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PHYSIOCHEMICAL EVALUATION OF PSIDIUMGUAJAVA LEAVES EXTRACT LOADED BUCCAL PATCH FOR ENHANCED MUCOSAL ABSORPTION

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ABSTRACT

Psidium guajava L. (guava), a member of the Myrtaceae family, is a widely cultivated tropical and subtropical plant known for its nutritional fruits and medicinal properties. Guava leaves, traditionally used in various folk remedies, are a rich source of bioactive phytochemicals, including flavonoids (such as quercetin), tannins, saponins, carotenoids, and essential oils. These compounds are associated with a wide range of pharmacological effects. In addition to antimicrobial and antioxidant activity, the extract showed promising anti-inflammatory and antidiabetic potential in vitro, likely due to its ability to inhibit key enzymes such as alpha-amylase and lipoxygenase. Cytotoxicity assays confirmed its safety at therapeutic doses, supporting its use in traditional medicine for treating conditions such as diarrhea, wounds, diabetes, and infections. Five patches of Psidiumguajava buccal patches were prepare by solvent casting technique. From the optimization, best two formulations psidiumguajava (drug), Polymer (hpmc), water, Propyel glycol, Glycerine were selected based on folding endurance and optimal tensile strength. Among these, the formulation showed maximum % Moisture uptake (3.57),% Moisture content (3.27), Thickness (0.35mm), Folding endurance (265),%Drug content (96.24), Percent Elongation (97), Tensile

strength (7.66 Kg mm2), Adhesive strength (21.66). Stability study was performed for period of three months. The physiochemical parameters like visual appearance, color, texture and drug content and drug release were studied. The results showed that there is no significant change from its initial nature till the period of three months at 40°C ±2°C/75±5% RH.

KEYWORDS: Paidium guava, Anti-inflammatory, amtidiabetic, buccal patch, hysiochemical parameters.

INTRODUCTION

1.1 Psidium guajava leaves

Guava leaves (from the Psidium guajava plant) have been traditionally used in various cultures for their medicinal properties, including their potential anti-inflammatory effects. These leaves are rich in bioactive compounds such as flavonoids, tannins, and essential oils, which contribute to their therapeutic benefits. Scientific research has shown that guava leaves possess anti-inflammatory, antioxidant, and antimicrobial properties, making them a promising natural remedy for inflammation related conditions.

The active compounds in guava leaves are thought to work by modulating the immune system, reducing the production of pro-inflammatory cytokines, and neutralizing free radicals. As a result, guava leaves are commonly used to relieve symptoms of inflammatory diseases such as arthritis, digestive disorders, and skin conditions. The leaves can be consumed as an herbal tea, or their extracts are used in various forms, including topical applications for inflammation relief.

While more studies are needed to fully understand the mechanisms and efficacy of guava leaves in treating inflammation, their historical use and the presence of bioactive compounds support their potential as a natural anti-inflammatory agent.

Fig 1. 1 Psidiumguajava plant.

What Is a Buccal Patch?

A buccal patch is a small, adhesive patch that is applied to the inside of the cheek (buccal mucosa) for the controlled release of a drug into the bloodstream. The buccal mucosa has a rich blood supply, which allows for the rapid absorption of medications through the tissues of the mouth.

Key Features of Buccal Patches

1. Non-invasive: Unlike oral pills or injections, buccal patches are placed inside the cheek, offering a non-invasive method of drug delivery.
2. Controlled Release: The patch gradually releases the medication into the bloodstream, which provide more consistent drug levels compared.
3. Avoids first-Pass Metabolism: When medications are taken orally, they pass through the digestive system and liver (first-pass metabolism), which can reduce the effectiveness of some drugs. With a buccal patch, the drug is absorbed directly into the bloodstream, bypassing the liver and improving its effectiveness.
4. Ease of Use: These patches are easy to apply and can be discreet, offering a convenient way to take medication without swallowing pills.

Biological Sources of Psidium guajava leaves

Guava leaves (from Psidium guajava) are known for their medicinal properties and are derived from the guava tree, which is native to tropical and subtropical regions of Central America, South America, and the Caribbean. Guava leaves are widely used in traditional medicine and are also explored for their potential health benefits in scientific research.

Chemical Constituents

Psidium guajava (guava) leaves contain a variety of bioactive chemical constituents, contributing to their medicinal properties.

These include: Flavonoids, Tannins, Essential Oils (eugenol, caryophyllene, α-pinene), Terpenoids

Therapeutic Activity

- Antioxidant Activity

- **Anti-inflammatory Activity**
- Antimicrobial and Antiviral Activity

- Anti-diabetic Activity
- Gastrointestinal Health

- **Analgesic** (Pain-Relieving) Activity
- Anticancer Activity

1.2 Control Drug Delivery

A control drug delivery system is aimed at releasing the correct dose of therapeutic direction in the desired zone and during the required period of time. This allow maximizing the effect of the therapeutic and minimizing the possible side effect controlled drug delivery system can include the maintain the drug administration, optimal use of the drug in question and increased patient compliance. The ideal drug delivery system should be inert, biocompatible, mechanically strong, comfortable for the patient, capable of achieving high drug loading, safe from accidental release, simple to administer and remove and easy to fabricate and sterilize. The goal of many of the original controlled release system was to achieve a delivery profit that would yield a high blood level of the drug over a long period of time, the key point with traditional drug administration is that the blood level of agent should remain between a maximum value, which may represent a toxic level and a maximum value, below which the drug is no longer effective.

Controlled drug delivery system are smart multifunctional platforms that are designed to improve the pharmacological activity of a therapeutic agent or active pharmaceutical ingredient by increasing the drug solubility, stability, and bioavailability reducing side effects and enhancing the selective delivery of drug with a predictable rate and mechanism to specific organ /tissue/ cell. Guava leaves, derived from the tropical guava tree (Psidium guajava), have been utilized for centuries in traditional medicine due to their remarkable health benefits. One of the most notable properties of guava leaves is their potent anti-inflammatory effect. Rich in antioxidants and various bioactive compounds, these leaves have been shown to help reduce inflammation in the body, making them a valuable natural remedy for a range of ailments. Research suggests that the phytochemicals present in guava leaves can inhibit inflammatory pathways, providing relief from conditions such as arthritis, digestive disorders, and skin irritations. As interest in natural remedies continues to grow, guava leaves stand out as a promising option for those seeking to harness the power of nature to support their health and wellbeing.[1]

A controlled drug delivery system (CDDS) is an advanced pharmaceutical technology designed to release therapeutic agents in a controlled and sustained manner over a specific period. Unlike traditional drug delivery methods, which may result in rapid fluctuations in drug concentration, CDDS aims to maintain a consistent and optimal drug level at the target site, improving therapeutic efficacy while minimizing side effects. These systems are engineered to deliver drugs at a predetermined rate, often in response to specific biological factors such as pH, temperature, or enzy activity.

CDDS can significantly enhance the treatment of chronic diseases, cancer, and other conditions that require long-term or continuous medication. By reducing the frequency of dosing, improving drug absorption, and offering targeted delivery, controlled drug delivery systems increase patient compliance and overall treatment outcomes. Technologies used in CDDS include polymers, liposomes, micelles, nanoparticles, and hydrogels, all of which help in precisely controlling the drug release profile.

(CDDS) is an innovative approach in modern medicine aimed at optimizing the administration of drugs by regulating the release rate and targeting the drug to specific sites within the body. Traditional drug delivery methods often result in fluctuating drug concentrations, which can lead to reduced therapeutic effectiveness or adverse side effects. CDDS technology allows for a more precise and sustained release, improving drug bioavailability, minimizing side effects, and enhancing overall treatment efficacy. These systems can be designed to release drugs over extended periods or in response to specific physiological cues, such as pH or temperature, making them invaluable for treating chronic conditions or diseases requiring continuous location.

A controlled drug delivery system (CDDS) represents a breakthrough in pharmaceutical technology, designed to provide a controlled and sustained release of therapeutic agents, improving the therapeutic efficacy of drugs while minimizing side effects. Traditional drug administration methods often lead to fluctuations in drug levels within the body, whereas CDDS ensures that medications are delivered at a consistent rate over time, enhancing patient outcomes. These systems are highly versatile, capable of releasing drugs in response to various physiological conditions, and are particularly useful in the treatment of chronic diseases, cancer, and pain management.

In the realm of modern drug delivery, a controlled drug delivery system (CDDS) offers a sophisticated solution for addressing the challenges of conventional therapies. By delivering drugs in a predictable and controlled manner, CDDS optimizes drug absorption, minimizes the risk of side effects, and improves patient compliance. These systems can be engineered to release therapeutic agents continuously or in response to specific biological signals, providing sustained effects over extended periods. With innovations in materials such as polymers, nanoparticles, and hydrogels, CDDS offers a highly customizable approach for treating a wide range of medical conditions, including chronic illnesses and targeted therapies.

1.2.1 TWO TYPES OF CONTROL DRUG DELIVERY SYSTEM

1. Sustained Release Control Drug Delivery System

A sustained release are the drug delivery system that achieve slow release of the drug over an extended period of time after administration of a single dose.

In other words, the drug release is simply extended in time [e.g] the rate and duration are not designed to achieve a particular profile. Sustained steadily over a long period of time.

2. Controlled Release Drug Delivery System

Controlled release are the drug delivery system which maintained constant level of the drug in the blood and tissue for the extended period of the time. It implies a predictability and producibility in the drug release kinetics.

Controlled release drug delivery system in a way of designing and formulating in a medicine so that the release of drug from it occur in controlled manner and desirable manner.[2]

1.2.2 ADVANTAGES OF CONTROLLED DRUG DELIVERY

- **Reduced Side Effects**: By controlling the release, drug concentrations remain within the therapeutic window, reducing the risk to toxic effects or side effects.
- **Improved Compliance**: Fewer doses are need which can be improve the patient adherences to the treatment region.
- **Targeted Action**: Drug can be directed to specific area of the body, making treatments more efficient.
- **Continue Drug Release**: Constant therapeutic level can be maintained avoiding peaks and troughs associated with traditional dosing.
- **Enhanced bioavailability:** Controlled system can improved the bioavailability of poorly

absorbed drugs bypassing digestive tract or releasing the drug in manner that increases its absorption.

- **Improved therapeutic outcomes**: By controlling relapse rate of a drug it ensure that a constant and optimal concentration is maintained in the bloodstream, leading to more consistent therapeutic effect.
- More uniformity in effect.
- Reduction in total drug usage will compared with conventional therapy.
- Stabilization of medical condition (because of more uniform drug levels)
- Interprets the movement of drugs across biological membranes and ensure a better understanding of drug transport methods.
- Favourable reach in plasma levels.
- Breached side effects and adverse reaction.[3]

1.2.3 DISADVANTAGES OF CONTROLLED DRUG DELIVERY

- **Limited Monitoring**: Lack of immediate feedback with control release system particularly those that are long acting are implanted, there's limited immediate feedback how to the body is reacting to the drug . This can complicated monitoring and adjustment by the healthcare providers.

- **Cost**: The development and use of advanced controlled delivery system often require more costly material and technologies which can increase the over all cost of treatment for patient and healthcare system.

- **Regulatory challenges:** Since controlled drug delivery systems can involve innovative technologies, they may face more stringent regulatory hurdles during development and approval. This can delay their availability on the market.

- Not all drugs suitable for formulation into CR dosage form.

- Delay in onset of drugs action.

- Increased potential for first pass metabolism.

- Possible toxicity or non-biocompatibility of the material used.[4]

1.2.4 IDEAL CHARACTERS OF CONTROL DRUG DELIVERY

1. Bio compatability

- **Non-Toxic** : The delivery system itself should not cause any adverse immune response or toxicity in the body
- **Safty Material**: Material used in drug delivery system (eg: nano particle polymer) should be safe for human use and should not elicit harmful reactions.

2. Controlled And Sustained Releases

- **Regulated Release**: The system should be able to release the drug at a consistent rate over and extended period to maintain the therapeutic level blood-stream without causes peaks or throughs.
- Long Lasting Effect: Ideally the system should minimize the frequent administration, improving patients compliance and conveniences.

3. Cost Effectiveness

Affordable: DDS should be affordable both in the terms of production and patient caused ensuring accessibility for a wide range bot the people particular in low resource setting.

4. Ease Of Administration

- **Convenience**: DDS should be easy to administer, wether orally, intravenously topically or via other methods
- Hormonal drugs, such as birth control or hormone replacement therapies, can be delivered.

Patient Friendly: it should be non-invasive or minimally invasive and required Effort on the part of patient, ideally improving adherence to the treatment.

5. Mulit Funcationality (Optional) **Therapeutic And Diagnostic**: Some drug delivery system can also serve diagnostic purpose (eg: Imaging or biomarker detection) while delivering the drug allowing for personalized plants and monitoring.[5]

1.2.5 APPLICATION

Chronic disease management

- **Diabetes:** Insulin pumps and patches are examples of controlled delivery systems that release insulin in a controlled manner, helping people with diabetes manage their blood sugar levels effectively.

- **Pain Management**: Controlled-release formulations of painkillers (like morphine) are used to provide sustained pain relief over time, which is particularly useful for chronic conditions.[6]

Hormonal Therapy

Hormonal drugs, such as birth control or hormone replacement therapies can be, Delivered in a controlled manner to maintain constant levels in the bloodstream, ensuring efficacy and reducing the need for frequent doses.

- **Vaccine**

Controlled release systems can be used in vaccine delivery to ensure slow, sustained release of the antigen, leading to enhanced immune responses and prolonged immunity.

- **Ocular Drug Delivery**

For eye diseases (like glaucoma), controlled release systems can be used in implants, eye drops, or contact lenses to provide a steady supply of medication, reducing the frequency of administration and improving patient compliance.[7]

- **Neurological Disorder**

Medications for neurological disorders (such as Parkinson's disease or epilepsy) can be delivered in a controlled manner to maintain a stable level of the drug in the brain, improving the consistency of treatment effects.

- **Gene Therapy**

Controlled release systems can be used to deliver gene therapy agents, like DNA or RNA, to specific cells, ensuring that the therapeutic agents are released gradually for sustained gene expression.

- **Biotheraputic**

In orthopedics, controlled release is used for drugs that aid in bone regeneration or prevent infections. For example, implants or scaffolds with drug reservoirs release therapeutic agents slowly to improve bone healing.

- **Inhalation Therapy**

For respiratory diseases like asthma or chronic obstructive pulmonary disease (COPD), controlled drug delivery systems like inhalers or nebulizers release medication in a controlled

manner to the lungs, providing sustained relief and improving treatment efficiency.[8]

BUCCAL DRUG DELIVERY SYSTEM

2.1 INTRODUCTION

The buccal mucosa line the inner check ad buccal formulation are placed in mouth between the upper gum and check to treat local and system condition. It is richly vascularized and more accessible for the administration and removal of dosage from. Additionally buccal drug delivery has highly patient acceptability compared to other non oral route of drug administration. Extensive first pass metabolism and drug degradation in the harsh gastrointestinal environment can be administering the drug via buccal route. After absorption, the drug is transported facial vein which then drains into general circulation via jugular vein, by passing the liver and there by sparing the drug from first pass metabolism. Buccal route provided one of the potential route for typically large, hydrophilic unstable protein, oligonudiotides and polysaccharide as well as conventional small drug.[9]

2.2 POLYMER

Hydrophilic polymer are commonly used in buccal drug delivery system as hydrophilic matries due to this compatibility and suitability to the buccal region.

Hydrophilic matures are dispersion of drug and other excipient incorporated in a hydrophilic polymer which swells upon water contact. Bioadversive or controlled drug delivery system various polymers are utilized to ensure sustained release, targeting, and bioavailability of the drug. Some of common polymer used in buccal drug delivery system include natural polymer.

2.2.1 Natural Polymer

1. Gelatin

Natural polymer that can be used to buccal patches, gel, and films.

2. Chitosan

Derived from chitin, it often used for it biocompatibility, musoadhesive properties and ability to form films for buccal drug delivery.

3. Gellan gum

Nature polymer often used for controlled release due to it’s ability to formhydrogel.[10]

2.2.2 Synthetic Polymers

1. Polyvinyl Alcohol

A synthetic polymer used to create films and matrices for buccal delivery.

2. Polyethylene glycol

Often used to improve the solubility and bioavailability of drug in buccal delivery mucoadhesive polymer.

2.3 ADVANTAGES

- Excellent accessibility
- Patient compliance
- Avoids first pass metabolism and involved robust mucosa
- Prolongation of contact time with mucosa
- Easy to administration

2.4 DISADVANTACES

- Complex installation Applying patch can require some technical knowledge and careful installation. If not done properly it can disrupt the buccal setup
- Compliance issues Uses may forget to apply the patches correctly or they may not be comfortable with the process leading to lower adherence to treatment regimens.[11]
- The drugs which are unstable at buccal pH can not be administrated.
- The drug requires with the small dose can only be administrated
- Eating and drinking may become restricted.
- Those drug which are passive deflation can only be adminstrated by this root.
- The drug which have bitter or unpleasant taste or an obnoxious odour or irritated the mucosa can not be administrated by this root.[12]

2.5 USES OF BUCCAL DELIVERY

- The oral cavity can be used for local and systemic therapy.
- Examples of local therapy would be the treatment of oral infections, dental caries, mouth ulcers, stomatitis, gingivitis etc.
- The buccal route is of particular interest with regard to the systemic delivery of small molecules that are subjected to first-pass metabolism.[15]

2.6 ENVIRONMENT OF BUCCAL MUCOSA

- The cells of the oral epithelia are surround by an intercellular ground substance, mucus.
- The oral cavity is marked by the presence of saliva produced by the salivary glands.
- Mucus which is secreted by the major and minor salivary glands as part of saliva.

1. Role of Saliva

- Continuous mineralization / demineralization of th tooth ename.
- Protective fluid for all tissues of the oral cavity
- To hydrate oral mucosal dosage forms

2. Role of Mucus

- Bioadhesion of mucoadhesive drug delivery systems
- Made up of proteins and carbohydrates
- Cell-cell adhesion
- Lubrication.[16]

2.7 BIOADHESION

Bioadhesion can be defined as the ability of a drug carrier system (synthetic or biological) to adhere to a biological substrate for an extended period of time.

- The biological surface can be epithelial tissue (skin) or the mucous coat on the surface of a tissue.
- If the adhesive attachment is to a mucous coat, the phenomenon is referred to as mucoadhesion.

2.8 MECHANISM FOR BIOADHERSION

Bio adhesion is an interfacial occurrence that occurs when two materials, in which any one should be biological, is kept intact together because of interfacial force. Adherence may occur between artificial materials, biologicals like the adhesion of polymer-copolymer to biological membrane. Bio adhesion is greatly influenced by the polymers hydration. Some critically know degree of hydration is required for optimal bio adhesion. The active adhesion site may not fully be freed and ready for interacting if there is partial hydration. Polymer is bound to mucosal tissue contain of much layers in the process of mucoadhesion. The mechanism go polymer-mucus interactions leading to mucoadhesion has been the subject of several theories. Hydrogen bond between polymer chain dissociate during hydration. The interaction between the polymer and the water becomes stronger than between the polymer and the other

polymer.[13]

Importance of Bioadhesion in Drug delivery Bioadhesion technique used to optimize either local or systemic drug delivery for various routes of administration by.

a. Extension of Contact Time

Prolong contact time of a drug delivery system to biological tissue can improve drug therapy.

b. Localization of Drug Delivery System

Some drugs are preferentially absorbed in a specified region "window for absorption". e.g., iron, riboflavin, chlorothiazide.

Theories of mucoadhesion, depending on the chemical nature of adhesive/ adherent combinations.

1. Diffusion Theory

The diffusion theory describes interpenetration of the mucoadhesive (polymer) and substrate (mucin) to a sufficient depth and creation of a semipermanent adhesive bond by physical entanglement which is dependent on the molecular weight of the polymer and flexibility and chain segment mobility of the mucoadhesive polymer.

2. Adsorption Theory

It is a surface force where surface molecules of adhesive and adherent are in contact. According to adsorption theory, bioadhesive systems adhere to tissue due to bond formation. Primary Chemical Bonds

- Many bioadhesives can form primary chemical covalent bonds with functional chemical groups in mucin.
- Aldehydes and alkylating agents can readily react with amino groups and sulfhydryl groups.
- Acylating agents react with amino and hydroxyl groups of serine or tyrosine.

3. Mechanical Theory

The adhesive flow into the pores and interstices to create mechanical embedding embedded adhesive solidifies and becomes inextractable. The mechanical theory depends on irregularities of the surface and Highly fluid adhesives which are able to penetrate into the cracks and crevices of the adherent create mechanical embedding.[17]

GINGIVITIS

Gingivitis is an inflammation of gum cause primarily by the accumulation of pleque a sticky, colourless film of bacteria that forms on yours teeth and gum. When it's usually caused by poor oral hygiene that encourage plaque to form on teeth, irritating the gum tissue. Gingivitis is a form of gum disease characterised by reversible gingival inflammation without destruction of tooth supporting tissues, periodontal ligament or bone.[18]

3.1 CLASSIFICATION

A. Plaque-induced gingival diseases

B. Non-plaque-induced gingival disease Plaque-induced gingival diseases.

1. Gingivitis Associated with Dental Plaque Only.

- Without local contributing factors
- With local contributing factors

2. Gingival Diseases Modified by Systemic Factors.

3. Gingival Diseases Modified by Medications.

4. Gingival Diseases Modified by Malnutrition.

Non-Plaque-Induced Gingival Lesions

1. Gingival Diseases of Specific Bacterial Origin.
2. Gingival Diseases of Viral Origin.
3. Gingival Diseases of Fungal Origin.
4. Gingival Diseases of Genetic Origin.
5. Gingival Manifestations of Systemic Conditions.
6. Traumatic Lesions.
7. Foreign-Body Reactions.

Classification according to course and distribution

- Acute Gingivitis
- Recurrent Gingivitis
- Chronic Oingivitis

ACUTE GINGIVITIS

- It is of sudden onset and short duration and can be painful

- A less severe from of acute condition is called sub- acute

RECURRENT GINGIVITI

Reappears after fuminated by a treatment by or dissapptarings pontanrously.

CHRONIC GINGIVITIS

- Sow in onset and long durations is painless
- Inflammation persists or resolves and normal areas become inflammated.[19]

3.2 COMMON SYMPTOMS

- Red, swollen or bleeding gums, especially when brushing or florsing
- Bad breath
- Receding gums
- Plague buildup
- Poor oral hygiene
- Smoking or chewing tobacco
- Poor nutrition
- Certain health condition

3.3 CAUSES

- Build-up of bacterial plaque on the teeth, adjacent gingivae, and pockets between teeth and gums, releasing toxins that cause an inflammatory response.
- Build up of calculus contributes to the chronicity of periodontal disease, if plaque is not removed, it form hard mass commonly called tartar, which traps bacteria that cause gingivitis.
- Smoking tobacco
- Faulty dental prosthesis
- Breathing through the mouth
- Local trauma (eg, an overly aggressive toothbrushing technique)
- Dry mouth because of loss of protective effect of saliva
- Vitamin deficiency, especially of vitamin C.[20]

3.4 OTHER CAUSES

- Changes in hormones- Which may occur during puberty, menopause, the menstrual cycle and pregnancy.

- The gingiva may become more sensitive, raising the risk of inflammation.
- Some diseases- Such as cancer, HIV, diabetes are liked to a higher risk of gingivitis
- Family history- Experts say that people who parent (s) has or had gingivitis, have higher risk of developing themself.

3.5 PREVENTION STRATEGIES

Mechanical biofilm removal

- Manual or powered toothbrush: 2-3 times per day for at least 2 minutes
- Interdental hygiene: dental tape or floss and interproximal brushes
- Oral irrigators
- Professional cleaning: removal of calculus • Chemical removal and/or alteration of bio Toothpastes:
- Cetylpyridinium chloric
- Fluoride
- VITIS
- VITES

Mouthwashes

- Chlorhexidine
- Cetylpyridinium chloride

3.6 TREATMENT

- OH instruction and motivation
- plaque control
- Eliminating poor habits: stop smoking
- Professional removal of biofilm: using ultrasound, curettes, polishing
- Improving local and systemic conditions
- (Advanced Periodontal Treatment) allows us to gain access to the root. of heroom for removal of calculus, plaque and diseased tissue.
- Kypeliths or other aids may be also be recommended.
- misaligned teeth or replacement of dental and orthodontic appliances Diagnosis
- Dental exam : A dental or hygienist will check the health of your gums, noting any sings of inflammation or bleeding
- X-ray : In some causes if the dentist suspect a more serious form of gum disease the might take X-ray to check for bone damage.

Marketed available drugs in gingivitis.

- Chlorhexi dinegly conats

This is antimicrobial mouthwash that helps reduce bacteria in mouth and is often prescribed by dentists for gingivitis treatment.

- Antiseptic mouthwash

Products like listerine (containing essential oil like eucalyptol, menthol and thymol) can help control plaque and reduce gingivitis.

- Fluoride toothpaste

It containing fluoride such as colgate or sensodyen, can help reduce ploque buildup and present gum disease progression. Hydrogen peroxid- sometimes recommended as a mouth rinse to reduse bacteria and help heal inflamed gums. Topical steroid creams in rate cases corticosteroid cream may be prescribed for saver inflammation but this is less common.

- Topical gels or paste

Doxycycline (arestin) a topical antibiotics gel often used in conjunction with scaling and root planing (deep cleaning) procedures for treating gum disease, including gingivitis.

- Chlorhexidine gel (c)

Some product delivery C in gel form to target infected gum assay.

- Antibiotics

Amoxicillin or metronidazole in cases where gingivitis by progressed to more severe form like priodontitis oral antibiotics may be prescribed to control bacterial infection.[21]

AIM AND OBJECTIVE

5.1 Guava Leaves (Psidiumguajava)

AIM: To investigate and Evaluate The anti inflammatory properties of quava (Psidiumguajava) leaves and Their potential as a natural Remedy for inflammation - Related condition.

OBJECTIVES

1. Phytochemical Analysis: To identify and quantify the phytochemical constituents present in guava leaves that may contribute to their anti-inflammatory properties.

2. In Vitro Evaluation: To assess the anti-inflammatory effects of guava leaf extracts using in vitro models, such as cell cultures treated with pro-inflammatory agents.
3. Mechanism of Action: To investigate the underlying mechanisms through which guava leaf extracts exert their anti-inflammatory effects at the cellular and molecular levels.
4. Dose-Response Relationship: To determine the dose-response relationship of guava leaf extracts on inflammation markers in relevant biological assays.
5. Comparison with Standard Anti-Inflammatories: To compare the efficacy of guava leaf extracts with established synthetic anti-inflammatory drugs in reducing inflammation.
6. Safety and Toxicity Assessment: To evaluate the safety profile and potential toxic effects of guava leaf extracts in relevant animal models.
7. Potential Applications: To explore the potential applications of guava leaves as a natural remedy for inflammation-related conditions in traditional and modern medicine.

5.2 Alpha pinene

AIM: To investigate the anti-inflammatory properties of alpha pinene in quava (Psidiumquajava) Kaves and Evaluate its potential as a Agent Natural anti-inflammatory.

1. Isolation and Characterization: To isolate and characterize alpha pinene from guava leaves and confirm its purity and identity through chromatographic techniques.
2. Anti-Inflammatory Activity Assessment: To evaluate the anti-inflammatory activity of alpha- pinene using in vitro assays, focusing on its ability to inhibit proinflammatory cytokines.
3. Synergistic Effects: To investigate whether alphapinene exhibits synergistic effects when combined with other phytochemicals present in guava leaves.
4. Mechanistic Studies: To elucidate the molecular mechanisms by which alpha-pinene exerts its antiinflammatory effects, including its impact on signaling pathways involved in inflammation.
5. Comparative Analysis: To compare the antiinflammatory efficacy of alpha-pinene with other known natural anti-inflammatory agents.
6. Pharmacokinetics and Bioavailability: To assess the pharmacokinetics and bioavailability of alpha-pinene when administered in various formulations.
7. Therapeutic Potential: To evaluate the therapeutic potential of alpha-pinene as a natural antiinflammatory agent in preclinical models of inflammation-related diseases.

PLAN OF WORK

- Literature review
- Drug
- Disease
- Excipient
- Dosage form.

- Drug and Excipient profile
- Preformulation studies
- Drug+Excipient - Compatibility
- Trail formulation.
- Evaluation.

1) Physicochemical

* Thickness
* Uniformity of weight
* Tensile strength
* Percent elongation
* Adhesive strength
* Folding endurance
* Moisture uptake test
* Moisture content
* Drug content
* Determination of surface pH

DRUG AND EXCIPIENT

6.1 Drug profile of Psidiumguajava

- DRUG NAME : The Leaves of Psidiumguajava
- SOURCE : Obtained from the guava tree
- SYNONYM : Guava folium
- FORMULA : $C_{10}H_{16}$
- DENSITY : 0.869/cm^3
- MOLAR MASS : 136.24g/mol
- BOILING POINT :156°C

- **STRUCTURE**

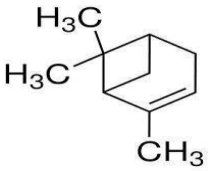


Fig 7.1 Alpha Pinene.

- IUPAC NAME : 2,6,6-Trimethylbicyclo [3.1.1]hep-2-ene
- ROUTE OF ADMINISTRATION : Inhalation, oral, topical
- THERAPEUTIC USE : Anti-inflammatory (cured for Pairs Relief and Swelling)
- PROPERTIES : Anti-inflammatory, Antioxidant and Anti diabetic

6.1.1 Mechanism of action

1. Inhibition of pro-inflammatory pathway Alpha pinene has been shown to inhibit pro inflammatory molecules such as prostaglandins and cytokines which are involved in the inflammatory response.[58]

2. Reduction of nitric oxide production

- Alpha pinene can decrease the production of nitric oxide (ND) a molecule that can contribute to inflammation in the body.
- Alpha pinene helps mitigate inflammation damage.[59]

6.1.2 Safety and toxicity

- Alpha pinene is generally regarded as safe for topical use
- The large amount of alpha pinene can cause toxicity and adverse effect such as haw, vomiting or dizziness.

Skin irritation: It can cause skin irritation or allergic reactions especially when used undulate.[60]

6.1.3 Uses of Alpha-Pinene

- Insect Repellent

Alpha pinene is used in natural insects repellents due to it’s ability to repel mosquitoes and other insects, it’s often found in essential oil or sprays that offer a natural alternative to chemical insect repellent like DDET.

- Essential oils

Often alpha-pinene is incorporated into natural products such as bag sprays, candles or diffusers to help keep insects at bay.[22]

- Flavoringagent

Food and beverage, due to its piney, fresh aroma, alpha pinene is used a flavoring agent in the food and beverage industry, particularly in mint-flavored products and beverages like tea or soda.

- Perfume and fragrance industry Fragrance ingredients

Alpha-pinene is used in the fragrance industry for its pine-like scent, which is refreshing and clean. It can be found in perfumes, air fresheners.

- Industrial

Alpha-pinene is used as a solvent in various industrial application such as in paint thinners, varnishes and cleaning agents. It helps dissolve versos, oil and other substances.[23]

6.2 HPMC

Characters

Hydroxy propyl methyl cellulose is a cellulose ether widely used in drug formulation due to its biocompatively, uncharged nature solubility in water and thermoplastic behavior.[68]

Properties

- HPMC is a white or affects odorless, tasteless powder soluble in water and someorganic solvents
- Viscosity, gelatine and forming ability.[24]

Source

Hydroxy propyl methyl cellulose is a cellulose ether derived from the wood pulp of soft wood trees scuhaspine and spruce. It is also obtained from cotton linters.

Uses

- Tablet binding
- Film coating
- Controlled-release matrix formulation
- Disintegration

- Viscosity modification
- Drug delivery system formulation.[25]

ADVANTAGES

- HPMC improves the work ability and consistency of construction materials enhance their performance and durability
- In pharmaceutical it aids in the controlled release of active ingredients, ensuring optimal drug delivery

DISADVANTAGES

- HPMC is derived from cellulose, which is a nature polymers. As a result, HPMC can lie hydrolyzed by enzymes, bacteria and others
- Some surfactants and other ingredients make HPMC incompatible with others
- HPMC can be difficult to remove form formulations.[26]

Stability

HPMC can improve the physical stability of the product by adjusting the viscosity of the detergent. The thickened detergent is more structured and can prevent the occurence of unstable phenomena such as phase separation, precipitation and gelation.[27]

APPLICATION OF HPMC IN PHARMACEUTICAL INDUSTRY

- HPMC not only has the properties of other cellulose of ethers such as thickning, dispersion, emulisification, adhesion, film forming, moisture retention and providing protecting colloids effects, but also better solubility in organic solvent then methy cellulose and hydroxyl ethyl cellulose.

- Pharmaceutical industry, hydroxypropyl methyl cellulose, is non toxic and safe Pharmaceutical Excipient

- It can also act as the adhesive of plastic bandage

- In recent year, hydroxypropyl methyl cellulose has been used as the matrix, adhesive, frame material, the porogen, the film forming material or coating material. Furthermore, it has been widely used in development of new formulation such as sustained released tablet, a variety of coating sustained release formulation, suppositories, ophthalmic preparation and sustained- release suppositories.[28]

6.3 GLYCERIN

Characteristics

It is colourless, odorless and viscous liquid with a sweet taste Chemical formula: $C_3H_8O_3$ Boiling point: above 290°C or 554°F

Viscosity : Syrup like consistency Sources

- Vegetable source
- Animal source
- Synthetic glycerin
- Fermentation Characters

Glycerol is a simple triol compound. It is a colorless, odorless, viscous liquid that is sweet-tasting and non-toxic. The glycerol backbone is found in lipids known as glycerides. It is also widely used as a sweetener in the food industry and as a humectant in pharmaceutical formulations. Because of its three hydroxyl groups, glycerol is miscible with water and is hygroscopic in nature. Modern use of the word glycerine (alternatively spelled glycerin) refers to commercial preparations of less than 100% purity, typically 95% glycerol Properties.

Glycerin is a simple polyol – having simple hydroxyl groups in its chemical structure. It is a sugar alcohol. It has a high viscosity and has greater resistance and opposition to flow against the surface.

It is odourless and colourless. It is sweet to taste and is non-toxic.

SOURCES

1. Glycerin can be obtained from various sources
2. Fermented foods and beverages, including beer, honey, vinegar, wine and wine vinegar.
3. Fats and oils, such as coconut, palm, and soybean oils and fats.
4. Tallow (beef or mutton fat) combined with water and heat and then chilled.
5. Petroleum-based synthetic glycerin produced from propylene.
6. Cane or Glycerin (also known as glycerol) has various uses in different fields
7. Corn syrup sugar

USES

- Glycerin (also known as glycerol) has various uses in different fields.
- Cosmetics: Used as a moisturizer and added to many cosmetic products.
- Medicine: Found in cough syrup and liquid medicines.
- Food: Used as a sweetener and to thicken and preserve some foods.
- Industrial applications: Used in antifreeze, cement, textiles, and waxes

ADVANTAGES

- It can be used as a cleanser.
- It can be used as a toner.
- It is a wonderful skin moisturizer.
- Applying the diluted version makes hands smooth.
- It helps retain moisture in the skin and thus nourishes dry skin.
- It plays an important role in cell maturation.
- It cures oily skin problems like pimples, acne and blackhead.
- It is used in cough syrups to reduce irritation of the throat
- Non-toxic : It is safe for consumption
- Preservative properties : It can help preserve the texture and shelf-life of products
- Solvent for active ingredient : In pharmaceutical and cosmetics, it helps dissolve and deliver active ingredients.

DISADVANTAGES

- In rare cases, people have experienced allergic reactions to ingesting and applying glycerol.
- It can cause skin rash and irritation or allergic reaction
- Some people may also experience burning or stinging when applied to their eyes.
- High viscosity- thick consistency
- Not ideal in hot and dry climates Stability.

Glycerin is generally chemically and microbiologically stable if kept near ambient temperatures1. It is very stable and can be easily stored under normal temperature 2.

However, product stored in vented tanks may increase in water over time due to the hygroscopic nature of glycerin1. The shelf life of glycerin is 24 months when stored below 100°F in a closed container.[29]

6.4 PROPYLENE GLYCOL

Characters

- Propylene glycol is viscous, colourless liquid
- It is mostly odorless and has a faintly sweet taste
- It is contain alcohol group
- Hygroscopic nature
- Low freezing point
- High boiling point Properties
- Colourless liquid
- Relatively viscous
- No odour
- Slightly sweet taste
- Non toxic.[30]

Sources

- Treating propylene oxide with water
- Direct hydrolysis of propylene oxide with water
- The chlorohydrin process or per oxidation starting with propylene
- Natural gas, petroleum, or vegetable sources.[31]

Uses

- As a chemical feed stock for the production of unsaturated polyester resin
- As a food additive and a preservative that improves the texture and moisture of foods
- As a solvent and an emollient for medicines, cosmetics, paints and varnishes.[32]

ADVANTAGES

1. An anticaking agent, helping to prevent lumps from forming in food
2. A solvent in food flavorings, helping to dissolve and mix ingredients in them
3. A dough strengthener
4. A way to improve flavors
5. A preservative, its antimicrobial properties help to kill or prevent the growth of microorganisms like bacteria and mold.A food thickener 6. A method to help retain moisture in food.[33]

Stability

[Stability and storage condition] It is very stable at room temperature, but is oxidized when left open at high temperatures (above 280 °C); has a chemical stability after mixing with 95% ethanol or water; can be sterilized by autoclaving or sterile filtration.

Boiling point: 187 °C (lit.) Density: 1.036 g/mL at 25°C (lit.) Melting point: 60°C (lit.) vapor density: 2.62 (vs air).[34]

6.5 EXTRACTION PROCEDURE FOR PSIDIUMGUAJAVA

Sample Preparation

- Collect fresh or dried Psidiumguajava plant material (e.g., leaves, fruits, stems).
- Wash fresh material thoroughly to remove dirt or contaminants.
- Grind the material into a fine powder using a mortar and pestle or grinder.

Solvent Selection

- Choose a solvent depending on the target compounds
- For hydrophilic compounds: Water or ethanol.
- For lipophilic compounds: Ethanol, methanol, or acetone.

Extraction

- Maceration Method (Simple Extraction)
- Soak the ground plant material in the chosen solvent in a container (e.g., beaker or jar).
- Stir the mixture occasionally and let it sit for 24-48 hours at room temperature or under mild agitation.
- Soxhlet Extraction (for continuous extraction):
- Place the plant material in a Soxhlet thimble and attach it to the Soxhlet apparatus.
- Add the solvent to the round-bottom flask of the Soxhlet extractor.
- Heat the solvent to initiate the extraction, allowing the solvent to repeatedly wash the plant material and condense back into the flask.
- Continue the extraction for 4-6 hours.

Filtration

- After extraction, filter the mixture using filter paper to separate the liquid extract from the plant residue.

Concentration (Optional)

- Remove the solvent by evaporation (using a rotary evaporator or gentle heat in a fume hood) to concentrate the extract.

Storage

- Store the final extract in amber bottles, protected from light and air, in a cool, dry place or refrigerated.

6.6 IDENTIFICATION TEST FOR ALPHA PINEN

Hpmc 300 mg +water 7ml + 0.15 ml+ 1 ml glycerin Infrared Spectroscopy (IR)

Purpose: IR spectroscopy can provide information on the functional groups present in alpha-pinene. Infrared (IR) spectroscopy is a powerful tool for identifying organic compounds like alpha- pinene based on their characteristic absorption bands corresponding to vibrational modes of atoms and functional groups in the molecule.

Procedure: The sample is exposed to infrared radiation, and the absorbance at different wavelengths is measured.

Identification: Key functional group stretches in alpha-pinene include: C-H stretch (aromatic or aliphatic) around 2960 cm-1

C=C stretch near 1640 cm-1

C-O stretches may appear around 1050 cm-1.

6.7 PREFORMULATION STUDIES

Preformulation testing is the first step in the rational development of dosage forms of drug substance. It can be defined as an investigation of the physical and chemical properties of the drug substance alone and when combined with excipients. The overall objective of reformulation testing is to generate information useful to the formulator stable and bioavailability dosage forms that can be man produced.

The following preformulation studies are carried out

- Physical appearance
- Solubility
- Melting point

6.7.1 Physical appearance Colour

Asmallquantity of psidiumguajava was taken in a test tube and viewed in well illuminated place.

Taste and odor : Very less quantity of psidium guava was used to get taste with help of tongue as well as smelled to get the odour.

Solubility: The spontaneous interaction of two or more substance to form a homogeneous molecular dispersion is called as solubility.

The solubility of psidiumguajava was studied in various solvents. Psidiumajava was suspended separately in a ml of different solvents at room temperature in tightly closed test tubes and shakes on wrist action. The solubility profiles of psidiumgavajava in various solvents are shown in the table:

The approximate solubility's of substance are indicated by terms in the accompanying.

Table: 6.1 Standard solubility profile.

Descrip-ve term	Parts of solvent required for 1 part of solute
Very soluble	Less than 1
Freely Soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Very slightly soluble	From 1000 to 10,000
PracIcallyinsoluble (or)insoluble	Greater than or equal to 10,000

6.7.2 Preparation of buccal patch of psidiumguajava

Psidiumguajava buccal patch was prepared by solvent casting method. The film was prepared in petriplate had a diameter of 7.6 cm with 6 ml capacity. The composition of polymer keeping the total 360mg in the buccal patch. The polymeric solution were prepared using water. The polymeric solution was added to the drug psidiumguajava. The plasticizer and glycerin were mixed and stirred well to get homogenous solution. The resulted uniform solution was casted on the mould and air dried for 24 hours. After 24 hrs the dried films were taken out and stored in desiccators for further studies.

Optimization

Before obtaining the appropriate formulation, various trails were made with respect to solvent, plasticizer and polymer concentration to get a buccal patch having good film

characteristics like uniform thickness, uniform weight, homogenous drug dispersion and optimum tensile strength. The obtained patch was visually compared with a commercially available buccal patch.

When the amount of polymer is less than 0.3 g or greater than 0.4 g the folding endurance of the patch was affected. If the quantity was less than 0.4 g, handing of the patch will affected and if it is greated than 0.4 g, the patch become thick or break with insignificant tensile strength.

0.05 ml of glycerine was added as plasticizer and to produce flexible patch without having major influence on their release property.

Table 6.2 Optimized Formula.

S. No.	Ingredence	T1	T2	T3
1.	Psidiumguajava (mg)	0.15	0.15	0.15
2.	Polymer (hpmc) (mg)	300	300	300
3.	Water (ml)	5	5	5
4.	Propyelglycol (ml)	1	1	1
5.	Glycerine	0.15	0.15	0.15

Fig 6.1 Physicochemical evaluation of Psidiumguajava.

Table 7.3 Optimizing of drug and polymer.

S. No	Ingredients	T1			T2			T3		
1	Drug (mg)	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
2	Polymer (mg)	300	300	350	350	300	300	300	300	350
3	Water (ml)	5	6	7	5	5	5	5	6	6
4	Glycerine (ml)	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
5	Proplylneglycol (ml)	1	1	1	1	1	1	1	1	1

6.7.3 Physicochemical evaluation of psidiumguajava coded buccal patch

Formulation films were subjected to preliminary evaluation tests. Films with any imperfections, entrapped air, or differing in thickness, weight (or) content uniformity were excluded from further studies.

Uniformity of weight

This was done by weighing five different patches if individual batch taking the uniform size at random and calculating the average weight of three. The tests were performed on strip which was dried at 60 °C for 4 hrs prior to testing. The result is shown in table:

Thickness of the patch

The thickness of the patch was assessed by using digital vernier caliper at different point of the patch. From each formulation three randomly selected patches were used. The average value for thickness of a single was determined. The result are shown in table.

Drug content determination

The patch were taken added to a beaker containing 100ml of phosphate buffer saline Ph 7.4. The medium was stirred magnetic bead for 5 hrs. The solution was later filtered and analyzed for drug content with proper dilution at 360nm spectrophotometrically. The result are shown in table.

Folding Endurance

This was determined by repeatedly folding one patch at the same place till it broke. The number of times the patch could be folding at the same place without breaking gave the value of folding endurance.

Percentage Moisture uptake

The patch of psidium guajava were weighed accurately and place in desiccators containing aluminum chloride. After 24hrs, the patch were taken out and weighed. The percentage moisture uptake was calculated as the difference final and initial weight.

With respect to initial weight. It is calculated by using following formula.

$$\text{Percentage moisture content} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Precentage Moisture Content

The patch were weighed and kept in desiccators containing calcium chloride. After 24 hrs the patch were taken out and weighed. The percentage moisture content was calculated using the following formula.

$$\text{Percentage moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Determination of surface pH

The patch were allowed to swell by keeping them in contact with 1 ml of distilled water for 2 hrs at room temperature and pH was noted down by bringing the electrode in contact with the surface of the patch, allowing it to equilibrate for1 min. The result are shown in table:

Percent Elongation

When stress is applied, a patch sample stretches and this is referred to as strain. Strain is basically the deformation of patch divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increase. It is calculated by using following formula.

$$\text{Percentage elongation} = \frac{\text{Increase in length of patch}}{\text{Initial length of strip}} \times 100$$

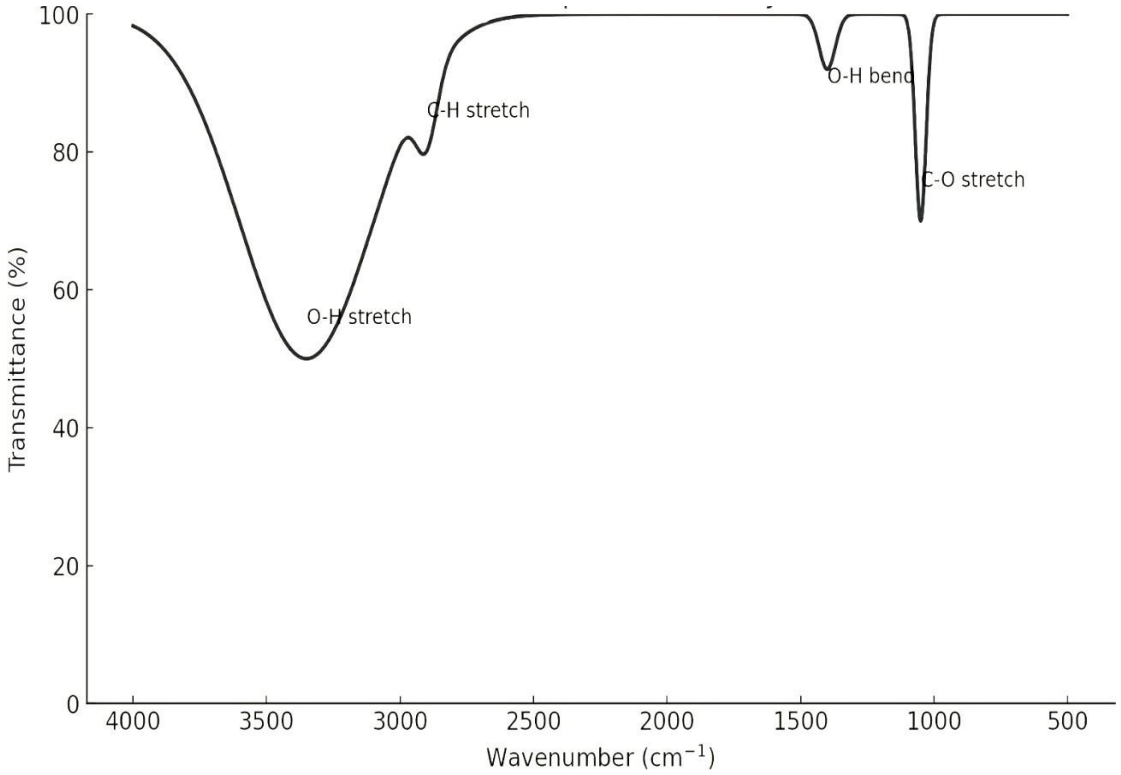
Tensile Strength

Tensile strength is the maximum stress applied to a point at which the patch specimen breaks. Its is calculated by applied load at rupture divided by cross sectional area of the strip as given in the equation below.

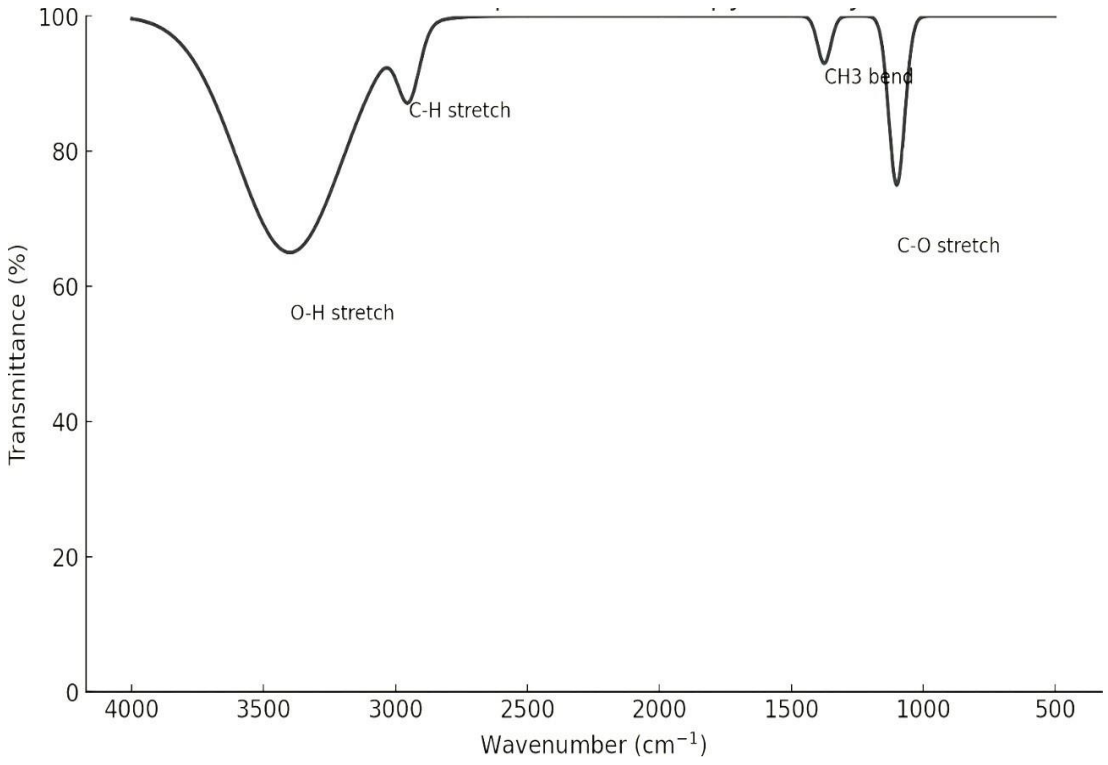
$$\text{Percentage elongation} = \frac{\text{Load at failure}}{\text{strip thickness x strip width}} \times 100$$

RESULT

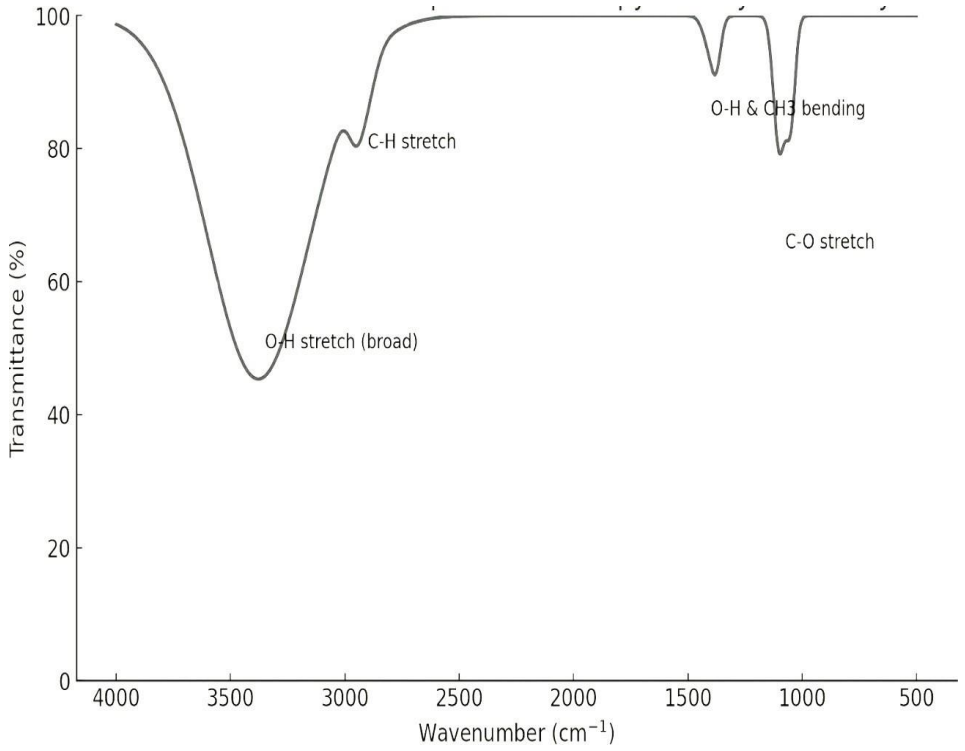
IR Spectrum of Glycerin



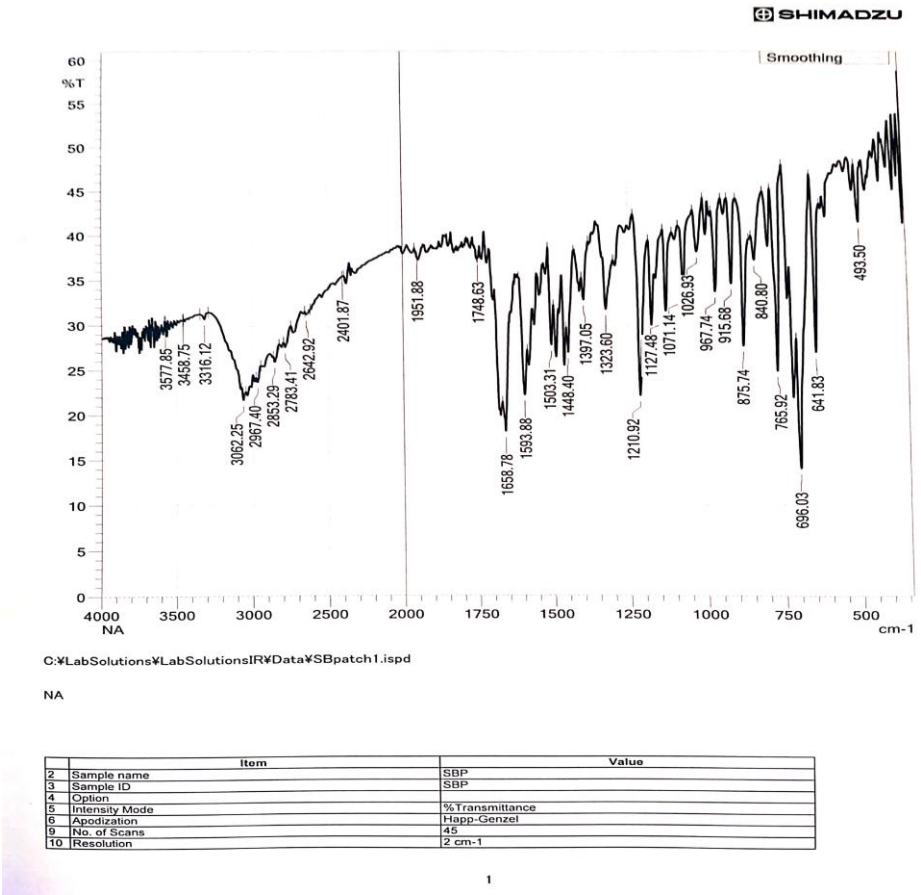
IR Spectrum of Propylene Glycol.



IR Spectrum of Glycerin and Propylene Glycol.



IR Spectrum for the Physiochemical Evaluation of Psidium guajava extract loaded.



	Item	Value
2	Sample name	SBP
3	Sample ID	SBP
4	Option	
5	Intensity Mode	%Transmittance
6	Apodization	Happ-Genzel
9	No. of Scans	45
10	Resolution	2 cm-1

1

Buccal Patch

Table 7.4 Physicochemical evaluation of Psidiumguajava.

Formulation	Information of weight (g)	Thickness (m m)	% drug content	Folding endurance (no's)	% MU	% MC	Surface pH determination	% Elongation (% mm)	TS (kg/mm^2)	Adhesive strength
T1	0.23±	0.17±	95.47	260±0	2.06±	0.572	6.4±0.	66±0.	3.410	10.0±
	0.73	0.52	±0.05	.06	0.54	±0.60	05	52	±0.05	0.63
T2	0.41±	0.29±	95.70	240±0	1.97±	1.642	6.2±0.	78±1.	6.461	21.66
	0.45	0.61	±0.68	.82	1.03	±0.05	72	21	±0.83	±0.15
T3	0.37±	0.35±	96.24	285±0	3.57±	3.271	7.4±0.	130±0	7.660	27.3±
	0.01	0.15	±0.65	.57	0.07	±0.4	11	.21	±0.21	0.29
T4	0.17±	0.24±	95.93	245±0	2.95±	3.431	7.2±0.	118±0	5.410	4.12±
	0.25	0.59	±0.81	.64	0.34	±0.62	9	.92	±0.72	1.04
T5	0.28±	0.11±	96.00	237±0	0.96±	1.481	7±0.6	98±0.	0.800	10.0±
	0.61	0.51	±1.04	.38	0.41	±0.45	5	06	±0.20	0.25

CONCLUSION

- Five patches of Psidiumguajava buccal patches were prepare by solvent casting technique.
- The various formulation parameter, drug-polymer ratios and excipients were optimized to get thin, transparent, smooth, stable and high permeable buccal patches using natural bioadhesive polymers.
- From the optimization, best two formulations psidiumguajava (drug), Polymer (hpmc), water, Propyel glycol, Glycerine were selected based on folding endurance and optimal tensile strength.
- It has been observed that the folding endurance and the handling of the patch is affected when the polymer concentration is less than 0.3 gm or greater than 0.5 gm. The polymer concentration of 0.4gm was found to be compatible for folding and handling. Hence it has been used in our study.
- 0.15ml of glycerine was added as plasticizer and to produce a flexible patch. If the amount exceeds, the film loses its flexibility and become stiff, hence the above two variables were controlled to form a good film.
- The plasticizer diffuses through the patch and softens the polymer particles. This softening promotes latex coalescence and patch formation.
- Among these, the formulation showed maximum % Moisture uptake (3.57), % Moisture content (3.27), Thickness (0.35mm), Folding endurance (265), % Drug content (96.24), Percent Elongation (97), Tensile strength (7.66 Kg mm2), Adhesive strength (21.66).
- The selected formulation visually compared with a commercially available buccal patch (Listerine pocket packs breath freshening patches).
- No significant difference in drug content was observed between the patch among the five.
- formulations. The results indicated that the process employed in the preparation of patch with uniform drug content and minimum patch variables inspection of the polymer used. This indicates the homogenous dispensing of drug during the patch preparation.
- Stability study was performed for period of three months. The physicchemical parameters like visual appearance, color, texture and drug content and drug release were studied. The results

showed that there is no significant change from its initial nature till the period of three months at 40℃ ±2℃/75±5% RH.

- It has been observed in our study along with the other literature reviews, periodontal disease is one of the risk factors for cardiovascular disease. By providing anti inflammatory effects through the buccal patches for the periodontal disease, there will be reduction of 50% of cardiovascular diseases.

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