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REVIEW ON PREPARATION AND EVALUATION OF ORAL DISINTEGRATING FILMS

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Abstract:

Recent modification are done in the conventional tablet to avoid the acceptance problem of pediatric , psychotics and bed ridden patient by improving disintegration capacity of formulation on that basis researcher prepare fast dissolving tablet by using super disintegrant on behalf of that patient having choking problem they prepare oral disintegrating film/ wafer for quick release of drug within few second. Without need of water formulation takes place in any condition like travelling or other emergency conditions. These are the formulation having thin film and larger surface area which is easily dissolves in the mouth saliva. Recently oral films containing breath freshener, vitamins supplement and API.

Different API containing formulation having avoided first pass metabolism effect this is easily given by od preparation.

Keywords: Oral disintegrating film, Oral fast dissolving films (OFDF), API, Fast dissolving tablet (FDT).

1. Introduction:

Recent development in the technology produce viable dosage alternative to oral route for the Pediatric, geriatric, bedridden, nauseous or noncompliant patients. Buccal delivery is latest technology in that buccal delivery bioadhesive dosage form have been produce a adhesive tablet, gel, ointment, patches more recently using polymeric film is called mouth dissolving films. Conventationl tablet formulation are acquired the 50 to 60 % maket⁷ in medicine, according to this data the tablet formulation most popular form but with this tablet having acceptance problem in the patients suffering from dysphagia, Parkinson's disease, mycosystis or vomiting,

geriatric, bed ridden, psychotics and pediatric patient due to unwilling to take solid preparations due to fear of choking. Even with the fast dissolving tablet they having choking problem due to their tablet appearance. According to survey out of 100 patient 26 patient are not acceptable tablet due to their swallowing disability, tablet size, surface form and taste. The problem of swallowing tablets was more evident in geriatric and pediatric patients, as well as traveling patients who may not have ready access to water²¹. This is largely as a result of the success of the consumer breath freshener product such as Listerine pocket packs in the US consumer market.²²

Conventional tablet having problem, that's why new development in it by using super disintegrants, researcher produce the fast dissolving tablet it is introduce in the 1970s with improving this technology to formulation wafer to the recent development of oral fast dissolving films (OFDF).⁶ This newly developed drug delivery system can also be beneficial for meeting the current needs of the industry are improved solubility/stability, biological half life and bioavailability enhancement of drugs⁷ new addition drug in the odf preparations are Metoclopramide (5mg), Dextromethorphan HBr, Diphenhydramine HCl, Simethicone, Phenylephrine HCl, Benzocaine Menthol⁶, Nicotine (Nicabate film)¹⁴.

2. Advantages of oral disintegrating films:

- i) Rapid disintegration than oral disintegrating tablet due to larger surface area.
- ii) Oral disintegrating tablet are having fragile and brittle nature due to they having special packing against the transport, but odf having flexible films they not having the fragile nature.
- iii) Odf are the recently formed material which are majorly accepted for the OTC counter than conventional product because having accurate dosing in the safe and effecious format and no need of water when it taken.
- iv) Patient of dysphasia, repeated emesis, motion sickness, and mental disorders prefer this dosage form as they are unable to swallow large quantity of water.⁹
- v) Those drug having first pass hepatic metabolism odf having advantage over them because oral or buccal mucosa is highly vascularised, that's why drug are absorbed directly in to the systemic circulation^{6, 27}.
- vi) Avoidance of first pass effect drug should be the improve potency by the sublingual or buccal route with low dose high efficacy and less side effect.

vii) With respective drops, syrup the precision is more about the dose in the oral disintegrating films.

i) Taste masking of drugs should be done.

3. Disadvantage of oral disintegrating films:

i) High dose is not incorporated in the odf formulation.

ii) Films are temperature and moisture sensitive that's why special type packing is needed.

iii) Uniformity in dose is technical problem.

4. Comparison between orally fast dissolving films and oral disintegrating tablets⁶.

Table 1

Orally Dissolving Films (odf\os)	Oral Disintegrating Tablets(odt\fdt)
I. Larger surface area gives greater dissolution	I. Less surface area gives less dissolution than odf
II. Odf are flexible and durable	II. Odt are brittle and less durable than odf
III. only Low dose can incorporated in formulation	III. High dose can incorporated in formulation
IV. Odf thickness are 50 to 500 μm	IV. Odt thickness as like convention tablet
V. Patient compliance more	V. Patient compliance is less than odf

5. Composition film.

Mouth dissolving films is thin film dosage form which is 50 to 500 μm in thickness with up to 30 mg active ingredient. Film dissolves in saliva at its pH for flexibility use plasticizer in the formulation, with water soluble polymer⁴.

Following general composition of drug & excipients in percentage

- i) Drug 1-25%
- ii) Water soluble polymer 40-50%
- iii) Plasticizers 0-20%
- iv) Fillers, colours, flavours etc. 0-4

i) Drug

In the odf formulation different types of drug are used like Levicitrizine (anti histamine), Verapmil (anti anginal), Montelukast (antiasthmatics), paracetamol, meloxicam, valdecoxib (NSAIDs), Metaclorpramide (antiemetic), tianeptine (antidepressant drug), cetirizine hydro chloride(anti histamine), Buprenorphine and Naloxone^{17,18,19,1,7,15,12,25,30}.

ii) Water soluble polymers

Film formation required film forming polymer which is having low molecular weight if not it affect on the disintegration time of the film. Natural gum are generally used as water soluble polymer derived from acacia, Arabic or tragacanth, guar, xanthun other available polymers are, acrylic based polymer polyethylene oxide, and several types of sodium carboxymethyl cellulose (CMC), several types of hydroxypropyl methyl cellulose (HPMC)³, Cellulose ethers are widely available and economical. Pullulan (pull), sodium chondroitin sulfate (CHS) an a-1, 6-linked maltotriose produced from the fungus Aureobasidium pullulans, has also been used⁵. A synthetic copolymer of polyethylene glycol–polyvinyl alcohol (Kollicoat IR) and sodium alginate. Five starches and maltodextrin⁶.

Table 2. Viscosities of polysaccharide solutions at 20⁰C^{5, 20}.

% of Disintegrant	Viscosity (mPa.s)
2% pull	< 10
4% pull	12
6% pull	48
1.5 %H-ALG	130
2% CHS	10
0.5% BSP	32

iii) Plasticizers

Plasticizer is used for improve Flexibility with reduce Brittleness of films PEG 400 as a plasticizer selection of plasticizer depend upon compatibility with polymer and type of solvent employed in this. Propylene glycol is used as plasticizer⁸, glycerol used as plasticizer in triclosan odf preparation⁷.with respect to this Pthalate derivative like dimethyl, diethyl, dibutyl pthalate, citrate, castor oil are also used as plasticizer in odf. Concentration generally used in 0- 20 % w/w dry polymer. Concentration changes affects on cracking, splitting, pilling effect on odf².

iv) colorings agent / Flavors :

Colouring agents approved by F D & C are generally used in not exceeding 1% w/w concentration eg. Titanium Dioxide⁶.

6) Method of Preparation:

Different methods for archiving odf formulation by following method⁴

1) Casting and drying

A) Solvent casting

B) Semisolid casting.

2) Freeze dried wafer

3) Extrusion

A) Hot melt extrusion.

B) Solid dispersion Extrusion

C) Rolling method.

Generally for formulation of odf we are using the solvent casting method and extrusion method. Their method of Descriptions is given below.

1) Casting and drying:

i) Solvent casting Method: All water soluble ingredient dissolve in water to form a homogenous mixture of viscous material in that drug add in small portion of solvent at high shear processor. Degassed the viscous material by sonicator²⁶ coated on film base, coated air is send oven for drying the film then film is cut into

different shape⁴. Film thickness measured by screw gauze²⁶. In the solvent casting method material is made viscous mix homogeneously and evaporates solvent at high temperature.

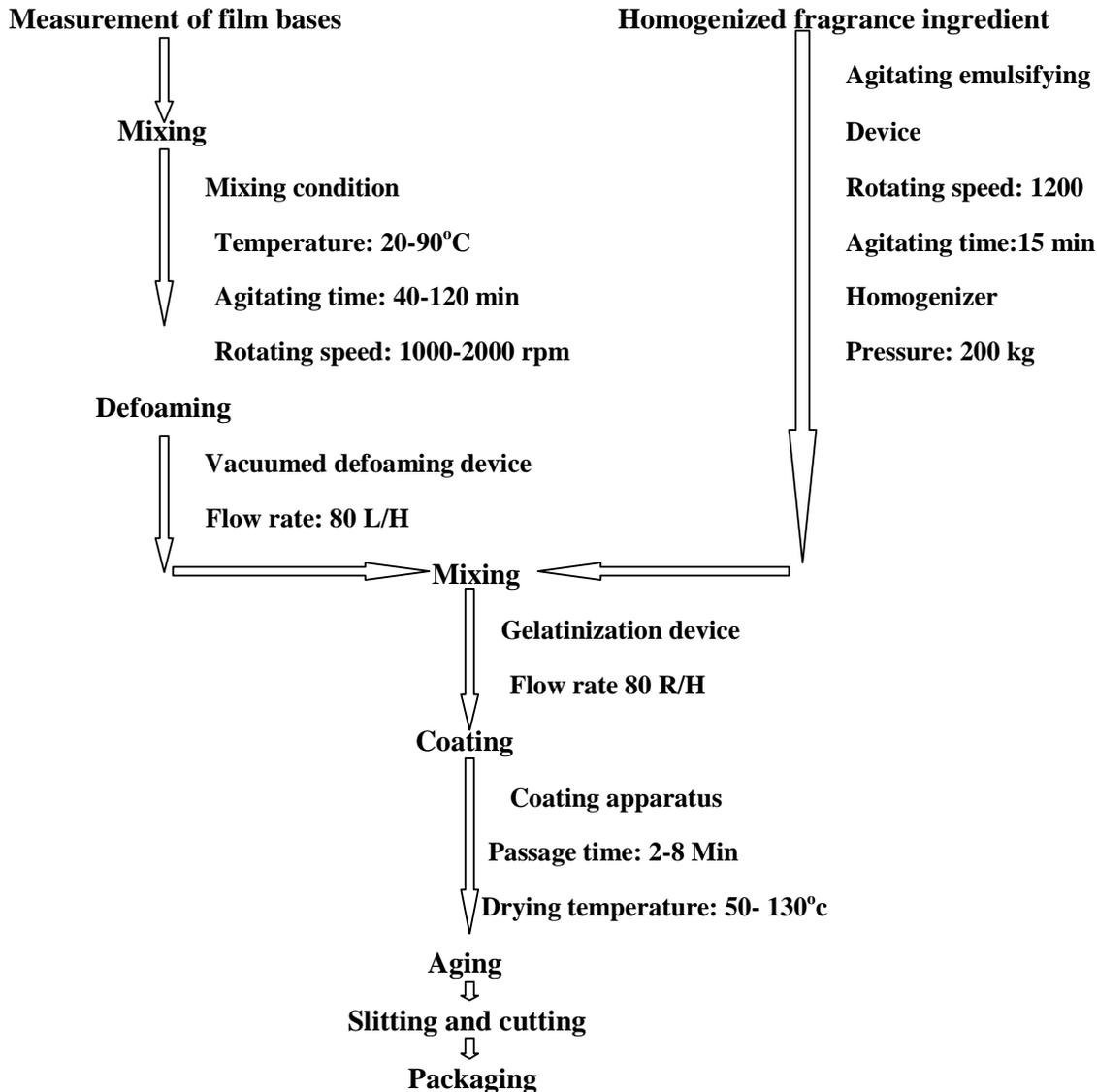


Fig.3 Flow chart of Procedures for the preparation of oral film (solution casting method)⁹.

ii) Semisolid casting:

In the semisolid preparation water soluble polymer add in it and this preparation add in acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate) which is prepared by the ammonium, sodium hydroxide then finally add sufficient amount of plastisizer form a gel and it casted. Acid insoluble polymer with film forming polymer ratio is 1:4 and film thickness is 0.015 to 0.05 inches⁴.

2) Freeze dried wafer:

Is also known as lyophilisation or cryodesiccation method in that dehydration of water and reduce pressure from surrounding to allow the water in material to sublime directly from solid phase to gaseous phase.

3) Extrusion

i) Hot melt extrusion:

In the hot melt extrusion drug mixed with carrier in the solid form. Extruder having extra facility with heater it melt the solid form carrier and drug then this melt is place in the dies and cut in to specific shape⁹.

eg. Maltodextrin can be used to produce fast-dissolving films with a high drug loading capacity by hot-melt extrusion technology¹.

ii) Solid dispersion Extrusion:

Those immiscible component are extruded then mix with drug and then solid dispersion prepared.

iii) Rolling method:

In this preparation drug containing suspension having water or alcohol as solvent which is add on drum then evaporate the solvent and cut in specified shape⁴.

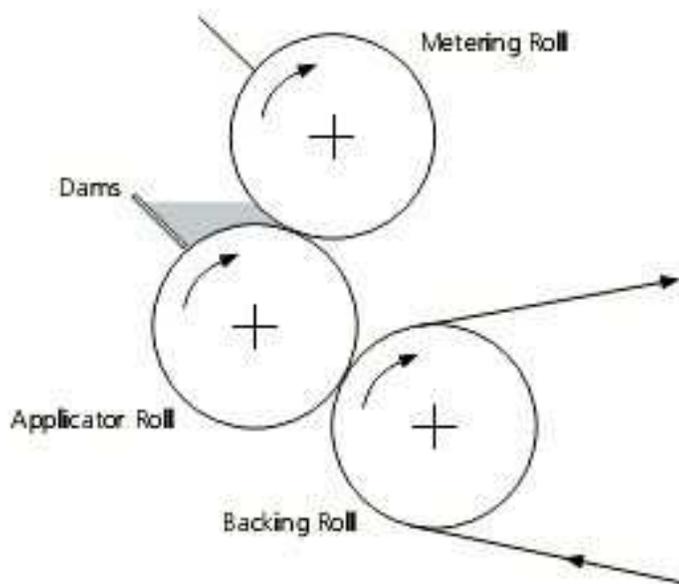


Figure-1. Three roll coating unit⁴.

7) Different technology used in oral disintegrating films formulation^{28,4}.

- i) Xgel:** This technology is produced by Bioprogress produce a newer technology to product manufacturing.
- ii) Soluleaves:** This technique is used to formulate the quick dissolving films by adding with active ingredient, flavor and colour to fill pleasant and easy acceptable form.
- iii) Foam burst:** This method gives effect like the melt in moth like sensation because at time of preparation of film gas is blown on the film due to this films gives honey comb like structure and this void are empty or filled with other material to acquire the specific test or odour.
- iv) Wafertab:** In this system drug load in film after casting.
- v) Micap:** Micap plc signed an option agreement in 2004 to combine its expertise in micro encapsulation technology with the BioProgress water-soluble films. Aim of this company to make the smoke sensation product.

8) Evaluating parameters:

i) Thickness:

Oral disintegrating film thickness measured by micrometer screw gauge. Films thickness check at five different points for uniform film thickness as well as content uniformity². By using calibrated digital micrometer (CLM1-15QM, Mitutoyo, Kawasaki, Japan)⁵. Three readings from all the batches were taken and mean thickness was evaluated¹⁷.

ii) Mechanical properties:

A) Tensile strength:

Tensile strength means the point at which films is break¹⁶.

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Film thickness} \times \text{film width}}$$

B) Percent elongation:

When tension is applied to the film and film strip is stretches this is a strain. If elongation of film increase means addition of plastisizer is increase⁶.

$$\% \text{ Elongation} = \frac{\text{Increase in length} * 100}{\text{Original length}}$$

C) Folding endurance:

Folding endurance is determined by folding a film up to it break at the folding point, attempt required to cut the film is folding indurance value.³¹

iii) Swelling property:

Swelling property of the oral film is check by using saliva solution. Keep the film on the pre weighed steel mesh one part is place in the 50 ml saliva solution. Weigh the film after specific time up to constant weight of film is come⁴.

Degree swelling property is calculated by following formula³¹.

$$SI = w_t - w_o / w_o$$

Where SI is the swelling index,

w_t is the weight of the film at time “t”, and

w_o is the weight of film at $t = 0$

iv) Contact angle:

Contact angle is measured by goniometer (AB Lorentzen and Wettre, Germany) in this method double distilled water drop place on dry film by using goniometer, digital picture is take within 10 second of drop add on film analyzed by imageJ 1.28v software (NIH, USA) for angle determination. Minimum five times at different position check the contact angle film⁴.

v) In vitro disintegration time:

Manually check the disintegration by placing the film in 10 ml water and time required to break or disintegrate the film¹¹. In vivo disintegration test take the volunteer (n =6) then place the odf in the mouth of volunteer and check the time to disintegrate the film²⁵.

vi) In vitro dissolution test:

Dissolution studies of films were performed by USP XXIII type II apparatus in 6.8 phosphate buffer (300ml) and 0.1N HCl (900ml). The temperature ($37 \pm 0.5^\circ\text{C}$) and the rotation speed was 50 rpm. The samples were withdrawn at various time intervals and analyzed spectrophotometrically¹¹.

vii) Permeation studies:

Permeation studies are done using modified Franz diffusion cell by using porcine buccal mucosa. Buccal mucosa is kept in between the donor and receptor compartment of Franz diffusion cell. In receptor compartment fill buffer kept at $37\text{ }^{\circ}\text{C} \pm 0.2\text{ }^{\circ}\text{C}$ and maintain the hydrodynamics by using magnetic stirring at 50 rpm. On buccal mucosa the oral disintegrating film is placed before placing mucosa will be moisten by few drop of simulated saliva, in the donor compartment add 1ml of simulated saliva of pH 6.8.

Samples withdraw at specific time interval fill with same amount of fluid. Percentage of drug permitted is calculated by taking absorbance by U.V method³¹.

viii) Assay/Drug Content and Content Uniformity:

Assay method determined by specification in different Pharmacopoeia. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85-115%²⁸.

Ix) Surface morphology:

Surface morphology is studied by using environment-scanning-electron microscopy method. In that absence of pore and surface uniformity, striations indicate the good quality of the ODF¹³.

x) Taste evaluation:

In vivo test evaluation studies going with panel of volunteers and In vitro studies by using the test sensor analyze the sweetness level of test masking agent¹³.

xi) Packaging:

At the starting single packaging of odf is kept but now this mandatory packing; 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. Rapid card are like ATM card which are easy to take dose individually⁴.

S.No	Product	Mfg By
1	Dextromethorphan(cough suppressant) , breath stripes	MonosolRx
2	Donezapil, Odansatron rapid dissolving films (under finaldevelopment)	A P R (Switzerland)-Labtec GmbH (Germany)

3	NC H has launched a pharmaceutical based in the 'film strip' format.	Novartis Consumer Health
4	MDFs of loratidine (10mg - 20mg), dextromthorphan (2.5mg - 5.5mg), which prescription is under development	Hughes Medical corporation
5	Listern pocket paks breath freshening strips	Pfizer's Warner-Lambert consumer healthcare division
6	Triaminic thin strip long acting cough and runny nose	Novartis
7	Oral pain relieving strips	Apothecus pharmaceutical corp.

9) Conclusion:

Oral disintegrating film is better acceptance than oral disintegrating tablet. Patient compliance is more due to low cost better mouth fill than other formulation. Especially in young and geriatric patient. Odf are the fast disintegrating quick drug release in systemic circulation. Avoid first pass metabolism and degradation in gastro intestinal tract.

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