Int J Biol Med Res. 2025; 16(1): 7991-7996

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Review Article

"EVALUTION OF MOUTH DISSOLVING FILM BY PHYSICO-CHEMICAL METHOD"

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ARTICLEINFO

Keywords:
Mouth
Dissolving
Pharmaceuticals
Physico-chemical

ABSTRACT

Orodispersible pharmaceuticals, especially those in film form, provide a suitable dose form for patients who have dysphagia or other swallowing issues. They are also useful for a variety of patient demographics, such as the elderly, young patients, and those receiving cancer therapy. These films rapidly dissolve or disintegrate in the mouth, ensuring quick drug release for efficient absorption. The films are manufactured using a variety of processes, including rolling, dissolvable projecting, hot liquefy expulsion, and semisolid projecting, in order to preserve important properties including thinness, flexibility, and consistent drug distribution. Evaluation of orodispersible films involves assessing both physical and chemical parameters to ensure quality, uniformity, and performance. Techniques include mechanical property testing, in vitro disintegration studies, in vivo drug release assessments, and characterization of key chemical properties. Despite their advantages in ease of administration, oral thin film drug delivery does have limitations in terms of drug load capacity. Solvent casting remains a common method for manufacturing ODFs, and further development and optimization efforts focus on enhancing mechanical properties and disintegration behavior. Overall, a multidisciplinary approach integrating formulation science, material engineering, and pharmacology is essential to ensure the successful development of safe, effective, and patient-friendly orodispersible medications.

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Introduction

1.BACKGROUND [1-6]

Orodispersible medications refer to those that break down or disperse in the mouth within a maximum of 3 minutes, meeting ideal criteria outlined in a specific monograph. This form of medication is particularly beneficial for patients experiencing difficulty swallowing, such as those with dysphagia, as well as for geriatric, pediatric, and cancer therapy patients. Available in tablet and mouth dissolving film forms, orodispersible dosage forms ensure rapid drug release upon placement in the mouth.Thin polymeric strips known as orodispersible films rapidly dissolve or disintegrate on the tongue and are recognized by various terms in the literature. The European Pharmacopoeia's monograph on "oromucosal preparations" now includes orodispersible films, however the exact specifications for disintegration time are still unclear. The perfect orodispersible film should have characteristics like elasticity, softness, resistance to breaking, short disintegration time, and pleasant flavor. It is essential to evaluate these characteristics during the formulation development phase, employing standardized protocols. To evaluate and characterize orodispersible films, the pharmaceutical industry, regulatory agencies, and drug delivery research use a range of techniques, such as the evaluation of mechanical and physical properties, in vitro crumbling testing, and in vivo drug discharge concentrates on in people.

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2. IDEALREQUIREMENTS [7 -9]

•Orodispersible films (ODFs) need to maintain a balance between thinness and flexibility, ensuring stability for efficient manufacturing and packaging, and facilitating easy handling and administration.

• It's crucial for the films to be non-tacky, easily transportable, and maintain a flat shape without curling.

• Ease of administration is particularly important, especially for patients with mental illness, disabilities, or those who may be uncooperative.

• For the purpose of enhancing patient compliance, ODFs have to have a pleasing flavor and texture.

• Avoiding the need for water during administration is essential.

• Rapid drug release requires minimal disintegration time.

• ODFs should exhibit resilience to environmental factors like temperature and humidity.

• They should capitalize on the benefits of liquid medications in solid form.

• Unit ODF size should be manageable to ensure patient compliance.

• A smooth and uniform surface is necessary for an optimal patient experience.

• ODFs must maintain physical and chemical stability throughout their shelf life.

• It is crucial to provide cost-effectiveness and commercial manufacturing simplicity of use top priority.

Table1:Benefits and drawbacks of ODFs [9]

Benefits	Drawbacks
Quick start of action	Medication loading is restricted.
A patient's grievance	Extra expense to cover up the harsh taste of medication
When not using water	Uniform dosage is a technological difficulty.
Precise dosage	Generally hygroscopic
Prevents the first pass metabolism	need unique packaging
Lowering of the dosage	

Table2: Percentage of different components utilized in the formulation of ODFs[8]

Serial no.	Components	
A	Medication (API)	5-30%
B	Polymer Soluble in Water	45%
C	Plastifier	0-20%
D	saliva-stimulating substance	2-6%
E	Surface Active Agent	q.s
F	Sweeteneraid	3-6%
G	Taste,Dye,Filler	q.s

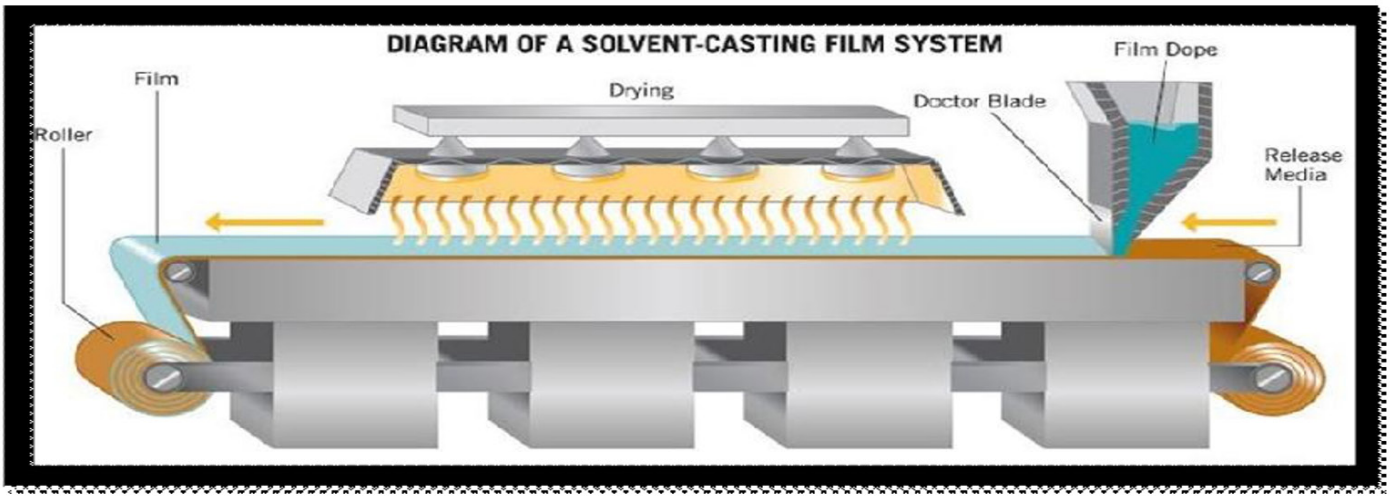
Table3:Ingredient examples usedinformationof ODTs[10]

Medicines	Polymeric Ingredients	Plasticizer	Sweetening Agents
Nicotine	Pullulan	Glycerin	D-glucose
Nitroglycerine	HPMC	PG(Propyleneg-lycol)	Fruit sugar
Zolmitriptan	Poly(acrylic acid) substitutions	The Dimethyl phthalate	Glucose
Loratidine	SodiumCMC	The Diethylphtha-late	maltobiose
Loperamide	Ethyl hydroxyce-llulose	The Dibuylphtha-late	wood sugar
Famotidine	HA (hydroxyalu-ronic acid)	Citrate tributyl	polyol
Flurazepam	Gum xanthan	triadcitrate	D-mannitol
Acrivastine	Gum from locust beans	Ethanoyl citrate	Sucralose
Dicyclomine	Gurr Gum	Glyceryl Triacetate	Nutrasweet
Omeprazole	Carragenan	vegetable oil	Sweetener

3. MANUFACTURING METHODS:

3.1 Casting Solution Technique [11]

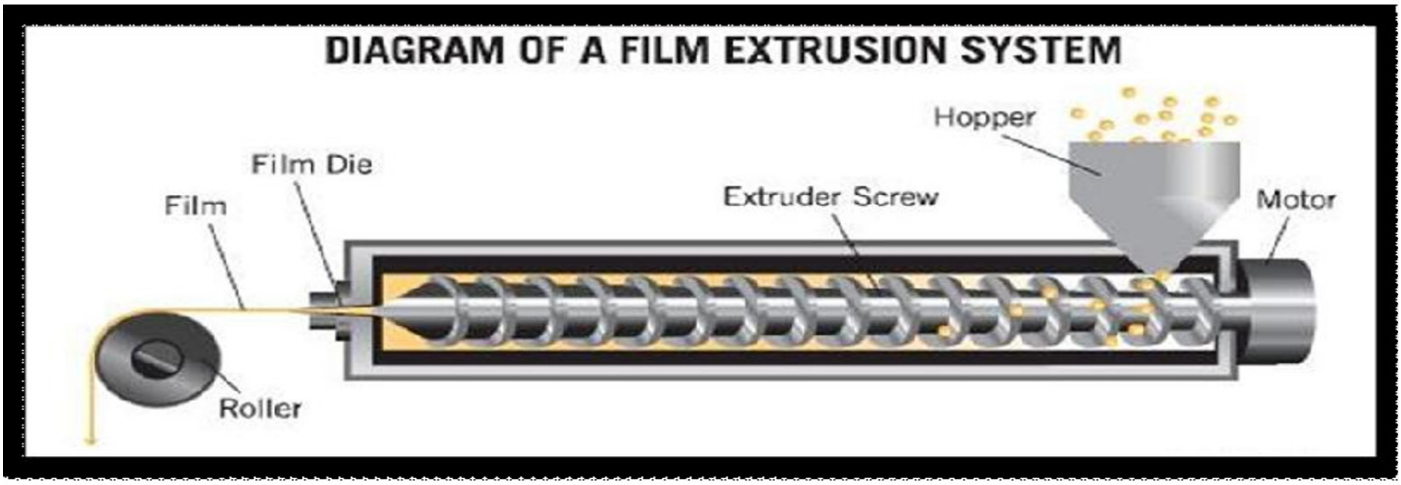
Using this technique, water-solvent polymers are disintegrated to create a steady arrangement.A tiny amount of water is used to dissolve the medication together with other components that dissolve in water. These solutions are blended together while continuously stirring to achieve uniformity. To remove any trapped air bubbles, vacuum pressure is applied. The resulting solution is then poured onto a surface that hasn't been treated, dried, and subsequently cut into pieces. For more information on the solvent casting method, refer to Picture 1 (source: particle science).



Picture 1:Film method for solvent casting

3.2 Heat Melt Extrusion [12]

Through the use of an extruder screw, hot melt extrusion entails heating and homogenizing the dry materials for the film until they are liquid and well combined.The liquid material is then pushed through a level expulsion kick the bucket to frame the legitimate film shape. The strength and thickness of the film might be adjusted utilizing stretching rollers while the material is as yet hot and pliable.Following extrusion, the film is chilled, sliced, and ready to be packed. For more information on the hot melt extrusion technique, refer to Picture 2(source: particle science).



Picture2:Heatmeltextrusionmethod

3.3 Method of Quasi-Solid Casting [13]

Initial, an answer of a corrosive insoluble polymer, for example, cellulose acetic acid derivation butyrate or phthalate, is joined with an answer of a water-solvent film-shaping polymer.A suitable amount of plasticizer is added to get a gel-like consistency.From that point forward, this gel mass is framed into movies or strips by warming and cooling drums.A film thickness of 0.015 to 0.05 inches is the ideal range, and a 1:4 proportion of corrosive insoluble and film-shaping polymers ought to be utilized.

3.4 Rolling Technique [14]

This multi-step procedure begins with the preparation of a pre-mix that contains the film-shaping polymer, polar dissolvable, and added substances —but not the medication.The first metering pump, control valve, and pre-mix are used to feed one or both of the first and second mixers after being added to aace clump feed tank.The required amount of medication is poured into the assigned mixer and mixed with the master batch pre-mix to create a homogenous matrix.The second metering pumps are then used to transmit a predetermined volume of this homogeneous matrix to the pan.Using support rollers, the film is created on the substrate and then removed.Lastly, controlled bottom drying is applied to the wet film.Water or a mix of water and liquor is the fundamental dissolvable carried out.

4.Evaluations of Orodispersible Films (ODFs)

After production using one of the aforementioned manufacturing methods, orodispersible films undergo thorough evaluation. In order to preserve homogeneity within and between batches, this procedure is essential.Evaluation takes into account a number of factors, which are grouped according to their chemical and physical characteristics.

4.1 Physical Specifications [15]

Physical characteristics are important because they enhance the final formulation's visual attractiveness and shed light on batch consistency. Albeit rigidity testing for careful stitches and fixes are generally illustrated in the US Pharmacopeia (USP), recommendations from other industries, such as the plastics industry, might be used as a point of reference.Tractable tests can be utilized, like those predefined in Racket EN ISO 527-1 and 527-3 guidelines or the ASTM Worldwide Test Strategy for Slender Plastic Sheeting (D 882-02).

4.1.1 Mechanical Specifications

a) Tamper / Dryness Test [13]

Tack is the film's solidarity of adherence to a piece of paper squeezed into contact with the strip; dryness is the estimation of the dissolvable or water content in the film. There are usually 8 steps in the process of film drying, spanning from set-to-contact to dried print-free.These qualities may be measured using a variety of devices; in the laboratory, a straightforward thumb push on the film is a typical technique.

b) Tensile Strength [16]

The best pressure applied forthright at which the film example breaks is addressed as rigidity.It may be computed using the cross-sectional region of the broke film and the applied load at rupture, which is the average of three observations.Details of various tensile testing instruments are provided in Table No. 4.

Tensile strength (N/mm2)=[Breakingforce (N)/Crosssectional area of sample (mm2)]

c) The % Elongation[11]

When a material experiences stress, it undergoes a sort of deformation called elongation.With the use of a texture analyzer, this shift in shape—usually perceived as an increase in length—can be measured.A sample essentially deforms and elongates when it experiences tensile stress. After the tensile measurement, the length increase of the film may be measured to determine the % elongation using the following formula:

%Elongation=[L-L0]X 100/L0

WhereLwas thefinallengthandL0was initiallength.

d) The Young's Modulus [17]

The elastic modulus, or Young's modulus, is a measurement of a film's stiffness. Young's modulus may be found using the same techniques as are used to measure tensile strength.It is addressed by the accompanying condition, which characterizes the area of versatile disfigurement as the proportion of applied pressure to strain:

Young'sModulus=Slopex100/Filmthicknessxcrosshead speed

Limited tensile strength and Young's modulus are seen in a thin, brittle layer with minimal elongation.

Table4: Various tensile testing instruments:

Instrument/Method	Procedure
A texture analyzer TA.XT2	It has a 5 kg load cell installed to measure the produced film's tensile strength. In short, film strips are held in place by two clamps that are spaced three centimeters apart. From that point forward, the strips were pulled at a speed of 2 mm/s by the top brace, and the force at which the film broke was recorded.
Palem et al. combined a motorized test platform with an improved force gauze that was based on a microcontroller	To secure the patch, sandwich the patch's strips between two clamps. The upper clamp pulls the strips apart at a speed of 2 mm/s until the strip breaks, while the bottom clamp remains motionless.
Tensiometer	Estimating the all out weight applied on the string to break the film yields the film's elasticity.
TheInstron	in addition to a five-kilogram load cell. Two clamps spaced three centimeters apart hold film strips of a specific size that are devoid of air bubbles or other physical flaws. At the point when the film breaks, the power and prolongation are estimated multiple times while the strips are being pushed at a speed of 100 mm/min by the top clamp.

e) Tear Resistant [18]

Plastic films or sheets that are resistant to tearing indicate their capacity to endure breaking under pressure. Typically, the power expected to begin tearing is estimated at an extremely low pace of stacking, as 51 mm (2 in.) each moment.The tear resistance number in Newton's (or pounds-force) represents the maximal stress or force required to rip the specimen, which is often close to the beginning of ripping.

f) Fold Endurance [16]

One essential physical property of a film that makes it easier to apply at the administrative site is its flexibility.Folding resilience provides a quantifiable measurement of the film's flexibility by folding it 300 times without breaking or at a 180° angle in the same plane.The folding endurance value of the film is determined by the number of folds it can withstand without breaking.

4.1.2 Other Physical Specification

a) Look / Appearance

The transparency or opaqueness of each manufactured film is evaluated based on its appearance.While surface qualities can also be assessed by use of tools such as microscopes, visual inspection is the usual method.

b) Density / Size (thickness) [16]

A micrometer screw gauge is used at many key spots to measure the size or thickness of the film.The middle and every one of the four corners ought to be estimated, and the mean thickness ought to then be processed.This guarantees consistency in the film's thickness, which has an immediate effect on the strip's dose precision.

c) Mass (Weight) Variation [16]

Weighing each film separately allows us to determine its average weight. Then, the singular loads are deducted from the typical load of the films. A significant variation in weight indicates method inefficiency and potential inconsistent drug content.

d) Angle of Contact [19]

A goniometer (e.g., AB Lorentz and Wettre, Germany) can be used to measure the contact angle at room temperature. This entails putting a drop of distilled water on a dry film's surface and using a digital camera to take pictures of the water droplet within ten seconds of it depositing. On both sides of the descent, contact angles are measured, and the average is computed.

e) Transparency [17]

A UV spectrophotometer is used to measure the films' transparency.The spectrophotometer cell is used to test the transparency of rectangular film samples at 600 nm.The following formula can be used to determine transparency is:

Transparency= (logT600)/b=—єC

Where,
T600=transmittanceat600nmb=thickness of the film (mm)
C=concentration

f) Content Moisture:[16]

The amount of dampness in a film has a big impact on how brittle and friable it is. The product's composition has a direct bearing on the film's moisture content.The moisture content can be ascertained using a variety of techniques, including Karl Fischer titration, weighing techniques, and moisture content testing equipment.Generally, a preweighed film of a particular size is heated to between 100 and 120°C until its weight remains constant.The quantity of moisture in the film may be determined by comparing the weight of the film before and after heating.

Moisturecontentcanbecalculatedas: -

%Content Moisture= [(Initial weight–Finalweight)×100/Initial weight]. The moisture content in an ideal film should be <5%.

4.2 ChemicalSpecifications:

a) Test for Surface pH [20-24]

By laying the film on top of a 1.5% w/v agar gel, the surface pH of the film may be measured.After that, pH paper with a color range of 1 to 11 is placed on the films, and any changes in the paper's color are noted and recorded.

b) Disintegration Time [11]

The film's disintegration and dissolution features may be understood through the analysis of disintegration time.A required-sized (2 x 2 cm2) film is inserted into a stainless steel wire mesh that holds 25 milliliters of artificial saliva at pH 6.8.The in-vitro disintegration time is a measurement of how long it takes for a film to break and disintegrate.

c) In Vitro Dissolution Studies [18]

For the purpose of performing dissolution testing, one may employ the standard basket or paddle apparatus as outlined in the pharmacopoeial guidelines. The selection of the dissolution medium is determined by the presence of sink conditions and the maximum dosage of the active pharmaceutical ingredient (API).Nevertheless, the examination could present difficulties occasionally because of the inclination of the strip to drift towards the dissolution medium when utilizing the paddle apparatus.

d) Thermic Analysis [16]

Thermal images of the specimens may be captured through the utilization of a differential scanning calorimeter (DSC).This procedure gives data on the state of the medication particles in the film.Phase transition, recrystallization, or molecular interaction of the drug molecule trapped inside the film is immediately indicated by any shift in the endothermic or exothermic peaks, or by an expansion of the peak area.In an aluminum pan, the sample is heated at a predetermined pace (~10 °C/min) from ambient temperature to a high temperature (~500 °C).

e) Crystallinity[16]

An X-ray diffractometer may be used for X-ray crystallographic investigations to identify whether the drug molecule in the film is crystalline or amorphous. Using a specific X-ray source, XRD transmission diffractograms are obtained over a predetermined diffraction angle, scan range, and scan speed after the films are placed in the sample holder.

f) Analysis / Uniformity of content[17]

Any standard assay procedure specified for the particular API in pharmacopoeial guidelines is used to ascertain this parameter.The limit of content uniformity is usually established at 85–115%. Content uniformity is evaluated by calculating the API content in individual strips

4.3 In Vivo Studies

In order to comprehend the swelling behavior of the films, efforts have been focused on modeling in vivo disintegration using techniques like contact angle measurements and thermo-mechanical analysis[4].

Using human volunteers and tasting panels, in vivo testing mainly involves assessing the films' flavor and in-vivo disintegration time.To evaluate the movie' flavor, electronic tongue testers are also used.

5. Discussion:

The provided content offers a comprehensive overview of orodispersible films (ODFs), focusing on their formulation, manufacturing methods, evaluation parameters, and importance in pharmaceutical development. Orodispersible medications, particularly in the form of films, provide a convenient dosage form for patients who have difficulty swallowing, such as those with dysphagia, as well as for certain patient populations like geriatric, pediatric, and cancer therapy patients. These films are intended to dissolve or break quickly in the mouth, releasing the medication for immediate absorption.

Dissolvable projecting, hot soften expulsion, semisolid projecting, and rolling are the accessible assembling strategies for ODFs; each has masters and disadvantages of its own. These methods ensure the films maintain essential characteristics such as thinness, flexibility, and uniform drug distribution.

Evaluation of ODFs is crucial to ensure their quality, uniformity, and performance. Physical parameters such as mechanical properties, appearance, thickness, weight variation, and transparency provide insights into the film's physical characteristics. Chemical parameters including surface pH, disintegration time, dissolution rate, thermal analysis, crystallinity, and assay/content uniformity assess the chemical properties and drug release behavior of the films.

In vivo testing further validates the performance of ODFs, particularly in terms of taste and disintegration time, often involving human volunteers and specialized equipment.

Overall, the development and evaluation of ODFs require a multidisciplinary approach, incorporating formulation science, material engineering, and pharmacology, to ensure the delivery of safe, effective, and patient-friendly medications.

6. Conclusion:

Oral thin film drug delivery offers numerous benefits, particularly in terms of ease of administration. ODFs (orodispersible films) are a great way to administer medication to kids and senior citizens since they're easy to swallow and don't cause choking hazards. Although ODFs are often made up of plasticizers, film-forming polymers, and other excipients to improve flavor, their ability to carry a medicine is limited. Solvent casting is a commonly employed method for ODF manufacturing. Key characterization methods involve assessing mechanical properties and disintegration behavior, laying a foundation for further development and optimization.

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