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ORAL WAFERS IN DRUG DELIVERY: AN EMERGING PARADIGM

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Abstract:

Oral fast dissolving wafers have been introduced in the market recently as they are convenience and easy to use over other dosage forms such as oral disintegrating tablets. This technology has been using since as they are gaining the interest of a large number of pharmaceutical industries. Fast-dissolving drug-delivery systems were first developed in the late 1970 an alternative to tablets, capsules, oral syrups for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms like tablets. Oral wafers are easy to swallow and can be used without water. Companies with experience in the formulation of polymer coatings to active pharmaceutical ingredients (APIs) for transdermal drug delivery capitalized on the opportunity to transition this technology to designing of oral thin wafers (OTW) formats. Today, OTWs are a proven and an accepted delivery systems for the systemic delivery of APIs for over-the-counter (OTC) medications and are in the early- to mid-development stages of prescription drugs.

Key Words: Fast dissolving wafers, Solvent casting, Semisolid casting, Disintegration time, Contact angle.

1. Introduction

Fast Dissolving Wafers/Films

Fig 1: Oral wafers.

Oral route has been the mostly preferred, convenient and popular route for drug delivery. Nearly 70% of all the formulation is solid dosage forms. But, the geriatrics, pediatrics and bedridden patients are experiencing difficulties in swallowing or chewing solid dosage forms.

Hence, many pediatric and geriatric patients are unwilling to take solid formulations due to fear of choking of dosage forms. The above said problems could be successfully addressed by formulating the drugs into oral wafers. This wafers dissolves in the oral cavity without water. Fast dissolving films are more flexible and developing based on the transdermal patch technology.

Oral wafers are intended to place on the patient's tongue and are hydrates rapidly and disintegrates to release the drug within seconds. Now a day's fast dissolving films/wafers accepting worldwide as advanced oral drug delivery systems. The fast dissolving films will be rapidly release the medication for oral mucosal, and intragastric absorption.

History:

Fast dissolving drug delivery system first developed in 1970 in North America. By today more than 80 oral thin wafers branches are launched.

Special features of mouth dissolving films are

- Thin, and elegant films
- Available in various sizes and shapes
- Excellent mucoadhesives capture
- Fast disintegration and dissolution
- Rapid drug release
- Can be administered without water

Advantages:

- Oral dissolving wafers can be administered without water, anywhere ,any time
- No risk of chocking
- Some drug is absorbed from the mouth and esophagus as the saliva passes down to the stomach, which will be improve the bioavailability of drugs.

- Pregastric absorption can result in improved bioavailability and results of reduced dosage forms. Then improved clinical performance through a reduction of unwanted effect.
- Good mouth feel property helps to change the perception of medication as the bitter pill particularly in pediatric patients
- Useful in cases where the rapid onset of action required, such as in motion sickness, sudden episodes of allergic attack or coughing, bronchitis or asthma
- Stability for longer duration of time, the drug remains in solid dosage forms till it is consumed than the compression to the stability on liquid dosage forms
- Oral dissolving wafers are flexible and portable in nature, so they provide ease in transportation, during consumers handling and storage
- As compared liquid formulation, precision in the administered dose is ensured from each strip of the weavers'
- Taste masking
- The oral or ducal mucosa being highly vascularized drug can be absorbed directly and can enter the systemic circulation without undergoing first pass hepatic metabolism, this will be improved oral bioavlability of molecules which undergo first pass metabolism.
- Wafers has the potential to improve the onset of action, lower the design and enhance the efficacy and safety profile of the medicament
- Provide new business opportunity like product differentiation, product proportion patent extension

Dis advantages:

- High doses cannot be incorporated
- Dose uniformity is a technical challenge
- It is hygroscopic in nature, so it must be kept in dry places
- It also shows the fragile, granule property
- They require special packaging for the product stability and safety
- The drug, which is unstable give buccal pH cannot be administered

Table-1: properties of the oral films.

Property	Flash release	Mucoadhesive melt release	Mucoadhesive Sustained release
Area (cm^2)	2-8	2-7	2-4
Thickness(µm)	20-70	50-500	50-250
Structure	Film single layer	Single or multilayer system	Multilayer
Excipient	Soluble, highly hydrophilic polymer	Soluble or hydro phallic polymer	Low/non soluble polymer
Drug phase	Solid solution	Solid solution	Suspension
Application	Tongue (upper plate)	Gingival or vocal region	Gingival or other region
Dissolution	Maximum sixty seconds	Disintegration within few mins, forming a gel	Maximum 8-10 hours
Site of action	Systemic or local	Systemic or local	Systemic or local

Overview of oral mucosa:

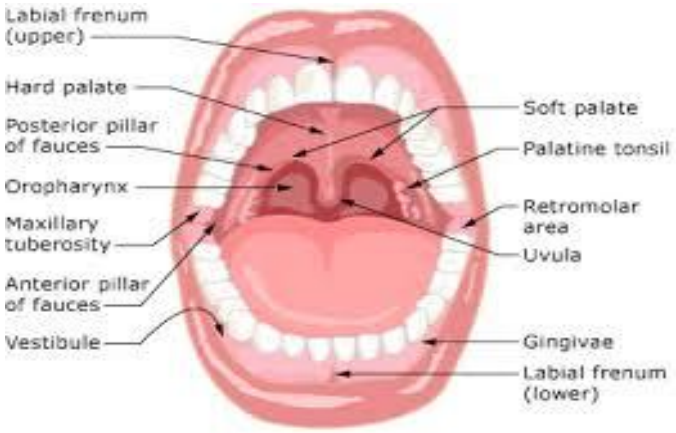

Fig 2: The vital areas of the buccal cavity

Structural features of oral mucosa

Structure: The oral mucosa contains an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the sub mucous as the innermost layer. The epithelium is similar to stratified squamous epithelia found in the rest of the body in that it has a mitotically active basal cell layer, advance through a number of differentiating intermediate layers in the superficial layer, where cells are shed from the surface of the epithelium .The turnover time for the buccal epithelium has been estimated at 5-6 days and this is probably representative of the oral mucosa as a whole. The oral mucosal thickness varies depending on the site: the buccal mucosa measures at 500-800 µm, while the maximal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue and the gingivae measure at about 100-200 µm.

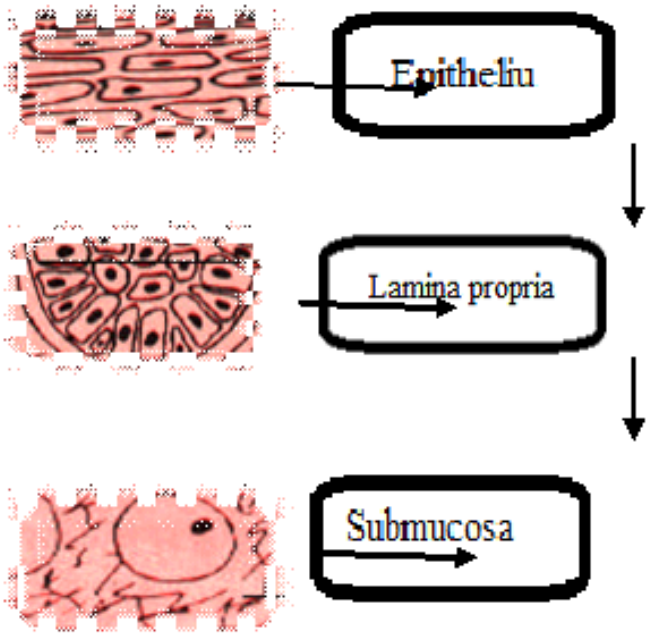

Fig 3: Various layers of oral mucosa.

Composition of oral mucosa:

The composition of the epithelium also varies depending on the site in the oral cavity. The mucosae of the gingivae and hard palate are keratinized similar to the epidermis, which contain ceramides and acylceramides (neutral lipids) which have been associated with the barrier function. The mucosa of the soft palate, the sublingual and the buccal regions are not keratinized which are relatively impermeable to water and only have small amounts of ceramide. They also contain small amounts of neutral, but polar lipids, mainly cholesterol sulfate and glucosyl ceramides. The figure 3 given above shows the layer of oral mucosa from outside to innermost.

Permeability: The oral mucosa in general is intermediate between that of the epidermis and intestinal mucosa in terms of permeability. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin. There is considerable differences in permeability between different regions of the oral cavity because of the diverse structures and functions of the different oral mucosa.

Oral mucosa: The oral mucosa contains proteins and carbohydrates. It is adhesive in nature and acts as a lubricant, allowing cells to move relative to one another with less friction. The mucus is also believed to play a role in bioadhesion of mucoadhesive drug delivery systems. In another part of body mucus is synthesized and secreted by the goblet cells, however, in the oral mucosamucus is secreted by the major and minor salivary glands as part of saliva. Up to 70% of the total mucus found in saliva is contributed by the minor salivary glands.

Table-2: Comparison between fast dissolving films (FDF) and fast dissolving tablets (FDT)

Fast Dissolving Film	**Fast Dissolving Tablet**
Gives Large surface area	Gives Less surface area
Gives greater dissolution	Gives less Dissolution than FDF.
Fast dissolving films are flexible and durable	Fast dissolving tablets are brittle and less durable than FDF.
Suitable for low dose drugs	Suitable High dose drugs
Thickness is0.015-.05 inches.	Thickness is more than 5 inches.
More patient compliance	Less patient compliance
No risk of choking	High risk of chocking

2. Formulation Considerations Of Designing Oral Wafers

The area of drug loaded FDF should be between 1-20cm^2. The drug can be loaded up toa single dose of 30mg.All excipients used in the fast dissolving film should begenerally regarded as safe (GRAS-listed) and authorized for use in oral strip. Formulation considerations have been reported as important factors which affect mechanical properties of the films.

Table-3: Formulation requirements of oral wafers.

Ingredients	**Amount %(w/w)**
Drug	1-30%
Film forming polymers	40-50%
Plasticizers	0-20%
Saliva stimulating agents	2-6%
Sweetening agents	3-6%
Flavoring agents	Qs
Surfactants	Qs
Colors, filler	Qs

Active pharmaceutical ingredient

A typical composition of the film contains 1-25% w/w of the drug. Variety of APIs can be delivered through fastdissolving films. Small dose molecules are the best candidates to be incorporated in OFDFs. Multi vitamins up to 10% w/w of dry film weight was incorporated in the films with dissolution time of less than 60 seconds. It is always useful to have micronized API which will improve the texture of the film and also for better dissolution and uniformity in the OFDFs. Many APIs, which are potential candidates for OFDF technology have bitter taste. This makes the formulation unpalatable especially for pediatric preparations. Thus before incorporating the API in the OFDF, the taste needs to be masked. Various methods can be used to improve the palatability of the formulation. Among the techniques employed, the simplest method involves the mixing and co-processing of bitter tasting API with excipient with pleasurable taste.

Table-4: Active pharmaceutical ingredients used in oral wafers.

Drug	**Dose**	**Therapeutic action**
Azatidine Maleate	1 mg	Anti histaminic
Nicotine	2mg	Smoking cessation
Loperamide	2mg	Anti diarrheal
Ondensetron	2.5mg	Anti emetic
Triplodine hydrochloride	2.5mg	Anti histaminic
Zolmitritpan	2.5mg	Anti migraine
Salbutamol	4mg	Anti histaminic
Chlorpheniramine Maleate	4mg	Anti allergic
Cortisone	5-10mg	Anti histaminic
Acrivastine	8mg	Anti histaminic
Loratidine	10mg	Anti histaminic
Omiprazole	10-20mg	Proton pump inhibitor
Famotidine	10mg	Antacid

Ketoprofen	12.5mg	Analgesic
Dicyclomine hydrochloride	25mg	Muscle relaxant
Diphenhydramine hydrochloride	25mg	Anti allergic
Sumatriptan succinate	35-70mg	Anti migraine

Film Forming Polymers:

Polymers are the most important ingredient of the oral fast dissolving film. Robustness of the film depends on the amount of polymer added in the oral strip. These polymers are mostly attracted considerable attention by medical and neutral ceutical industry. Generally 45% w/w of polymer is used which isbased on total weight of dry film. Mainly hydrophilic polymers are used in the oral strip as they rapidly disintegrate in the oral cavity as they come in contact with saliva.

Ideal Property of Film Forming Polymer:

- It should be non-toxic and non irritant
- Polymer must be hydrophilic
- It should have excellent film forming capacity.
- It should have good wetting and spread ability property.
- Polymer should be readily available & should not be very expensive
- Polymer should have low molecular weight
- It should have sufficient shelf-life.
- Polymer must be tasteless, colorless.
- It should not cause any secondary infection in oral mucosa
- It should exhibit adequate peel, shear and tensile strengths.

Water soluble polymers:

Water-soluble polymers are used as film formers. The film forming polymers in dissolvable films have attracted considerable attention in medical and nutraceutical application. The water-soluble polymers achieve rapid disintegration, good mouth feel and mechanical properties to the films. The disintegration rate of the polymers is decreased by

increasing the molecular weight of polymer film bases. Some of the Water soluble polymers used as film former are HPMCE-3 and K-3, Methyl cellulose A-3, A-6 and A-15, Pullulan, carboxy methylcellulose, cekol 30,Polyvinylpyrollidone (PVP) K-90, Pectin, Gelatin, Sodium Alginate, Hydroxy propyl cellulose, Polyvinyl alcohol, Maltodextrins and Eudragitrd-10Polymerized rosin is a novel film forming polymer.

Table-5: List of polymers used in the formulation of oral wafers.

Natural polymers	**Synthetic polymers**
pullulan	Hydroxypropylmethyl cellulose
Starch gelatin	Polyvinyal pyrrolidone
Pectin	Polyvinyl alcohol
Sodium alginate	Carboxy Methyl Cellulose
Malt dextrin	Poly ethylene oxide
Polymerized rosin	Kollicoat
Amylose	Hydroxy propyl cellulose
Xanthan gum	Hydroxyl ethyl cellulose

Plasticizers:

Plasticizer havebeen reported as important factors affecting mechanical properties of films. The mechanical properties such as tensile strength and elongation to the films have also been improved by the addition of plasticizers. Variation in their concentration may affect these properties. The commonly used plasticizers are glycerol, propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, citrate derivatives such astributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizers.

Surfactants:

Surfactants are used as solubilizing or wetting or dispersing agent so that the film is getting dissolved within seconds and release active agent immediately. Some of the commonly used surfactants are sodium lauryl sulfate, benzalkonium chloride, bezthonium chloride, tweens etc. One of the most widely used surfactant is polaxamer407 that is used as solubilizing, wetting and dispersing agent.

Saliva Stimulating Agents:

The rationale of employing saliva stimulating agents is to increase the rate of production of saliva that would be aid in the faster disintegration of the film these are generally acids which are used in the preparation of food can be utilized as salivary stimulants, like- citric acid, malic acid, lactic acid, ascorbic acid etc. These are used alone or in combination between concentration of 2 to 6%w/w of the film. Sweeteners are also act & as saliva stimulating agent

Flavoring agents:

Preferably up to 10%w/w flavors are added in the OFDF formulations. The acceptance of the oral disintegrating or dissolving formulation by an individual is largely depends on the initial flavor quality which is observed in first few seconds after the product has been consumed and the after taste of the formulation which lasts for at least about 10 min. The selection of flavor is dependent on the type of drug to be incorporated in the formulation. It was observed that age plays a significant role in the taste fondness. The geriatric population like mint or orange flavors while younger generation like flavors like fruit punch, raspberry etc. Flavoring agents can be selected from synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavors can be used alone or in the combination. Peppermint oil, cinnamon oil, spearmint oil, oil of nutmeg are examples of flavor oils while vanilla, cocoa, coffee, chocolate and citrus are fruity flavors. Apple, raspberry, cherry, pineapple are few examples of fruit essence.

Coloring agents:

FD & C approved coloring agents are used (not exceeding concentration levels of 1 %(w/w) in the manufacturing of orally fast dissolving films. Eg. Titanium dioxide silicon dioxide are also used as prominent coloring agents for oral films

3. Manufacturing Methods of Oral Wafers

The following methods are generally used in the preparation of oral wafers

1. Solvent casting method
2. Hot melt extrusion method
3. Semisolid casting method
4. Rolling method
5. Solid dispersion extrusion

1. Solvent casting method:

In this method water soluble polymer and plasticizer are dissolved in the distilled water. The solution is stirred up for 2 hrs in the magnetic stirrer and kept aside to remove all their entrapped air. Meanwhile, the excipient and API are dissolved and stirred well for 30 min, after the completion of stirring both the solutions are mixed and casted on a suitable solid substrate.

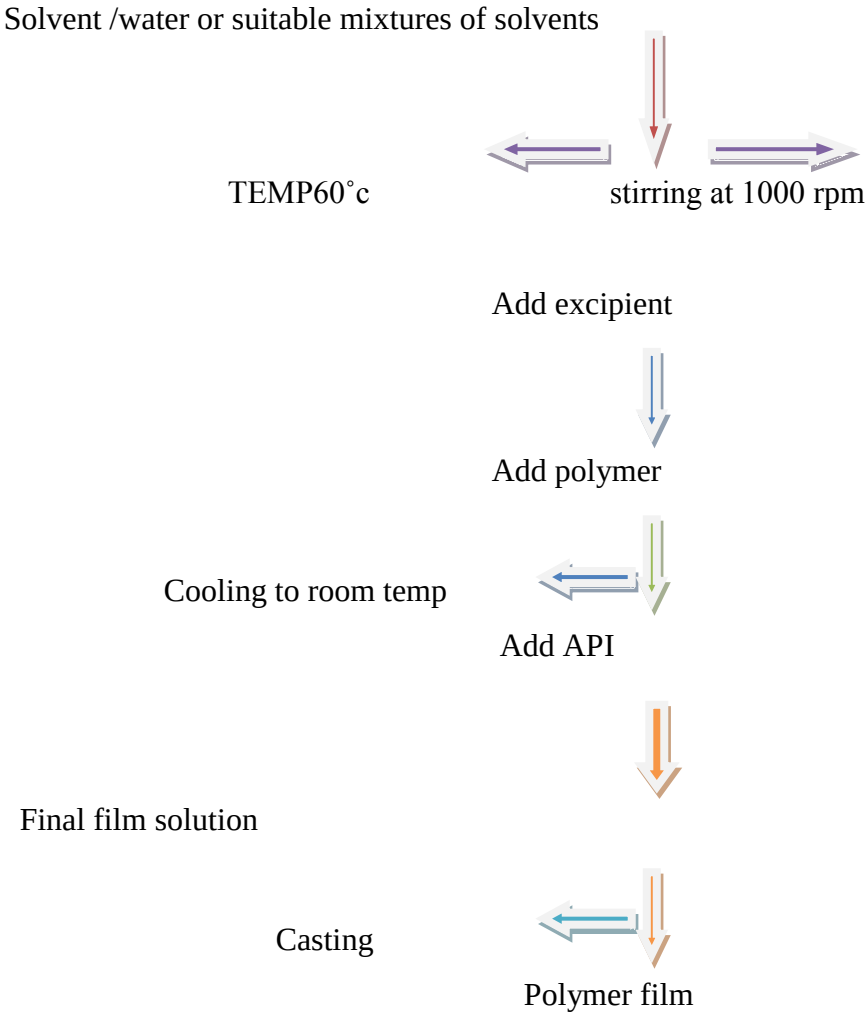

Fig:4: Flow chart of solvent Casting method.

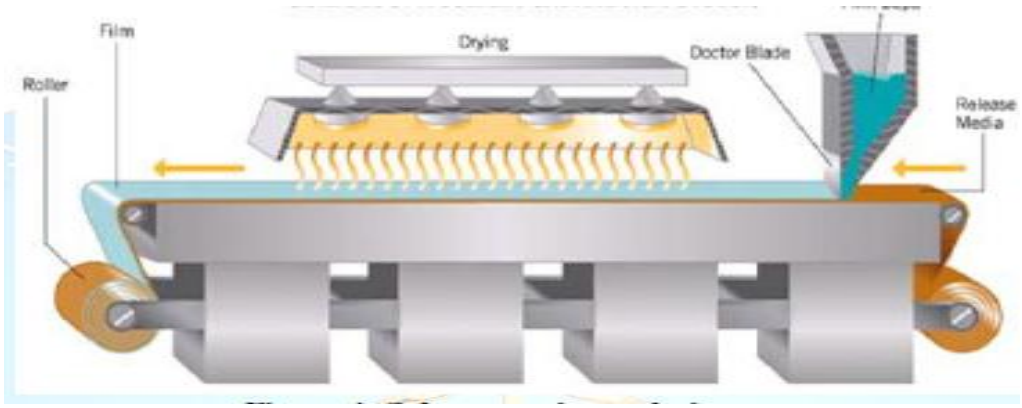

Fig 5: Industrial manufacturing of oral wafers by Solvent casting method.

2. Hot melt extrusion method:

In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally the melt is shaped in to films by the dies.

The advantages of hot melt extrusion method are as follows

1. Fewer operation units

2. Better content uniformity

3. An anhydrous process

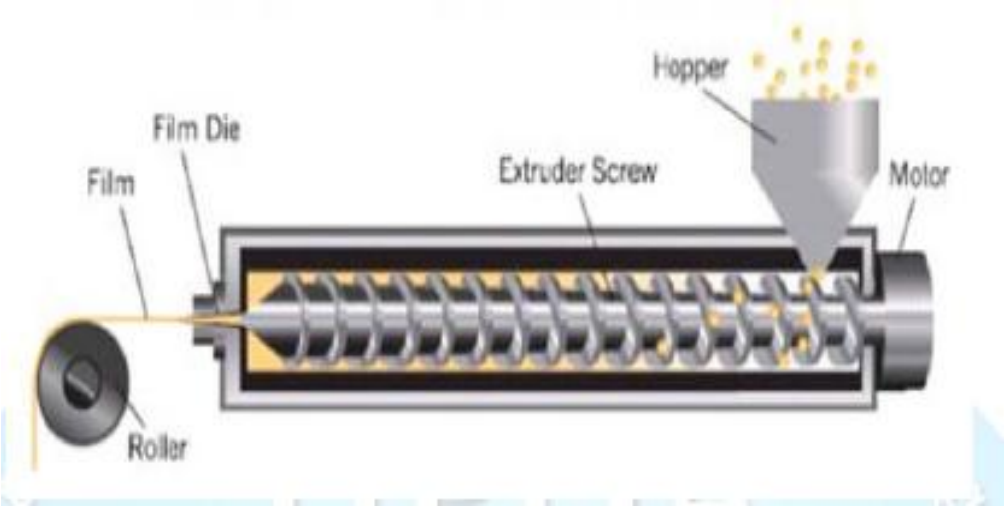

Fig 6: Apparatus for hot melt extrusion method of preparing oral wafers.

3. Semisolid casting:

In this method at first a solution of water soluble film forming polymer is prepared. Then the resulting solution isadded to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate) which was prepared in ammonium orsodium hydroxide. The ratio of the acid insoluble polymer to film forming polymer should be 1:4. A gel mass is obtained on addition of suitable amount of plasticizer. By the means of heat controlled drums, finally the gel mass is casted in to the films or ribbons

4. Rolling Method:

In rolling method a solution or suspension of drug with film forming polymer is prepared and subjected to the rolling. The solution or suspension should have specific rheological consideration. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cut in to desired shapes and sizes. The film is dried and carefully removed.

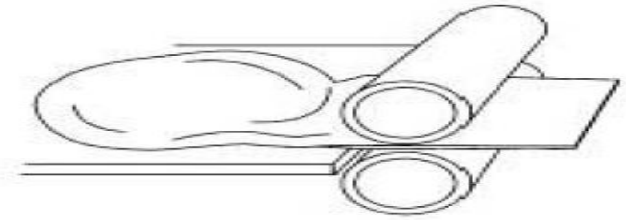

Fig :7 Apparatus used in Rolling Method of preparing oral wafers.

5. Solid dispersion extrusion:

Solid dispersion extrusion refers to the dispersion of two or more active ingredients in an inert carrier in the presence of amorphous hydrophilic polymers in solid state. The API is dissolved in suitable solvent and incorporated into PEG. The drug and solvents are immiscible in nature. Solid dispersions are then shaped into flat surface to form a film. The film is dried and carefully removed.

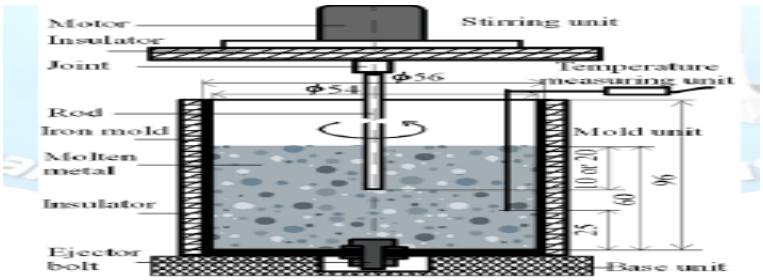

Fig 8: Solid dispersion extrusion methodof preparing oral wafers.

4. Patented Technologies of Wafer Production

1) SOLULEAVES™: This technology is used to produce an array of oral delivery films that can incorporate active ingredients, colors and flavors. SOLULEAVES™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavors. This quality makes edible films an excellent delivery method for a large range of product requiring fast release in the mouth. For pharmaceutical uses this method of administration is especially useful for pediatric or elderly patients who may have difficulty in swallowing traditional tablets or capsules. The delivery system can be used for the cough/cold, gastrointestinal and pain therapeutic areas as well as delivering nutritional products. SOLULEAVES™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 minutes.

2) WAFERTAB™: It is a drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB™ filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely

dosed and integrated into the body of a pre-manufactured XGEL™ film, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. The WAFERTAB™ system lends itself to many possibilities for innovative product design, enabling. Multiple films with different actives to be bonded together. WAFERTAB™ can be prepared in a variety of shapes and sizes and is an ideal method for delivery of medicines, which require fast release, or for use by patients who have difficulty swallowing.

3) FOAMBURST™: It is a special variant of the SOLULEAVES™ technology where an inert gas is passed into the film during production. This results in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation. FOAMBURST™ has attracted interest from food and confectionary manufacturers as a means of carrying and releasing flavors.

4) XGEL™: *XGEL* film is as IPR of Meldex International's, used in all its film systems and its ingestible dosage delivery technologies. GEL™ film provides unique product benefits for healthcare and pharmaceutical products: it is not are animal-derived, approved on religious grounds and is suitable for vegetarians; the film is GMO free and continuous production processing provides an economic and competitive manufacturing platform. GEL™ film can be taste masked, colored, layered, and capable of being enteric properties whilst also having the ability to incorporate active pharmaceutical ingredients. The XGEL™ film systems can be made to encapsulate any oral dosage form, and can be soluble in either cold or hot water. XGEL™ film is comprised of a range of different water-soluble polymers, specifically optimized for the intended use. All of the XGEL ingredients are well known and generally regarded as safe (GRAS).

5) Micap: Micap plc. Signed an option agreement in 2004 to combine its expertise in micro encapsulation technology with the Bio Progress water-soluble films. The developments will be aimed at providing new delivery mechanisms for the $1.4bn global market for smoking cessation products (SCPs).

4. Quality Control Test for Fast Dissolving Film:

1. Morphology Study:

The morphological studies are done by using of oral scanning electron microscopy (SEM) at a definite magnification. Study refers the differences between upper and lower side of films. It also helps in determination of the distribution of API.

2. Mechanical properties:

Mechanical properties of films are evaluated using texture analyzer equipment equipped with a 5kg load cell. Films are held between two clamps positioned between 3cm. During measurement the strips were pulled at rate of 2mm/sec. The force and elongation were measured when film breaks. Three mechanical properties namely tensile strength, elastic modulus and % elongation are calculated.

a) Thickness test

A micrometer screw gauge is used to measure the strip thickness. In order to obtain uniformity of film, thickness is measured at 5 different locations. The thickness of the film should be less than 5%.

b) Tack test

Tack is the tenacity with which the film adheres to the accessory that has been pressed into contact with strip. This test also determines the dryness.

c) Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by Formula

$$\text{Tensile strength} = \frac{\text{Load at Failure X 100}}{\text{Strip thickness X Strip Width}}$$

d) Percentage elongation: Percentage elongation of wafers is calculated by using the following equation.

$$\% \text{ Elongation} = \frac{\text{Increase in length of strip x 100}}{\text{Intial length of strip}}$$

e) Young's modulus:

Young's modulus or elastic modulus is the measure of stiffness of strip. It is represented as the ratio of applied Stress over strain in the region of elastic deformation as follows

$$\text{Young's modulus} = \frac{\text{Slope X 100}}{\text{Strip thickness X Cross-head speed}}$$

Hard and brittle strips demonstrate a high tensile strengthand Young's modulus with small elongation. Typical Young's modulus value for film is 0.30 ± 0.07MPa.

f) Tear resistance:

Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. The maximum stress or force (that is generally found near the Onset of tearing) required to tear the specimen is recorded as the tear resistance value in Newton's (or pounds-force).

g) Folding endurance:

To determine folding endurance, a strip of film is cut and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gives the value of folding endurance. Typical folding endurance for film is between100-150.

3. Organoleptic evaluation:

For these purpose *invitro* methods of utilizing taste sensors and specially designed apparatus are being used. These *invitro* taste assessment apparatus are opted for high-throughput taste screening of oral pharmaceutical formulations.

4. Swelling index:

The studies of swelling index of the film are conducted in simulated salivary fluid. The film sample is weighed and placed in a pre-weighed stainless steel wire sieve. The mesh containing the film is submerged into 50ml of simulated salivary medium contained in a mortar. Increase in weight of the film is determined at each interval until a constant weight is observed. The degree of swelling is calculated using the formula:

SI = wt - wo / wo

Where,

SI = swelling index,

Wt. = weight of the film at time "t", and

wo = weight of the film at t = 0

5. Surface of pH**:**

Surface pH of the film was determined by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on film. The change in the color of pH paper was observed and report.

6. Contact Angle: Contact angle are measured by Goniometer at room temperature. Take a dry film and place a drop of distilled water on the surface of the dry film. Images of water droplet were recorded with in 10 sec of deposition by means of digital camera. The contact angle was measured on both side of drop and average is considered.

7. Transparency:

The transparency of the films can be determined using a simple UV spectrophotometer. Cut the film samples into Rectangles and placed on the internal side of the spectrophotometer cell. The determine transmittance of films at 600 nm. The transparency of the films was calculated as follows:

Transparency = (logT600)/b = - €c

Where,

T600 is the transmittance at 600 nm

b is the film thickness (mm)

c is concentration

8. Uniformity of drug content:

This parameter can be determined by dissolving known weight of film by homogenization in 100 ml of simulated Saliva of pH 6.8 for 30 min with continuous shaking. Content uniformity is determined by estimating the API Content in individual film. Limit of content uniformity is85-115%.

9. Moisture content:

Initially the prepared film was weighed and placed in the desiccators containing cadmium chloride. After 3 daysthe film was reweighed to obtain the percentage of moisture loss

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final Weight}}{\text{Initial weight}} \times 100$$

10. Disintegration test:

Disintegration time is defined as the time (seconds) at which a film breaks when brought in contact with water or saliva. The disintegration time limit of 30 s or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral film. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for film is5-30 s.

- **Slide frame method:** one drop of distilled water was dropped by a Pipette onto the oral films. Therefore theFilms were clamped into slide frames and were placed planar on a Petri dish. The time until the film dissolved and caused a hole within the film was measured.
- **Petri dish methods:** 2 mL of distilled water was placed in a Petri dish and one film was added on the surface of the water and the time measured until the oral film was dissolved completely.

11. *In-vitro* Dissolution test:

By this method cumulative drug release and cumulative percentage of drug retained were calculated. *In-vitro* drug dissolution was performed using USP paddle type apparatus. The studies were carried out at 37°C with Stirring speed of 75 rpm in 900 ml phosphate buffer (pH6.8). 5 ml of samples were withdrawn at predetermined Time intervals of 2, 4, 6, 8, 10 min and replaced with the same volume of buffer. The samples were collected and the concentration was determined at appropriate wavelength using UV-visible spectrophotometer.

5. Packaging of Oral Wafers:

A variety of packaging options are available for fast dissolving films. Single packaging is mandatory for Films, which are pharmaceutical products; an aluminum pouch is the most commonly used packaging format. APR-Labtec has developed the Rapid card, a proprietary and patented packaging system, which is specially designed for the Rapid films. The rapid card has same size as a credit card and holds three raid films on each side. Every dose can be taken out individually2.A variety of packaging optionsare available for fast dissolving Wafers. Single packaging is mandatory for Wafers. An aluminum pouch isthe most commonly used packaging format.

1) Single pouch: Soluble Film Drug Delivery Pouch is appealable pouch for "quick dissolve" soluble films with high barrier properties. The pouch is transparent for product display. Using a 2 structure combination allows for one side to be clear and the other to use a cost effective foil lamination. The foil lamination has essentially zero transmission of both gas and Moisture. The package provides a flexible thin film alternative for nutriceutical and pharmaceutical applications. The single dose pouch provides both product and dosage protection.

2) Blister card with multiple units:

The blister Container consists of two components: the blister, which is the formed cavity that holds the product, and the lid stock, which is the material that seals to the blister. The film selection should be based upon the degree of protection

required. Generally the lid stock is made of aluminium foil. The material used to form the cavity is typically aplastic, which can be designed to protect the dosage from moisture.

3) Polyvinyl Chloride: The most commonly used blister material is polyvinyl chloride (PVC). This material, which provides a nominal or zero barriers to moisture, is used when the product does not require Effective moisture protection.

4) Barrier Films: Many drug preparations are extremely sensitive to moisture and therefore require High barrier films. Several materials may be used to provide moisture protection such as Poly-chloro trifluoroethylene film, Polypropylene.

5) Continuous roll dispenser: An automatic drug tape dispensing and metering device and a disposable Cassette containing a roll of drug tape housed in a Small reusable portable dispenser unit. The dispenser contains a measurement device for carefully measuring the length of tape as it is dispensed. A Counter monitors the remaining doses of drug tape remaining within the dispenser. A timer device may be provided to alert the patient that it is time for the Medicament to be dispensed. As the lid of the dispenser unit is opened, the measured length of drug Tape is severed from the roll by a cutter blade in corporate into the lid. The administration of the dose to the patient may be set by adjusting the tape length released for each single dose and selecting the time Intervals between dosages. The invention comprises also ingestible tapes of medicament

Table 6: Marketed medicated wafers.

Product	**Manufacturer**	**Active Pharmaceutical Agent**	**Strength (mg)**
Triaminic	Novartis	Dextromethorphan HBr	7.5
Triaminic	Novartis	Diphenhydramine HCl	12.5
Theraflu	Novartis	Dextromethorphan HBr	15
Gas-x	Novartis	Simethicone	62.5
Sudafed	Pfizer	Phenylephrine HCl	10
Benadryl	Pfizer	Diphenhydramine HCl	12.5
Chloraseptic	Prestigine	Benzocmenthol	3/3
Suppress	Innozen	Menthol	2.5
Orajel	Del	Menthol/pectin	2/30
Listerine	Pfizer	Cool mint	-

Conclusion:

Fast dissolving oral films have several advantages over the conventional dosage forms. So they are of great importance during the emergency cases such as allergic reactions and asthmatic attacks whenever immediate onset of action is desired. Oral fast dissolving films have emerged as revolutionary trend and an extensive research activities involving various categories of drug are going on in this field. This technology is useful for vast category of patients specially geriatrics, pediatrics and also it offers many advantages like enhanced bioavailability and faster action over other dosage forms like tablets and capsules and also have great potential of delivering the medicinal agent systemically as well locally. So it can be concluded that the oral films are highly advantageous with high patient compliance hence they have glowing futuristic opportunities. OFDFs are not well defined in the literature but these are considered as revolutionary and an innovative drug delivery systems for all the population groups, specifically geriatric, pediatric patients and patients with swallowing difficulties.

References:

1. Priya Y D, Chaudhary Y A, Murthy T E G K, SeshagiriB. Approaches for taste masking of bitter drugs: a Review. Journal of Advances in Drug Research. 2011;(2): 58-67.
2. Parul Saini, Anoop Kumar, Pankaj Sharma, Sharad Visht, Fast Disintegrating Oral Films: A Recent Trend of Drug Delivery International Journal of Drug Development & Research, October-December 2012 **,** 4**(**4) **,** 80-94.
3. Banker G S, Film coating theory and practice Journal of Pharmaceutical Sci.1966, 55, 81- 89.
4. Chien M J, Tirol. G, Charles. B, Corniello. C, Waston G, Sanchez. I., Castable edible pharmaceutical films, Dow Chemical Company, West Haven, USA. 2007, 1-7.
5. Thakur Smriti. Mouth dissolving films: a review, International Journal of Pharma and Bio Sciences,2013 Jan; 4(1), 899 – 908.
6. Naga Sowjanya Juluru, Fast dissolving oral films: areview,International Journal of Advances in Pharmacy, Biology and Chemistry Vol. 2(1), Jan- Mar, 2013, 108-112.
7. Gowri R Narayanan N, Revathy S Prabhavathy P, et.al, Melt in Mouth Films- an effective alternative drug delivery system, International Journal of Biological &Pharmaceutical Research. 2013; 4(9): 645-650.

8. Malke M, Shidhaye S, Kadam VJ. , Formulation and evaluation of Oxacarbazine fast dissolve tablets. Indian Journal Pharmaceutical Sci. 2007;69: 211-214.
9. Vollmer U, Galfetti P. Rapid film: Oral thin films as an innovative drug delivery System and dosage form.Drug Dev Report. 2006; 64-67. http:// www.apr.ch
10. Frey.Film Strips and Pharmaceuticals. Pharma Mfg & Packag Sourcer. 2006:92–93.
11. Vondrak B, Barnhart, Scott. Dissolvable Films: Dissolvable Films for Flex Product Format in Drug Delivery. Pharmatech. 2008; 1-5.
12. Suresh B, Halloran D, James L. Quick dissolving films: A novel approach to drug delivery. Drug Development and Technology. 2006;1-7. http://www.drugdeliverytech.com
13. Mashru R C, Sutariya BC, Parikh PP. Development and evaluation of fast dissolving films of salbutamol sulphate. Drug Dev Ind Pharm. 2005;31:25-34.Doi: 10.1081/DDC-200043947
14. Gohel MC, Sharma R, Soniwala MM. Development of taste masked film of Valdecoxib for oral use. Indian journal of Pharmaceutical Sciences. 2007;69:318-320.
15. http://www.hughes-medical.com/products/fast-dissolving-film.htm
16. Cilurzo F, Paola M, Andrea C. Maltodextrin Fast –Dissolving Film: A Feasibility Study. Pharma Films Srl, Milano Italy. http://www.tecnova-srl.it/download/film@EUFEPS051.pdf
17. Chien M J, Tirol G, Chien C, Schmitt R.Film forming polymers in oral films. Poster presented at the 2006Annual Meeting and Exposition of the American Association of Pharmaceutical Scientist Oct. 29–Nov.2AAPS. 2006; 1-5.
18. Cilurzo F, Minghetti P, Como A, Montanari L. Feasibility study of fast-dissolving film containing Piroxicam. The American Association of Pharmaceutical Sciences, W4148-W4148. AAPS Annual Meetingand Exposition, Nashville, 2005
19. Chien M J, Tirol G, Charles B, Corniello C, Waston G, Sanchez I. Castable edible pharmaceutical films. Dow Chemical Company, West Haven, USA. 2007; 1-7.
20. Fulzele S V, Satturwar P M, Dorle A K. Polymerised rosin: Novel Film Forming Polymer for drug delivery. International Journal of Pharmaceutical sciences. 2002; 249:175-184. Doi : 10.1016/S0378-5173(02)00529-X.

21. Habib W, Pritchard JF, Bozigian HP, Gooding AE, Griffin RH, Mitchell R, Bjurstrom T, Panella TL, Huang AT, Hansen LA, Fast-dissolve drug delivery system. Crit. Rev. Ther. Drug Carrier Syst. 17: 2000: 61–72.
22. Liang C A, Chen HL, Fast dissolving intraoral drugdelivery systems. Expert Opin. Ther. Patents. 11: 2001:981-986. 3. Anderson O, Zweidorff OK, Hjelde T, Rodland EA, Problems when swallowing tablets. Tidsskr NorLaegeforen. 115: 1995: 947-949.
23. Joseph F Standing, Catherine Tuleu, Paediatric formulations: Getting to the heart of the problem.International Journal of Pharmaceutics. 300: 2005: 56–66.
24. Goel Honey, Rai Parshuram, Rana Vikas, Tiwary K Ashok, Orally Disintegration systems: Innovations in formulation and Technology. Recent Patents on Drug Delivery &Formulation. 2: 2008: 258-274.
25. Bhowmik Debjit, Chiranjib B, Krishnakanth, Pankaj, Margret R Chandira, Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research. 1(1):2009: 163-177.
26. Patel RA, Prajapati SD, Fast dissolving films (fdfs) as anewer venture in fast dissolving dosage forms. International Journal Drug Development & Research.2(2): 2010: 232-246
27. Technology catalysts International Corporation, accessedon 2011 feb 14th Available fromhttp://www.technologycatalysts. com.
28. Zhang H, Zhang J, Streisand JB, Oral mucosal drug delivery: clinical pharmacokinetics and therapeutic applications. Clinical. Pharmacokinetics. 41: 2002: 661-680.
29. Mashru RC, Sutariya BC, Parikh PP, Development andevaluation of fast dissolving films of salbutamol sulphate. Drug Delivery Industrial Pharmacy. 31; 2005:25.