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A Review of Polyherbal Oral Care Strips for Managing Gingivitis and Oral Infections

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ABSTRACT:
Oral strips offer a convenient and effective method of medication delivery, with the market valued at $500 million in 2007. The advantages of oral strips include a larger surface area, convenient dosing, reduced dosage, taste masking, and cost-effectiveness. However, limitations include low flux, difficulty retaining the dosage form, and accidental swallowing. Gingivitis, a disease caused by bacterial plaque accumulation, can lead to tooth loss and calculus, requiring removal by dental specialists. Oral strips provide a promising solution for the prevention and treatment of gingivitis, offering a targeted and efficient delivery of antibacterial agents.

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INTRODUCTION:

In terms of patient compliance, the oral route is the most acceptable of the delivery methods. The majority of medicinal dosages are taken orally as liquids, tablets, granules, and powders [1]. Numerous fast-dissolving medication delivery devices have been created in order to address this issue. In the late 1970s, researchers at Wyeth Laboratories in the UK invented fast dissolving medication delivery [2]. Many technologies, such as direct compression, wet granulation, and freeze-drying, can be used to create fast-dissolving drug delivery systems. In reality, none of the fast-dissolving systems dissolve as their names imply; instead, some of them employ distinct disintegrating mechanisms, such as the use of large concentrations of disintegrates or

effervescent chemicals, which cause tables to disintegrate quickly during the month [3].

An oral strip is a thin layer made of hydrophilic polymers that dissolves quickly in the buccal cavity or on the tongue. When Listerine pocket strips, a new mouthwash product, were introduced and widely used in the early 2000s, oral strips were already well liked by the public [4]. The market for pharmaceutical items in oral thin film formulations was estimated by Technology Catalyst to be worth $500 million in 2007 and might grow to $2 billion by 2010. However, due to the OS's complexity, only a small number of goods with bitter compounds have been able to reach the market.

Over the past two years, a number of breath-freshening products have been introduced to the market, exposing consumers to this idea. Oral thin films, or OTFs, are now in the early to mid-stages of research for prescription medications and are a recognized and tested technology for the systemic administration of APIs for over-the-counter medications [5].

Need of quick dissolving oral strips:

A tablet that dissolves or disintegrates in the oral cavity without the need for water or chewing is the most common type of fast-dissolving drug delivery device. The primary distinction between the oral strips or quick-dissolving drug delivery system and the majority of traditional fast-dissolving dose forms is that the former is not a tablet.

The film's enormous surface area, which wets quickly when exposed to the moist oral environment, is primarily responsible for its swift dissolving effect. By offering a fresh and simple approach to treatment, the oral strip represents a significant advancement in drug administration. ODT goods that would provide a better barrier to generic entry and product differentiation to over-the-counter brands are still being considered for OS technology [6].

Advantages:

- Availability of larger surface area.
- Convenient dosing.
- No water needed.
- Reduction in the dose leads to decrease side effects associated with drug.
- Taste masking.
- Not expensive as prepared with simple method.
- No risk of chocking.
- Easy to handle, transport and store.
- Improved patient convenience.
- Reduction in the dose leads to decrease side effects associated with drug.

Disadvantages:

- The low flux that in turn results in low drug bioavailability.
- Difficulty in retaining dosage form for long periods.
- High dose cannot be incorporated into the strip.
- Accidental swallowing of dosage forms and salivary scavenging.

DISEASES:

Gingivitis:

Gingival fluid transudation is the first clinical indication of gingival inflammation. A fluid made primarily of serum and leukocytes gradually replaces this thin, nearly cellular transuded. The clinical signs and symptoms of persistent gingivitis are generally painless and nebulous. Most patients are unaware of the condition because of these characteristics, and dentists tend to underestimate them. In rare cases, spontaneous bleeding occurs in chronic gingivitis. The vascular transfigurements and epithelial alterations are quite noticeable, as evidenced by the fact that the gingival tissues can be made to bleed simply by contacting the gingival border with a blunt tool. Diverse microbial populations are present in the sub gingival crevice. When gingivitis and periodontitis develop, which are thought to be sequential stages of periodontal health degradation, changes in the composition of these communities take place [7].

The degrees of protection provided by health and gingivitis-associated microbiota, as well as whether these communities support the subsequent emergence of periodontitis-associated taxa, are unclear [8].

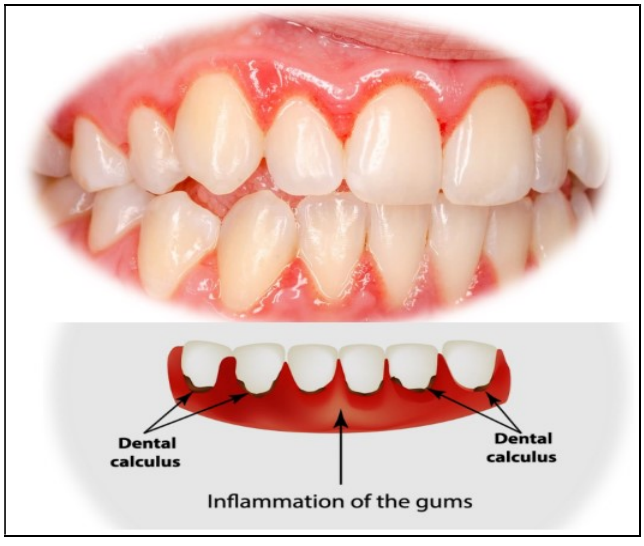

Fig 1. Clinical symptoms of Gingivitis.

Symptoms:

- Puffy or swollen gums
- Gums that are darker than normal, or gums that are bright red or dark red.
- Gums that bleed readily when flossing or brushing.
- Gums that are sensitive.
- Foul breath.

Causes:

The build-up of bacterial plaque between and around teeth is the most frequent cause of gingivitis. Dental plaque is a naturally occurring biofilm that builds up on teeth. It happens when bacteria adhere to a tooth's smooth surface.

Plaque and tartar accumulation can set off immunological reactions that destroy gingival or gum tissue. It may eventually result in other issues, such as tooth loss [9].

Near the gum line at the base of the teeth, this plaque can solidify into calculus, also known as tartar. The colour of this is yellow-white. Calculus may only be removed by dental specialists [9].

Types of oral strips:

- Flash release strips.
- Mucoadhesive melt away strips.
- Mucoadhesive sustained-release strips.

Standard Composition of oral strips [10].

The orals trip is a drug-containing thin film that is 1 to 20 cm in size. A single dose of the medication cannot contain more than 30 mg. An oral strip's makeup consists of following things.

- Drug.
- Water-soluble polymers.
- Plasticizer.
- Surfactants.
- Sweetening agents.
- Saliva stimulating agents.
- Fillers, colours, and flavour.

Table 1. Composition of the oral strips [11].

Composition	Conc. (w/w)
Drug/ API	5-30%
Polymer	45%
Plasticizer	0-20%
Surfactant	Q.S.
Sweeting agents	3-6%
Saliva stimulated agents	2-6%
Fillers, color, flavours	Q.S.

ORAL STRIPS (FORMULATION CONSIDERATION):

Drug:

A range of APIS could be delivered by the Oral Strips technology. The following medications or APIs can be used in strip delivery [12].

- Depending on the required final release profile, they can be milled, micronized, or transformed into Nano crystals or particles.
- That need to be taste-masked.
- People who experience the first pass effect.
- Which call for prompt response.

Water-soluble polymers:

- The selection and concentration of polymers play a crucial role in determining the development and mechanical strength of a film.
- Polymers can be used alone or in combination with others to enhance strength and modify film properties.
- Typically, 45 % w/w concentration of the polymer is utilized in creating an oral strip.
- However, the concentration can be increased to 60-65% w/w to achieve specific desired characteristics.

Plasticizer:

Plasticizers are indeed crucial in the formulation of oral strips, as they enhance the flexibility and workability of the polymer films used in these products. By incorporating plasticizers, formulators can achieve desired mechanical properties, such as improved tensile strength and reduced brittleness, which are essential for the performance and stability of oral strips [13].

Surfactant:

Surfactants are utilized as dispersing, wetting, or solubilizing agents to breakdown the film in a matter of seconds and release the active ingredient right away. Among the often-utilized ones are Tweens, Sodium Lauryl Sulphate, Benzalkonium Chloride, and Bezthonium Chloride. Poloxamer 407 is a crucial surfactant that is utilized as a dispersing, wetting, and solubilizing agent.

Sweeting agents:

One of the key components in pharmaceutical products nowadays is sweeteners, which help to cover up the bitter taste of the medication. Sweeteners, both natural and artificial, are employed. Natural sweeteners include sucrose, dextrose, fructose, glucose, liquid glucose, and is maltose, among others; artificial sweeteners include

monosaccharides, disaccharides, and polysaccharides, including Galactose, Glucose, Mannose, Fructose, Xylose, Ribose, Dextrose, Maltose, Sucrose, Sugar, Sorbitol, Xylitol, Mannitol, And Soluble Saccharin Salts, Cyclamate Salts, Acesulfame-K, Aspartame, and notate, respectively. Artificial sweeteners are becoming more and more common in medicinal formulations these days. Compared to sucrose, neonate and alitame have a sweetening potential that is more than 2000 to 8000 times greater [14].

Saliva stimulated agents:

Increasing the rate of saliva production is the goal of using saliva stimulating chemicals, which will help the rapid dissolving strip formulations dissolve more quickly. Generally speaking, salivary stimulants can be made from acids used in meal preparation. The few examples of salivary stimulants are citric acid, which is the most preferred, followed by malic acid, lactic acid, ascorbic acid, and tartaric acid. Between 2 and 6 % w/w of the strip's weight, these chemicals are applied either alone or in combination. Sweeteners and other OS components also stimulate saliva [15].

Colouring and flavouring agents:

Natural colouring compounds that have been approved by the FDC are frequently utilized. The colouring agent's concentration should not exceed 1 % w/w.

In order to enhance flavour and make the formulation appealing to young patients, flavouring ingredients are typically used. Various flavour, including sour fruit (lemon), fruit essence (apple, raspberry, cherry, and pineapple), powerful mint (peppermint, sweet mint, and spearmint), wintergreen, cinnamon, clove, and essential oils or water-soluble extract of menthol, can be employed [16].

MANUFACTURING METHOD [18,19]:

One or combination of the following processes can be used to manufacture the mouth dissolving films.

- Solvent casting.
- Semisolid casting.
- Hot melt extrusion.
- Solid dispersion extrusion.
- Rolling.

Solvent casting method:

The solvent casting process involves dissolving water-soluble polymers in water and the medicine and other excipients in an appropriate solvent. The two solutions are then combined, swirled, and eventually placed onto a Petri plate to dry.

Semisolid casting method:

First, a water-soluble film-forming polymer solution is made for the semisolid casting procedure. A solution of an acid insoluble polymer (such as cellulose acetate phthalate or cellulose acetate butyrate) made in sodium hydroxide or ammonium is mixed with the resultant solution. After that, the right amount of plasticizer is added to create a gel mass. Finally, heat-controlled drums are used to cast the gel mass into the films or ribbons. The film is between 0.015 and 0.05 inches thick. A 1:4 ratio should be maintained between the acid-insoluble polymer and the film-forming polymer [17].

Hot melt extrusion method:

The medication and carriers are initially combined in a solid state using the hot melt extrusion process. The mixture is then melted by the extruder's heaters. Lastly, the dies form the melt into films.

Solid dispersion extrusion method:

Using this technique, drug-immiscible components are extruded to create solid dispersions. Lastly, dies are used to meld the solid dispersions into films.

Rolling method:

The rolling method involves rolling a drug-containing solution or suspension on a carrier. Water and water-alcohol mixtures make up the majority of the solvent. After drying on the rollers, the film is cut into the appropriate sizes and shapes. [18]

Marketed Formulation of Oral Strip:

The marketed formulations of oral strips are given in the Table 2.

List of Patent for oral care strips:

The patent detail of oral care strip is given in Table 3.

CONCLUSION:

The novel dose form known as oral strips fills a need in both general and specific populations, including children, the elderly, and immobile patients who are nauseous or do not complain. Advances in techniques for enhancing the drug's dissolving and release properties, as well as the palatability of dosage forms, allow for the inclusion of a wide variety of pharmaceuticals in oral strips.

Table 2. List of the Marketed Formulation of Oral Strip [17,18].

Product/ Brand Name	Manufacturer/ Distributor	Uses
Diphenhydramine Hydrochloride films	MonoSol RX	Antihistaminic
Benadryl	Pfizer	Anti-allergic
Klonopin Wafers	Solvay Pharmaceuticals	Treatment of anxiety
Triaminic Thin Strips	Novartis Pharmaceuticals	Nasal decongestant
Orajel	Del	Mouth ulcer
Suppress	InnoZen, Inc.	A cough suppressants
Ondansetron Rapid films	Labtec Pharma	Postoperative nausea and vomiting
Caffeine films	Dow chemical company	CNS stimulant
Dextromethorphan fast dissolving films	Hughes medical corporation	Antitussive agent
Theraflu	Novartis	A cough suppressant
Chloraseptic	Prestige	A sore throat
Listerine Cool Mint Pocket Paks	Pfizer, Inc.	Mouth Fresheners
Zuplenz	MonoSol Rx	Prevent nausea and vomiting caused by cancer drug treatment
Ondissolve	Labtec Pharma	Prevent nausea and vomiting
Sub Oxone	MonoSol Rx	Treatment of opioid
Set film	Labtec Pharma	Nausea and vomiting
Sudafed PE	Wolters Kluwer Health, Inc.	Relieving Congestion
Chloraseptic® Relief strips	InnoZenInc.	A minor irritation, pain, and sore throat
Folic acid-fast Dissolving films	Hugs Medical Corporation	Anaemia
Gas-X	Novartis	Anti-flaunting

Table 3. The Patent list of oral care strips [17,18].

Authors	Title	Patent no.	Submission/ Publication date
Jin-Kyu Park, Won-suk Yang, Kyoung Tae Jung	Quickly soluble oral film dosage containing steviosides as a unpleasant taste masking agent	US9492379B2	2012-08-10/ 2016-11-15
Eric Allen, Robert Davidson, Tony LaRosa, David Reid	Oral dissolvable film that includes plant extract	US11701339B2	2022-03-04/ 2023-07-18
Michael Li, Markus Krumme	Edible oral strip or wafer dosage form containing ion exchange resin for taste masking	US10744176B2	2019-07-15 2020-08-18
Robert K. Yang, Richard C. Fuisz, Garry L. Myers, Joseph M. Fuisz	Uniform films for rapid dissolve dosage form incorporating taste-masking compositions	US20170290777A1	2017-06-27/ 2017-10-12
Robert K. Yang, Richard C. Fuisz, Garry L. Myers, Joseph M. Fuisz	Thin film with non-self-aggregating uniform heterogeneity and drug delivery systems made therefrom	US10111810B2	2013-03-29/ 2024-10-17

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