# REVIEW ON A ORAL FILM FOR THE TREAMENT OF MIGRAINE

Sohan S. Thipe[1], Shailesh G. Jawarkar[2]

[1]*Student of Vidhya Bharti college of pharmacy, Naidu marg camp, Amravati, India*

[2]*Assistant Professor of Vidhya Bharti college of pharmacy, Naidu marg camp, Amravati, India*

**ABSTRACT**

*Patients suffering migraines accompanied by nausea, vomiting, and sensitivity to light and sound should be provided with an oral film of an anti-migraine medication to help remove their pain. These severe headaches are often recurrent and are particularly prevalent in women. While weekly occurrences are typical, they can also present once every few years or even less frequently. The duration of these headaches can range from a few hours to three days, depending on their intensity. Generally, morning headaches tend to affect just one side of the head, usually the side of the forehead. Such headaches can be extremely debilitating and are very frequently reported. These conditions comprise the leading causes of headaches, accounting for 95 percent or more of all complaints. Utilizing transdermal patch technology, mouth-dissolving films and oral film represent an innovative method of drug delivery. When a patient's tongue or any mucosal surface comes into contact with saliva, a thin film forms on the area, which quickly hydrates and adheres to the site of application. Upon swallowing, it rapidly breaks down and dissolves, allowing the medication to be absorbed through the oral mucosa. In contrast to traditional methods, these fast-dissolving films can be produced at a cost similar to that of standard tablets, making them an innovative and promising option for delivering anti-migraine medications in the treatment of migraines.*

*Among the various methods of administration, the oral route is the most preferred by patients. Many pharmaceutical companies have focused their research efforts on creating effective oral dosage alternatives for children, the elderly, patients with adherence issues, or those suffering nausea. Advancements in the oral drug delivery field have transformed dosage forms from basic traditional tablets and capsules to modified-release versions, as well as oral disintegrating tablets, culminating in the latest innovation of oral films.*

**Keywords:** *Oral film, Migraine, oral route, Headache,*

## 1.INTRODUCTION [(1)]

Migraine is currently ranked as the sixth most disabling condition worldwide, holding the top position among all neurological disorders. The biology of migraine is complex, multi-dimensional, and still unresolved in certain areas. A likely complex genetic predisposition, coupled with environmental and behavioral factors, appears to lead to changes in sensory processing in the brain, resulting in heightened sensitivity to sensory stimuli. Consequently, what would be normal sensory experiences may become distressing for those who suffer from migraines. Over the years, our understanding of migraines has significantly advanced, largely due to foundational scientific research and imaging techniques that have enhanced our comprehension of the complex models necessary to elucidate the wide array of migraine symptoms. Pain, the primary symptom of the condition, is not always the most distressing aspect for every patient at all times. Migraine is defined by a series of essential phases that frequently overlap, including the premonitory (prodromal), aura, pain, and postdrome stages. Improved understanding of these phases has enabled us to view migraine as a network disorder that involves various cortical, subcortical, and brainstem areas, producing a diverse array of signs and symptoms. We will examine these regions in detail in the following sections, which exhibit changes in both function and structure in patients with migraine and in animal models of the condition.

### 1.1 Definition of migraine [(2)]

A migraine is an intense headache that typically causes a throbbing, pulsating pain on one side of the head. The headache stage of a migraine generally lasts for several hours, but it can sometimes persist for an entire day. This pain tends to intensify with

1. Physical exertion

2. Bright lights

3. Loud sounds

4. Strong odors

### 1.2 Types of migraine

There are mainly two types are fallowing

1. Migraine with aura (Classic migraine)
2. Migraine without aura (Common migraine).

### 1.3 Phases of migraine

There are four phase or stages of migraine

**1. Prodrome** - The initial phase occurs within 24 hours prior to the onset of a headache.

**2. Aura** - An aura consists of a series of sensory, motor, and speech symptoms that serve as a warning sign for an impending migraine headache. The duration of the aura phase can be as brief as five minutes or extend up to 60 minutes. It's possible to experience the aura and headache simultaneously.

**3. Headache** - A migraine headache typically persists for a duration of four to 72 hours.

**4. Postdrome** - The postdrome phase usually lasts anywhere from a few hours to 48 hours. The symptoms resemble those of a hangover caused by alcohol, which is why it's often referred to as the "migraine hangover."

### 1.4 Migraine Symptoms

Migraine symptoms based on phases or stage

**1. Prodrome**

Altered mood, trouble with focus, sleep difficulties, tiredness, queasiness, heightened hunger and thirst, increased frequency of urination.

**2. Aura**

Weakness in muscles, alterations in vision, tinnitus, heightened sensitivity to touch.

**3. Headache**

Nausea and vomiting, increased sensitivity to light, sound, and odors.

**4. Postdrome**

Exhaustion, neck stiffness, sensitivity to light and sound, challenges with concentration, queasiness, dizziness.

### 1.5 Diagnosis [3]

**1. When suspecting a migraine:**

1. A recurring headache that is of moderate to severe intensity.

2. The presence of a visual aura.

3. A family history indicating migraines.

4. Symptoms beginning around the time of puberty.

**2. Migraine diagnosis:**

1. Gather the patient's medical history.

2. Use established diagnostic criteria.

3. Consider other possible diagnoses.

4. Examine the patient to rule out alternative causes.

**3. Focusing on the patient and their education:**

1. Offer suitable reassurance.
2. Establish realistic goals together.
3. Identify any predisposing or triggering factors.
4. Develop a strategy to tailor therapy based on individual symptoms and needs.

### 1.6 Acute and preventive treatment

**Acute treatment**

1.First line medication

NSAIDS (Acetylsalicylic acid, ibuprofen, diclofenac sodium)

2.Second Line medication

Triptans

3.Third one medication

Diptan, Gepants, Prokinetic antiemetic (Domperidone or metoclopramide)

**Preventive treatment**

1.First line medication

Beta blocker (Propranolol, metoprolol, atenolol, bisoprolol), Topiramate, Candesartan

2.Second line medication

Flunarizine, Amitriptyline, Sodium valproate

### 1.7 Managing migraines in specific demographics

1. Elderly individuals
2. Children and adolescents
3. Pregnant or breastfeeding women
4. Women experiencing menstrual migraines

### 1.8 Clinical supervision and follow-up

1. Assessment of treatment efficacy and handling treatment failures
2. Addressing complications
3. Identifying and managing comorbid conditions
4. Organizing long-term follow-up care

## 2 Oral Thin Films [4]

Oral film are another term for these products. In recent years, oral thin films have emerged in the confectionery and oral care industries as breath strips. These innovative products have gained widespread consumer acceptance for the delivery of vitamins and personal care items. At present, fast-dissolving oral films (FDOFs) are recognized and validated technology for the systemic administration of active pharmaceutical ingredients (APIs) in over-the-counter (OTC) medications and are currently in the early to mid-development phases for prescription drugs.

The success of breath freshener products like Listerine Pocket Packs can be credited to consumer preferences in the US market. These systems employ various hydrophilic polymers to create a film measuring between 50 and 200 mm. This film is produced as a large sheet and subsequently cut into individual doses for packaging in various pharmaceutically acceptable formats. Classfication of oral films There are three types of oral films. They are:

 Flash release/ Fast dissolving films (Placed on the tongue).

 Mucoadhesive melts away films (Gingival or buccal region).

 Mucoadhesive sustained release films (adhere to the buccal mucosa).

**1.Flash Release:**

The area and thickness of the film range from approximately 2 to 8 square centimeters and 20 to 70 micrometers, respectively. It features a single-layer structural design that necessitates the use of soluble, highly hydrophilic polymers for its formulation. This wafer is positioned on the upper palate of the tongue and can fully disintegrate within a maximum of sixty seconds.

**2. Mucoadhesive Melt Away films:**

This system can be either single or multilayered and requires soluble, hydrophilic polymers as excipients. The drug phase can consist of a solid solution or suspended drug particles. It is applied in the gingival or buccal area and disintegrates within a few minutes, resulting in the formation of a gel. The film's thickness ranges from 50 to 500 micrometers, with an area of 2 to 7 square centimeters.

**3.Mucoadhesive Sustained Release films:**

This wafer is used in the gingival area (another part of the oral cavity) and employs a multilayer system. The drug phase may exist as a solid solution or a suspension, and the excipients could be low- or non-soluble polymers. With an area of 2 to 4 square centimeters and a thickness of 50 to 250 micrometers, it takes 8 to 10 hours to dissolve.

## 2.1 Benefits of oral films 5,6,7,8,9

The benefits of buccal films include:

1. There is no need for specially trained personnel.

2. They are flexible and portable, making them easy to transport and store.

3. They provide accurate dosing.

4. They offer improved stability and safety.

5. Each film contains a specific amount of the drug.

6. They have a quick onset of action and enhanced bioavailability.

7. They help in freshening breath.

## 2.2 Drawbacks of oral films

1. Eating and drinking are restricted while using them.

2. They can only administer drugs that require lower doses.

3. Special packaging is necessary to maintain product stability and safety.

4. There is a limited selection of polymers available.

## 3 MATERIALS AND METHODS 10,11,12

**MATERIALS:**

**3.1 Composition of film:**

A oral film is a thin layer containing an active ingredient and ranges in size from 2 to 8 $cm^2$. The swift disintegration occurs in water, transforming into saliva or water through a specialized matrix. Polymers that are capable of dissolving are utilized. A single dose of medication can be incorporated, with amounts reaching up to

30 mg. Research has indicated that formulation factors significantly influence the mechanical characteristics of the films. Additionally, there is an in-depth analysis of the excipients used in the development of rapid-dissolving films. From a regulatory standpoint, each excipient included in the formulation must be approved for use in oral pharmaceutical products and must be generally recognized as safe. All the components regarding their percentage proportions are presented in Table No. 1

**Table No.1:-** Material used in formulation of film

| Sr. No. | Category | Percentage (%) Amount |
|---|---|---|
| 1 | Drug (API) | 1-30% |
| 2 | Polymer | 40-50% |
| 3 | Plasticizer | 0-20% |
| 4 | Surfactant | Qs |
| 5 | Saliva stimulating agent | 2-6% |
| 6 | Sweetning Agent | 3-6% |
| 7 | Flavoring Agent | 0-10% |
| 8 | Coloring Agent | Qs |
| 9 | Stabilizing agent | 0-5% |

## 3.2 FORMULATION INGREDIENTS AND COMPONENT

### 3.2.1 Active Pharmaceutical Ingredient:

The active medicinal component constitutes 1-30% w/w of the film formulation. Since combining high doses of medications into fast-dissolving films can be challenging, it is generally advisable to use low-dose active pharmaceutical ingredients. Various drugs, including antihistamines, antidiarrheal agents, antidepressants, vasodilators, anti-asthmatics, and antiemetics, can be employed in the formulation of fast-dissolving oral films. Additionally, optical dissolvable films can be noted for their taste-masking properties. Table 2 presents a list of some common medications that have been developed as films.

**Table No 2:-** Below List of few drug that can be incorporated in fast dissolving oral film

| Drug | Dose Action | Therapeutic |
|---|---|---|
| Azatidine maleate | 1mg | Anti histaminic |
| Nicotine | 2mg | Smoking cession |
| Loperamide | 2mg | Anti diarroheal |
| Ondensetron | 2.5 mg | Anti emetic |
| Triplodine Hydrocholride | 2.5 mg | Anti histaminic |
| Salbutamol | 4 mg | Anti histaminic |
| Chlorpheniramine maleate | 4 mg | Anti allergic |
| Cetrizine | 5-10 mg | Anti histaminic |
| Acrivastine | 8 mg | Anti histaminic |
| Loratidine | 10 mg | Anti histaminic |
| Omeprazole | 10-20 mg | Proton pump inhibitor |
| Famotidine | 10 mg | Antacid |
| Ketoprofen | 12.5 mg | Analgesic |
| Dicyclomine hydrochloride | 25 mg | Muscle relaxant |
| Diphenhydramine hydrochloride | 25 mg | Anti allergic |
| Sumatriptan succinate | 35-70 mg | Anti migraine |

### 3.2.2 Drug

A variety of drug classes can be included in oral dissolving films, such as anti-histamines, anti-diarrheal agents, antidepressants, vasodilators, anti-asthmatics, anti-emetics, and others. Dimenhydrinate can also be added to oral dissolving films for the purpose of taste masking. Common examples of drugs found in oral dissolving films include salbutamol sulfate, rizatriptan benzoate, verapamil, ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, and indomethacin. An oral dissolving film was formulated using prochlorperazine, an anti-emetic agent, by incorporating microcrystalline cellulose along with other film-forming polymers.

### 3.2.3 Polymers

The effective creation of oral dissolving films relies heavily on the appropriate selection and concentration of polymers, as the mechanical strength of the films is closely linked to these aspects. Polymers can be utilized singly or in combination with others to adjust the film's characteristics. The concentration of the polymers is a crucial consideration in the development of oral dissolving films. The stability of fast-dissolving oral films hinges on the careful choice of the type and proportion of polymers used. Typically, the polymer concentration in the preparation of oral dissolving films is about 45% w/w of the total dry strip weight, but it can be raised to 60-65% w/w to achieve the desired film qualities and attributes. Polymers utilized as film-forming agents in the formulation of thin strips need to possess specific characteristics. Recently, both natural and synthetic polymers are employed in the preparation of oral dissolving film formulations. Due to the low cost of this excipient, it is often used in combination with pullulan to lower the overall product cost. Pullulan is a natural polymer derived from non-animal sources and does not require chemical modifications. Around 50 to 80 percent w/w of pullulan can be substituted with starch during the manufacturing of fast-dissolving films without compromising the necessary properties of pullulan. The combination of microcrystalline cellulose and maltodextrin has also been utilized to produce fast-dissolving films. Various polymers such as HPMC E15, HPMC K4M, HPMC E5, PVP, PVA, and gelatin were employed in the formulation of oral films using the solvent casting method. Findings indicated that HPMC is the most suitable polymer for oral fast-dissolving films.

### 3.2.4 Plasticizers

Plasticizers improve the mechanical characteristics of the film, including tensile strength and elongation, by lowering the glass transition temperature of the polymer. They also decrease the brittleness of the strip, thereby enhancing its flexibility. The selection of a plasticizer is influenced by the type of solvent used and its compatibility with the polymer. Commonly used plasticizers include phthalate derivatives like dimethyl, diethyl, and dibutyl phthalate, low molecular weight polyethylene glycols, castor oil, and citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin, and glycerol. Improper application of plasticizers can result in issues like blooming, cracking, splitting, and peeling of the film.

### 3.2.5 Surfactants

Surfactants act as wetting, solubilizing, or dispersing agents to ensure that the film dissolves rapidly and releases the active ingredient promptly. Frequently used surfactants include polaxamer 407, bezathonium chloride, sodium lauryl sulfate, tweens, and benzalkonium chloride. Among these, polaxamer is the most commonly used surfactant.

### 3.2.6 Sweetening agents

Sweeteners play a crucial role in the formulation designed to be disintegrated or dissolved in the mouth. Generally, sweeteners are utilized at concentrations ranging from 3 to 6% w/w, either individually or in combination. Both natural and artificial sweeteners are incorporated into these fast-dissolving films. However, it's important to limit the use of natural sugars in preparations intended for those on a diet or individuals with diabetes. For this reason, artificial sweeteners have become increasingly popular in both food and pharmaceutical products. The first generation of artificial sweeteners includes saccharin, cyclamate, and aspartame, while the second generation comprises acesulfame-K, sucralose, alitame, and neotame. Acesulfame-K and sucralose are over 200 and 600 times sweeter, respectively, while neotame and alitame boast sweetness levels exceeding 2000 and 8000 times that of sucrose. Aspartame has been utilized in the manufacture of oral strips containing valdecoxib, and sucralose and neotame have been reported to mask the bitter flavors of fast-dissolving films for diclofenac and ondansetron, respectively.

### 3.2.7 Saliva stimulating agents

Saliva stimulating agents are utilized to enhance the production rate of saliva, aiding the rapid disintegration of strip formulations. Citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid are examples of salivary stimulants, with citric acid being the most preferred. These agents can be used alone or in combination at a concentration of 2 to 6% w/w relative to the weight of the strip.

### 3.2.8 Flavoring agents

The amount of flavoring agent needed to mask taste varies based on the type and intensity of the flavor. Commonly used flavors include fruity options (such as vanilla, cocoa, coffee, chocolate, and citrus) as well as flavor oils (like peppermint oil, cinnamon oil, and nutmeg oil). Flavors can also be derived from oleo resins, synthetic flavor oils, and extracts from various plant parts, including fruits and flowers. Ideally, flavor additions should not exceed 10% w/w.

**3.2.9 Coloring agents**

Typically, coloring agents used include synthetic colors, natural colors, and pigments such as titanium dioxide. Approved coloring agents are employed in the production of fast-dissolving films, with concentrations kept below 1% w/w.

## 4 Method of preparation of oral Film 13,14,15

a. Solvent casting method

b. Semi-solid casting method

c. Hot melt extrusion

d. Solid dispersion extrusion

e. Rolling method

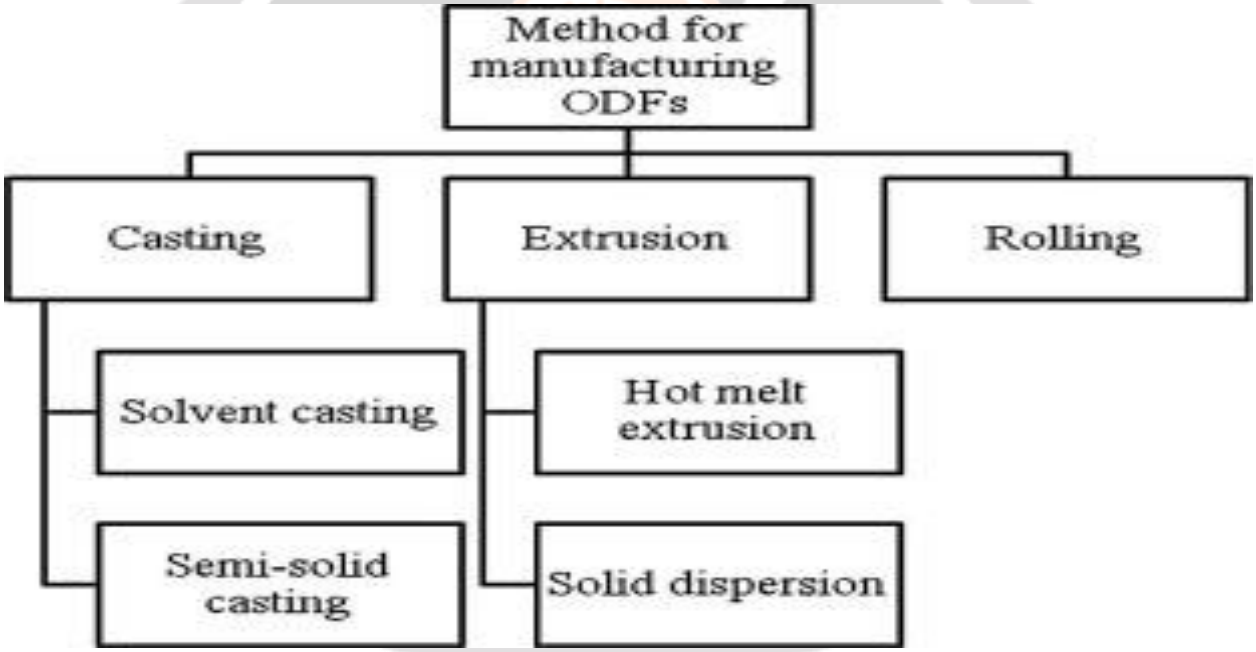


**Fig no. 1:-** Traditional method of manufacturing of oral dissolving film

**4.1 Solvent casting method**

The required quantity of polymer is added and dissolved in distilled water when utilizing the solvent casting method. A small quantity of the active medicinal ingredient is incorporated into this solution. The solution is then modified with a plasticizer and mixed thoroughly. Afterward, the solution is poured onto a baking plate and dried in a hot air oven at 40°C. Once dried, it is carefully cut out of the petri dish using a knife and placed in a desiccator for 24 hours. Finally, it is cut into the desired size and shape. Steps in the solvent casting method:

Step 1: Prepare the casting solution.

Step 2: Deaerate the solution.

Step 3: Pour the appropriate amount of solution into the mold.

Step 4: Dry the casting solution.

Step 5: Cut the final dosage form to the required dosage.

**4.2 Semi-solid casting method**

The flow diagram for the semi-solid casting method is presented below.

Mixing of hydrophilic acid-insoluble

↓

Addition of plasticizer to create a gelled mass

↓

Rolling

↓

Drying and cutting

**4.3 Hot melt extrusion**

The procedure utilizes a hot melt extruder. In this approach, a polymer is heated and shaped into a film. A combination of dry pharmaceutical substances, including the active pharmaceutical ingredient (API), is introduced into the hopper, where it is transported, mixed, and heated before being extruded in a molten state by the extruder. The film is cast from the molten mass, which solidifies thereafter. The casting and drying stages are critical steps in this process.

Steps involved in hot melt extrusion technique

Step 1: The medication is blended with solid carriers.

Step 2: A heater-equipped extruder melts the blended mixture.

Step 3: The melted material is finally shaped into films using dies.

**4.4 Solid dispersion extrusion**

Initially, solid dispersion is produced by extruding immiscible components along with the drug and then formed into films using dies.

The drug is dissolved in a suitable liquid solvent.

↓

The solution is then mixed into the melt of polyethylene glycol, which is achievable below 70°C.

↓

Ultimately, the solid dispersions are shaped into films using dies.

**4.5 Rolling method**

The primary solvents used in this technique are water and combinations of water and alcohol. Through a high shear process, the active ingredient and other components are dissolved in a small amount of aqueous solvent. Water-soluble hydrocolloids are dissolved in water to create a uniform viscous solution. Subsequently, the resulting solution or suspension containing the drug is rolled onto a carrier. Finally, the film obtained is cut into the desired shapes and sizes.

Prepare a pre-mix with film-forming polymer, polar solvent, and other additives except for the drug.

↓

Introduce the pre-mix into the master batch feed tank.

↓

Feed it via a first metering pump and control valve to either or both the first and second mixers.

↓

Incorporate the required amount of drug into the chosen mixer.

↓

Blend the drug with the master batch pre-mix to form a uniform matrix.

↓

A specific quantity of the uniform matrix is then fed into the pan using two metering pumps.

↓

The film is then formed on the substrate and transported away by a support roller.

↓

The wet film is subsequently dried utilizing controlled bottom drying.

## 5 EVALUATION TEST 16,17,18,19

1.Thickness

2.Weight Variation

3.Folding endurance

4.Surface pH

5.Drug Content Uniformity

6.Disintegration test

7.In vitro drug release

### 5.1 Thickness

The film's thickness is crucial for maintaining consistent drug content, making it essential to verify uniformity across the film's thickness. This can be assessed using a micrometer screw gauge or calibrated digital Vernier Calipers at various strategic points.

### 5.2 Weight Variation

The patches underwent a mass variation study, where randomly selected patches were weighed individually. The average from five measurements of each batch was calculated, with these assessments conducted for every batch.

### 5.3 Folding Endurance

Folding endurance refers to the number of times the film can be folded at the same location before showing visible cracks or breaking. This measure indicates the film's brittleness, with the test conducted by repeatedly folding the strip at the same point until a noticeable crack appeared, and the resulting values were recorded.

### 5.4 Surface pH of Film

The surface pH of the films was measured by placing the film on the surface of a 1.5% w/v agar gel, followed by placing pH paper (with a range from 1 to 11) on the films. Observations of the color change in the pH paper were noted and reported.

**5.5 Drug Content Uniformity**

Content uniformity involves evaluating the active pharmaceutical ingredient (API) content in individual strips. The acceptable range for drug content uniformity is between 85-115%, while a more stringent target is 95% to 105%.

**5.6 Disintegration Time**

The disintegration of orally fast-dissolving films is assessed using the USP disintegration apparatus. The guideline for disintegration time is set at 30 seconds or less for orally disintegrating tablets, which can also apply to fast-dissolving oral strips. Although disintegration times can differ based on formulation, they generally range from 5 to 30 seconds, and no formal guidance exists for oral fast-dissolving film strips.

**5.7 In-vitro Drug Release**

For in-vitro dissolution testing, each film was carefully placed using forceps into a 50 ml glass beaker containing 25 ml of phosphate buffer at pH 6.8. The dissolution media's temperature was maintained at 37±0.5ºC with stirring at 50 rpm. During the study, 3 ml aliquots were taken at intervals of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 minutes, and replaced with fresh buffer. The amount of drug released into the media was measured using a UV-Visible Spectrophotometer (Shimadzu-1800) at 225 nm.

## 6 Conclusions

According to this study, an migraine medication is Among the novel method in the pharmaceutical science field are oral films that dissolve quickly. They have enhanced patient compliance and acceptance since they are safer and more effective than traditional forms. Oral film was created to assist dysphasic patients who had trouble swallowing traditional oral dose forms. Today, a range of oral films are accessible to treat ailments like acidity and hypertension. When they are administered without water, they satisfy the needs of the public who want easier drug administration and avoid hepatic metabolism, which improves therapeutic response. The patient will benefit from it.

## 7 REFERENCE

1.Francesca Puledda et.al Migraine: from pathophysiology to treatment April 2023 page no 3654-3666

2. https://my.clevelandclinic.org/health/diseases/5005-migraine-headaches

3. Hakan Ashina et.al Diagnosis and management of migraine in ten steps 2021 Vol 17 page no 501 -514

4. Pavan Kumar Kothapuvari et.al Preparation of fast dissolving oral film of new generation anti migraine drugs by solvent casting method may 2016 vol 8(5) page no 30704-30710

5. Buccal film – an updated review

6. Jangra PK, Sharma S, BalaR.Fast dissolving oral films: Novel way for oral drug delivery. Int. J. Uni. Pharm. Bio. Sci., 2014; 3(1): 6-27.

7. Heer D, Aggarwal G, Kumar SLH. Recent trends of fast dissolving drug delivery system-An overview of formulation technology. Pharmacophore, 2013; 4(1):1-9.

8. Mahajan A, Chhabra N, Aggarwal G. Formulation and Characterization of Fast Dissolving Buccal Films: A Review. Der Pharm Lett., 2011; 3(1): 152-165.

9. Kakri, S., Kim, H., Shin. D. and Lee, JThin films as an emerging platform for drug delivery. Asian Journal of Pharmaceutical Sciences. (2016); 2(1) : 559-574.

10.Bhura, N., Sanghavi, K., Patel, U. and Parmar, B. (2012). A Review on Fast Dissolving Film. International Journal of Pharmaceutical Research and Bio Science, 1(3), pp. 63-89,

11. AS Kulkarni: HA Deokule: MS Mane: DM Ghadge. J current Pharm. Research, 2010;2 (1): 33-35.

12.Mclndoe; RC Rowe; PJ Sheskey; SC Owen. In Handbook of Pharmaceutical Excipients, Pharmaceutical press, London, 2006;: 128 - 130.

13.Bala, R., Pawar, P., Khanna, S. and Arora, S. Orally dissolving strips: A new approach to oral drug delivery system. International Journal of Pharmaceutical Investigation (2013); 3(2): 67-76.

14.Patel, A., Prajapati, D. and Rawal. J. Fast dissolving films (FDFs) as a newer venture in fast dissolving dosage forms. International Journal of Drug Development & Research (2010); 2(2): pp. 232-246.

15. Pandya Ketul, K.R.Patel, M.R.Patel, N.M.Patel. Fast Dissolving Films: A Novel Approach to Oral Drug Delivery. IJPTP, 2013, 4(2), 655-661.

16. Dixit R. Puthli S. Oral strip technology: Overview and future potential. Journal of Controlled Release 2009: 94-107.

17. Hirpara F. Debnath KS. Saisivam S. Optimization and Screening of Different Film Forming Polymers and Plasticizer in Fast Dissolving Sublingual. Int J Pharm Pharm Sci, 2013, 6; 41-42.

18. NA Nafee: NA Boraie: FA Ismail: LM Mortada. Acta Pharm 2003. 53. 199-212.

19. R Patel: N Shardul: J Patel: A Baria. Arch Pharm Sci & Res. 2009. 1 (2), 212-217