

# Effect of Glycerin as Plasticizer in Orodissolving Films of Losartan Potassium

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**Abstract:** *The preparation of orodissolving films of Losartan Potassium with the purpose of developing a dosage form for a very quick onset of action, which is very convenient for administration, without the problem of swallowing and using water. Losartan Potassium is antihypertensive agent, antagonist of angiotensine. 2. The Films of Losartan Potassium were prepared by using polymer as HPMC 15 Cps, Glycerin as plasticizer, polysorbate 80 as a surfactant, sodium saccharin as a sweetening agent, Menthol as a flavoring agent, ethanol as preservative by solvent casting method. The fast dissolving oral films were designed using optimal design and numerical optimization technique was applied to find out the best formulation. The formulated orodissolving films were evaluated for physical characteristics such as thickness, Folding endurance, drug content uniformity, percentage elongation, gave satisfactory results. The formulations were subjected to disintegration, In-Vitro drug release tests. The marked increase in the % drug release was exhibited by mouth dissolving firms of Losartan potassium containing HPMC 15 cps as a polymer at 15 min., orodissolving films of Losartan potassium shows 84.29 drugs release at 15 min. orodissolving films of Losartan potassium F3 Formulation (Containing 14% glycerin) shows percent elongation 25, folding endurance 32, disintegration time 28. 15 sec, thickness 0.09 mm and % content uniformity 81.4%.*

**Keywords:** orodissolving, losartan potassium, glycerin, plasticizer

## Objectives:

- To formulate orodissolving films of Losartan potassium by solvent casting method.
- The study the effect of various concentration of glycerine as plasticizer in orodissolving films.
- To evaluate orodissolving films of Losartan potassium of thickness, folding endurance, percent elongation, disintegration time, percent content uniformity and invitro drug release.

## 1. Introduction

The oral route is the most popular route for the administration of therapeutic agent. Because of its low cost and ease of administration lead to high levels of patient compliance. The most popular oral solid dosage forms are tablets and capsules. Many patients have difficulties to swallow tablets and hard gelatin capsules particularly pediatric and geriatric irritation. Patients do not take their medicines as prescribed. Difficulty in swallowing or dysphasia is seen to affect nearly 35% of the general population. In some cases such as motion sickness, sudden episode of allergic attack or coughing, fear of choking and an unavailability of water, the swallowing of tablet or capsules may become difficult. To overcome these difficulties, several fast – dissolving drug delivery systems have been developed. Oral fast dissolving films is relatively a new dosage form in which thin film is prepared using hydrophilic, which rapidly dissolves.

### 1.1 Salient Features of Fast Dissolving Drug Delivery System

1. Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and, psychiatric patients.
2. No need of water to swallow the dosage form, which is highly convenient feature for patients.
3. Who are traveling and do not have immediate access to water.
4. Good mouth feels properly of MDDS helps to change the basic view of medication as “bitter Pill” particularly for pediatric patients.
5. Rapid dissolution of drug and absorption which may produce rapid, onset of action.

6. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.
7. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.
8. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
9. Stability for longer of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

### 1.2 Characteristics of orodissolving film:

#### 1. Ease of Administration :

Fast Dissolving Delivery Systems are easy to administer and handle hence, leads to Better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (tablets, capsules, solutions and suspensions) because of tremors of extremities and dysphasia. Fast Dissolving Delivery Systems may offer a solution for these problems.

#### 2. Taste of the medicament :

Mouth dissolving delivery systems usually contain the medicament in taste masked form. Taste – masking is of critical importance in the formulation of an acceptable FDDT. Traditional tablet formulations generally do not address the issue of taste masking, because it is assumed that the dosage form will not dissolve until passing the oral cavity. Many oral suspensions, syrups and chewable tables simply contain flavors, sugars and other

sweeteners to overwhelm or complement the bitter taste of the drug. Current methods of taste masking in fast dissolving / disintegrating tablets includes sweeteners and flavors; however these are not a sufficient means for taste masking many bitter drugs.

### 3. Hygroscopicity :

Several fast dissolving dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions from humidity which call for specialized product packaging.

### 4. Friability :

In order to allow fast dissolving tablets to dissolve in the mouth, they are made of either very porous or soft moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable and / or brittle which are difficult to handle, often requiring specialized peel-off blister packaging.

### 5. Mouth Feel :

Mouth feel is critical, and patients should receive a product that feels, pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth feel by reducing the "dryness" of a product.

## 1.3 Classification of Fast Dissolving Technology

For ease of description, fast – dissolve technologies can be divided into three broad groups:

### 1. Lyophilized systems :

The technology around these systems involves taking a suspension or solution of drug with other structural excipients, through the use of a mould or blister pack, forming tablet shaped units. The units or tablets are then frozen and lyophilized in the pack or mould. The resulting units have very high porosity, which allows rapid water or saliva penetration and very rapid disintegration.

### 2. Compressed tablet – based systems :

This system is produced using standard tablet technology by direct compression excipients. Depending on the method of manufacture, the tablet technologies have different levels of hardness and friability. The speed of disintegration for fast dissolve tablets compared with a standard tablet is achieved by formulating using either water soluble excipients Superdisintegrant or effervescent components, to allow rapid penetration of water into the core of the tablet.

### 3. Thin oral film

Oral films also called oral wafers, evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers for delivering vitamins and personal care products. Today, FDFs are proven and accepted technology for the systemic delivery of APIs for over – the counter (OTC) medication and are in the early – to mid development stages for prescription drugs.

This has been attributed to the success of the breath freshener products by consumers such as Listerine Pocket packs in the US consumer market. Such systems use a variety of hydrophilic polymers to produce a 50-200 mm film. The film is manufactured as a large sheet and then cut into individual dosage units for packaging.

## 1.4 Structural Features of Oral Mucosa Structure

The oral mucosa is composed of an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the submucosa 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, advancing through a number of differentiating intermediate layers to the superficial layers, where cells are shed from the surface of the epithelium considerably more permeable to water than keratinized epithelia.

## 1.5 Composition of Oro-mucosal Region

Oro-mucosal Cell: Are made up of proteins and carbohydrates. It is adhesive in nature and acts as a lubricant, allowing cells to move relative to one another, while the mucosa with less friction. The mucus is also believed to play a role in bioadhesion of mucoadhesive drug delivery. In other parts of the body mucus is synthesized and secreted by the goblet cells, however in the oral mucosa; mucus is secreted by the major and minor salivary glands. Up to 70% of the total mucin found in saliva is contributed by the minor salivary glands.

## 1.6 Classification of oral Films

There are three different subtypes of oral films :

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

## 1.7 Advantages of Orodissolving film:

1. Ease of administration to pediatric, geriatric, bedridden patients and psychiatric patients who refuse to swallow tablets.
2. No need of water to swallow the dosage form, which is highly convenient feature for parties who are travelling.
3. Rapid dissolution and absorption of drug, which may produce rapid onset or action.
4. Some drug is absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, which enhances bioavailability of drugs.
5. Pre – gastric absorption can result in improved bioavailability and as a result of reduced dosage; improved clinical performance through a reduction of unwanted effect.
6. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
7. The risk of choking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.

8. Useful in cases where a rapid onset of action required such as in motion sickness, sudden episodes of allergic attack or coughing, bronchitis or asthma.
9. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
10. Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

### 1.8 Disadvantages of Orodisolving films

1. Drugs which are unstable at buccal pH cannot be administered.
2. Drugs which irritate the mucosa cannot be administered by this route.
3. Drug with small dose requirement can only be administered.
4. Taste masking most drugs have bitter taste, and need taste masking.

### 1.9 Composition of the Formulation –

A typical composition contains the following:

- a) Drug – 5% to 30% w/w.
- b) Water soluble polymer – 45% w/w
- c) Plasticizers – 0-20% w/w
- d) Sweetening agent- 3% to 6% w/w.
- e) Saliva stimulating agent – 2 to 6% w/w
- f) Fillers, Colors, flavor surfactant etc. q.s.

#### a) Drug:

The ideal characteristics of a drug to be selected –

1. The drug should have pleasant taste.
2. The drug to be incorporated should have low dose up to 40 mg.
3. The drugs with smaller and moderate molecular weight are preferable.
4. The drug should have good stability and solubility in water as well as in saliva.
5. It should be partially unionized at the pH of oral cavity.
6. It should have the ability to permeate oral mucosa.

#### b) Polymer

For the preparation of FDR the various polymers can be used in the film up to 40% w/w of the film content. The polymers are responsible for the strength of the film. The film should be tough to prevent damage during handling and transportation. The polymers can be used as single or in combination as per requirement. Polymers are – Hydroxyl Propyl methyl cellulose (HPMC), Hydroxy Propyl cellulose, starch and modified starch, Pullulan, pectin, Gelatin, carboxy, methyl cellulose, PVP+Cross linked PVP, Alginate, Poly vinyl Alcohol, Maltodextrin, and Polyox.

#### c) Plasticizer

The role of Plasticizer is beneficial for preparation FDF. Plasticizer helps to improve the flexibility of the film and reduces the brittleness of the film. The plasticizer should be compatible with polymer and solvent. The flow of polymer

will get better with the use of plasticizer and enhances the strength of the polymer. Propylene glycol (PG), Poly ethylene Glycol (PEG), Glycerol, Phthalate derivative like di-methyl, diethyl and dibutyl phthalate, citrate derivative such as tributyl, triethyl, acetyl, citrate, triacetin and castor oil are some of the commonly used plasticizer. Plasticizer may lead to film cracking, splitting and peeling of the film. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug. The plasticizer should be volatile in nature.

#### d) Flavors

Flavors include:

1. Both natural and artificial flavor such as artificial vanilla, cinnamon, and various fruit flavors; either individual or mixed.
2. Mints such as peppermint, menthol.
3. Essential oils such as thymol, eucalyptol and methyl salicylate.

#### e) Sweeteners

Sweeteners have become the important part of the formulation intended to be Disintegrated or dissolved in the oral cavity. Generally sweeteners are used in the Concentration of 3 to 6% w/w either alone or combination. Both nature sweeteners as well as artificial sweeteners are used in the formulation of these fast dissolving films. Polyhydric alcohols such as sorbitol, mannitol and isomalt can be used in combination as they additionally provide good mouth feel and cooling sensation. However it should be noted that the use of natural sugars in such preparation need to be restricted in people who are on diet or in the case of diabetic patients. Due to this reason, the artificial sweeteners have gained more popularity in food and pharmaceutical preparation. Saccharin cyclamate and aspartame is the first generation of the artificial sweeteners followed by acesulfame – K, Sucralose, alitame and neotame which fall under the second generation artificial sweeteners. Acesulfame – K and sucralose.

#### f) Saliva Stimulating Agent

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving strip formulations. Generally acids which are used in the preparation of good can be utilized as salivary stimulants. E.g. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid. These agents are used along or in combination between 2 to 6% w/w of weight of the strip.

#### g) Coloring Agent

FDA approved coloring agents are used (not exceeding concentration levels of 1 percent; w/w) in the manufacturing of orally fast dissolving film E.g. Titanium dioxide.

## 2. Method of Preparation

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

**1. Solvent Casting Method –**

In solvent casting method excipients are dissolved in water, then water soluble polymers and in last drug is added and stirred to form homogeneous solution. Finally solution is casted in to the Petri plate and dried.

**Semisolid Casting –**

This method is preferably adopted when acid insoluble polymers are to be used in the preparation of the films. In semisolid casting method gel mass is casted in to the films or ribbons using heat controlled drums. Gel mass is obtained by adding solution of film forming to a solution of acid insoluble polymer in ammonium or sodium hydroxide. Acid – insoluble polymers used to prepare films include: cellulose acetate phthalate, cellulose acetate butyrate. Acid insoluble polymer and film forming polymer should be used in the ratio of 1:4

**2. Hot Melt Extrusion –**

In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then dried granular material is introduced into the extruder. The crew speed should set at 15 rpm in order to process the granules inside the barrel of the extruder for approximately 3-4 min. The processing temperatures should be 800C (Zone 1), 1150C (Zone 2), 1000C (Zone 3) and 650C (zone The extrudate (T=650 C) then pressed into a cylindrical calendar in order to obtain a film. There are certain benefits of hot melt extrusion –

- Fewer operation units.
- Better content uniformity.
- An Anhydrous process.

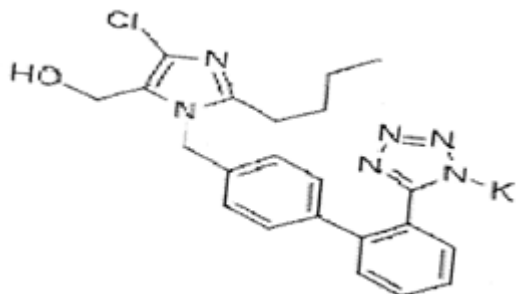
**3. Solid dispersion Extrusion –**

In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

**4. Rolling Method –**

In rolling method a solution or suspension of drug with film forming polymer is prepared and subjected to the roller. 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 an cut in to desired shapes and sizes.

- Drug Profile
- Chemical Structure



- Chemical Name – 2 Butyl -4-choro-1 {[2' – tetrazzol-5-yl] [biphenyl]-4y) methl} – 1H-imidazol-5-methanol mono – potassium salt.
- Empirical Formula – C<sub>22</sub>H<sub>22</sub>ClKN<sub>6</sub>O
- Molecular Weight – 461.0
- Category – Antihypertensive agent
- Dose – 25 mg – 100mg

h) Solubility – In water – freely soluble

i) In ethanol – Low

**5. Pharmacology**

- The main effect of angiotensin 2 vasoconstriction, aldosterone secretion and nor – epinephrine release from sympathetic nerve terminal.
- Losartan is a specific and selective antagonist of angiotensine – 2 AT1 site.
- It is able to block the contractile effect of angiotensine – 2in isolated strip of rabbit aorta, isolated guinea pig ileum.
- Losartan causes an acute dose dependant blood pressure falls in renal hypertensive rat.

**6. Pharmacokinetics:**

Losartan is well absorbed rally but undergoes pre-systemic metabolism, forming an active metabolite E-3174. Both the losartan and its metabolites are 99% bound to plasma protein, primarily albumin. Volume of distribution is relatively low. Plasma half life is about 2 hrs. losartan is extensively metabolized in liver. Approximately 35% of oral route is excreted in urine.

- Use – In all grades of hypertension.
- Synonym – Hypromollose, Methocel, Hypromellosum.
- Molecular weight – Approximately 10000 – 1500000.
- Category – Bioadhesive material, coating agent, controlled release agent, dispersing agent, emulsifying agent, film forming agent, release modifying agent.
- Description – It is an odorless, testless, white or creamy – white fibrous or granular powder.
- Typical Properties :
  - PH – 5.0 – 8.0 for 2% w/v
  - Density (bulk) – 0.341 g/cm<sup>3</sup>
  - Density (tapped) - 0.557g/cm<sup>3</sup>
  - Melting Point – Browns at 190-200c
  - Specific gravity – 1.26
  - Solubility – Forming colloidal solution with cold water.

**7. Glycerin**

- Synonym – Glycerol, Glycerolum, glycon g-100, optima, trihydroxypropane glycerol.
- Chemical Name – Propane – 1, 2, 3 Triol.
- Empirical Formula C<sub>3</sub> H<sub>8</sub> O<sub>3</sub>
- Molecular Weight – 92.09
- Category – Antimicrobial agent, cosolvent, emollient, humectants, plasticizer, sweetening agent.
- Description – Racemic menthol is a mixture of equal parts of the (1R, 2S, 5R) and (1S, 2R, 5S) isomers of menthol. It is a free flowing crystalline powder, or colorless, prismatic or acicular shiny crystal, strong characteristic odor and taste.
- Typical Properties – Boiling Point – 2120c
- Melting Point -340c
- Solubility – very soluble in ethanol (95%) chloroform, ether, liquid paraffin. Freely soluble in glacial acetic acid. Soluble in acetone and benzene.
- Saccharin Sodium:
  - Synonym – Crystallose, saccharinum natricum, sodium o-benzosuifimide, sucaryl sodium.
  - Chemical name – 1, 2 Benzisothiazol – 3 (2H) One, 1, 1-dioxide, sodium salt.



- m) Empirical Formula – C<sub>7</sub>H<sub>4</sub>NNaO<sub>3</sub>s  
 n) Molecular weight – 217.24  
 o) Category – Sweetening agent  
 p) Description – it occurs as a white odorless or faintly aromatic, crystalline powder. It has intensively sweet taste.  
 q) Typical Properties :
- PH – 6.6
  - Density (bulk) – 0.8-1. 1g/cm<sup>3</sup>
  - Melting point – Decomposes on heating.

### 8. Ethanol

- Synonym – Ethanolum, ethyl alcohol, ethyl hydroxide, grain alcohol.
- Chemical name – Ethanol
- Empirical Formula – C<sub>2</sub>H<sub>6</sub>O.
- Molecular weight – 46.07
- Category – Antimicrobial Preservative, disinfectant solvent.
- Typical Properties –
- Boiling point – 78.15
- Flammability – Readily flammable burning with blue flame.
- Solubility – miscible with chloroform ether, glycerin, water.
- Specific gravity – 0.8119-0.8139 at 200c

## 2. Materials and Method

Losartan potassium, HPMC 15 CPS, Glycerin Polysorbate 80, Sodium saccharin, Menthol, Ethanol, Distilled water.

Method of preparation of Film:

The preparation of film was done by using solvent casting method. The polymer was dissolved in hot water. The drug and other excipients were dissolved in ethanol. This solution was added to the polymeric solution. Then the solution was mixed by using mixing device for 45 minutes with rotating speed 60-80 rpm. The entrapped air is removed by vacuum. The resulting solution was casted slowly and with continuous flow on glass plate. The plates were kept in a hot air oven at 60 for 24 hours. The dried film was gently separated from glass plate and cut into desired sizes of about 4 cm<sup>2</sup>.

**Table 1:** Different formulation batches F1 to F3 of orodissolving film

Batches	F1	F2	F3
Losartan Potassium	25 mg	25 mg	25 mg
HPMC 15 CPS	400 mg	400 mg	400 mg
Glycerin	60 mg	72 mg	84 mg
Polysorbate 80	40 mg	40 mg	40 mg
Sodium Saccharin	40 mg	40 mg	40 mg
Menthol	20 mg	20 mg	20 mg
Ethanol	1 ml	1 ml	1 ml
Dist. Water	9 ml	9 ml	9 ml

Evaluation test for mouth dissolving firm:

### 1. Mechanical Proprieties

- Thickness
- Dryness / tack test
- Tensile strength
- Percent Elongation
- Young's Modulus
- Tear resistance

Folding endurance

2. Organoleptic test
3. Swelling test
4. Surface pH test
5. Contact angle
6. Transparency
7. Assay / Content Uniformity
8. Disintegration test
9. In – Vitro Dissolution test

### Thickness:

As the thickness of film is directly concern with drug content uniformity so it is necessary to ascertain uniformity in the thickness of the film. It can be measured by micrometer screw gauge or calibrated digital vernier Calipers at different strategic locations.

### Dryness Test / Tack Tests:

About eight stages of film drying process have been identified and they are set – to touch, dust – free, tack – free (Surface dry), Dry – to touch, dry – hard, dry – through (dry – to – handle), dry-to-recoat and dry print – free. Although these tests are primarily used for paint films most of the studies can be adapted intricately to evaluate pharmaceutical OFDF. The details of evaluation of these parameters can be checked elsewhere and are beyond the scope of this review track is the tenacity with which the strip adheres to an accessory (a piece of paper) that has been pressed into contact with the strip. Instruments are also available for this study 30.

### Tensile Strength:

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross – sectional area of the strip as given in the equation below:  $30 \text{ Tensile Strength} = \text{Load at breakage} / \text{Strip Thickness} \times \text{Strip width}$

### Percent Elongation:

When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increase as the plasticizer content increase

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

### 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: Hard and brittle strips demonstrate a high tensile strength and Young's modulus with small elongation 30.

**Tear Resistance:**

Tear resistance of plastic film or sheeting is a complex function of its ultimate to rupture. Basically very low rate of loading 51 mm (2 in) / min is employed and is designed to measure the force to initiate tearing. 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)

**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:

$$\text{Transparency} = (\log T600) / b =$$

Where T 600 is the transmittance at 600 nm and b is the films thickness (mm) and c is concentration 33, 34.

**Drug Content:**

A film of size 2 x 2 cm<sup>2</sup> is cut and put in 100 ml of breaker containing. This is then shaken in a mechanical shaker for 30 min to get homogeneous solution and filtered. The drug is determined spectroscopic ally after appropriate dilution. Limit of content uniformity is 85-115%

**Disintegration test**

It is determined by manually dipping the film in beaker containing 10ml distilled water. Time required to break or disintegrate the film is disintegration time.

**Standard calibration curve**

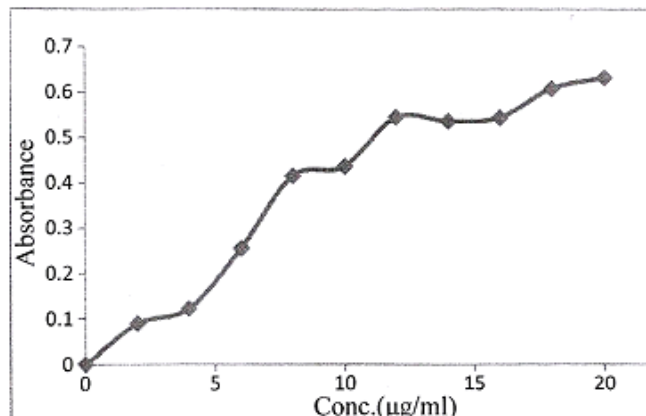
1. Preparation of phosphate buffer pH 6.8 – Place 50ml of 0.2 M Potassium dihydrogen phosphate in 200ml volumetric flask, add 22.4ml sodium hydroxide solution add water to make up the volume.
2. Preparation of stock solution :
3. Weigh accurately 10mg Losartan Potassium and transfer in to 100ml volumetric flask makeup the volume up to 100ml using phosphate buffer pH 6.8

**Parameters**

1. Beer's Lambert Rang – 2-20ug / ml.
2. Solvent – Phosphate buffer – pH 6.8.
3. Maximum wavelength – 254 nm.
4. RPM – 10

**Table 2:** Observation table of calibration curve

Sr. No.	Concentration ( g/ml)	Absorbance
1	2	0.09
2	4	0.123
3	6	0.256
4	8	0.415
5	10	0.436
6	12	0.544
7	14	0.536
8	16	0.544
9	18	0.608
10	20	0.632
R2 = 0.96		Slope – 0.062
		Intercept – 0.043



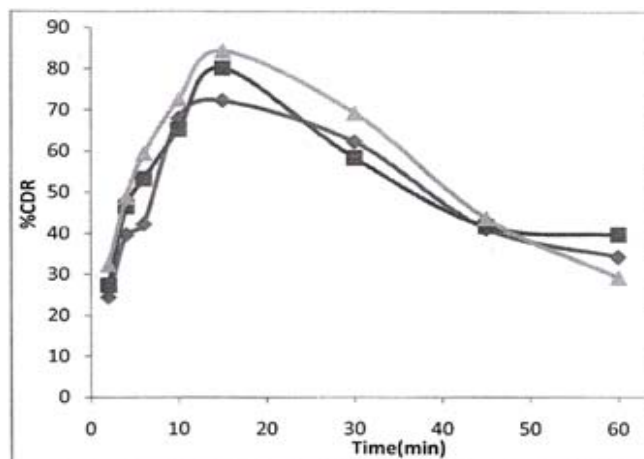
**Figure:** Calibration curve of Losartan Potassium

**In Vitro drug Release:**

Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopoeia. The dissolution is carried out in 900ml of PH 6.8 Phosphate buffer maintained at 37± 0.050c at 100 rpm. 10 ml of samples were taken at 2, 4, 6, 10, 15, 30, 45, 60 min which replaced with same volume of fresh PH 6.8 phosphate buffer. After appropriate dilution samples was then determined spectroscopic ally at 254 nm.

**Table 3:** Invitro drug release of formulation batches F1 to F3

Time (Min)	% CDR		
	F1	F2	F3
2	24.48	27.36	32.4
4	39.6	46.44	48.8
6	42.3	53.25	59.4
10	67.96	65.23	72.6
15	72.23	80.12	84.29
30	62.21	58.3	69.23
45	41.11	41.7	43.53
60	34.2	39.6	29.16



**Figure 2:** Invitro Drug release of Losartan Potassium

### 3. Result and Discussion

**Table 3:** Evaluation of orodissolving film formulation batches F1 to F3

Batches	F1	F2	F3
Thickness (nm)	0.09	0.1	0.09
% Elongation	5	10	25
Folding endurance	21	28	32
% Drug content	73.1	78.36	81.4
Disintegration time (sec.)	42	34.12	28.15
In vitro drug release	72.23	80.12	84.29

#### 1. Thickness -

The result shows that thickness of mouth dissolving film does not depend on the concentration of plasticizer.

#### 2. Percent elongation -

A result showed that as the concentration of plasticizer increases % elongation of orodissolving film also increases.

#### 3. Folding endurance -

As a result shows as the concentration of plasticizer increase folding endurance of orodissolving film also increases.

#### 4. Disintegration time -

As the concentration of plasticizer increases, disintegration time of orodissolving film decreases.

#### 5. Percent drug content-

As a result shows concentration of plasticizer increases percent drug content also increases.

#### 6. In vitro drug release -

As a result shows F3 formulation shows best release of drug .

### 4. Conclusion

The Losartan potassium orodissolving films were successfully prepared as orodissolving dosage form. In vitro dissolution studies showed fast release at 15 min. The formulation F3 showed fast drug release as compared to F1 & F2.

Order of release of Losartan potassium is as follows:

F3 > F2 > F1

Order of disintegration time is as follows:

F1 > F2 > F3

Thus, F3 formulation showed fast drug release 84.29% at the end of 15 min because glycerin also acts as cosolvent and enhances dissolution of Losartan potassium, so disintegrate rapidly and release is fast. Hence, as the concentration of plasticizer increases drug release increases.

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