest package label or manufacturer information before including a product as currently marketed. [16,18]

Product category	Example or composition	Relevance to proposed gel
Amla-containing herbal mouthwash	Herbal mouthwashes containing Amla alongside ingredients such as neem, liquorice or tulsi have been reported in oral-health literature.	Demonstrates use of Amla in oral hygiene, but a mouthwash has limited contact time compared with a mucoadhesive gel.
Triphala oral-care preparations	Triphala contains Amla (Phyllanthus emblica), Terminalia chebula and Terminalia Billerica. It is used in some herbal oral-care products.	Supports interest in Amla-containing herbal oral care, but the effects of the individual ingredients cannot be assumed.
Choline salicylate + lignocaine oral gels	Examples include Soregel and Eragel-CT; these are marketed for temporary relief of mouth-ulcer pain.	Useful conventional comparators for dosage form and local application, but they are not Amla-based gels.
Amla chewing gum studied for oral health	Amla fruit extract has been investigated in chewing gum and other oral-care approaches.	Indicates research into oral delivery of Amla, although chewing gum is not a mucoadhesive gel.

Existing research specifically on Amla oral gel [8, 4, 11, 12, 25]

A particularly relevant publication to check is the following:

Verma S, Prasad P, Kushwaha SK. A Systematic Review on: Oral Gel Infused with Phyllanthus emblica Linn and Curcuma longa Based on Natural Herb for Dental Gum Care Solution. Published in the World Journal of Pharmaceutical Science and Research in 2025, 4(4):1049–1060.

Zenodo: The record describes an herbal oral gel combining Amla and turmeric. This is directly relevant to your literature search, but it is not the same as an Amla-only mucoadhesive gel. Read the full paper and assess its methods and references before drawing conclusions about the quality of its evidence.

Based on the literature identified above, the following areas could justify further investigation:

- Formulation optimization: identify a suitable mucoadhesive polymer system for Amla extract.
- Standardization: quantify a marker compound, such as gallic acid, and control extract variability.
- Mucoadhesion and residence time: determine how well the gel adheres to oral mucosa and how long it remains in place.
- Release and stability: investigate marker-compound release, extract stability and microbial quality.
- Biological evaluation: test antioxidant or antimicrobial activity using appropriate validated methods.
- Safety: establish mucosal compatibility before considering clinical use.

Potential Applications [5, 6, 7, 8, 9, 13, 14]

Amla (Phyllanthus emblica L.), commonly known as Indian gooseberry, is a medicinal plant rich in polyphenols, tannins, flavonoids, and vitamin C. Its reported antioxidant, anti-inflammatory, and antimicrobial properties make it a promising candidate for developing herbal oral formulations. Incorporating Amla fruit extract into a mucoadhesive oral gel may improve local retention and provide prolonged contact between the active constituents and the oral mucosa.

Potential applications of the proposed formulation include:

1. Antioxidant protection: Amla-derived polyphenols may help neutralize reactive oxygen species and protect oral tissues from oxidative stress.
2. Anti-inflammatory effects: Its phytochemicals may have potential for reducing local inflammation, subject to confirmation in oral tissue models.
3. Antimicrobial activity: Amla extracts have demonstrated antimicrobial potential in experimental studies, suggesting possible applications against selected oral microorganisms.
4. Oral mucosal care: The gel could be investigated for its potential use in minor oral irritation and inflammatory conditions.
5. Periodontal applications: Its antimicrobial and anti-inflammatory properties warrant investigation for adjunctive use in gingival and periodontal care.
6. Herbal local drug delivery: The formulation may offer localized delivery, ease of application, and improved residence time compared with conventional liquid preparations.

Future Perspectives [1, 2, 3, 4, 20, 21, 23]

Future research on Amla-based mucoadhesive oral gels should focus on improving formulation quality, establishing therapeutic potential, and generating evidence of safety and efficacy.[17]

1. Phytochemical standardization: Identify and quantify suitable marker compounds to ensure consistent extract quality.
2. Polymer optimization: Compare polymers such as Carbopol, hydroxypropyl methylcellulose (HPMC), sodium carboxymethylcellulose (NaCMC), and chitosan for their effects on viscosity, adhesion, spreadability, and drug release.
3. Advanced delivery systems: Investigate suitable combinations of mucoadhesive polymers with nanoparticles or other delivery platforms if they offer demonstrable benefits.
4. Improved stability: Evaluate suitable antioxidants, packaging systems, and storage conditions to protect sensitive phytochemicals.
5. Biocompatibility studies: Conduct appropriate in vitro mucosal irritation and cytotoxicity assessments before progressing to more advanced studies.
6. Mechanistic investigations: Study the release, diffusion, mucosal interaction, and retention of selected Amla constituents.
7. Preclinical and clinical research: Following satisfactory quality and safety results, investigate efficacy for a clearly defined oral health application.
8. Scale-up and quality assurance: Develop reproducible manufacturing procedures and assess batch consistency, microbial quality, and long-term stability.

Conclusion

Amla (Phyllanthus emblica L.) is a promising herbal candidate for pharmaceutical research because of its diverse phytochemical composition and reported antioxidant, anti-inflammatory, and antimicrobial activities. Incorporating its fruit extract into a mucoadhesive oral gel may provide a practical approach for investigating localized delivery and prolonged contact with the oral mucosa. However, the success of such a formulation depends on appropriate polymer selection, extract standardization, acceptable pH, suitable rheological and mucoadhesive properties, microbial quality, and adequate stability. [4, 6, 9, 11, 12]

References:

[1] Variya BC, Bakrania AK, Patel SS. emblica officinalis (Amla): A review for its phytochemistry, ethnomedicinal uses and medicinal potentials with respect to molecular mechanisms. Pharmacol Res. 2016;111 :180–200. https://doi.org/10.1016/j.phrs.2016.06.013

[2] Saini R, Sharma N, Oladeji OS, et al. Traditional uses, bioactive composition, pharmacology, and toxicology of Phyllanthus emblica fruits: A comprehensive review. J Ethnopharmacol. 2022;282: 114570. https://doi.org/10.1016/j.jep.2021.114570

[3] Begum MA, Hossain R, Jain D, et al. Recent Insights into the Antimicrobial Properties of Phyllanthus emblica L.: A Comprehensive Review of Wonder Berry. Chem Biodivers. 2024;21(9): e202400747. https://doi.org/10.1002/cbdv.202400747

[4] Li G, Yu Q, Li M, et al. Phyllanthus emblica fruits: a polyphenol-rich fruit with potential benefits for oral management. Food Funct. 2023;14(17):7738–7759. https://doi.org/10.1039/D3FO01671D

[5] Grover S, Tewari S, Sharma RK, Singh G, Yadav A, Naula SC. Effect of subgingivally delivered 10% emblica officinalis gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A randomized placebo-controlled clinical trial. Phytother Res. 2016;30(6):956–962. https://doi.org/10.1002/ptr.5600

[6] Jairam LS, et al. Development and Characterization of an Oral Mucoadhesive Patch Containing Amla (Phyllanthus emblica) Bark and Fruit Extracts to Promote Healing of Oral Ulcers: An In Vitro Study. International Journal of Clinical Pediatric Dentistry. 2025;18(10):1234–1242. https://pubmed.ncbi.nlm.nih.gov/33726644/

[7] Gaire BP, Subedi L. Phytochemistry, pharmacology and medicinal properties of Phyllanthus emblica Linn. Chin J Integr Med. 2014. https://doi.org/10.1007/s11655-014-1984-2

[8] Ahmad B, Hafeez N, Rauf A, et al. Phyllanthus emblica: a comprehensive review of its therapeutic benefits. S Afr J Bot. 2021; 138:278–310. https://doi.org/10.1016/j.sajb.2020.12.028

[9] Harris D, Robinson JR. Drug delivery via the mucous membranes of the oral cavity. Journal of Pharmaceutical Sciences. 1992;81(1):1–10. https://doi.org/10.1002/jps.2600810102?utm

[10] Smart JD. The basics and underlying mechanisms of mucoadhesion. Advanced Drug Delivery Reviews. 2005;57(11):1556–1568. https://pubmed.ncbi.nlm.nih.gov/?term=Smart+basics+underlying+mechanisms+mucoadhesion&utm

[11] Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Advanced Drug Delivery Reviews. 2005;57(11):1666–1691. https://doi.org/10.1016/j.addr.2005.07.003?utm

[12] Shaikh R, Singh TRR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. J Pharm Bioallied Sci. 2011;3(1):89–100. https://doi.org/10.4103/0975-7406.76478

[13] Woertz C, Preis M, Breitkreutz J, Kleinebudde P. Assessment of test methods evaluating mucoadhesive polymers and dosage forms: An overview. European Journal of Pharmaceutics and Biopharmaceutics. 2013;85(3):843–853. https://doi.org/10.1016/j.ejpb.2013.06.023?utm

[14] Andrews GP, Laverty TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009;71(3):505–518. https://doi.org/10.1016/j.ejpb.2008.09.028

[15] Bansil R, Turner BS. Mucin structure, aggregation, physiological functions and biomedical applications. Current Opinion in Colloid & Interface Science. 2006;11(2–3):164–170. https://doi.org/10.1016/j.cocis.2005.11.001?utm

[16] Mizrahi B, Domb AJ. Mucoadhesive polymers for delivery of drugs to the oral cavity. Recent Pat Drug Deliv Formul. 2008;2(2):108–119. https://doi.org/10.2174/187221108784534126

[17] Shinkar DM, Dhake AS, Setty CM. Drug delivery from the oral cavity: A focus on mucoadhesive buccal drug delivery systems. https://doi.org/10.5731/pdajpst.2012.00877?utm

[18] Prananda AT, Dalimunthe A, Harahap U, et al. Phyllanthus emblica: a comprehensive review of its phytochemical composition and pharmacological properties. Front Pharmacol. 2023; 14:1288618. https://doi.org/10.3389/fphar.2023.1288618

[19] Ma Q, et al. Phyllanthus emblica Linn: A comprehensive review of botany, traditional uses, phytonutrients, health benefits, quality markers, and applications. https://www.sciencedirect.com/science/article/pii/S0308814624002261?utm

[20] Verma S, Prasad P, Kushwaha SK. A Systematic Review on Oral Gel Infused with Phyllanthus emblica Linn and Curcuma longa. 2025. https://zenodo.org/records/17130220?utm

[21] QbD Approach for Development of a Mucoadhesive Thermosensitive Gel for Oral Application: Risk Assessment Followed by Screening and Optimization. https://pmc.ncbi.nlm.nih.gov/articles/PMC13115452/?utm

[22] Khanna S, Das A, Spieldenner J, Rink C, Roy S. A study of Phyllanthus emblica and its biological effects. J Med Food. 2015;18 :415–420. https://doi.org/10.1089/jmf.2014.0178

[23] Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Advanced Drug Delivery Reviews. 2005;57(11):1666–1691. https://doi.org/10.1016/j.addr.2005.07.003?utm

[24] Russo E, Selmin F, Baldassari S, et al. A focus on mucoadhesive polymers and their application in buccal dosage forms. J Drug Deliv Sci Technol. 2016;32 :113–125. https://doi.org/10.1016/j.jddst.2015.06.016

[25] Krishnaveni M, Mirunalini S. Research on the therapeutic and biological properties of Phyllanthus emblica. J Basic Clin Physiol Pharmacol. 2010; 21:93–105. https://doi.org/10.1515/JBCPP.2010.21.1.93