ORO-DISPERSIBLE FILMS:A MODERN EXPANSION IN FAST DISSOLVING DOSAGE FORMS

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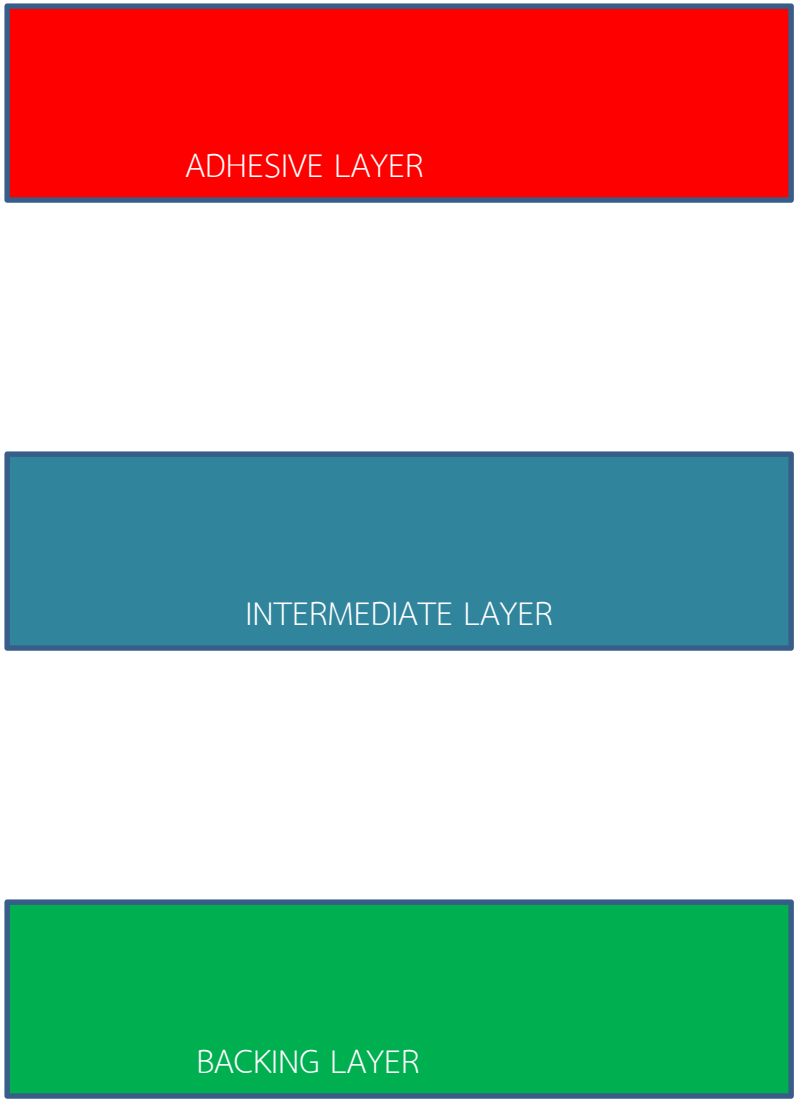
INTRODUCTION

- Oro-dispersible film drug-delivery systems were initially created in the late 1970s, utilizing the technology utilized for transdermal patches.
- For paediatric and geriatric patients who encounter difficulties in swallowing conventional oral solid-dosage forms, oro-dispersible film drug-delivery systems provide a substitute for tablets, capsules, and syrups.

Definition:

- An oral fast-dispersing dosage form refers to a solid dosage form that swiftly dissolves or disintegrates in the oral cavity, resulting in a solution or suspension, without requiring the administration of water.
- These types of dosage forms are also commonly referred to as orally dissolving films, flash release wafers, quick-dissolving films, soluble or buccal films, and are favored by the FDA. In addition, the European Medicines Agency employs the term "oro-dispersible films" to refer to this type of medication delivery.


ADHESIVE LAYER
Contains API
Or
Adhesion purpose only
INTERMEDIATE LAYER
Contains API Drug dissolution
Or
Shielded between layers
BACKING LAYER
Permanent Or
Dissolvable

SPECIAL FEATURES

- Oro-dispersible films are characterized by their thin and elegant nature, and are available in a variety of sizes and shapes.
- They are less fragile than orally disintegrating tablets and demonstrate excellent mucoadhesion, resulting in more accurate dosing.
- These films provide rapid release and can be administered without the need for water, making them highly suitable for dysphagic patients.

GENERAL PROPERTIES

Oro-dispersible films have a thickness that can range from 2-500mm and a surface area that spans 1-20 cm^2. These films are easy to handle and apply due to their low dry tack. They feature a rapid hydration rate, allowing for quick softening and absorption. In particular, a 2mm thick film can begin to disintegrate within 5-10 seconds.

ADVANTAGES:

Oro-dispersible films provide numerous benefits, including improved oral absorption, faster onset of action, minimized first-pass effect, and increased bioavailability, resulting in more accurate dosing. Additionally, these films can be easily administered without any special training and are associated with reduced gastrointestinal irritation.

DISADVANTAGES:

Limitations of oro-dispersible films include the inability to incorporate h doses, the inability to administer drugs that are unstable in the buccal pH, ar the requirement for special packaging to protect the films from moisture. Additionally, drugs with strong or unpleasant odors cannot be administered via oro-dispersible films.

APPLICATIONS OF ORAL STRIPS

- Topical application:

- Oro-dispersible films are a suitable option for delivering active agents, such as analgesics or antimicrobial agents.

- Gastro retentive dosage systems:

- Oro-dispersible films can accommodate the incorporation of poorly water-soluble and high molecular weight molecules, with dissolution being triggered by factors such as pH or enzymatic secretions.

- Diagnostic devices:

- Oro-dispersible films offer the ability to incorporate multiple agents, allowing for timed release in diagnostic devices.

Comparison between fast dissolving tablets and films

Fast dissolving Tablets	Fast dissolving Films
Lesser dissolution due to less surface area	Greater dissolution due to large surface area
Less durable as compared with oral films	Better durable than oral disintegrating tablets
Less patient compliance than films	More patient compliance
High dose can be incorporated	Low dose can only be incorporated
It has fear of chocking	No risk of chocking

Classification of Oral thin films:

1. Flash release wafers
2. Mucoadhesive melt away wafers
3. Mucoadhesive sustained release wafers

PROPERTIES	FLASH RELEASE WAFERS	MUCO-ADHESIVE MELT AWAY WAFERS	MUCO-ADHESIVE SUSTAINED WAFERS
Area(cm2)	2-8	2-7	2-4
Thickness(mm)	20-70	50-500	50-250
Structure	Single layer system	Single or multilayer	Multilayer system
Excipients	Soluble hydrophilic polymer	Soluble hydrophilic polymer	Low/non-soluble polymer
Drug phase	Solid solution	Solid solution or suspended solution	Suspension and/or solid solution
Dissolution	60 sec	Few min	Max 8-10 hrs
Application	Tongue	Gingival or buccal region	Gingival (other region in oral cavity)

Formulation development

Category	Conc(%)	Examples
Drug	1-25	NSAIDS, Antiemetic, Anti asthmatic, Snoring agents, Erectile dysfunction drugs
Hydrophilic Polymers	40-50	Pullulan, Gelatin, Starch, Sodium alginate, Pectin, Maltodextrin, HPMC, HPC, PEO, Kollicoat, PVA, PVP. Novel film forming polymer: Rosin
Plasticizer	25-35	PEG,PG, PHTHALATE Derivatives
Saliva secreting agents	2-6	Citric acid, Malic acid, Tartaric acid
Sweetener	2-10	Sucrose, Glucose,Fructose Aspartame, Sucralose
Flavor	2-5	Peppermint, vanilla,cofee, chocalate, Strawberry, Lemon

METHOD OF PREPARATION

- There are five methods available for preparing mouth-dissolving films.
  - Solvent casting method
  - Semisolid casting method
  - Hot melt extrusion
  - Solid dispersion technique.
  - Rolling method
- The most commonly preferred method for the production of mouth-dissolving films is the solvent casting method.

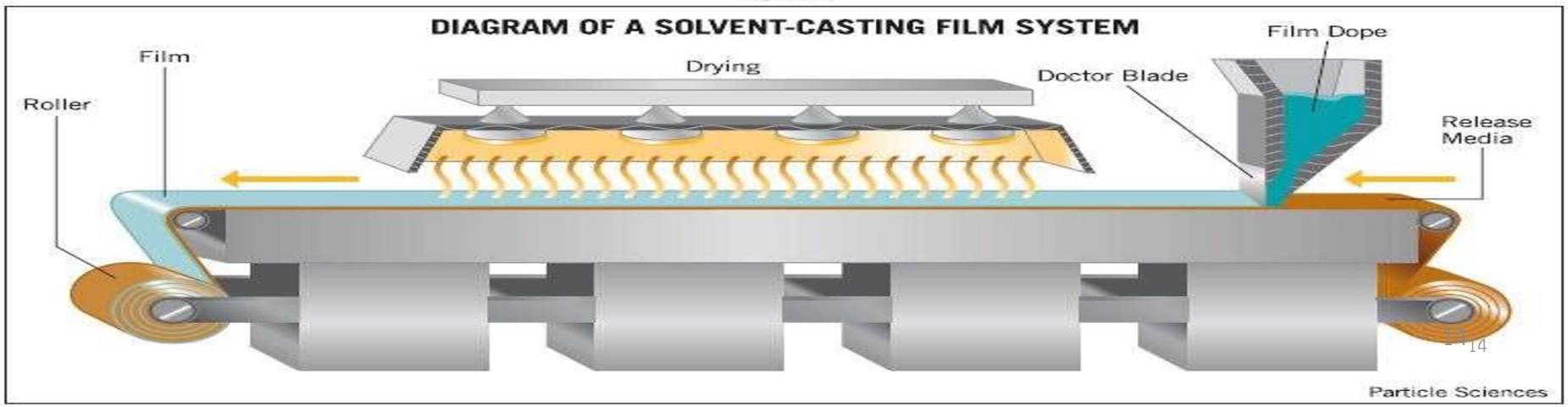
SOLVENT CASTING METHOD

1. In the solvent casting method, the excipients are initially dissolved in water, followed by the addition of water-soluble polymers. The drug is added last.

2. The solutions are mixed with the aid of a magnetic stirrer for 5 minutes to create a homogenous solution

3. Afterward, the solution is poured into a Petri plate and dried at a temperature of 40°C in a hot air oven.

Figure 1



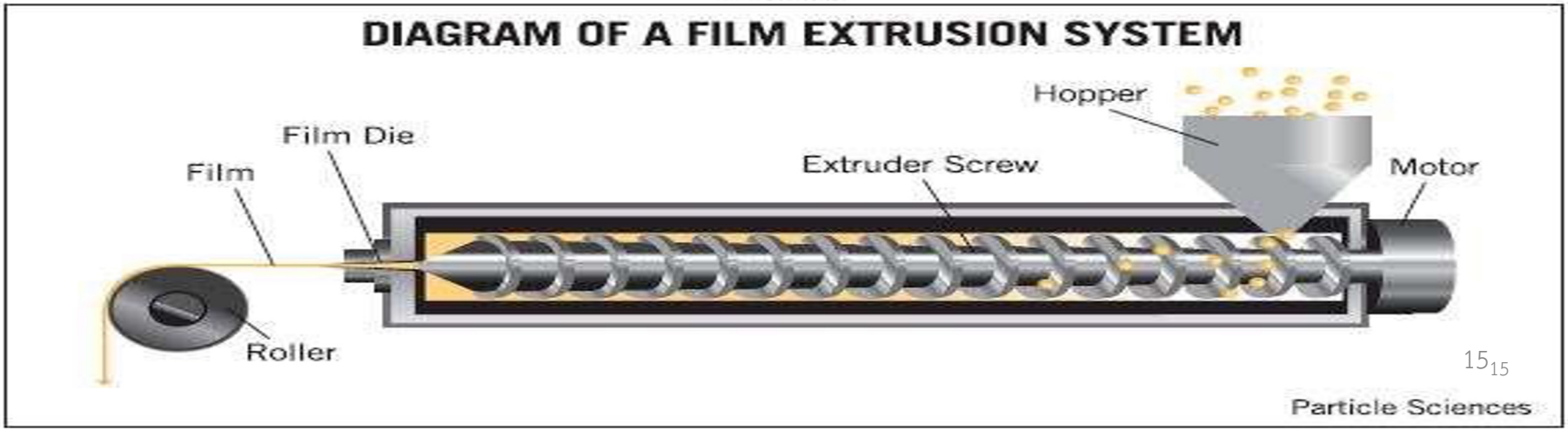
HOT – MELT EXTRUSION

The drug is mixed with carrier in solid form

Extruders having heaters melts the mixture Finally the

melt is shaped in films by the dies

Figure 2



SOLID DISPERSION EXTRUSION

Drug is dissolved in a suitable liquid solvent

Then solution is incorporated into the melt of polyethylene glycol, obtainable below 70^0c

Solid dispersions are shaped into the films by means of dies.

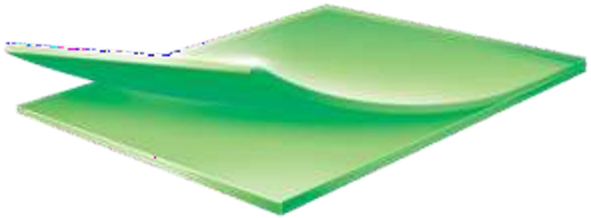
ROLLING METHOD

In this method firstly solutions or suspension of the drug is prepared

Either water or mixture of water and alcohol are mainly used

Suspension or solution containing drug is rolled on the carrier

Films are dried on the rollers and cut in to desired shapes and sizes



Evaluation

MORPHOLOGY STUDY	Scanning electron microscope Visual inspection
THICKNESS	Micrometer screw gauge WEIGHT VARIATION
Digital vernier callipers	
TENSILE STRENGTH	. (Load at failure * 100) / (Strip thickness * Strip width)
FOLDING ENDURANCE	A typical folding endurance for a film is 100 – 150
TRANSPARENCY	Transperancy=(logT600)/b=-€c

PERCENTAGE ELONGATION	(Increase in length of strip / initial length of strip) * 100
SWELLING PROPERTY	$(W_t - W_0)$ / W_0 SURFACE P^H OF
FILM P^H meter	
MOISTURE CONTENT	Karl Fischer titration method or weight variation $(W_t - W_0)$ / W_0
PERMEATION STUDIES	Franz diffusion cell
DISINTEGRATION TIME	Typical disintegration time for film is 30s Tests: Slide frame method Petri dish method
CONTACT ANGLE	Goniometer
DISSOLUTION	USP Type I or Type II

Packaging of orally disintegrating films

- Packaging options for oral thin films comprise of foil paper or plastic pouches, aluminum pouches, single pouches, blister packaging with multiple units, and barrier films.
- Barrier films are typically used for drugs that are extremely moisture-sensitive.
- Oro-dispersible films are manufactured using the Rapid Film Technology, which incorporates primary packaging in the form of a sealing pouch, providing sufficient space for logos, codes, instructions, and other necessary information.
- Barrier films are prepared through a laminating process, and the cost of packaging is comparable to that of tablets.

Market potential

According to a study conducted by Research and Markets in January 2015, the oral thin films market is projected to experience substantial growth from 2015-2025.

1. As of the time of the study, there were already 10 oral films on the market, with an additional 29 in varying stages of clinical and pre-clinical trials.
2. Roughly 38% of the market is occupied by 10 proprietary technologies, including PharmFilm, RapidFilm, and Bio-FX, among others.
3. As a result, there is significant potential for research and development within this technology.

FDA Approved ODF

Drug	Year	Company
Versafilm(Rizatriptan)	Feb /4 /2014	IntelGenx and RedHill Biopharma
Suboxone (Buprinorphine or Naloxone)	31/08/2010	Reckitt Benckiser Pharmaceuticals Inc.
Zulpenz	January 2010	Pharmfilm technology
Ondansetron	23rd march 2010	APR Applied Pharma research s.a (“APR”) and Labtech GmbH(“Labtech”)
Zelapar	October 2005	Valent Pharmaceuticals Interanational Inc

EXAMPLES OF MARKETED ODFs FOR SYSTEMIC DRUG DELIVERY

Brand	Distributor	Drug
Benadryl® Allergy quick dissolve strips	McNeil-PPC	Diphenhydramine HCL
Gas –X® thin strips	Novartis consumer health	Simethicone
Risperidon HEXAL® SF Schmelzfilm	Hexal AG	Risperidone
Sudafed® quick dissolve strips	McNeil-PPC	Phenylephrine HCL
Theraflu® Thin strips long acting cough	Novartis consumer health	Dextromethorphan HBr
Zulpenz™	Sativa Pharmaceuticals	Ondansetron

EXAMPLES OF MARKETED ODFs FOR LOCAL DRUG DELIVERY

Brand	Distributor	Drug
Chloraseptic® Sore Throat Relief Strips	Prestige brands	Benzocaine
Orajel® Kids Sore Throat Relief Strips	Church & Dwight Co.	Pectin
Snoreez Oral Strips	Passion For Life Healthcare	Peppermint oil, vitamin E, sodium hyaluronate, guar gum

LifeStrong MARKETING INC

Marketed OTF

CONCLUSION

In summary, oral films are considered to be one of the most promising and essential drug delivery systems due to their ability to rapidly disintegrate, dissolve, and facilitate absorption, especially for paediatric and geriatric patients.

While most formulations are currently developed as orally disintegrating tablets (ODTs), oral films have gained popularity due to their portability, improved patient compliance, and ease of administration.

- Oral films can be administered via both oral and buccal routes and are utilized not only as medicament films (for local anesthetics, vitamin supplements, and cold allergy remedies) but also as breath fresheners.
- The fast-paced growth of this technology is driving many pharmaceutical companies to develop oral films for a wide range of active pharmaceutical ingredients.

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