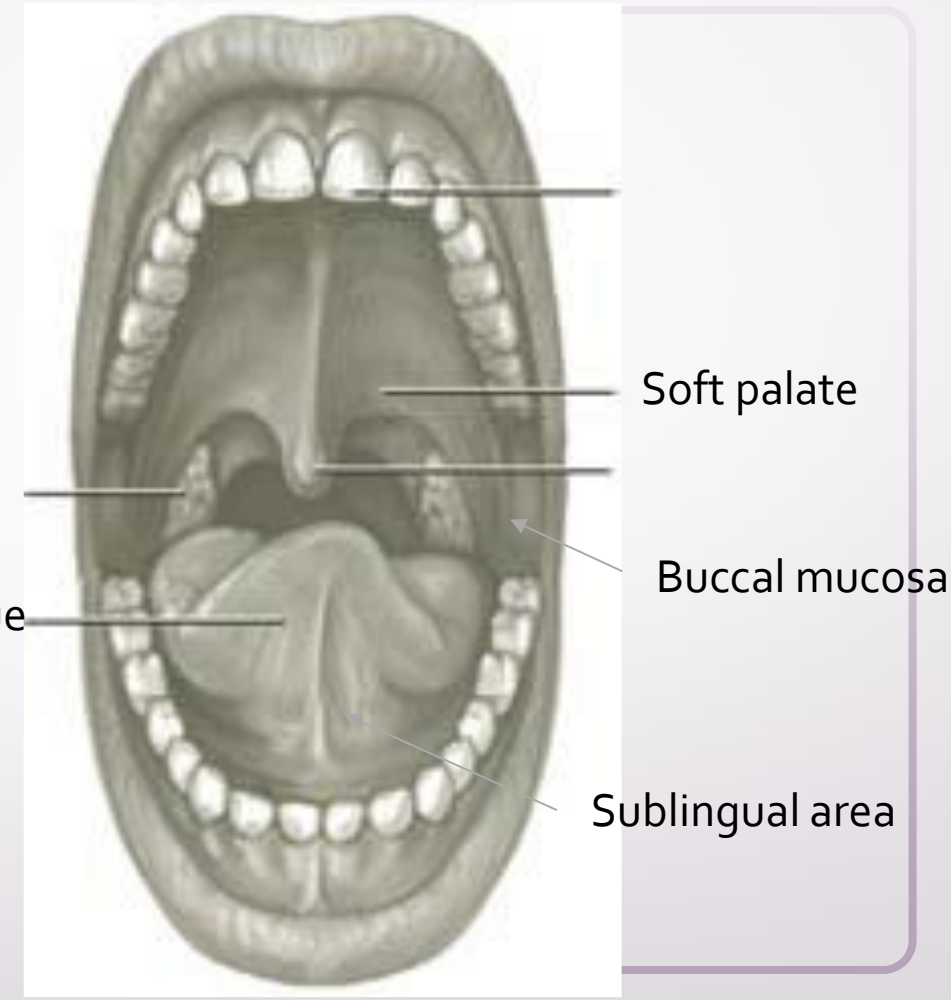
Beyond Conventional Tablets: Advancing Oral Drug Delivery through Fast Dissolving Formulations

By

Sara adnan

- There is considerable interest in developing dosage forms for the delivery of drugs from the oral cavity to drug targets in the systemic circulation.
- The absorbing membrane is easily accessible
- There are significantly fewer drug metabolizing enzymes in the mouth
- The considerable blood flow to the area
- circumventing the first pass losses to the liver that occur when drugs are swallowed

Drugs are applied to the entire oral mucosa for treatment of local conditions of the mouth or to the sublingual area and the buccal mucosa for treatment of conditions outside the mouth



The following properties affect the design of dosage forms for the oral cavity.

- must have good water solubility because of the relatively small volume of saliva there.
- Favorable log P for the oral cavity is between 2.0 and 4.0.
- Preferred molecular weight for moving through the multiple layers of epithelia is less than 500 Da.
- Drugs with stability problems may be formulated as solid dosage forms.
- Drugs with high first pass loss will have improved bioavailability when applied to the oral cavity. (peptide drugs)

Dosage forms designed for the oral cavity must

- 1. One dose in a manageable size unit

  The dimensions of solid dosage forms are limited to 1–3 cm2 and the dose contained generally needs to be 25 mg or less to maintain patient comfort with the size of the unit.

- 2. Palatable

  Because of its proximity to taste buds the drug must be rendered tasteless or masked with sweeteners and flavors.

- 3. Stable

paediatric oral dosage forms challenges

- While liquid dosage forms are traditionally preferred for children, there is growing interest in the use of orally administered solid dosage forms that are safe for all paediatric age groups.
- It is believed that solid dosage forms would avoid major disadvantages of oral liquids: poor stability, dosing inaccuracy, wastage, and non-compliance.
- limitations of conventional compact delivery systems (tablets and capsules) are issues with swallowing and the potential for choking
- Orally disintegrating drug carriers are thought to overcome several of the these challenges.

- There are several classes of orodispersible drug formulations that currently exist or already being investigated, and these include :

  Orodispersible tablets, films, granules, lyophilisates/orodispersible wafers, mini-tablets, and electrospun fibers or webs.

Orodispersible tablets

- intended to rapidly disintegrate in the mouth, rapidly forming a suspension or solution within 0 - 180 s.
- Requires minimal water, has good mouthfeel and taste, sufficient mechanical strength, and has high bioavailability.
- Although ODTs do not need to be swallowed, they should ideally be small: no larger than 8 mm.
- ODTs are manufactured to achieve a critical balance between mechanical strength and porosity.

Manufacture process

- Currently, several techniques such as direct compression, sublimation, mass extrusion, molding, and melt granulation are employed to produce ODTs.
- Another growing area of manufacturing for the pharmaceutical industry is 3D printing, which has recently been applied to develop orodispersible drug carriers.

- Spritam®, an orodispersible tablet formulation of levetiracetam was the first US FDA approved 3D printed orodispersible drug carrier.

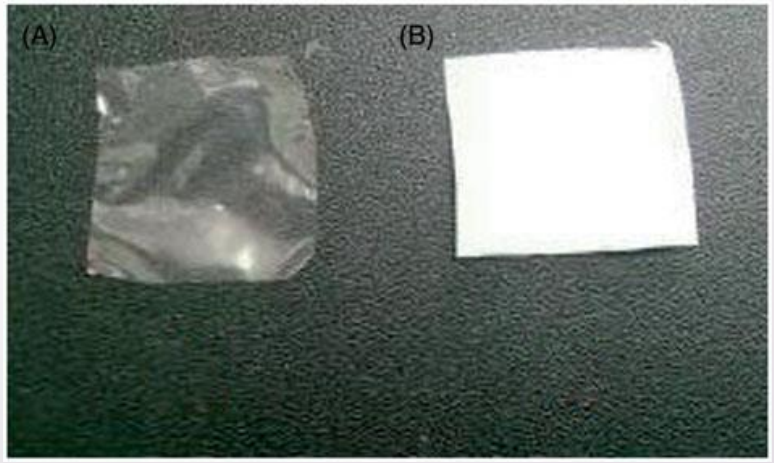
Orodispersible films

- Orodispersible films (ODFs) are single or multilayered sheets rapidly disperse when placed in the mouth
- They are most commonly rectangles or squares; however, circles and U-Shaped ones exist
- They inherently have a larger surface area than ODTs and as such, often have faster disintegration time
- often easier to handle, and store compared to ODTs since they are generally less brittle

Manufacture process

- Casting method. This method is commonly used due to its low cost and simplicity
- Extrusion through a sheet-die
- Printing technologies
- Rolling method.
- Freeze-drying

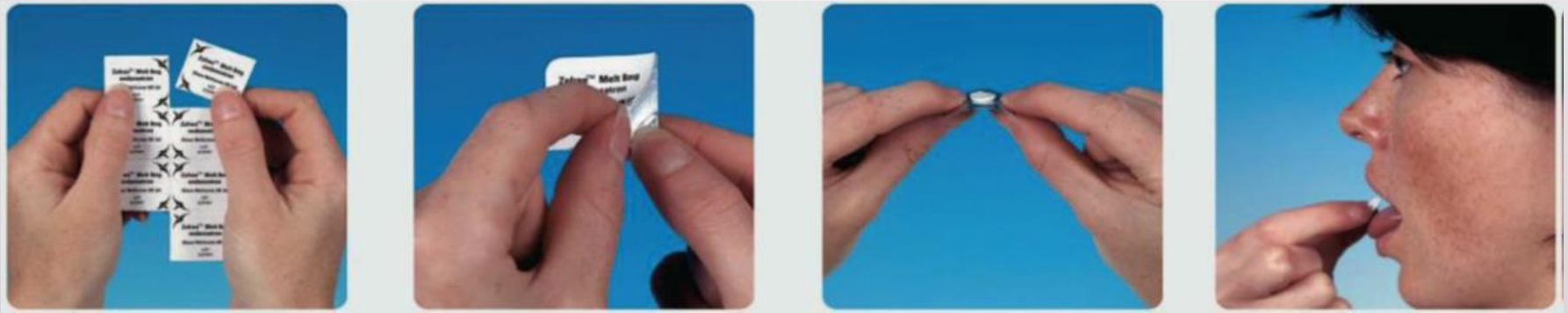
- Freeze-dried films generally showed lower tensile strength, but better folding endurance and disintegration time compared to heat-dried film.



Orodispersible lyophilisates/wafers

- produced from a solution or suspension of APIs and then freeze-dried directly in the blister package.
- They are a highly porous solid dosage forms with diverse dimensions depending on the type of casting mold employed
- commonly require special peel-off blister packaging because they are very fragile.
- Additionally, ORLs have low mechanical strength and poor stability at higher temperatures and humidity

- An example of a commercially available product that follows this process is Zofran Zydis®



Orodispersible granules and pellets

- multiple small-size carriers
- can be administered directly into the oral cavity.
- Additionally, they can be mixed with a drink or soft food before administration, which may help mask the taste of unpleasant drugs.
- Both granulation and palletisation techniques can be used to produce ODGs

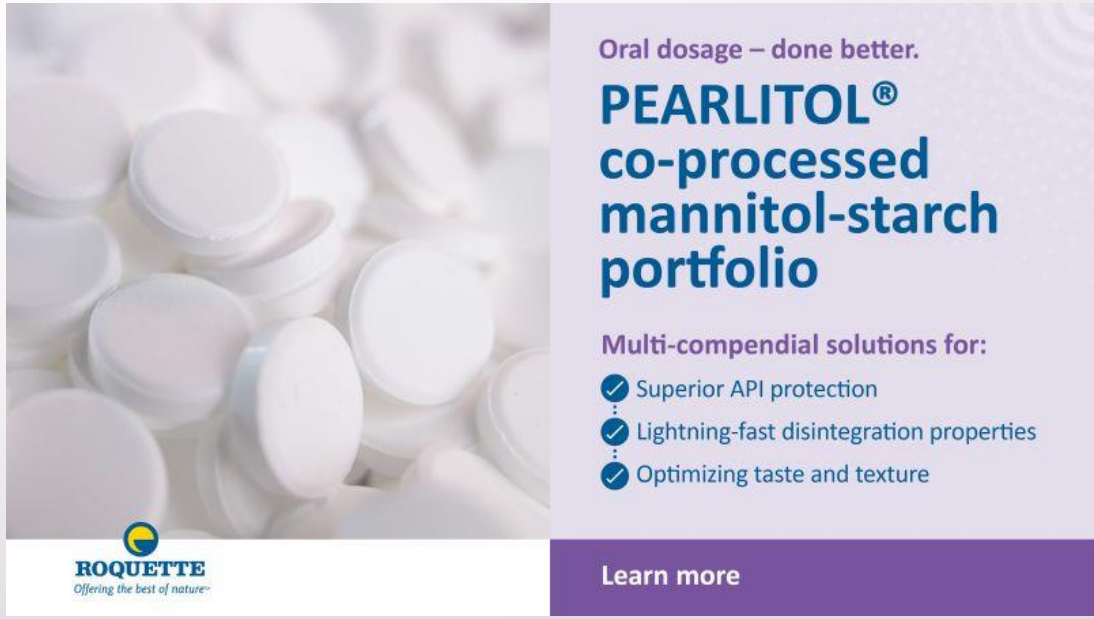
Orodispersible electrospun fibers and webs

- a newer advancement in the development of orodispersible drug carriers.
- The process starts by generating a high electrical field which is used to form a charged jet of polymer solution.
- The solvent evaporates in the air, leaving behind a charged fiber that is retrieved on a metal screen as solid nanofibers, which subsequently can be formed into an orally dissolving web (ODW)

- Advatages:
- large surface area created in the process
- fast disintegration (less than 15 s)
- good mechanical properties
- allows for two or more APIs to easily be incorporated

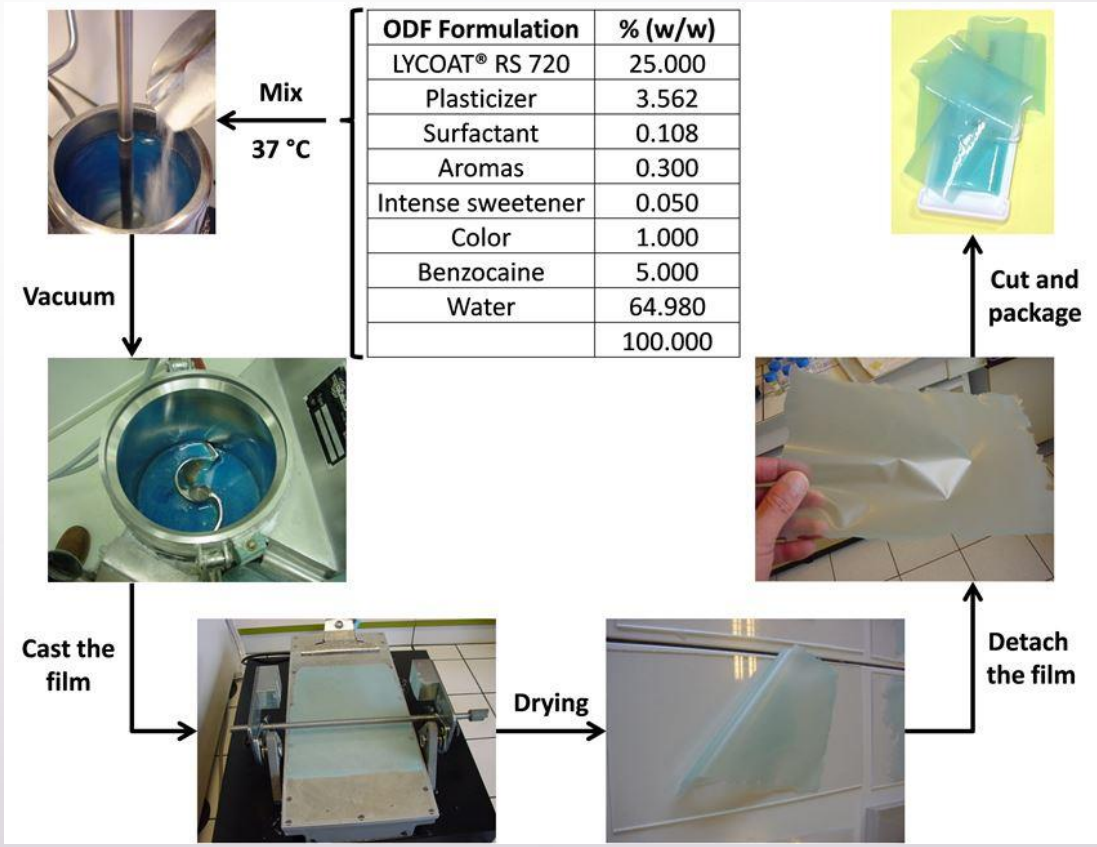
ODT platform

- PEARLITOL® Flash Co-processed Mannitol Starch provides excipient functional properties of **filler/binder** as well as some **disintegrant** benefit
- It is a direct compression excipient offers excellent chemical inertness and consistent rapid disintegration time. It brings a pleasant taste and texture and is suitable for swallowable and orally dispersible tablets.



Lycoat® RS 720 (as a film former)

- Pregelatinized hydroxypropyl pea starch
- is cold water soluble and offers film-forming and coating properties in various oral dosage forms
- It is a new alternative for the formulator with benefits such as instant dispersion at room temperature, excellent mechanical properties, high gloss and smoothness and a neutral taste.



ODF Formulation	% (w/w)
LYCOAT® RS 720	25.000
Plasticizer	3.562
Surfactant	0.108
Aromas	0.300
Intense sweetener	0.050
Color	1.000
Benzocaine	5.000
Water	64.980
	100.000

Thank you