

# A Novel Venture in Oral Formulation: Wafer

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## Abstract:

The Fast Dissolving / Disintegrating is a novel drug delivery system .Fast-dissolving / Disintegrating oral drug delivery systems are the solid oral dosage forms, which get disintegrate or dissolve within 1 min when placed in the oral cavity without drinking water or chewing. It enhances the safety and efficacy of the drug molecule. It enhance the fast onset o set of action which improve the bioavailability by avoiding the first pass metabolism and enzymatic degradation in GI tract. These dosage form is convenience to the special category patients such as Pediatrics, geriatrics and bedridden patients who having difficulty in Swallowing the conventional dosage form. These system consist of Thin Film or Wafer, which is placed on the patient's tongue or oral mucosal tissue, it instantly get wet by the saliva and it rapidly get hydrates and adhere on the site of application. It is get disintegrates and dissolve rapidly and release the medication to the mucosal absorption. Recently the Fast Dissolving Film or Wafer are gaining the interest as alternative to the fast dissolving tablets which definitely eliminates the fear of patients of choking. These formulation are formulated by using the polymers, plasticizers, sweeteners, flavours and colors. These are prepared by using the various methods like casting, extrusion etc. the film/ wafer is evaluated by using various evaluation parameters like disintegration time, dissolution time, thickness, etc.

**Keywords:** Fast Dissolving Oral Wafer, Polymer, Solvent Casting Method, Bioavailability Enhancement.

## Introduction:

The priority has been focused for more patient compliant dosage forms. Oral transmucosal route for drug delivery system is preferred over the other routes because of its versatility. The conventional pharmaceutical dosage forms are incapable of the controlling the rate of the drug delivery system; over which the novel drug delivery system maintain the drug concentration in the therapeutic range for a long period of time. Fast-dissolving drug delivery were first developed in the late 1970s which is an alternative to other dosage forms,

The rationale for development and the use of a novel drug delivery systems may include one or more of the following argument (Vibhooti *et al.* 2013):

- It Decreases the toxicity and occurrence of the adverse drug reactions by controlling level of drug and metabolites in the blood at the target sites.
- Improve drug utilization by applying the smaller drug dose in the controlled – release form to produce the same clinical effect as larger dose in a conventional dosage form.
- Control rate and the site of release of drug that acts locally so that the drug is released where the activity is needed rather than at the other sites where it may cause the adverse reactions.

Wafer – It is an innovative oral dosage form: New oral thin films, so-called the wafers, thus the creating new possibilities for the action profiles and patient compliance. Wafers are the paper-thin polymer films used as a carriers for pharmaceutical agents. The innovative dosage form is taken orally but does not require any water for swallowing.

**Benefits** (Rekha *et al.*2014):

- It provides direct entry of drug into the systemic circulation.
- Increasing the bioavailability of the oral administered drugs that otherwise undergo hepatic first-pass metabolism
- It improved the patient compliance due to the elimination of pain with injections.
- Drug absorption can be terminated in case of the emergency.
- It offers passive system, which does not require any activation process.

**Salient Features** (Shaheda *et al.*2014):

- Thin elegant film
- Available in various size and shapes
- Excellent mucoadhesion
- Fast disintegration
- Quick dissolution
- Rapid release
- Adaptable and amenable to existing processing and packaging machinery
- Cost effective

**Types of Wafers:** (Alpesh *et al.* 2010):**1] Flash release water:**

Sr.no.	Property	Flash release water
1.	Area (cm sq.)	2-8
2.	Thickness ( $\mu\text{m}$ )	20-70
3.	Structure	Film: Single layer
4.	Excipients	Soluble, highly hydrophilic polymers
5.	Drug Phase	Solid solution
6.	Application	Tongue (upper palate)
7.	Dissolution	Maximum 60 seconds
8.	Site of action	Systemic or local

**2] Mucoadhesive melt-away wafer:**

Sr.no.	Property	Mucoadhesive melt-away wafer
1.	Area (cm sq.)	2-7
2.	Thickness ( $\mu\text{m}$ )	50-500
3.	Structure	Single or multilayer system
4.	Excipients	Soluble, hydrophilic Polymers
5.	Drug Phase	Solid Solution or suspended drug particles
6.	Application	Gingival or buccal region
7.	Dissolution	Disintegration in few minutes, forming gel
8.	Site of action	Systemic or local

**3] Mucoadhesive sustained released wafer:**

Sr.no.	Property	Mucoadhesive sustained released wafer
1.	Area (cm sq.)	2-4
2.	Thickness ( $\mu\text{m}$ )	50- 250
3.	Structure	Multi layer system
4.	Excipients	Low / Non – soluble Polymers

5.	Drug Phase	Suspension and / or solid solutions
6.	Application	Gingival, (other region in oral cavity)
7.	Dissolution	Maximum 8-10 hours
8.	Site of action	Systemic or local

### Formulation Consideration:

Sr.No	Ingredients	Amount (w/w)
1.	Drug	1-30%
2.	Film Forming Polymer	40-50%
3.	Plasticizer	0-20%
4.	Saliva Stimulating Agent	2-6%
5.	Sweetening Agent	3-6%
6.	Flavoring agent	q.s.
7.	Surfactant	q.s.

### Formulation Aspects (Sri Rekha *et al.* 2014):

#### 1] Wafer Forming Polymer:

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

#### ❖ List of polymers:

Sr.no.	Natural Polymers	Synthetic Polymers
1.	Pullulan	Hydroxypropylmethyl cellulose
2.	Starch, Gelatin	Polyvinyl pyrrolidone
3.	Pectin	Polyvinyl alcohol
4.	Sodium alginate	Carboxy methyl cellulose
5.	Maltodextrin	Poly ethylene oxide
6.	Polymerized rosin	Kollicoat
7.	Lycoat	Hydroxypropyl cellulose
8.	Xanthan gum	Hydroxyl ethyl cellulose

**2] Plasticizer:**❖ List of Plasticizer:

Sr.no.	Plasticizer
1.	Glycerol
2.	Propylene glycol
3.	Polyethylene glycol (400,200,600)
4.	Dimethyl, Dicyetyl and Dibutyl Phthalate
5.	Triacetin
6.	Castor oil
7.	Citrate ether
8.	Try ethyle citrate

**3] Sweating agent:**❖ List of Sweating Agent:

Sr.no.	Sweating agent
1.	Sorbitol
2.	Sucrose
3.	Cyclamate
4.	Erosin red
5.	Aspartame
6.	Neotame
7.	Sacchrin
8.	Mannitol, Acesulfame- K

**4] Saliva Stimulating agent:**❖ List of Saliva Stimulating agents:

Sr.no.	Saliva Stimulating Agent
1.	Citric acid
2.	Tatric acid
3.	Malic acid
4.	Lactic acid
5.	Ascorbic acid

**5] Surfactant:**❖ List of Surfactants:

Sr.no.	Surfactant
1.	Polaxamer 407
2.	SLS
3.	Tweens
4.	Spans
5.	Benzalkonium Chloride

**6] Flavouring agents:**❖ List of Flavouring Agents:

Sr.no.	Flavouring agent
1.	Peppermint oil
2.	Cinnamon oil
3.	Menthol
4.	Lemon oil

**7] Colouring agents:**❖ List of Colouring Agents:

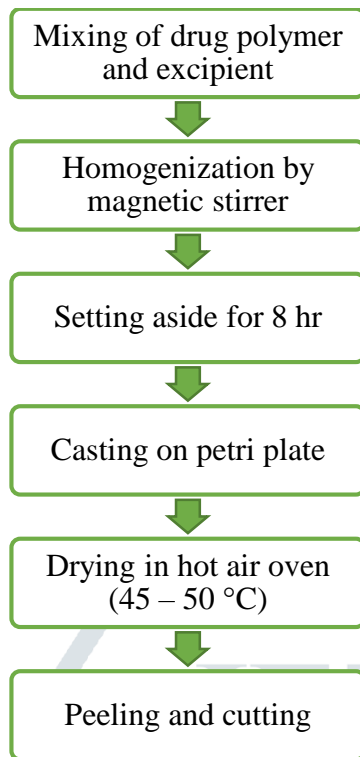
Sr.no.	Colouring agent
1.	Titanium dioxide
2.	Sunset yellow

**8] Drug:**

- Drug should have pleasant taste.
- Incorporated drug should have low dose.
- Possess smaller and moderate molecular weight.
- Good stability and solubility in water as well as saliva.
- Partially unionizes at the pH of the oral cavity

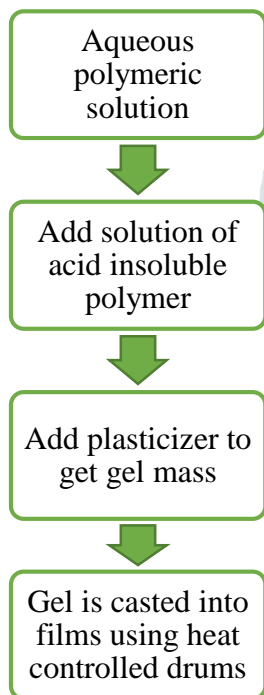
**Method of formulation of Wafer (Puja Chaurasiya *et al.* 2016):**

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

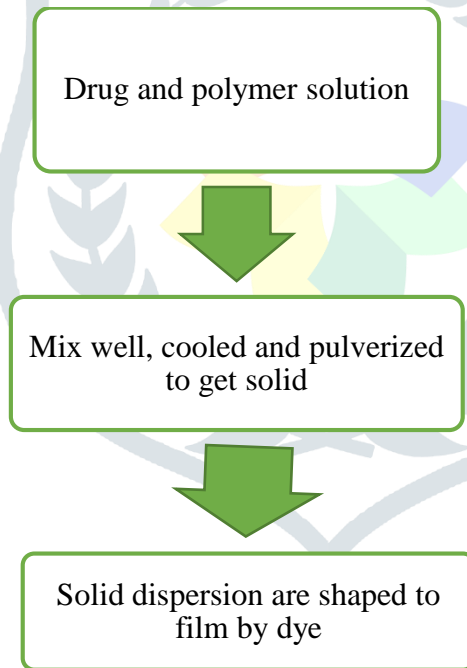
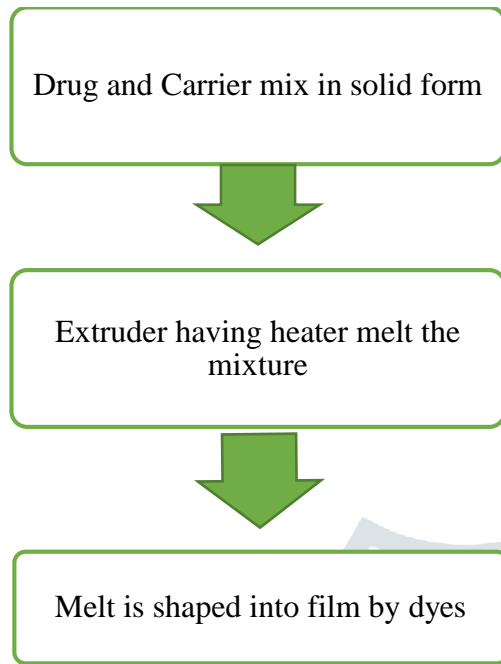


1] Solvent casting:

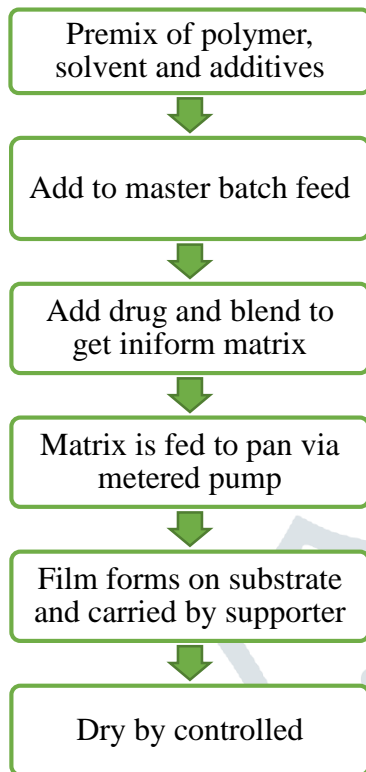
2] Semisolid Casting:



3] Hot melt extrusion



4] Solid dispersion method:

5] Rolling method:**Advantages** (Jain *et al.*2018):

- Improve oral absorption
- Fast onset of action
- Minimizes the first pass effect
- Improves the Bioavailability
- For administration no first pass is required
- It reduces the gastrointestinal irritation
- Easy For Handling and transportation
- Enhance the stability of dosage form
- Accurate dosing is present

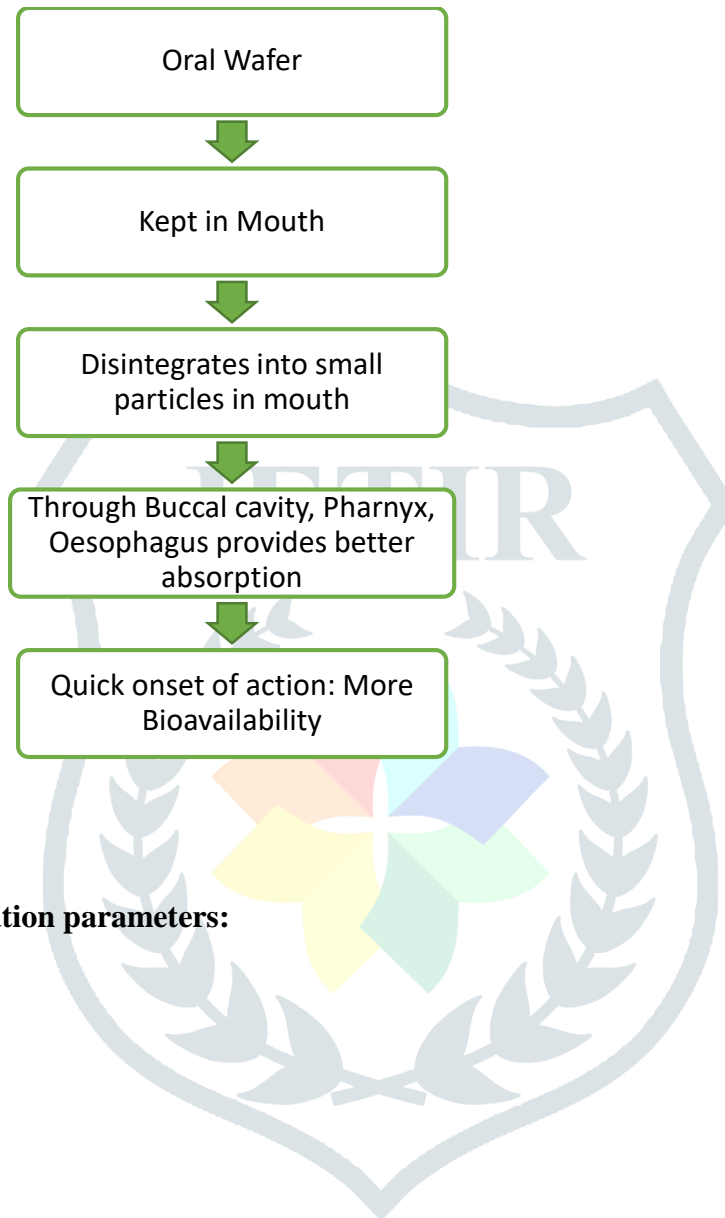
**Diadvantages** (Ahirwar *et al.*2018):

- High dose cannot be incorporated in this dosage form
- Drug unstable in the buccal pH cannot be determined
- It requires the special packaging that must be protected from water
- Eating and drinking phenomenon may be restricted
- It shows the fragile and granule proper



**Mechanism** (Lade *et al.*2013):

Mechanism of wafer are as follows:

**Characterization /Evaluation parameters:**

1. Appearance
2. Color
3. Weight
4. Thickness
5. Disintegration time
6. Dissolution time
7. Folding endurance
8. Drug content uniformity / Assay
9. Water uptake and erosion test
10. Surface pH
11. Elongation at break
12. Tensile strength
13. Tear resistance
14. Young's modulus / Elastic modulus
15. Diffusion studies
16. Contact angle
17. Transparency test
18. Dryness / Tack test
19. Burst strength
20. Percentage elongation
21. SEM

## 22. DSC

**1] Appearance, Size and Shape:** The formulated wafer were checked for their appearance, shape and thickness. The thickness of the wafer was determined at two different places using a digimatic micrometer and mean value was calculated (Sumedha *et al.*2014).

**2] Color:** It should be attractive and good patient compliance (Garg *et al.*2014).

**3] Weight:** The wafer were subjected to mass variation study by individually weighing randomly selected patches. The average of 5 observations of each batch was calculated. Same done for each batch (Mayank *et al.*2014).

**4] Thickness test:** Thickness is determined by calibrated digital micrometer and then subsequently mean average is calculated. Generally, three readings from all the batches are determined and average is calculated. (Soad AY *et al.*, 2009). Uniformity in thickness is important for dose accuracy. (Mandeep *et al.*, 2013).

**5] Disintegration time:** Disintegrating time is defined as the time (seconds) at which a wafer breaks when brought in contact with water or saliva. Typical disintegration time for wafer is 5-30 seconds. (Dey *et al.*2016).

**6] Dissolution time:** The cumulative drug release and the cumulative percentage of the drug is calculated. In-vitro drug dissolution is performed by using USP paddle type apparatus. The studies were carried out at 37°C of stirring speed 75 rpm in 900 ml phosphate buffer (pH 6.8). 5 ml of the samples withdrawn at the predetermined time intervals of 2, 4, 6, 8, 10 min and they are replaced within the same volume of buffer. The samples were collected and the concentration were determined at the appropriate wavelength by using UV-visible spectrophotometer (Naga *et al.* 2013).

**7] Folding endurance:** To estimate the mechanical properties of a wafer. It is measured by repeatedly folding a wafer at the same point until it breaks. Folding endurance value is number of times the wafer is folded without breaking. Higher folding endurance value depicts the more mechanical strength of a wafer. As mechanical strength is governed by plasticizer concentration so it is clearly evident that plasticizer concentration also indirectly affects folding endurance value (Mandeep *et al.*, 2013).

**8] Drug content uniformity / Assay:** Wafer dissolved in simulated saliva (100 ml pH 6.8) by homogenization for 30 min continue shaking. Content uniformity estimating the API content in individual wafer. Limit: 85-115% (Dey *et al.* 2016).

**9] Water uptake and erosion test:** The Wafer is weighed (W1) added to stainless steel mesh basket. The weight immersion in the water then measured (W2). Similarly the weight after immersion of basket without the Wafer (W3). The amount of absorbed (W) is determined by the following equation;

$$W \text{ (g/g)} = \frac{(W2 - W1 - W3)}{W1}$$

**10] Surface pH:** Done by placing the wafer on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on wafer. The change in the colour of pH paper was observed and report (Nisreen *et al.* 2009).

**11] Elongation at break / Percent elongation:** Upon exerting stress on a wafer, the specimen stretches which is referred as strain. Strain is defined as change in length of wafer divided by its original/initial length of the wafer specimen. Percent elongation is related quantitatively to the amount of plasticizer used in wafer formulation. Increased plasticizer concentration in the wafer generally results in enhanced elongation of the strip (Mandeep *et al.* 2013).

It is determined by the following formula:

$$\text{Percentage elongation} = (\text{Change in length} / \text{Initial length}) \times 100$$

**12] Tensile strength:** Tensile strength is defined as maximum stress applied at which the wafer breaks. Basically, this test is performed to measure the mechanical strength of wafer. It can be calculated from applied load at rupture divided by the strip cross-sectional area given in the equation below (Mandeep *et al.*, 2013)

$$\text{Tensile strength} = (\text{Load at failure} / \text{wafer thickness} \times \text{wafer width}) \times 100$$

**13] Tear resistance:** Tear resistance of wafer is the intricate function of its ultimate resistance to rupture. Maximum force required to tear the wafer is measured as tear resistance value (Mandeep *et al.*, 2013). This test is typically attributed to plastic industry. The rate of loading employed is 2 inch/minute which is planned to determine the magnitude of force required to initiate tearing in the wafer specimen. The maximum amount of force necessary for tearing is generally found near the tearing onset which is ranked as tear resistance value (Bhyan *et al.*, 2011).

**14] Elastic modulus:** It is the measure of wafer stiffness. It is found as ratio of applied stress to the strain in the elastic deformation region. It is determined by the following formula (Mandeep *et al.*, 2013):

$$\text{Young's Modulus} = (\text{Slope} / \text{wafer thickness} \times \text{Cross head speed}) \times 100$$

It can also be written as:

$$\text{Young's modulus} = \text{Force at corresponding strain} / \text{Cross-sectional area} \times \text{Corresponding strain}$$

Hardness and brittleness are characteristics of the wafer which are related with Young's modulus and tensile strength. A hard and brittle wafer depicts higher value of tensile strength and Young's modulus with small elongation (Bhyan *et al.*, 2011).

**15] Diffusion study:** Before the diffusion study, drug assay and uniformity of OME within the wafer was determined. This is measured by weighing wafer accurately 5mg and hydrated in 8 mL of drug dissolution media. These hydrated wafer was stirred at the  $37 \pm 0.5^\circ\text{C}$  until it completely get dissolved. The concentration of OME was analyzed by using UV Spectrophotometry.

**16] Contact angle:** Contact angle are measured by Goniometer at room temperature. Take a dry wafer and place a drop of distilled water on the surface of the dry wafer. 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 taken (Muhammad *et al.* 2016).

**17] Transparency test:** The transparency of the wafer can be determined using a simple UV spectrophotometer. Cut the wafer samples into rectangles and placed on the internal side of the spectrophotometer cell. The determine transmittance of wafer at 600 nm. The transparency of the wafer was calculated as follows (Bhyan *et al.* 2011):

$$\text{Transparency} = (\log T_{600}) / b = - \epsilon c$$

Where,  $T_{600}$  is the transmittance at 600 nm

b is the wafer thickness (mm)

c is concentration

**18] Dryness test/Tack test:** This test is performed to find out the ability of a wafer to get adhered to a piece of paper pressed between wafer (Chaudhary *et al.*, 2013; Mandeep *et al.*, 2013). Obstnacy with which the wafer adheres with the piece of paper or any other accessory pressed in between the wafer is known as tack. Almost there are eight stages of wafer drying process which are identified viz dry-to touch, dry-to-recoat, dry hard, set-to-touch, dust-free, dry-through, tack-free and dry print-free. Primarily these tests are used to evaluate dryness of wafer in paint industry but are also adoptable for assessing orally fast disintegrating wafer. Dryness or tack test can also be performed by with the help of some newly invented instruments (Bhyan *et al.*, 2011).

**19] Burst Strength:** Wafer burst strength is the force required to break or rupture the wafer, which is an indicator of the flexibility of the wafer. Burst strength of the wafer was studied using 5mm spherical stainless steel ball probe (P/5S) with the probe adapter which was connected to the load cell. A circular strip wafer with an area of  $7.07\text{cm}^2$  was placed in wafer supporting rig and moving probe reached the surface of the wafer with the pretest

speed of 2.0mm/sec. When the probe reached the surface of the wafer, probe speed was changed to 1.0mm/sec test speed with the trigger load of 5g and the data were recorded.

**20] Percentage elongation:** Folding endurance is another procedure to estimate the mechanical properties of a wafer. It is measured by repeatedly folding a wafer at the same point until it breaks. Folding endurance value is number of times the wafer is folded without breaking. Higher folding endurance value depicts the more mechanical strength of a wafer. A direct relation exists between mechanical strength and folding endurance of wafer. As mechanical strength is governed by plasticizer concentration so it is clearly evident that plasticizer concentration also indirectly affects folding endurance value (Mandeep *et al.*, 2013).

**21] Scanning Electron Microscopy (SEM):** Scanning Electron Microscopy study is used to identify the difference between the upper and lower Sides of the Wafer. It also help to determine the uniform distribution of API (Verena *et al.*2009).

**22] Differential Scanning Calorimetry (DSC):** DSC was to characterize the thermal behavior of Wafer and changes in their properties with introduction of Polymer and the drug, Analysis of the wafer and starting material was carried out on Q2000(TA instruments) calorimeter. About 2.5mg of each sample was placed into hermetically sealed T zero aluminium pans with a pin hole in the lid and heated from -40°C to 180°C at a heating rate of 10°C/min under constant purge of the nitrogen (100 ml / min) (Prithviraj *et al.*2013).

**23] % Moisture Uptake:** % Moisture Uptake Formulation was exposed to an atmosphere of 84% RH at 28°C for three days using a saturated solution of NaCl. After three days the wafer was removed, weighed and percentage moisture absorbed was calculated. Average percentage moisture absorption of each wafer was calculated (Satishbabu *et al.*2008).

**24] Stability studies:** The purpose of the stability testing is to provide evidence on how the quality of the drug substance or the drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and the light, enabling the recommended storage condition, retest periods and the shelf life. The stability studies were carried out as per the International Conference of harmonization (ICH) Guidelines. The Stability studies were carried out at 40° C / 75% RH for 3 months. The optimized wafer formulations were packed in amber colored bottles, which were tightly plugged with cotton and capped. They are stored at 40°C / 75% RH for 3 months and these are evaluated for their physical appearance, drug content and in-vitro dispersion time at specified intervals of time (Lade *et al.*2010).

**27] Taste evaluation:** Taste acceptability was measured by a taste panel (n=5) with 3 mg drug and subsequently film sample containing 3 mg drug held in mouth until disintegration, then spat out and the bitterness level was then recorded. The volunteers were asked to gargle with distilled water between the drug and film sample administration. The scale for the bitterness study was as follows (Panchal *et al.*):

+ = very bitter

++ = moderate to bitter

+++ = slightly bitter

++++ = tasteless/taste masked

+++++ = excellent taste masking

**3] Texture analyzer:** These studies were conducted manually by visual inspection. This study the films made of PEG 400 were shown good physical appearance and texture when compared with the films formulated by using propylene glycol (Ali MS *et al.* 2016).

## Conclusion:

In the recent trend of obtaining a palatable dosage form, wafers as an orodispersible film have made its own place & met in the expectation of the rising demand. Wafers are formulated as a advancement to oral fast dissolving films with its special properties of the high absorption and the high bioavailability. It is so popular among the people of all ages but particularly among geriatric and paediatric population because of its compatibility and the good mouth feel. The marketed products of the wafers are still less but there are so many more to come in the market.

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