International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1952-1959 www.ijprajournal.com ISSN: 2456-4494

# Patidar, et al.: Topiramate mouth-dissolving film for tranuillizers

# Formulation and Evaluation of the Topiramate Mouth-Dissolving Film for Tranquillizers

MOHINI PATIDAR*, BHOOPENDRA PATIDAR, NITIN DESHMUKH, NILESH MANDLOI, ESHA GUPTA, KOUSHAL PATEL

*Department of Pharmaceutical Chemistry, GRY Institute of Pharmacy, Khargone, MP, INDIA-451228*
*Department of Pharmaceutics, GRY Institute of Pharmacy, Khargone, MP, INDIA-451228*

Date of Submission: 04-12-2023 Date of Acceptance: 17-12-2023

## ABSTRACT

The objective of the current study is to create and assess a Topiramate mouth-dissolving film formulation from HPMC-15, with a combination of microcrystalline cellulose and PEG 6000. Topiramate is an antiepileptic drug used to treat migraine and epileptic seizures. Drug has poor water soluble properties. Topiramate mouth dissolving films are the new approach in NDDS System to administer drugs with combination of polymer and solubilizing agent which will improve solubility in water, improve drug efficacy and bioavailability, avoid first pass metabolism, and decrease patient noncompliance. Materials and Methods: The water soluble polymers HPMC E 15 and CMC have good film-forming abilities and a high elastic modulus. As plasticizers, stabilizing agents, and taste modifiers, PEG 6000, Tween 80, and saccharin were utilized, respectively. Films were prepared by solvent casting method. Result: The IR spectrophotometer was used to investigate the medication and polymer compatibility; no interactions of any type were found. A new analytical technique wasdeveloped and validated in accordance to ICH guideline for the estimation of topiramate in bulk utilizing pH 6.8 buffer solutions. The analytical method's results showed the λmax at 238 nm, the regression equation y = 0.0179x + 0.0571, and a correlation coefficient of 0.9989. ($R^2$). Among all the formulations F1 was selected as an optimized formulation, the results showed homogenous and transparent, devoid of particulate matter, good folding endurance properties 93, thickness 0.096±0.00, weight variation 35.30±0.002, and pH 6.85 reassembled with the pH of saliva. The result of dissolution study reveals 97.92% drug release within 80 second which is an essential characteristic for faster absorption. Topiramate mouth dissolving formulation was significantly improved the drug solubility and release. Thus, mouth dissolving film formulation of topiramate was successfully developed.

**Key world:** Topiramate, Mouth dissolving film, Analytical method, Solvent casting method.

## I. INTRODUCTION

Mouth dissolving films are novel medication delivery technology for oral drug delivery. MDF is highly beneficial to use in the acute drug delivery such as pain, epilepsy, seizures, emesis, migraine, hypertension, congestive heart failure, asthma, etc. These are designed to dissolve or disintegrate in a matter of seconds. They provide benefits such administration without water, simplicity of ingesting, quick beginning of action, and ease of dosing. Absorption through the oral mucosa is a possibility for quickly dissolving active medicinal substances, which may enhance bioavailability. Polymers with good film-forming qualities that are water soluble and quickly disintegrate are mostly used to create RDF, including hydroxy propyl methylcellulose (HPMC), polyethylene oxide (PEO), polyvinyl pyrrolidone (PVP), and hydroxy propyl cellulose (HPC).[1]

In light of the proposed research work's reasoning, the current study's objective was to create and formulate topiramate-based fast-dissolving aprepitant films using the solvent casting process for the drug's direct absorption into the systemic circulation through the mucosa.The proposed formulation, which is used in patients with certain types of seizures such as primary generalized tonic-clonic seizures (previously known as a grand mal seizure; a seizure that affects

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1952-1959 www.ijprajournal.com ISSN: 2456-4494

the entire body) and partial onset seizures (seizures that affect only one part of the brain), has the potential to improve compliance and offers numerous competitive advantages over its marketed oral dosage.

## II. Materials and Methods:

**Material:** Topiramate and hydroxyl propylmethyl cellulose (k15) were purchased as samples from Yarrow Chem.**,** Mumbai and microcrystalline cellulose, saccharin sodium, citric acid were purchased from Loba chemie, Mumbai. Polyethylene glycol 6000, Tween -80 were purchased from SD fine chemical limited, Mumbai, coloring (quinoline yellow) & flavoring agent (Red rose) were purchased from A S Attarwala & sons, Mumbai.

**Instrumentation:** Venire caliper, In–vitro dissolution apparatus, pH meter, UV-1800 shimadzu with UV probe software system were utilized for qualitative determination of Topiramate.

**Pre –formulation studies:**

**Drug-excipients compatibility study:**

FTIR is an effective method for examining the interaction between drugs and excipients. Surfactant, co-surfactant, and oil were added to the pure medication individually then KBr pellets are prepared and the resulting mixture was scannedin the 400–4000 cm-1 range. To reduce the possibility of significant functional groups in the drug interacting with the excipients, the comparison was conducted using the FTIR spectrum of the pure drug. (Fig N0. 4,5)

**Drug solubility analysis**

A solubility analysis was carried out in order to create a new analytical method. Topiramate powder was added to this drug in excess to the solvents water, acetone and the mixture was then vortexed. The samples were left at room temperature for 30 minutes to achieve equilibrium. The undissolved drug was subsequently removed from the equilibrated samples using sonication for 30 minutes. Whatman filter paper was used to filter the mixture so that the drug's solubility could be seen. The formulation of the mouth dissolving film depends on the drug's solubility in surfactant, and co-surfactant that the drug shows maximum solubility in is necessary before beginning formulation in order for the drug to be in the desired solubility range, which is crucial for the formulation of a mouth dissolving drug delivery system drug delivery system. The same approach was used to test the solubility of Topiramate in surfactants, and co-surfactants.

**Table no. 1 composition formula**

| Composition | F1 | F2 | F3 | F4 |
|---|---|---|---|---|
| Topiramate(drug) | 25mg | 25mg | 25mg | 25mg |
| HPMC-15 | 30mg | 20mg | 20mg | 10mg |
| Microcrystalline Cellulose | 50mg | 40mg | 20mg | 30mg |
| PEG6000 | 0.1mg | 0.1mg | 0.1mg | 0.1mg |
| Saccharin | 60mg | 60mg | 60mg | 60mg |
| Tween80 | 0.1ml | 0.1ml | 0.1ml | 0.1ml |
| Coloringagent | q.s | q.s | q.s | q.s |
| Flavoringagent | q.s | q.s | q.s | q.s |
| Water | q.s | q.s | q.s2 | q.s |

**Method**

**Formulation method of fast dissolving film:** A principal of formulation of fast dissolving film was optimised from various composition formulas (Table 1). A homogenous aqueous solution of HPC and HPMC was created by dissolving the materials in 50 ml of hot water($80^0$C) while stirring continuously to avoid lumps formation, and the solution was then stored to facilitate the swelling of the polymer for overnight In 10ml of distilled water, polyethylene glycol, tween 80, citric acid, aspartame, and flavors were dissolved, as per the composition formula(F1-F4) Separately, the medication was dissolved in distilled water. In order to get rid of the air bubbles, both of these solutions were combined in a polymer solution while being constantly stirred. The produced solution was then placed in Petri plates and allowed

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1952-1959 www.ijprajournal.com ISSN: 2456-4494

to air dry for 24 hours. The film was taken off from the plate and sliced to a size of 2cm by 2cm.

**Evaluation parameter of mouth dissolving film**

**Interpretation of IR Spectra of Baclofen and other excipients:**

**Solubility:** Topiramate shows great solubility with water thus water is used as solvent in development of formulation.

**Evaluation of composition formula :**HPMC is odorless ,transparent ,stable, oil-resistant ,nontoxic and edible material with good film forming properties .It is a nonionic polymer with a linear structure of glucose molecules ,in which its matrix is stabilized using hydrogen bonds which provide great stability when combined with microcrystalline cellulose, PEG 6000 is very soluble in water which provides excellent solublity thus compatible with water soluble drug like topiramate

**Appearance of the film:** Film appearances were rated using visual cues like translucent, semi-transparent, and fuzzy.[4]

**Weight variation:** One square inch film was cut at five different places in the caste film. The weight of each films trip was taken and the weight variation was calculated.[4]

**Folding endurance:** This test was performed by cutting the mouth dissolving film ofsize3×2cm2.The films were folded at same place until it breaks apart.[5]

**Thickness:** Film thicknesses were measured by using the Vernier Caliper and them an thickness was calculated.[6]

**Surface pH:** To check for any potential adverse effects in vivo, the pH of the film's surface was measured. Keep the pH of the film as close to neutral as you can because an acidic or alkaline pH may irritate the oral mucosa. For this, a pH meter was used to measure the pH after the film had been dissolved in 10 ml of distilled water. The process was carried out three times, and the standard deviation was recorded.[2]

**Drug content:** Films were dissolved in 100ml of pH 6.8 phosphate buffer solution, shaken until the film was fully dissolved, and then the solution was filtered. In order to test absorbance at238 nm using the placebo film as a blank solution, 1ml of theaforesaidsolutionwasdilutedto10ml usingthesamesolvent.Thepercentdrugconcentration wasthencomputed.[2]

**In-vitro dissolution studies:** Using 400ml of 6.8pH phosphate bufferas the dissolution media, a dissolution investigation was conducted in a USP basket-type apparatus at 100 rpm and $37.5^0$ C temperature. At 30-second intervals up to 6 minutes, 4ml aliquots were removed, and the same volume of new solution was then added. The aliquots were diluted with the same solvent up to 10 ml, and the absorbance at 238 nm was measured to compute the percent drug release.[2]

## III. Result and discussion:

**Formulation Preparation Result:** Different composition formula was prepared for the formulation of the mouth dissolving film contains topiramate as active pharmaceutical ingredient mentioned in table No.2, four batches was prepared from the above formula from which F1 provide excellent output and their result of evaluation are mentioned below.

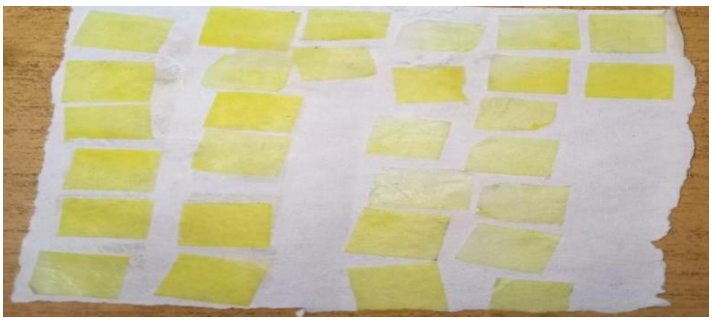

**Fig No. 1: Formulation Preparation**

**Appearance of the film:** This parameter was simply checked with visual inspection of films and evaluation of texture by feel or touch. Prepared oral film showed in figure. (Table N0.2)

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1952-1959 www.ijprajournal.com ISSN: 2456-4494

**Table No. 2: Appearance of Film**

| Formulation | Appearance of the film |
|---|---|
| F1 | Transparent |
| F2 | Transparent |
| F3 | Transparent |
| F4 | Transparent |

**Weight variation:** Onesquare inch film was cut at five different places in the caste film. The weight of each film strip was taken and the weight variation was calculated. (Table N0.3)

**Table No. 3: Reading of Comparative Evaluation of weight Variation**

| S. No. | Formulation code | Mean Weight(mg) |
|---|---|---|
| 1. | F1 | 35.30±0.002 |
| 2. | F2 | 32.10±0.002 |
| 3. | F3 | 36.52±0.003 |
| 4. | F4 | 38.20±0.001 |

**Folding Endurance:** This test was performed by cutting the mouth dissolving filmofsize2×2 cm2. The films were folded at same place until it breaks apart. (Table N0.4)

**Table No. 4: Reading of Comparative Evaluation of Folding Endurance**

| S. No. | Formulation code | Mean Endurance |
|---|---|---|
| 1. | F1 | 93 |
| 2. | F2 | 91 |
| 3. | F3 | 90 |
| 4. | F4 | 90 |

**Thickness:** Film thicknesses were measured by using the Vernier Caliper and the mean thickness was calculated. (Table N0.5)

**Table No. 5: Reading of Comparative Evaluation of Thickness**

| S. No. | Formulation code | Mean Thickness(mm) |
|---|---|---|
| **1.** | F1 | 0.096±0.00 |
| 2. | F2 | 0.076±0.01 |
| 3. | F3 | 0.11±0.01 |
| 4. | F4 | 0.08±0.01 |

**Surface pH**: To check for any potential adverse effects in vivo, the pH of the film's surface was measured. Keep the pH of the film as close to neutral as you can because an acidic or alkaline pH may irritate the oral mucosa. For this, a pH meter was used to measure the pH after the film had been dissolved in 10 ml of distilled water. The process was carried out three times, and the standard deviation was recorded. (Table N0.6)

**Table No. 6: Reading of Comparative Evaluation of Surface pH**

| S. No. | Formulation code | pH |
|---|---|---|
| 1. | F1 | 6.85 |
| 2. | F2 | 6.66 |
| 3. | F3 | 6.77 |

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1952-1959 www.ijprajournal.com ISSN: 2456-4494

| | | |
|---|---|---|
| 4. | F4 | 6.48 |

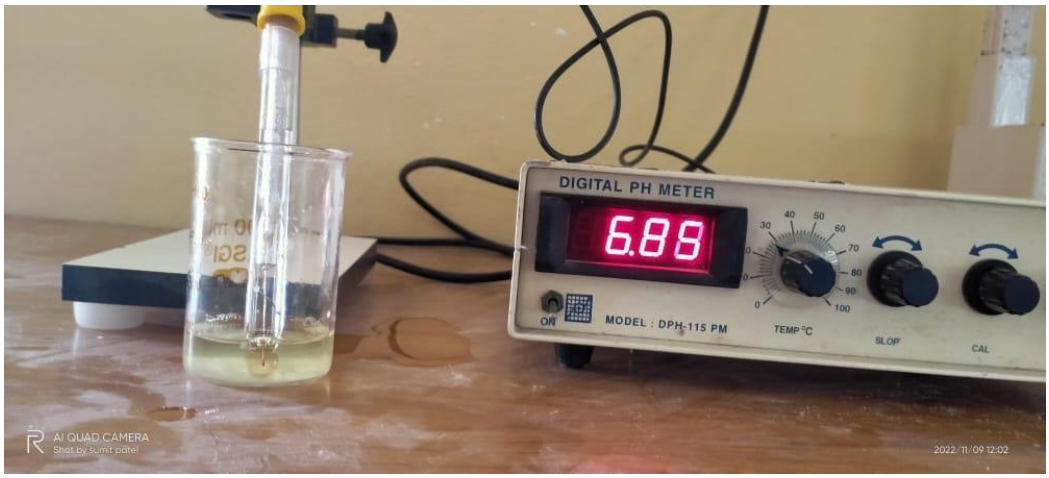


**Fig No. 2: Surface pH**

**Drug content:** Films were dissolved in 100ml of pH 6.8 phosphate buffer solution, shaken until the film was fully dissolved, and then the solution was filtered. In order to test absorbance at 238 nm using the placebo film as a blank solution, 1 ml of the solution was diluted to 10 ml using the same solvent. The percent drug concentration was then computed**.** The absorbance of solution is determined by UV Spectrophotometer (Shimadzu 1800). The absorbance of solution is 0.120, Therefore the drug present in solution is 9.79µg/ml. The % purity of drug present in solution is 97.92%.

**In –vitro dissolution studies:** Using 400ml of 6.8 pH phosphate buffer as the dissolution media, a dissolution investigation was conducted in a USP basket-type apparatus at 100 rpm and 37.5$^0$C temperature. At 30-second intervals up to 6minutes, 2ml aliquots were removed, and the same volume of new solution was added. The aliquots were diluted with the same solvent upto10ml, and the absorbance at 238nm was then measured to compute the percent drug release. (Fig No. 3) (Table No.7)

**Table No. 7: Reading of Comparative Evaluation of In-vitro Dissolution**

| S. No. | Time(sec.) | F1 | F2 | F3 | F4 |
|---|---|---|---|---|---|
| 1. | 0 | 0 | 0 | 0 | 0 |
| 2. | 10 | 11.30 | 8.50 | 9.32 | 7.59 |
| 3. | 20 | 22.10 | 15.79 | 19.54 | 15.68 |
| 4. | 40 | 37.80 | 25.56 | 39.10 | 27.43 |
| 5. | 60 | 73.69 | 62.11 | 67.89 | 60.74 |
| 6. | 80 | 99.85 | 90.66 | 91.20 | 89.63 |

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1952-1959 www.ijprajournal.com ISSN: 2456-4494

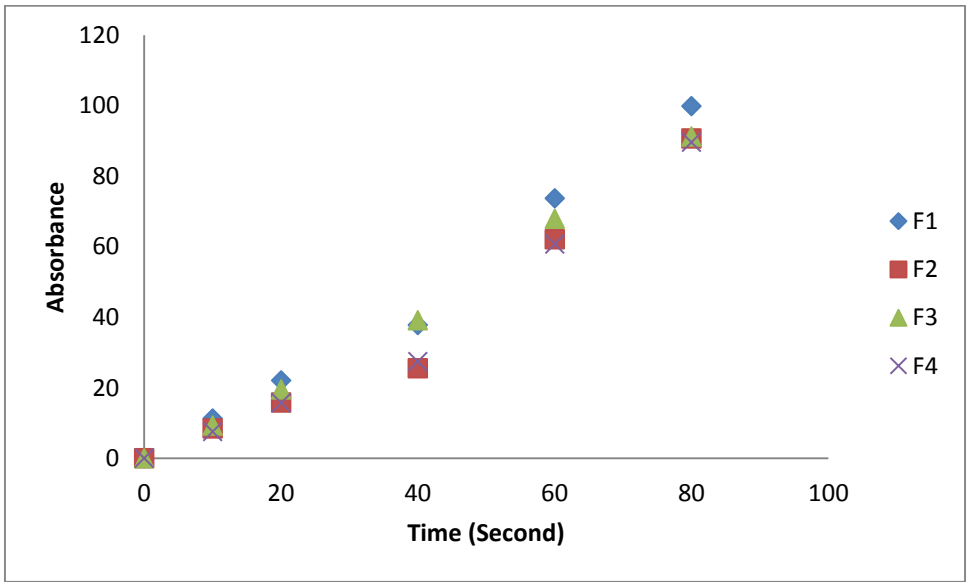


**Fig No. 3: In-Vitro Dissolution**

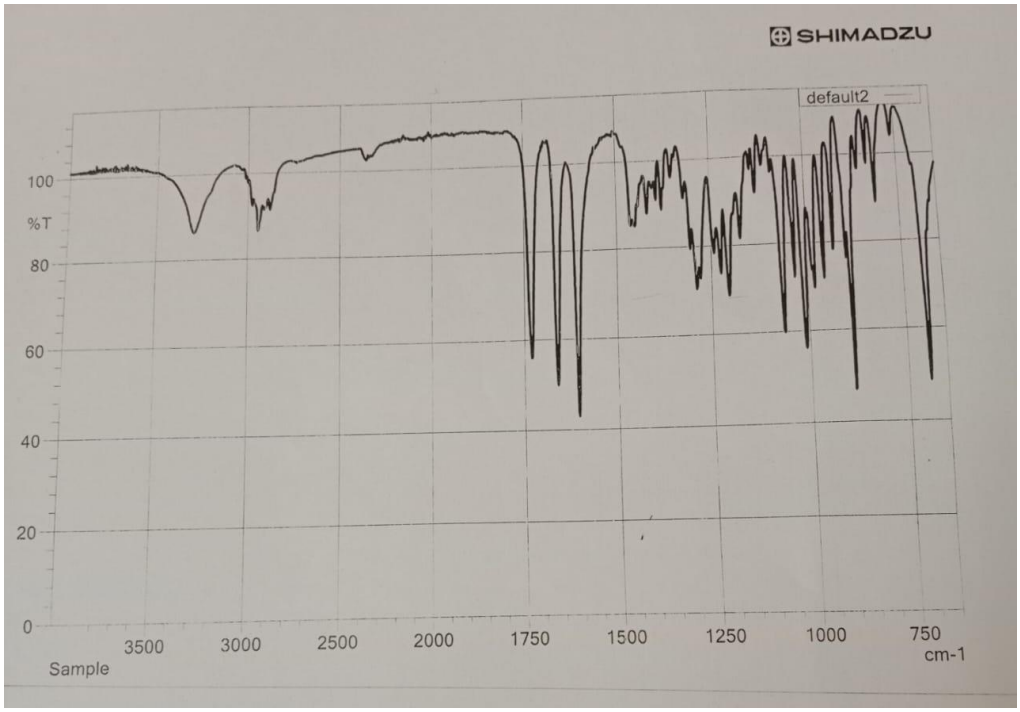


**Fig No. 4: FTIR Spectrum of Topiramate**

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1952-1959 www.ijprajournal.com ISSN: 2456-4494

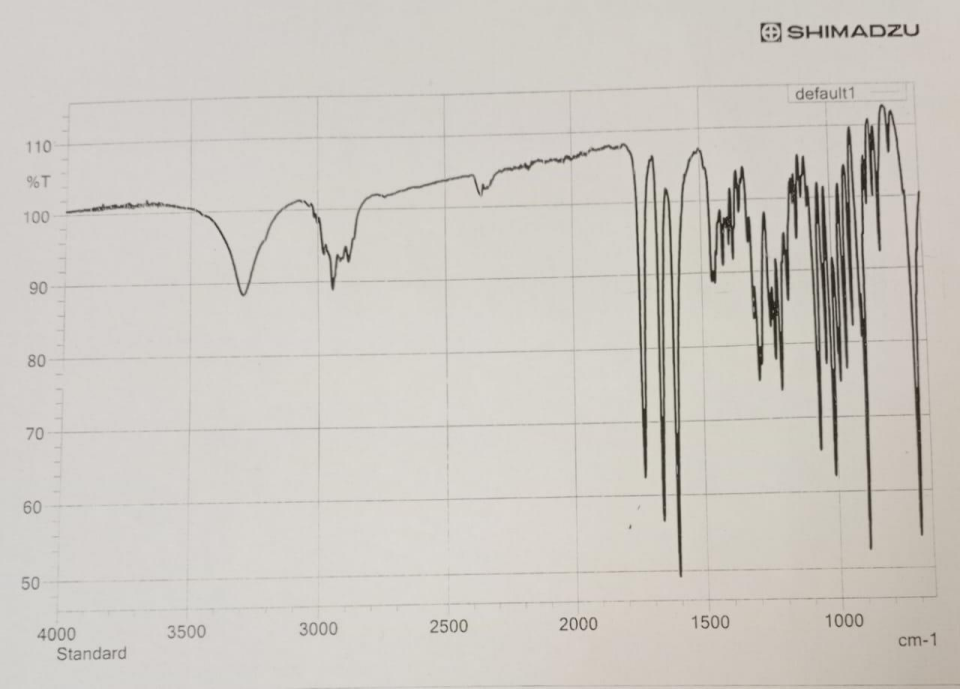


**Fig No. 5: FTIR Spectrum of Topiramate Mouth Dissolving Film**

## IV. CONCLUSION:

In the present work, an attempt had been made to prepare fast dissolving buccal films of Topiramate. Since Topiramate is a poorly soluble drug and the rate of absorption is often controlled by the rate of dissolution. The rate of dissolution can be increased by incorporating the drug in a fast dissolving buccal film.The fast dissolving films of optimized Topiramate were prepared by solvent casting method using HPMC-15,Microcrystalline cellulose and PRG-6000 as a plasticizer. The formulated films were evaluated for their physiochemical parameters like thickness & weight of the films, surface pH, folding endurance, disintegration time, drug content, in vitro release study.

The prepared films were clear, homogenous, devoid of particulate matter, showed good folding endurance and all the films disintegrated with in 60sec. Thickness & weight of the films increases, as the concentration of polymer increases. Content uniformity study showed that the drug is uniformly distributed throughout the film. In vitro dissolution studies were conducted for all film formulations by using USP type I (basket) apparatus in simulated salivary fluid i.e. phosphate buffer of pH 6.8 to check the effect of polymer & plasticizer concentration on the drug release profile and compared with Topiramate film. Among all the formulations F1 was selected as a optimized formulation, due to folding endurance value and showed 96.79 % drug release within 80 sec. which is an essential character for faster absorption. Overall, these findings indicate that fast dissolving buccal films of Topiramate was the most suitable dosage form for clinical use in the treatment of anti-migraine where a quicker onset of action for a dosage form is desirable along with the improved bioavailability and convenience of administration.

## ACKNOWLEDGEMENTS

Without the assistance of Dr. Sujit Pillai, Mr. Sumit Patel, Ms. Esha Gupta and my family, this research would not have been feasible. I'd like to take this initiative to thank GRY Institute of Pharmacy for providing the required equipment and materials to enable me to conduct the research project.

## REFERENCES

[1]. Muggu Sankara Bhavani, B. Divya Kanthi , B. Jyothi , G, “Sailaja and G. Naga Mani. Formulation and evaluation of topiramate fast dissolving oral films”, World Journal of Pharmaceutical Research 2021, Volume 10, Issue 3, Pages:1278-1291.

[2]. M.K. Patidar, F.A. Karjikar, F.A. Patel, S.S. Rathi, S.B. Thokal, C.L. Bhingare. “Formulation and evaluation of mouth dissolving films of Zolpidem tartrate by

exploration of polymers combination," Int J Pharm. 2013;3(4).Pages:716-721.

[3]. Kapoor VP. "Herbal Cosmetics for Skin and Hair care", Natural Product Radiance, 2005;4(4) : 306 -314.

[4]. Parthasa rathi Keshav arao, Dixit Mudit, Gunashekara K, ShahnawazAnis, SinghMangla N and Kulkarni Ajay. Formulation and evaluation of mouth dissolving film containing Rofecoxib, 2011,Pages:273-278.

[5]. Ms. Mital S. Panchal, Mr. Hiren Patel, Mrs. AartiBagada, Dr. K. R. Vadalia, "Formulation and Evaluation of Mouth Dissolving Film of Ropinirole Hydrochloride by Using Pullulan Polymers", 2012,1(3), Pages:60-72.

[6]. Pratik kumar Joshi**,** Harsha Patel**,** Vishnu Patel , "Formulation development and evaluation of mouth dissolving film of domperidone", Journal of pharmacy and bio alliet sciences,2012, 4(5) Page:108-109.

[7]. K. Senthil kumar and C. Vijaya, "Formulation Development of Mouth Dissolving Film of Etoricoxib for Pain Management", Hindawi Publishing Corporation Advances in Pharmaceutics Volume 2015,Pages:1-11.

[8]. Gailany I Ouda, Eman Z Dahmash, Hamad Alyami, AffiongIyire, "A novel technique to improve drug loading capacity of fast/extended release orally dissolving films with potential for paediatric and geriatric drug delivery", AAPS PharmSciTech,2021.volome 21, issue 4, Pages 1-14.

[9]. Daud, A. S., Sapkal, N. P., & Bonde, M. N. "Development of Zingiber officinale in oral dissolving films: Effect of polymers on in vitro, in vivo parameters and clinical efficacy. Asian journal of pharmaceutics (AJP)2014.Volume.5,No.3,Pages183-189.

[10]. Bilal Quazi, Unhaleshrikrushna ,shelkesnehal ,kale purva, "A review on mouth dissolving film, European journal of pharmaceutical and medical research", ejpmr, 2020,7(3),pages 232-238.

[11]. Pawar R, Sharma R, Sharma P, Darwhekar G, "A Review on Mouth Dissolving Film. Journal of drug delivery and pharmaceutics", 2019,9(6),Pages206-210.

[12]. Chougule, P. C, "Design and Evaluation of Formulated Mouth Dissolving Film of Domperid one and Study the Effect of Concentration of Polymers on Drug Release", Asian journal of pharmaceutics ,*11*(04). Pages 846-852.

[13]. Ghodake prasanna p., karande kailas ,Osmani Riyazali, "Mouth Dissolving Films : Innovative Vehicle for Oral Drug Delivery", International Journal of Pharma Research & Review ,2013,2(10),pages 41-47.

[14]. Patil Pallavi, Shrivastava S.K, "Fast Dissolving Oral Films: An Innovative Drug Delivery System", International Journal of Science and Research ,2012,3(7),Pages 2088-2093.

[15]. Lu Xiao, Tao Yi & Ying Liu, "A new self-microemulsifying mouth dissolving film to improve the oral bioavailability of poorly water soluble drugs", Drug Development and Industrial Pharmacy, 2013, 39(9), pages1284-1290. DOI:10.3109/03639045.2012.723716.

[16]. Shank,R.P. and Maryanoff,B.E., "Molecular Pharmacodynamics, Clinical Therapeutics, and Pharmacokinetics of Topiramate", CNS Neuroscience & Therapeutics, 2008, 14(2), pages120-142. doi.10.1111/j.1527-3458.2008.00041.x.

[17]. Arya Arun ,Chandra Amrish ,Sharma vijaya, "Fast dissolving oral film: Aninnovative drug delivery system and dosage form", International journal of cemtech. Research CODEN(USA), 2(1), pages576-583.

[18]. Kaminski RM, Banerjee M., Rogawski M.A, "Topiramate selectively protect against seizure induced by ATPA, aGluR5 kainate receptor agonist.Neuropharmacology, 2010, 46, page1097-1104.

[19]. Sarro Giovam battista, Gratteri Santo, Bonacci Fedrico, "Topiramate potentiate the antiseizure activity of some anti-convulsantin DBA/2 MICE", European journal of pharmacology 2000, 388(2), pages163-170.

[20]. Perucca Emilio, "Pharmacological and clinical review on Topiramate, a new antiepileptic drug", Pharmacological research 1997,volume 35, issue 4, pages 241-256.

[21]. Prabhu P, Malli R, Koland M, Vijaynarayana K, D'Souza U, Harish N, Shastry C,Charyulu R, "Formulation and evaluation of fast dissolving films of levocitirizine dihydrochloride", Int J Pharm Investig. 2011,1(2),pages 99-104. doi:10.4103/2230-973X.82417.