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Current overview of fast dissolving oral films of clove oil

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ABSTRACT:
In the late 1970s, rapid disintegrating drug delivery systems were developed to address. swallowing issues in geriatric and pediatric patients. Orally disintegrating tablets disintegrated within one minute without chewing or drinking water. Recently, oral fast dissolving films (OFDFS) have gained interest in the market due to their convenience and ease of use. Similar to postage stamps, OFDFs can deliver drugs systemically through intragastric, sublingual, or buccal routes and can be used for local action. Some companies have introduced more robust forms of fast-dissolving drug delivery, which dissolves instantly on the tongue, enhancing drug bioavailability and providing a good mouth feel.Orally fast dissolving films (OFDFS) have been introduced in the market as they are convenient to use .Fast dissolving oral films of clove oil have been use for oral health application like pain relief from toothache . These films are developed for quickly dissolving in the mouth so clove oil gets absorbed rapidly. Clove oil is a natural product obtained from distillation of flower stem and leaves of clove tree syzygiumaromaticum (eg. eugeniaaromaticum or eugeniacaryophyllata). It is a dark brown liquid with a rich aromatic odor and flavor. Clove is expensive and is gaining interest in a large number of pharmaceutical industries . This technology is a convenient way of medication for pediatric , geriatric , bedridden patients , mentally ill patients and also the general population .Fast-dissolving oral films (FDOFs) have garnered considerable attention in pharmaceutical research due to their convenience, ease of administration, and rapid onset of action. Among various active ingredients incorporated into FDOFs, clove oil stands out for its wide-ranging pharmacological properties, including antimicrobial, analgesic, anti-inflammatory, and antioxidant effects. This comprehensive review aims to summarize the recent advances in FDOFs containing clove oil, focusing on formulation strategies, characterization techniques, pharmacokinetic aspects, and clinical applications. Various methods for enhancing the solubility, stability, and bioavailability of clove oil in FDOFs are discussed, including the use of solubilizers, surfactants, and complexation techniques. Additionally, advancements in film-forming polymers, such as natural and synthetic polymers, are explored for their role in optimizing the mechanical properties and drug release kinetics of FDOFs. Furthermore, the review highlights the importance of evaluating the physicochemical attributes and in vitro/in vivo performance of clove oil-loaded FDOFs to ensure their efficacy and safety for oral administration. Finally, potential challenges and future perspectives in the development of FDOFs containing clove oil are outlined, with an emphasis on innovative formulation approaches, scale-up strategies, and regulatory considerations. Overall, this review provides valuable insights into the current state of research and the promising prospects of clove oil-based FDOFs as a novel drug delivery system for oral healthcare and pharmaceutical applications.

Keywords: Clove oil, Anti inflammation, fast dissolving films, Antimicrobial, Biopreservative

I. INTRODUCTION:

Plant-based essential oils (EOs) are abundant in volatile terpenoids and phenolic chemicals. Such substances have the ability to kill harmful germs both directly and when they are in the vapor phase. Commercially, edible films created from produce containing EOs can be utilized to shield food against pathogenic bacterial infection. Clove oil taken by mouth can provide anti-inflammatory effects that help relieve toothache. When applied orally, the rapidly dispersing films soon reach the watery wood at the site of application & then disintegrate to release the drug. Fast-dissolving films are a unique and stable oral formulation and have valuable advantages.Rapidly dissolving films are an attractive quantity for delivery of the poorly soluble triclosan water. Problems with swallowing medications are most evident in pediatric medical licenses and passports, which may not be ready for water to enter.This rapid oral disintegrating system was developed. This dosage typically dissolves or disintegrates within 3 minutes in a dehydrated

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mouth. Oral medications are associated with many problems such as gritty feeling in the mouth, difficulty swallowing medications , fear of swallowing. Clove oil is an effective, local and natural anesthetic.clove oil is probably more appropriate for use in commercial aquaculture situations.Increased use of clove oil may reduce fish survival, distort physiology or outcome. Clove oil is known to destroy cell walls of bacteria.(1,2)

The oral route is the most popular method for administering drugs with a systemic impact since it is non-invasive, flexible, patient-acceptable, and easy to administer. Because they are easier to manufacture, ship, and administer, tablets are the most common dose type. Patients who are elderly, young, queasy, confined to bed, and noncompliant typically have trouble swallowing traditional oral dosage forms and don't take their medications as directed. This issue is thought to have affected 50% of the population, which ultimately raises the risk of noncompliance and inefficient therapy". The majority of people in today's population are old, primarily due to longer life expectancies." Dysphagia, or difficulty swallowing, is a widespread issue that is associated with a number of medical conditions. Illness, radiation therapy to the head and neck, other neurological conditions, and encephalopathy. The most frequent pill complaints are related to size and choking anxiety. The inability to take tablets is particularly noticeable in elderly and young patients, as well as in patients on the go who might not always have easy access to water. To get past this In order to provide juvenile and geriatric patients who have trouble swallowing conventional oral solid dose forms with an alternative to tablets, capsules, and syrups, oral fast disintegrating drug delivery systems were created in the late 1970s. Without the need for water, these dose forms usually dissolve or disintegrate in the mouth in three minutes. Oral fast-disintegrating dose forms are beginning to be recognized as a novel. (3,4)

Rapid dissolving films and mouth-dissolving tablets make up the oral rapid disintegrating dose type. Tablets that dissolve in the mouth are linked to a number of issues, including residues that produce a grittiness in the mouth, a fear of choking, and difficulties swallowing tablets. A new drug delivery technology for the oral distribution of the pharmaceuticals, called as Fast dissolving films,oral dispersible film,mouth dissolving films,oral disintegration film,oral dissolving film, was investigated to overcome the problems with mouth dissolving tablets. Based on the transdermal patch technology, a fast-dissolving oral film was created for drug delivery orally.The patient's tongue or mucosal surface is covered with a postage-stamp-sized thin film that serves as the delivery.(6)

II. MATERIAL AND METHODS :

Natural essential oils include clove oil:

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Numerous species, including Streptococcus aureus . Monocytogenes
and Aspergillus, are inhibited by clove oil., clove e ssential oil is particularly beneficial.
Clove oil's active component, eugenol, is a local an aesthetic and antiseptic.
Eugenol is used to reduce toothache discomfort bec ause it fights mouth microorganisms.
There are some antibacterial and antioxidant proper ties in clove oil.
Dissolving oral films were initially released on the market as personalcare items like dental strips and soap strips and breath fresheners.However, they are made available on the pharmaceutical markets in Europe and the United States for medicinal purpose s.
Due to its flexibility, increased effectiveness of the AP! (ActivePharmaceutical Ingredient), and faster dissolution and disintegration
9than dissolving tablets, fast dissolving oral ffilms are the most advanced form of solid dosage form.
The development of sensitive pharmacological targ ets that might not otherwise be attainable in tablet o r liquid formulations may be made
possible by thin films .
The most popular and traditional method of deliver y, using pills, is oral consumption.(7)

Technology:

Umang Pharmatech Pharmaceuticals has d eveloped Actifims with the incorporation of desirab le actives in personal care to obtain better visual im pact, deliver desirable actives ingredients, and prov ide stable films within the formulation by using the well-
known technology, namely encapsulation and film casting technology.(8)

Principles:

Modified release dosage forms were created and, instead of oral disintegrating tablets, rapid dissolving films were created as a result of advancements in oral drug delivery technology. When inserted in the mouth, oral disintegrating film or strips containing water-dispersing polymer dissolve and release medication for oromucosal absorption, while also retaining the dosage form to be rapidly hydrated by saliva, cling to mucosa, and disintegrate within a few seconds. An other approach with first pass metabolism is oral film technology(9).

Methods for formulation:

They are as follows:
1) Solvent casting method
2) Hot melt extrusion method
3) Rolling method

1) Solvent casting method :

The solvent casting method is the preferred method for formulating fast dissolving buccal films. In this method, the drug and other excipients are dissolved in a suitable solvent after the water-soluble ingredients have been dissolved to form a clear, viscous solution. The two solutions are then combined, swirled, and dried in a Petri plate.

2) Hot melt extrusion method :

Granules, prolonged release tablets, and transdermal and transmucosal medication delivery systems are frequently made via hot metal extrusion. The pharmaceutical sector began using melt extrusion as a manufacturing tool in 1971.

3) Rolling method :

The film by first making a pre-mix, adding an active, and then forming the film. Prepare the film-forming polymer pre-mix. Components, such as polar solvents, aside from drugs Fill the master batch feed tank with pre-mix. It is supplied to the first or both of the mixers through a control valve and metering pump on the Ist. Add the appropriate amount of medication to the mixer. To create a homogenous matrix, blend the medication with the master batch premix. The pan is subsequently supplied with a predetermined volume of homogeneous matrix via the second metering pumps. Finally, the film forms on the substrate and is removed by the support roller.(10)

Phytoconstituents

Compounds	**Compounds**
Eugenol	Antibacterial
Betacaryophyllene	Antibacterial
Eugenyl acetate	Antioxidant, antivirulance, antibacterial

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Clove buds contain 15-20% essential oil, predominantly eugenol, eugenyl acetate, and -caryophyllene, according to research. Vanillin, crategolic acid, tannins, gallotannic acid, methyl salicylate, flavonoids, and triterpenoids are among the other essential oil components. Methyl amyl ketone, methyl salicylate, and -humulene, benzaldehyde, -ylangene, and chavicol are also found in the oil. (11)

Application:

1.Dosing that is simple.
2.No need for water.
3.No chance of choking.
4.Stability.
5.Administration simplicity.
6.Its bioavailability is improved by bypassing the GIT.
7.Low dose means less adverse effects.
8.Pleasant mouthfeel.
9.In cases of asthma attacks and allergic reactions, there is a quick commencement of activity.
10.Drugs that are released under controlled conditions absorb more quickly and completely.
11.Does not hinder everyday activities like speaking, drinking, etc. It is possible to provide API that are very susceptible to gastrointestinal tract degradation.(12)

Fast dissolving drug delivery system, also known as fast dissolving/disintegrating film for oral drug delivery, is a new generation delivery system that was developed in the late 1970s as an alternative to tablets, capsules, syrups, and other formulations for pediatric and geriatric patients who have trouble swallowing traditional solid dosage forms. It combines the benefits of both liquid and conventional tablet dosage forms. This administration technology uses solid dosage forms that dissolve in the mouth in a matter of seconds without the need for liquid.

Water administration. The delivery method is a very thin oral strip that is applied to the patient's tongue or any other mucosal tissue in the mouth and is immediately moistened by saliva. At the application site, the film hydrates quickly. It then quickly dissolves and breaks down, releasing the drug for absorption through the oral-mucosa. Because of its mobility, correct dose, and ease of distribution, fast-dissolving oral thin films are well-liked by both patients and caregivers . The kind and quantity of polymer utilized determines how sturdy the film is, and pharmacopeia states that the typical dissolution period for an oral dissolving film is between 5 and 20 minutes 1Additionally, as the medicine is absorbed across the oro-mucosal barrier, they offer a prompt commencement of action in a matter of seconds.(13)

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Anatomy of oral cavity:

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Advantages of Orally Fast Dissolving Oral Films:

Oral disintegration therapies (ODTs) and rapidly dissolving or oral soluble formulations (OTFs) continue to expand in sales and have been introduced in patient-tailored formulations, and products easily dealing well with pharmacological and nutritional issues in typical doses as solid oral products.

Fast-dissolving thin oral films are rapidly gaining popularity in the pharmaceutical industry rather than breaking tablet technology because they are easier for patients with trouble swallowing or chewing solid dosage forms Companies identified which actively developing OTF delivery technologies that range from tablets to fast-dissolving, highly wafer or films of water soluble. Additionally, the report lists nine OTF products introduced and 47 OTF products under development by 12 companies. Technology Catalysts had forecast that the market for thin solution formulations would be worth $500 million in 2007 and by 2010 could reach $2 billion OTFs have evolved in recent decades into respiratory devices from the confectionery and oral care markets, becoming the new widely accepted quantity for delivering vitamins and personal care products by consumers The companies expertise in polymer coatings developers for transdermal drug delivery focused on converting this technology to OTF. Today, OTFs are a well-proven and globally validated technology for producing active pharmaceutical ingredients (APIs) that are systematically dispensed for over-the-counter (OTC) pharmaceuticals and prescription drugs are in the early stages of development to in the middle. (16)

Disadvantages of Orally fast dissolving Oral films

Fast-dissolving oral films drawbacks Drugs that become unstable at buccal pH can't be given. Drugs that irritate the mucosa cannot be given by this route of administration. Drugs that just require a minimal dose can only be administered. Most medications have a bitter taste, hence taste masking is necessary. Special packaging is required since OFDFs are delicate and must be protected from moisture. Dose homogeneity is a difficult technical problem. Oral film is packaged in a pricey manner.(17)

Fast-Dissolving Oral Films Restrictions:

1. It is impossible to incorporate high doses.
2. It is impossible to make excessively bitter medications.
3. Dose uniformity presents a technological difficulty.
4. They need particular packaging to ensure the stability and security of the products.
5. This route cannot be used to provide medications that irritate the oral mucosa.(18)

The ideal qualities of the drug must be chosen:

1. The medication should taste good. The medication ought to have low molecular weight and tiny molecules.
2. Both in water and saliva, the medication should be well soluble and stable.
3. The pH of the oral cavity should cause it to partially unionize.
4. The medication should show no sensitivity to environmental circumstances.
5. It should be able to penetrate the tissue of the oral mucosa.
6. The drug's therapeutic dose shouldn't be higher than 40mg.

The transformation of dosage forms from straightforward traditional tablets or capsules to modified release tablets or capsules, oral disintegrating tablet (ODT), wafer, and the oral drug delivery system has been made possible by research and development in the oral.(19)

Fast-dissolving film creation:

Rapid dissolution for the creation of oral films, a variety of components are used, including Active component of a medication,Producing polymers for films, Plasticizer, Superdisintegrants, Savouring agent, Agent that stimulates

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saliva,Surfactants, Flavored substance, Coloured substance.

The complex use of aesthetic and functional qualities, such as flavor masking, quick dissolution, physical appearance, mouth feel, etc., is required in the formulation of FDFs. From a regulatory standpoint, every excipient utilized in the creation of OS must be GRAS-listed and permitted for use in pharmaceutical dosage forms intended for oral administration.The complex use of aesthetic and functional qualities, such as flavor masking, quick dissolution, physical appearance, mouth feel, etc., is required in the formulation of FDFs. From a regulatory standpoint, every excipient utilized in the creation of OS must be GRAS-listed and permitted for use in pharmaceutical dosage forms intended for oral administration.(20)

Pharmaceutically Active Ingredient:

1-30% weight-per-weight of the active medicinal component is included in the film mixture. Always utilize low dose active pharmaceutical ingredients because it is challenging to put high doses of medication into fast-evaporating films. Several medications, such as antihistamines, anti-diarrheals, antidepressants, vasodilators, anti-asthmatics, and antiemetics, can be utilized as fast-acting oral films.

For taste masking, dimenhydrinate can also be added to ODFs. Salbutamol sulfate, rizatriptan benzoate, verapamil, ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, etc. are typical examples of medications included in ODFS.

Polymers for Making Films The primary and most crucial component of is polymer the creation of oral films, a range of polymers are available. These polymers are typically employed in concentrations of 40–45% weight per weight of the final product, but they can be increased to up to 65% weight per weight of the final product either alone or in combination to achieve the necessary oral film qualities.1391 The acquired film needs to be durable enough to prevent damage during handling or shipping. The kind of polymer and its quantity in the formulation affect the film's durability. The resulting disintegration time of the prepared film is greatly influenced by the physicochemical properties of the polymer or polymers chosen for film production.(21)

Ideal Film Forming Polymer Properties.

1. The polymer used must not be poisonous, irritating, or contain any leachable contaminants.
2. It should have no flavour.
3. It should have good spreading and wetting characteristics.
4. The polymer needs to have strong enough peel, shear, and tensile properties.
5. The polymer needs to be affordable and widely accessible.
6. A lengthy shelf life is required.
7. It shouldn't result in any secondary infections in the tooth or oral mucosa.
8. It ought to have a satisfying mouthfeel.
9. Having a polymer with local enzyme inhibitory effect would be desirable.(22)

Limitations of solution filming:

Several obstacles have to be encountered when delivering drugs through solution-based films which can be enumerated as follows.

Only low-dose medications can be administered.

Rapid drug clearance for local action is due to continuous salivation (0.5-2L/day), which subsequently dilutes the drug, resulting in larger doses of the drug

This method cannot give chemicals, which force a liquid or have a bitter or unpleasant taste or unpleasant odour.

Drugs absorbed by passive diffusion can only be administered in this way.

Food and drink should be banned. 17. The 17th century

The advantages of various drug delivery systems and recent advances offset the disadvantages of inexpensive solvent-based films and therefore solvent-based films are ideal for drug delivery for orally is a promising method for further research**.** (23)

III. CONCLUSION

From the foregoing, it can be inferred that quickly dissolving oral films have shown to be a cutting-edge method of medicine administration for all populations.of people or patients who have swallowing issues. When used quickly, dissolving oral films have proven to be useful.The need for an immediate response, such as during an asthma attack, cardiacepilepsy and cardiac failure. A useful tool is the use of oral thin films.To prolong the life of the current product by obtaining a patent forsame thing as oral films that dissolve quickly. The technology accelerating and posing challenges

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to the majority of the pharmaceutical organisations to create oral films for a variety of active ingredients for pharmaceuticals. There is a tonne of study being done, and will commence.

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