Journal of Drug Discovery and Health Sciences

journal home page : https://jddhs.com/index.php/jddhs/index

Research Article

Effect of Variation in Concentration of Film Forming Polymer and Superdisintegrating Agent on Release Profile of Mouth Dissolving Film of Telmisartan

Diwas Adhikari[1*], Sharada Pokhrel[1], Meenakshi Kandwal[2], Shivanand Patil[2]

[1]Madho Singh Bhandari Uttarakhand Technical University, Dehradun, India.*
[2]Shree Dev Bhoomi Institute of Education, Science and Technology (Affiliated with Veer Madho Singh Bhandari Uttarakhand Technical University), Dehradun, India.

ARTICLE INFO

Article history:
Received: 02 January, 2025
Revised: 10 February, 2025
Accepted: 02 March, 2025
Published: 25 March, 2025

Keywords:
Film forming polymer, Plasticizers, Superdisintegrants, Mouth dissolving film

DOI:
10.21590/jddhs.02.01.01

ABSTRACT

Mouth dissolving films offer the extensive range of benefits and among them patient compliance and easiness for taking the drug without water are the superior one. For the formation of the mouth dissolving films different material can be used such as film forming polymer, superdisintegrants, saliva stimulating agents, surfactants or wetting agents, buffering agents, plasticizers etc. Combination of these agents at suitable concentration helps in the formation of mouth dissolving film of required quality. Disintegration time and In-vitro dissolution rate are the key factors for determining the effect of the concentration of polymer and Superdisintegrating agents on release profile of mouth dissolving film of telmisartan. Role of the superdisintegrants is considered crucial. Higher concentration of superdisintegrant contributes for the better release profile whereas the lower concentration of superdisintegrant hinders the release pattern of drug from the mouth dissolving film. Similarly, higher amount/concentration of polymer hinders the release pattern. Role of plasticizer also arise simultaneously in the film as lower amount of the plasticizer enhance the release pattern of the drug as the higher concentration leads to the gel formation thus affecting the drug release. Thus optimum formulation containing high concentration of super disintegrating agent and minimum concentration of the polymers for film formation shows the better outcome. Conclusively, it can be recommended that comparatively lower concentration/amount of film forming polymer can be used for the routine formation of matrix due to which thickness of the film will also be controlled and thus % drug release rate will be higher. Moreover the higher concentration of the superdisintegrant, Kyron –T is effective for formulation of mouth dissolving film of telmisartan.

INTRODUCTION

Background

Study of anatomy is the pre-requisite of mouth/buccal dissolving film. It is lined with the special cells called mucosal cells which allow the molecules to enter into systemic circulation and bypass the "first pass metabolism". Lubricating mucus gets spread over its it's epithelium due to which it is slippery in nature and provides sufficient fluid for wetting (Gupta *et al.*, 2019). Mouth dissolving films are recent advancement mainly targeting the pediatric, geriatric and patients with dysphagia. Dysphagia is seen to affect 35% of general populations.(Patil *et al.*, 2014) They have difficulty in swallowing and thus feel uncomfortable for taking the drugs though the oral routes in the forms of tablets and

***Corresponding Author:** Diwas Adhikari

Address: Madho Singh Bhandari Uttarakhand Technical University, Dehradun, India.

Email ✉**:** adhikaridiwas51@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

capsule(Adhikari *et al.*, 2024). Mouth dissolving films when placed on the tongue easily get hydrates with the saliva in the mouth thus promoting rapid disintegration or dissolution thus releasing the therapeutic molecules, in other words known as active pharmaceuticals ingredients thus allowing the faster relief to the patients (Patil *et al.*, 2014).

Due to convenience in application, oral routes are considered as the best among others since they enhance the higher patient compliance, promotes adaptability along with acceptability and non-invasiveness (Pawar *et al.*, 2019).

In case of mouth ulcers, toothache, oral ulcers, cold sores and if there is the requirement of the local anesthetic, they play a significant role (Neeta *et al.*, 2012).

First pass metabolism is bypassed through these dosage forms thus leading to the higher availability of the active congener in the systemic circulation. Fear of chocking of the drugs in the neck is prevalent among the patient which is solved through the development mouth Dissolving Films (Panchal *et al.*, 2012).

Super disintegrating agent-Kyron T

Polacrillin potassium (Kyron-T)

It is the resin which exchanges ions. It is acidic (weak) in nature. Its molecular formula is $C_4H_{11}NO_3$ and has structure as in figure 1. It is used in manufacturing due to the various reasons like enhancing the disintegration of solid formulation. It helps in increasing the bioavailability of the formulation. Solubility of the poorly soluble drugs also gets enhanced using Kyron-T. It has been established as the novel superdisintegrant(Gandhi *et al.*, 2011).

Film forming polymer-HPMC E5

HPMC

It is most commonly used excipient and being used traditionally for a long time. It is a basis of matrix formation and its grade, concentration; amount determines the quality of the matrix that is required for the formulation. Its molecular formula is $C_{56}H_{108}O_{30}$ and has molecular structure as in figure 2. It has excellent mucoadhesive properties and due to this property, it is extensively used in the mucosal drug delivery system. It forms the matrix along with the other excipients and provides the best release pattern. Various viscosity grades of Hydroxypropyl methyl cellulose are available in the market and these provide the variability in the physical and chemical properties .HPMC is mostly used in the formulation of tablets and films. It has a great role in the pharmaceutical development and is the future of modern pharmaceutics. HPMC has great printability and spin ability features due to which they are extensively applicable in the 3D printed Drug Products.

Being a water soluble electro neutral cellulose derivative, they are not broken or cleaved by enzymes. FDA and EMA have considered HPMC as safe excipient. Commercially they are available under different trade names such as methocel, metolose etc. Enhancement of solubility of poorly soluble drug is a greatly desirable property of the HPMC.

Due to its ability to get easily wetted and form the gel, it is being used widely in the controlled drug delivery system. Moreover in combination with different superdisintegrant, HPMC is being used in the Orodispersible film formation. For the formation of Orodispersible film, low grade and low concentration of HPMC are used. Higher grades and higher concentration hinders the dispersion of the matrix within the oral cavity (Panraksa *et al.*, 2020).

Drug profile of Telmisartan

Telmisartan is non-peptide in nature and it works on the "Angiotensin Receptor". Its molecular formula is C33H30N4O2 and has molecular structure as in figure 3. Telmisartan inhibits the activity of Angiotensin-II on the muscle which is vascular and smooth in nature. Comparatively lesser solubility is observed in the water which has become the major problem associated with it for the formulation of different dosage form. Bioavailability study also shows that telmisartan does not have good bioavailability i.e. Not more than 45 percentage (Rajeswari *et al.*, 2017).

Telmisartan is also used in other cardio vascular disorders like cardiac arrhythmias and pectoris angina. Telmisartan is the drugs of choice for many cardiovascular patients because of its safe therapeutic effects (Shewale *et al.*, 2008).

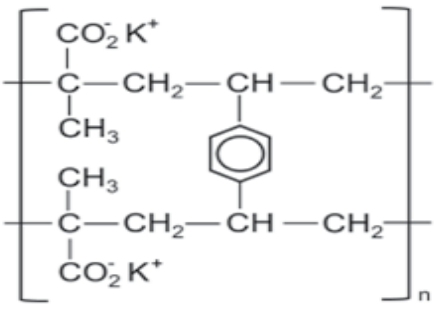

Figure 1: Chemical structure of Polacrillin Potassium

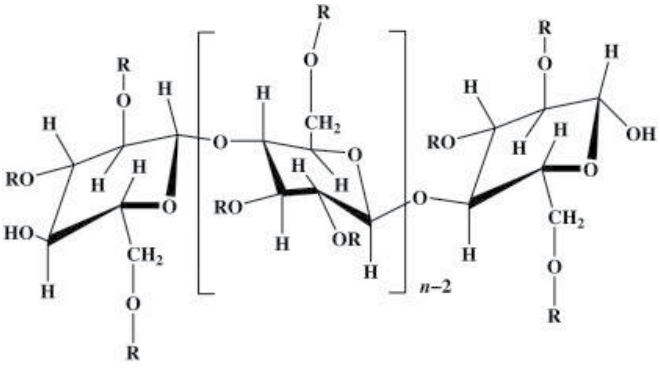

Figure 2: Chemical structure of Hydroxypropyl methyl cellulose

Table 1: Formulation of mouth dissolving film

S.N	*Components*	*TF1*	*TF2*	*TF3*	*TF4*	*TF5*	*TF6*	*TF7*	*TF8*	*TF9*
1	Telmisartan +Betacyclodextrin Complex (mg)	1330.4	1330.4	1330.4	1330.4	1330.4	1330.4	1330.4	1330.4	1330.4
2	HPMC E5	2000	2000	2000	1600	1600	1600	1200	1200	1200
3	Povidone-K 30(ml)	0.5	1.75	3	0.5	1.75	3	0.5	1.75	3
4	Trisodium Citrate(ml)	10	10	10	10	10	10	10	10	10
5	Polacrillin Potassium (Kyron-T)	2%	5%	8%	2%	5%	8%	2%	5%	8%
6	Tween 80 (ml)	5	5	5	5	5	5		5	5
7	Aspartame(mg)	75	75	75	75	75	75	75	75	75
8	Distilled Water (ml)	50	50	50	50	50	50	50	50	50

Note: Concentration of Kyron T is expressed in percentage of concentration of HPMC E5.

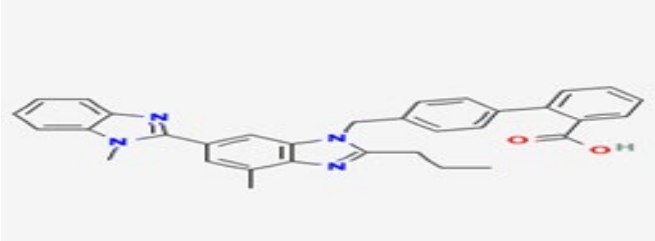

Figure 3: Structure of Telmisartan

Table 2: Disintegration time of different formulation

S.N.	*Formulation*	*Disintegration time (Sec)±SD*
1.	TF1	51.67±0.82
2.	TF2	42.17±0.75
3.	TF3	26.33±0.82
4.	TF4	53.33±1.03
5.	TF5	41.50±1.05
6.	TF6	27.50±1.05
7.	TF7	54.00±0.63
8.	TF8	42.33±0.82
9.	TF9	28.67±0.52

Description: White crystalline powder
Molecular weight: 514.6
Melting point of 261-263°C
Lipophilicity: Highly lipophilic
Partition coefficient: Log p=3.2

Rationale of choosing film forming polymer

HPMC E5 was chosen as film forming polymers as it is seen that in many research intermediate viscosity grades of HMPC has been proven effective during the formulation in compared to higher viscosity grade of HPMC.

Rationale of choosing super disintegrants

Enhancement of solubility of telmisartan in the mouth dissolving film is required for higher bioavailability. Since Kyron-T has been established as the novel superdisintegrants, it plays the synergistic role for the rapid disintegration and higher solubility of the drug in mouth dissolving film, thus bioavailability is enhanced.

Formulation Method

Development of drug-inclusion complex

It was prepared by kneading method. Telmisartan was mixed with Beta-cyclodextrin at ratio of 1:1 and was

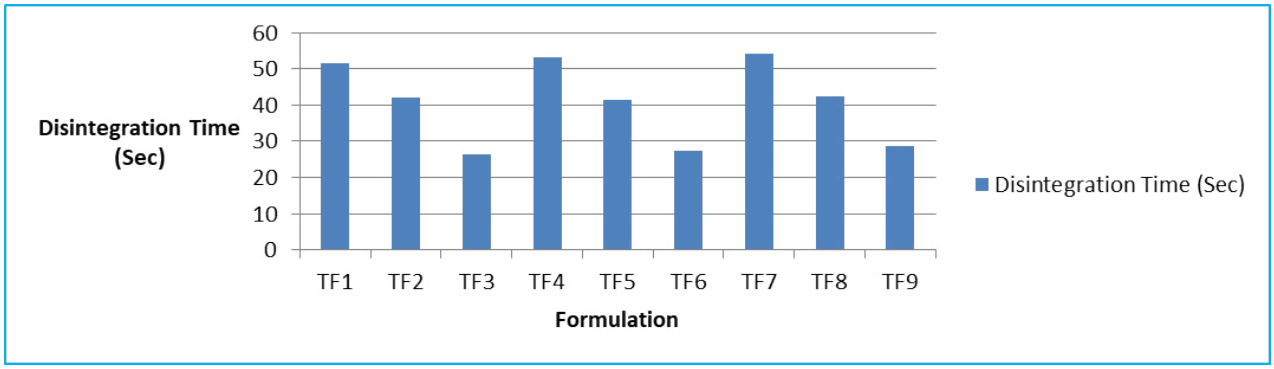

Figure 4: Bar graph for disintegration time

Inferences: Maximum disintegration time is seen in the formulation number TF7 i.e. 54 seconds. Similarly formulation number TF4 and TF1 have also disintegration time in maximum range i.e. 53.33 and 51.67 seconds respectively. Formulation number TF3, TF6 and TF9 have the disintegration time in the lower range i.e. 26.33, 27.5 and 28.67 Seconds respectively.

Table 3: % Drug release of different formulation at different time interval

S.N	Formulation number	3 Minutes	6 Minutes	9 Minute	12 Minutes	15 Minutes
1.	TF1	14.69	32.00	51.49	74.41	87.49
2.	TF2	17.08	38.15	55.56	76.89	92.49
3.	TF3	15.99	33.40	54.29	75.42	89.55
4.	TF4	18.16	39.42	57.09	76.73	94.37
5.	TF5	20.41	41.59	59.68	80.52	98.01
6.	TF6	19.66	40.76	58.81	78.64	95.65
7.	TF7	21.81	43.93	63.03	81.07	99.62
8.	TF8	22.64	44.26	65.85	83.25	100.78
9.	TF9	21.64	44.45	66.64	83.44	100.22

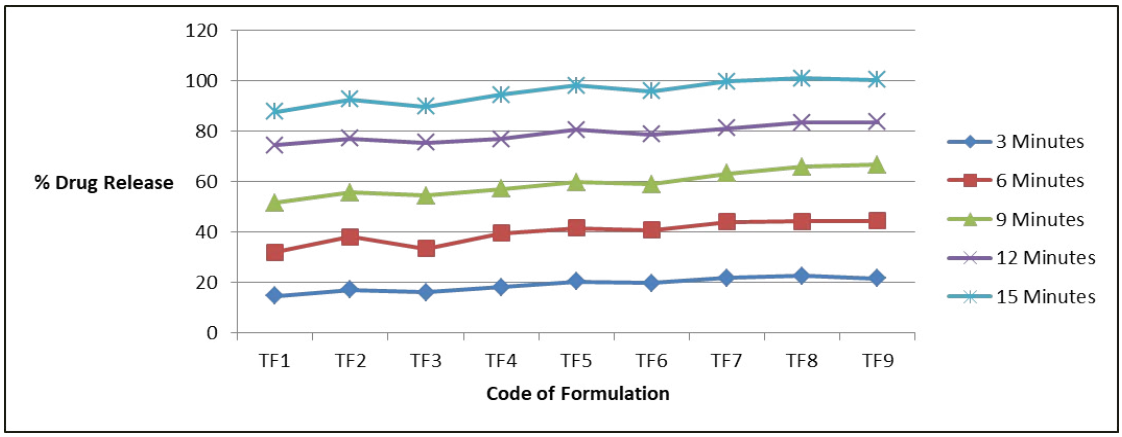

Figure 5: Drug release at different time interval

Inferences: % Drug release is seen in the increasing trend at different time interval in each formulation from TF1 to TF9.

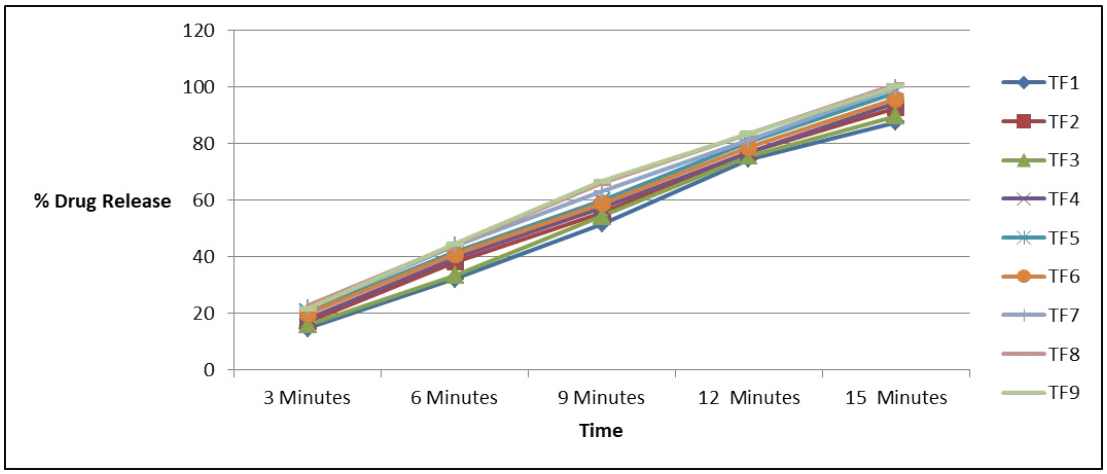

Figure 6: Graph showing percentage drug release of different formulation at different time

Inferences: % Drug release is following the linear trend from 3rd minute to 15th minute. It shows that linear fashion is followed for drug release.

wetted by adding distilled water in it. The wet mass was kneaded thoroughly and paste was obtained with high consistency. Sample was subjected for drying at normal temperature of room and final dried product was passed through the #80 mesh size. Prepared Inclusion complex was then stored at desiccator for further use.

Formulation of film of telmisartan using "Solvent Casting Method"(Raza et al., 2019)

Different trials were taken and different formulations were designed altering the concentration of HPMC E5 along with Superdisintegrating agent Kyron-T as in Table 1. Formulation Film forming polymer (HMPC E5) was

dispersed in distilled water and the inclusion complex of telmisartan was added in it with continuous stirring. Superdisintegrating agents (Kyron-T) was added in the above polymeric solution and stirring will be done vigorously. Tribasic sodium citrate, Tween 80, Povidone-K 30 and Aspartame was added with continuous stirring. Solution was subjected for sonication for 10 min in the sonicator. Viscous solution was obtained and it was poured into the petridish and it was placed in oven in 40°c for twenty four hours. The prepared films were into2*2 cm^2 area and evaluated.

Evaluation of effects on disintegration time and release pattern of the drug

Disintegration time

Prepared mouth dissolving films were kept at the disintegrating test apparatus when the apparatus gain the temperature of 37±2ºC. Time at which the film completely gets disintegrated was noted and represented graphically (See table 2 and figure 4).

Drug release profile

Prepared mouth dissolving films were kept at the dissolution test apparatus when the apparatus gain the temperature of 37±0.5ºC. % drug release at different time interval was noted and represented graphically (See table 3 and figure 5, 6).

From the result obtained from the data of formulation vs. disintegration time and formulation Vs. drug release pattern, it is seen that formulation containing the higher concentration of Superdisintegrating agent and lower concentration of film forming polymer shows better result.

Table 4: Optimized formulation

S.N	*Components*	*Amount*
1	Telmisartan-Betacyclodextrin Complex	1330.4 mg
2	HPMC E5	1200 mg
3	Povidone-K 30	1.75
4	Trisodium Citrate	10 ml
5	Polacrillin Potassium (Kyron-T)	8 % (96 mg)
6	Aspartame	75 mg
7	Tween 80	ml
8	Distilled Water	ml

Table 5: Evaluation of optimized formulation

S.N	*Evaluation parameters*	*observation*
1	General appearance	Transparent
2	Taste	Acceptable
3	Thickness	0.2
4	Folding endurance	140
5	Surface pH	8.2
6	In-vitro disintegration time	28 Sec
7	Assay (%)	100.71

Table 6: Drug release (%)

S.N	*Formulation*	*3 Min*	*6 Min*	*9 Min*	*12 Min*	*15 Min*
1	Optimized Formulation	23.24	47.81	65.97	83.82	100.53

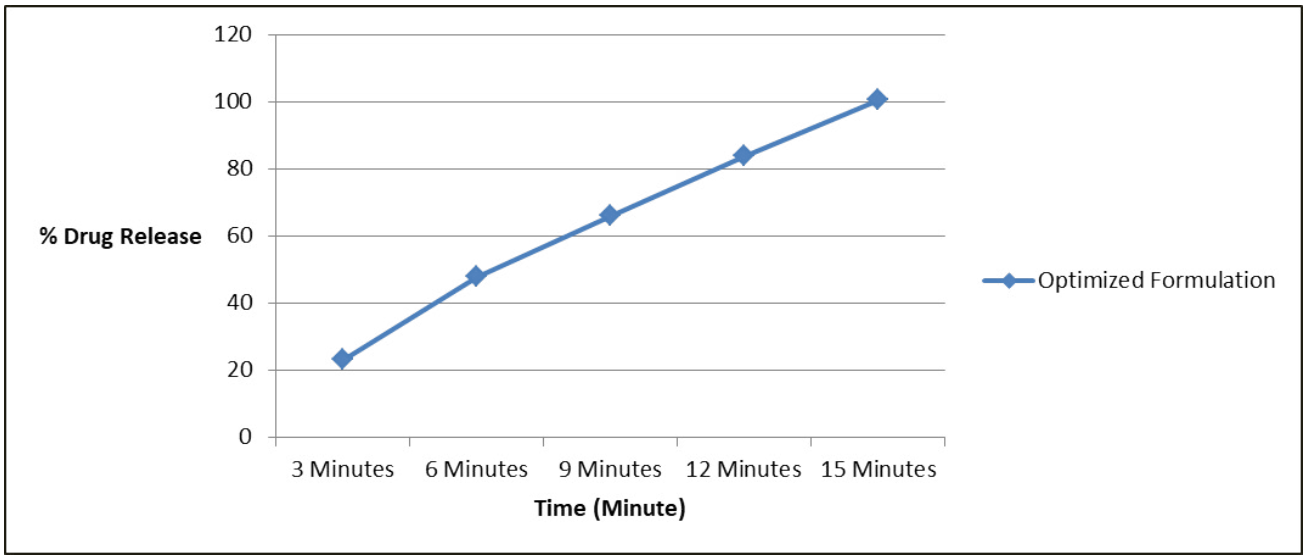

Figure 7: Scatter plot showing percentage drug release

Inferences: Optimized value of the different parameters is obtained for the optimized formulation. In-vitro DT was 28 second. % drug release also follows the best linear fashion in different time interval.

For the confirmation, Optimized formulation was designed taking the lower concentration of film forming polymer and higher concentration of super disintegrating agent.

Formulation Optimization

It was designed with lower concentration of the HPMC E5, higher concentration of Superdisintegrating agents, Kyron-T as in table 4. Optimized formulation was also prepared in similar way as other formulation using the solvent casting technique. Prepared optimized formulation was evaluated for different parameters as in other formulation and results were noted (see table 5, 6 and figure 7).

Discussion

Disintegration time and In-vitro dissolution rate are the key factors for determining the effect of the concentration of polymer and Superdisintegrating agents on release profile of mouth dissolving film of telmisartan. Formulations using the different concentration of film forming polymer i.e. HPMC E5 and Superdisintegrants i.e. Kyron T shows the different results and based on which optimization is possible. Development of the optimized formulation assists for the confirmation of the results to draw the conclusion from the study. All the formulation including optimized formulation follows the linear kinetics in the release pattern with the variation in the released rate, which can be seen from the respective graphical representation.

Conclusion

Polymer concentration effect

Concentration of intended polymer plays important role in the film formation and its quality. Thickness determination and drug release pattern determination helps in the finding of best concentration of polymer (film forming) for better result. From the study, we can have conclusion that, with increased concentration of the film forming polymers retards the release rate of the concerned drug. It is because, as the concentration of polymer goes on increasing, orally disintegrating film with higher thickness is formed and as the film hydrates in the mouth, it forms the thick gel inside the mouth than the ODF having lower concentration of the film. Thus the drug release rate is degraded upon increasing the concentration of film forming polymer.

Effect of Superdisintegrating agent

Concentration of super disintegrating agents plays important role for increasing the rate of disintegration of the film. From the study it has been observed that higher concentration of super disintegrating agent i.e. Kyron-T lowers the disintegrating time compared with the ODF having the lower concentration of super disintegrating agent, thus enhancing the release rate of drug.

Recommendation

Comparatively lower concentration/amount of film forming polymer shall be used for the formation of matrix due to which thickness of the film will also be controlled and thus % drug release rate.
Higher concentration of the superdisintegrant, Kyron –T is effective for mouth dissolving film of telmisartan.

Authors Contribution

Diwas Adhikari and Sharada Pokhrel have contributed for research and gathering results, Meenakshi Kandwal and Dr. Shivanand Patil supported through supervision.

Source of Funding

Self-funding for the research

Conflict of Interest

None

References

1. Adhikari, D., Pokhrel, S., Kandwal, M., Kori, A., & Patil, S. (2024). Study on Synergistic Effect of Dioctyl Sodium Sulfosuccinate, Sodium Starch Glycolate and Crospovidone on Drug Release Profile of Orodispersible Tablets of Rizatriptan Benzoate. *Journal of Drug Discovery and Health Sciences, 1*(04), 244-248.
2. Gandhi, B., Mundada, A., & Gandhi, K. (2011). Evaluation of KYRON T-314 (polacrillin potassium) as a novel super disintegrant. *International Journal of Drug Delivery, 3*(1).
3. Gupta, P., Bisht, A., & Rao, N. G. R. (2019). Fast Dissolving Oral Films:A Comprehensive Review. *World Journal of Pharmaceutical and Medical Research, 5*(7), 116-127.
4. Neeta, Dureja, H., Bhagwan, S., Seema, & Dahiya, J. (2012). Fast Dissolving Tablets: An Overview. *Novel Science International Journal of Pharmaceutical Science, 1*(5), 228-232.
5. Panchal, M. S., Patel, H., Bagada, A., & Vadalia, K. R. (2012). Formulation and Evaluation of Mouth Dissolving Film of Ropinirole Hydrochloride by Using Pullulan Polymers. *International Journal of Pharmaceutical Research & Allied Science, 1*(3), 60-72.
6. Panraksa, P., Udomsom, S., Rachtanapun, P., Chittasupho, C., Ruksiriwanich, W., & Jantrawut, P. (2020). Hydroxypropyl Methylcellulose E15: A hydrophilic polymer for fabrication of orodispersible film using syringe extrusion 3D printer. *Polymers, 12*(11), 2666.
7. Patil, P. C., Shrivastava, S. K., Vaidehi, S., & Ashwini, P. (2014). Oral Fast Dissolving Drug Delivery System:A Modern Approach for Patient Compliance. *International Journal of Drug Regulatory Affairs, 2*(2), 49-60.
8. Pawar, R., Sharma, R., Sharma, P., & Darwhekar, G. N. (2019). A Review on Mouth Dissolving Film. *Journal of Drug Delivery and Therapeutics, 9*(6), 206-210.
9. Rajeswari, D., Babu, B. N., Desu, P. K., Rao, P. V., & Anitha, B. (2017). Formulation and Evaluation of Fast Dissolving Film of Telmisartan. *World Journal of Pharmacy and Pharmaceutical Sciences, 6*(11), 1038-1047.
10. Raza, S. N., Kar, A. H., Wani, T. U., & Khan, N. A. (2019). Formulation and Evaluation of Mouth Dissolving Film of Losartan Potassium Using 3^2 Factorial Design. *International Journal of Pharmaceutical Sciences and Research, 10*(3), 1402-1411.
11. Shewale, B., Patil, P., Deshmukh, P., & Fursule, R. (2008). Effect of Hydroxypropylated-β-Cyclodextrin and pH on Solubility of Telmisartan. *International Journal of Chemical Sciences, 6*(3), 1449-1454.

HOW TO CITE THIS ARTICLE: Adhikari, D., Pokhrel, S., Kandwal, M., Patil, S. Effect of Variation in Concentration of Film Forming Polymer and Superdisintegrating Agent on Release Profile of Mouth Dissolving Film of Telmisartan. J. of Drug Disc. and Health Sci. 2025;2(1):1-6. **DOI:** 10.21590/jddhs.02.01.01