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AN ACCOUNT ON PREPARATORY METHODS AND CHARACTERIZATION OF ORODISPERSIBLE FILMS - A REVIEW

GUDA SHAILAJA[2], PASHAPU RUCHITHA[3], VUDATHALA MADHUKAR[4], M. SWETHA[*1]

[*1]Assistant professor, Department of Pharmaceutics, CMR College of Pharmacy, Hyderabad, Telangana, India.

[2,3,4] Department of Pharmaceutics, CMR College of Pharmacy Hyderabad, Telangana, India.

Email : swetha.thangallapalli@gmail.com

ABSTRACT :

This review aims to Formulate and Evaluate Oro dispersible Films in current study and future prospective,assure safety, efficacy, compliance, and patient acceptability, researchers and businesses have been working to create novel drug delivery systems during the past few decades. Although the processes of drug discovery and development are currently costly, difficult, and time-consuming, there is a trend towards novel drug delivery systems. Through a variety of local and systemic actions, this delivery system aids in achieving drug response. Orodispersible films (ODFs) prepared using this innovative method are advantageous for pediatric, elderly, and bedridden patients. In addition to focusing on the positive and negative aspects of film formulation, this review paper seeks to provide information on the creation, characterisation, and assessment of ODFs. It also wants to provide insight into prospective drug candidates and polymers for use in ODFs, advantage includes Patients with psychological disorders, elderly people, and children can easily Apply Orodispersible films Patients with mental disorders, dysphagia,vomiting, hypertension, motion sickness. The major disadvantages of ODFs are limited drug loading capacity, possible unpleasant taste of certain active ingredients, sensitivity to moisture and the higher cost of the manufacturing process compared to conventional products.The major limitations of ODFs includes High doses cannot be added to strips.It takes special tools and is challenging to package orodispersiblefilms.It is prohibited to deliver medicines that irritate the mucosa. Since orodispersible films are typically hygroscopic, extra care should be given throughout Prolonged preparation. The co-administration of drugs in films hindered both the dissolving and the disintegration time.

Different drugs used to Formulate ODFs include Glycopyrrolate, Vildagliptin, Chlorpromazinedihydrochloride, Levocetirizine,Domperidone, Rosuvastatin Calcium etc.Solvent Casting method is commonly used method is Solvent casting method,This technique involves dissolving water-soluble polymers in a suitable solvent, then adding the medication and other excipients. dissolved in an appropriate solvent. The two solutions are then combined and agitated.The air bubbles in this solution are subsequently settled by degassing it while under vacuum The final step is to cast the bubble-free solution into a Petri dish and let it dry. more clarity than extrusion and greater thickness consistency. Films have a nice sheen and are defect-free Films are more flexible and have better physical characteristics than die lines. Evaluation of ODFs includes Tensile strength, viscosity, Surface area, PH, Wettability, Dissolution, Disintegration, palatability studies, Physical and chemical properties.

KEYWORDS: Mouth dissolving buccal film, Anti-diabetic, Super Disintegrants,Chitosan. Muco-adhesive polymers. Drug delivery, Stabilizer.

INTRODUCTION

The goal of a wide range of pharmaceutical research is to create novel dosage formulations.The Majority of initiatives have been directed on either developing new drug delivery systems improving patient compliance. Orally disintegrating systems have been the top choice of product development scientists, the dosage forms created to make Formulation easier.

Hence, it may be expected that orally disintegrating systems will quickly acquire the necessary peak plasma concentration for medicines that are stable in the gastric pH. The administration of active medicinal components via oral films is receiving increased attention (API). The cavity offers clear benefits such as simple delivery, no gastrointestinal fluid degradation of API, avoiding the initial hepatic metabolism, and potentially increased bioavailability ensuring quick entrance and fast onset. Recently, a number of this route's benefits have come to light, and numerous products are currently being developed. There is no universally accepted definition of oral films, so for practical purposes, it is defined as "A thin flexible, non-friable polymeric film comprising dispersed active medicinal ingredients that is meant to be placed on the tongue for quick absorption[1]

For people who have an active lifestyle, symptoms could include coughing, diarrhea, or acute allergy episodes. In situations when local action is sought, such as for local anesthesia. formulated as a very thin oral strip that is easily applied to the patient's tongue or any other oral mucosal tissue, rapidly moistening,To quickly release the medication for oral mucosal absorption, the film quickly hydrates, clings to the application site, disintegrates, and dissolves when exposed to saliva. Depending on the active pharmacological ingredients, it also has a proven shelf life of between two and three years[2]

Pullulan and PEG400 are used as a plasticizer and film-forming polymer in the formulation of the mouth-dissolving Glycopyrrolate film. Pullulan, a naturally occurring polysaccharide composed of repeating maltotriose units, is an effective film-former that produces a heat-sealable film with good oxygen barrier qualities Water serves as the medium while sodium saccharin serves as the sweetener

As the medication dose is ingested, no liquid or measuring device is necessary. Because the mouth mucosa is highly vascularized and hence extremely permeable, absorbing drugs through it into the systemic circulation is a desirable strategy. Because of their huge surface area and ability to dissolve quickly in the mouth, fast dissolving films have become a favored oral administration form for a number of drugs. disintegration, which enhances patient adherence[3].

Solvent casting method is one of the methods frequently used in the production of ODFs. In this method, after the film-forming agents are dissolved in designated solvent, the solution is poured onto a flat surface and dried.When placed on the tongue, formulations are immediately moistened with saliva and then rapid disintegration and dissolution occurs and the release of the active pharmaceutical substance happened.

Drug delivery methods known as orodispersible films (ODFs) are designed to quickly disperse after oral administration. Because of their optimal size, thickness, and ease of administration, ODFs, which are frequently made using hydrophilic polymers, are dosage forms that facilitate patient access.. One of the procedures widely employed in the fabrication of ODFs is the solvent casting Method.
The current study includes formulation development, in vitro testing, and preformulation tests of mucoadhesive ODFs[4]

Several terminologies, such as wafer, oral film, thin strip, orally dissolving film, flash release wafer, quick dissolve film, and melt-away film, can be found in the literature. ODFs have just been added to the European Pharmacopoeia's monograph on "oromucosal preparations." However, no specifications about time limits for disintegration have yet been made.

An ideal ODF should have sufficient flexibility, elasticity, softness, resistance to breaking, quick disintegration, and conformity with taste. All of these factors must be taken into consideration while developing a formulation and following the necessary standard procedures[5].

The intraoral route is favored over many other routes because it is simple to administer and allows for a possible quick medication effect. Without the use of water to aid in swallowing, these delivery systems either dissolve or disintegrate in the mouth quickly, releasing the active medication. They are helpful for patients who may have trouble swallowing standard pills, capsules, liquid orals, or syrups, such as children, the elderly, bedridden patients, or patients with developmental disabilities(5-7), which could result in inefficient therapy[6]

The oral mucosal epithelium is a multicellular layer that is 40–50 cells thick and composed of proteins and carbohydrates. Mucus is a gel-like fluid that is expelled from the mucosal epithelium. It contains 90–99% water, with the remaining ingredients being (water-insoluble) glycoproteins, nucleic acids, electrolytes, and enzymes. saliva from the salivary glands close to the sublingual canals; these glands release 1-2 mL of saliva every 60 seconds. Saliva serves as a barrier and is made up of water, mucus, lysozymes, amylase, immunoglobulin, clotting factors, and mineral salts[7]

A medicated oral film with a patented bilayer technology that was designed as a new medication delivery system.The ingredients in these films include an effective dose of the active ingredient, water-soluble hydrocolloids like HPMC, pullulan, pectin, and carboxymethyl cellulose, as well as palliatives, preservatives, flavorings, and saliva-stimulating substances[8]

Special features of Mouth Dissolving Films :
1· Thin elegant films
2· Various sizes
3· Unobstructive
4· Mucoadhesion
5· Quick dissolving
6· Fast disintegrating

Ideal Qualities of a Good Drug Candidate :
1. The medicine should taste well.
2. The recommended drug dosage is a modest amount of up to 40 mg,and more moderately-sized molecules being preferred.
3. The medication should be able to penetrate oral mucosal tissue, be partially unionized at the pH of the oral cavity, and have good stability and solubility in water and saliva[9].
Based on the transdermal patch technology, mouth-dissolving films are a revolutionary drug delivery device for oral drug administration. The delivery device is a very thin oral strip that the patient simply places on their tongue or any other oral mucosal surface [10].

Advantages of Oro dispersible Films of patients perspective
Over traditional dose forms, orodispersible films have a number of Advantages

• Patients with psychological disorders, elderly people, and children can easily Apply orodispersible films
•Patients with mental disorders, dysphagia, recurrent vomiting, hypertension, sickness should consider
• Because the administration of films doesn't require water, there is no risk of choking.
• Because they have a wide surface area, orodispersible films quickly dissolve and disintegrate in the oral cavity, reducing the time between doses and improving the drug's efficacy, safety, and efficacy.

Major Limitations Related to Oro dispersible Films :

There are a few drawbacks to orodispersible films.
• High doses cannot be added to strips.
• It takes special tools and is challenging to package orodispersible films.
• It is prohibited to deliver medicines that irritate the mucosa.
• Since orodispersible films are typically hygroscopic, extra care should be given throughout Prolonged preparation. The co-administration of drugs in films hinders both the dissolving and the disintegration time, combining more than two pharmaceuticals is particularly challenging[11].

Formulation Aspects for fast dissolving films.

1) Drug Category.
2) Polymers for Film Formation.
3) Plasticizers.
4) Artificial Sweeteners.
5) Saliva stimulating agents.
6) Cooling Agent.
7) Flavouring Agent.
8) Colouring agent.
9) Surfactants.
10) Thickening and stabilizing agents.

The complex use of aesthetic and functional qualities, such as flavor masking, quick dissolution, physical appearance, mouth feel,every excipient utilized in the creation of OS must be GRAS-listed and permitted for use in pharmaceutical dosage forms intended for or administration[12].

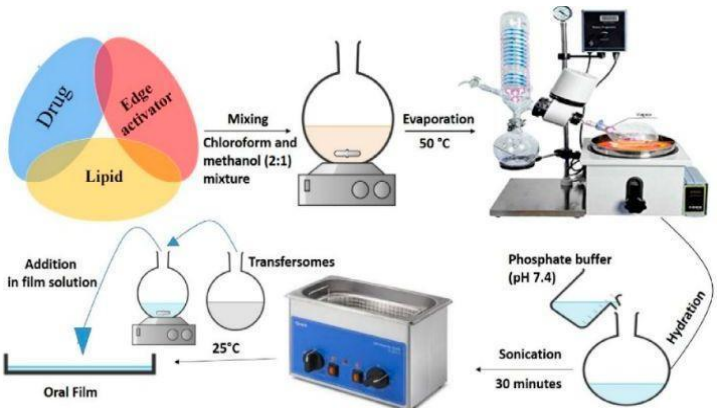

Fig 1 : Schematic Representation of the Transfersomes formulation process [13]

Approaches For Formulation of Oro dispersible Films :

ODFs are thin films that quickly dissolve and have an area between 5 and 20 cm^2, in which the active pharmaceutical ingredient (API) is consolidated into a matrix using a hydrophilic polymer. The active pharmaceutical ingredient is frequently combined with various excipients, such as plasticizers, sweeteners, flavor modifiers, colorants, etc., to a maximum concentration of 15 mg. Table I provides an overview of an ODF's general makeup.

Table 1: A typical Composition of ODFs.

Components	Concentration (%)
Active pharmaceutical Ingredient (API)	1-25
Hydrophilic polymer	40-50
Plasticizer	0-20
Colour,Flavour, Filler	0-40

Table 2 : polymers employed in the preparation of ODFs

S.No	Polymer	Examples
1	Natural polymer	Pullulan,starch,Gelatin,pectin,Maltodextrins,sodiumalginate,polymerized Resin.
2	Synthetic polymer	Hydroxypropyl methyl cellulose, sodium carboxymethyl cellulose,poly ethylene oxide,poly vinyl pyrrolidone, poly vinyl alcohol.

The development of orodispersible films has not yet been thoroughly studied, despite the fact that there is currently a wealth of research on such dosage delivery systems available in the form of patents and other forms. The lack of acceptable guidelines for the quality assurance and production of orodispersible films with a focus on enhancing their performance from a pharmaceutical aspect, will add to providing experiences on thorough understandings for the formulation and characterisation of orodispersible films [14].

Table 3 : Suitable polymers used for preparation of ODFs [15].

Excipients	Excipient role	Excipient Example
Polymers	Shows immediate and rapid disintegration when contact with saliva.	**Natural polymers :** starch, sodium alginate,zein,pectin, maltodextrin,Gelatin, collagen,amylose,cellulose derivatives, Chitosan.

		Synthetic polymers : Polyvinyl alcohol, poly vinyl acetate, methacrylic acid, Hydroxypropyl methyl cellulose, copolymers.
Plasticizers	Reduce brittleness, improves tensile strength and intense elongation, improves the Plasticity of polymer which affects film flexibility.	Glycerol,mannitol, sorbitol, propylene glycol,citric acid esters,triethyl Citrate, diethyl phthalate.
Surfactants	Enables film disintegration within seconds during the contact with saliva. solubilizing, dispersing, and wetting agent.	sodium lauryl sulfate, polysorbate.
Sweetening agents	Mask the bitter taste.	Sucrose, glucose, fructose, maltose,Oleoresin,mannitol, aspartame,ribose.
Saliva stimulators	Develop the stimulation of saliva in the oral cavity.	tartaric acid,malicacid,lactic acid, ascorbic acid.

Method of preparation of fast dissolving films can be prepared by:
a.Solvent casting method.
b.Semisolid casting method.
c.Hot melt extrusion.
d.Solid dispersion extrusion.
e.Rolling method.

a.Solvent casting method :
This technique involves dissolving water-soluble polymers in a suitable solvent, then adding the medication and other excipients.dissolved in an appropriate solvent. The two solutions are then combined and agitated.The air bubbles in this solution are subsequently settled by degassing it while under vacuum The final step is to cast the bubble-free solution into a Petri dish and let it dry. more clarity than extrusion and greater thickness consistency.Films have a nice sheen and are defect-free Films are more flexible and have better physical characteristics than die lines.

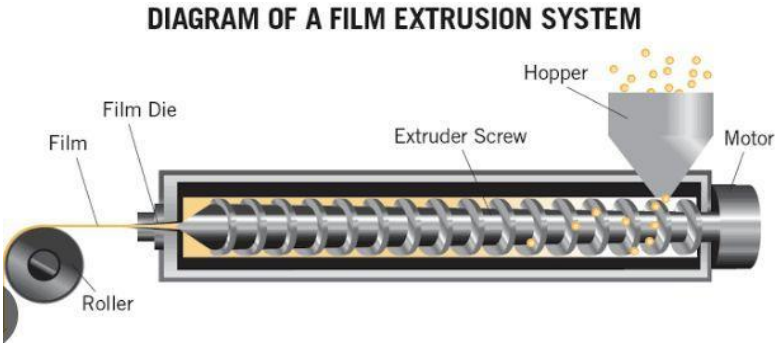

Fig 1: Represents the working of film extrusion system.[16]

b. Semi Solid casting method :

This procedure creates a water-soluble film-forming polymer solution. Then the resultant solution is mixed with an acid-insoluble polymer solution (cellulose, for instance).cellulose acetate butyrate, acetate phthalate, etc.). The right quantity of plasticizer is then added to create a gel mass. The films or ribbons are then cast using heat-controlled drums from the gel bulk. The films should be between 0.015 and 0.05 inches thick. The ratio of the film-forming polymer to the acid-insoluble polymer should be 1:4 [16].

c. Hot melt extrusion :

This method can be used based on knowledge from the plastics sector, where formulators can extrude the mixtures of medications, polymers, and other relevant excipients into desired final forms to achieve adequate drug-release profiles. Twin screw extruders have shown to be useful in pharmaceutical formulations because they can mix various formulation materials uniformly and consistently, which improves bioavailability and dissolution rates. The API and other materials are combined in a dry state, heated till the mixture turns into molten, and then extruded out to create thin films. Using the right method, the solvent is fully eliminated. After being created, the strips are further chilled and sized as needed.

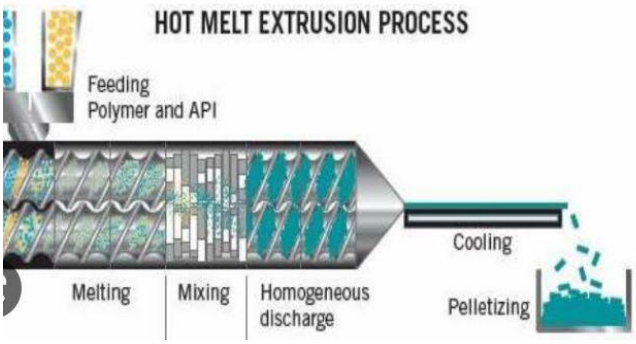

Fig :2 Represents the working of the Hot melt extrusion process.[16].

d. Solid dispersion extrusion :
In this method, the medication and immiscible components are both extruded together before solid dispersions are made. Using dies, solid dispersions are molded into acceptable thin-sized films [17].

e. Rolling method :
This process involves mixing the API, polymers, and other excipients with the appropriate solvents, such as water and alcohol. The API-containing solution or suspension is then rolled onto the carrier. The film is then dried and shaped and sized as needed [18].

EVALUATION TESTS FOR ODFs :
The basic evaluation tests were performed on the prepared films.Films with any flaws, air entrapment, thickness asymmetry, weight deviation, or uneven content were not considered.The produced films physicochemical characteristics were measured, including their thickness, weight uniformity, folding durability, surface pH, and drug content uniformity.

Compatibility studies :
To determine the compatibility between the drug and other excipients using the KBr pellet method, Fourier transform-infrared (FTIR) experiments were carried out for the pure drug, excipients, and the physical mixture.

Physical and chemical properties :
Morphological investigations (visual approach)Morphological research was done to evaluate color and transparency of films against a background of white and black [19].

In vitro dissolution studies :
Studies on in-vitro dissolution were conducted using a USP type II paddle-type dissolution device (Lab India). pH 6.8 phosphate buffer (900 ml), maintained at 37°5°C, was the dissolving medium, rotating at 50 rpm. At intervals of 1, 5, and 10, a 10ml sample was taken. Replaced after 10, 15, or 30 Using a UV-Visible spectrophotometer-1800 (Shimadzu, Japan), the absorbance of this solution was measured at 278 nm. Calculated and reported as a cumulative proportion of the drug released, drug concentration.

Drug release kinetics :

To describe the in-vitro drug release mechanism, the cumulative amount of drug released from the manufactured tablets was fitted to zero order kinetics, first order kinetics, Higuchi's model, and Korsmeyer-Peppas model [20].

Palatability studies :
It serves as a gauge for how good a movie tastes because the comic strip has to be enjoyable. For taste approval, film batches are given grades ranging from A to C. One A grade is considered average for a product, two A grades are considered good for a formulation, and three A ratings are considered very good for a formulation.

Disintegration Test :
The disintegration time is the amount of time it takes for a film to break down after coming into touch with saliva or water. Oral thin films are subjected to the same disintegration standards for oro-dispersible tablets, i.e. the 30s or less, as established by CDER.

Dissolution Test :
The conventional dissolution assembly mentioned in pharmacopeia is generally employed for performing the dissolution test. The selection of medium depends on sink conditions and maximum drug dose. Most basket assembly is used, because the film can float in the medium in case of paddle apparatus, creating trouble during testing Dissolution studies performed in triplicate.

Swelling Index :
This test is carried out with simulated saliva. Weigh the film sample, set it on a wire sieve that has already been weighed, and then immerse the entire system in 50 cc of medium, or simulated saliva. Until a uniform value is obtained, the weight gain is measured at each interval[21].

Drug content and Drug uniformity :
The drug content can be determined using any of the common test techniques mentioned for the specific API. Calculating the API content in each film allows one to estimate the consistency of the content. The range of the content uniformity is 85-115% [22].

Contact Angle :
A goniometer is used to measure contact angles at room temperature (AB Lorentz and Wetter, Germany). On the dried film's surface, a drop of distilled water is applied. Digital cameras can record images of water droplets within 10 seconds of their deposition. The visual pictures are analyzed using imaging software to determine the contact angle.

Wetting Time :
The petridish is filled with 6 ml of a 0.1% w/v amaranth dye solution, and a circular piece of paper is placed within to gauge the amount of time the paper has been wet. The tissue paper is placed on top of the film strip (2x2 cm2). The amount of time needed for the dye to show up on the film's surface is known as the wetting time [23].

Tensile strength : The highest stress that may be applied to a strip specimen before it breaks is its tensile strength. As shown in the equation below, it is computed by dividing the applied load at rupture by the strip's cross-sectional area.

CONCLUSION :
In recent years, it has become common practice to incorporate various kinds of drugs into films. This drug delivery system is being monitored by both emerging and seasoned pharmaceutical firms. ODFs

were mostly used in over-the-counter (OTC) products when they first entered the market, but today prescription medications are also using them. The businesses work to create a wide range of thin Due to patient compliance (particularly in geriatrics and pediatrics), films are used for oral, sublingual, ophthalmic, buccal, transdermal routes.Therefore, anticipated that these polymeric thin films will replace traditional dosage forms as dosage form to get around the drawbacks of current dosage forms. Even though mouth dissolving tablets (MDTs) are widely used, there are some drawbacks to consider.Several benefits come with drug delivery via oral thin film.ODFs are an excellent dose form for usage with youngsters and the elderly because they are simple to swallow and pose no choking hazard.They typically include plasticizers, film-forming polymers,additional excipients, like those that enhance flavor. The low medication load of ODFs is their principal drawback. Solvent casting is a typical method for producing ODFs. Determining mechanical characteristics and disintegration behavior are fundamental characterisation procedures.

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