Original Article

Formulation and Evaluation of Oral Trans-mucosal Delivery System of Eletriptan Hydrobromide

Manan Patel[1,*], Radhika Pandya[2]

[1]Department of Pharmaceutics, SAL Institute of Pharmacy, Ahmedabad, Gujarat, INDIA.
[2]Department of Pharmaceutics and Pharmaceutical Technology, L. M. College of Pharmacy, Ahmedabad, Gujarat, INDIA.

ABSTRACT

Background: To formulate, develop and evaluate sublingual tablet of anti-migraine agent (Eletriptan Hydrobromide). **Materials and Methods:** The sublingual tablet was prepared by direct compression method and the tablets were formulated using Kyron T-314, Sodium Bicarbonate, Mannitol, Neusilin US2, Stevia, PVP K-30, Magnesium Stearate and Talc as excipients. The prepared tablets were evaluated for various parameters like hardness, thickness, friability, weight variation, wetting time, *in vitro* disintegration time, *in vitro* dissolution and ex-vivo permeation study. A 3^2 full factorial design was applied to optimize the concentration of Kyron T-314(X1) and Sodium Bicarbonate (X2). Disintegration time (Y1) and % drug release at 15 min (Y2) were taken as dependent variables. **Results:** From the all batches, B9 was found to be the best batch with 3.5% of Kyron T-314 and 40% Sodium Bicarbonate. The optimized batch gave the best disintegration time of 9 sec and % drug release of 92.23% in 15 min. It showed maximum permeation of 93.17% in 30 min which is significant compared to the formulation without alkalizing agent. **Conclusion:** This indicates that the amount of the drug which remains unionised after the addition of the alkalizing agent lead to increase in permeability. Stability testing of the optimised batch was carried out and the results showed no significant change in the results of % drug release.

Key words: Anti-Migraine, Alkalizing agent, Permeation, Sublingual, Eletriptan Hydrobromide.

INTRODUCTION

Migraine is a neurological condition that can cause multiple symptoms. Migraine is characterized by pulsating headache of severe or moderate intensity that last for 3 – 72 hr and increase with normal physical activity. Vomiting, photophobia and nausea are the common symptoms of migraine. There are various causes of migraine such as hormonal changes in women, stress, medication, degraded food, changes in the environment etc. Various drugs are used in the treatment of migraine and amongst them triptan class drugs are widely used.[1-3] In present work, Eletriptan Hydrobromide which belongs to triptan class is selected as drug of choice.[4-6] Oral trans-mucosal delivery have many advantages like, ease of administration, larger contact surface area leading to rapid and extensive drug absorption, greater bioavailability, reduced dose related side effect and most important the drugs which are not stable in the acidic or alkaline environment of the intestine can be taken by this route.[4,7,8] Conventional tablet formulations are available of Eletriptan Hydrobromide in market by companies like Pfizer and Intas Pharmaceuticals. This drug shows extensive first pass metabolism in the liver with 50% bioavailability. This problem is here in the present work by formulating oral trans-mucosal delivery system,[12]Where in a suitable sublingual dosage form is prepared of Eletriptan Hydrobromide to avoid first pass effect and have quick onset of action.

Submission Date: 08-10-2021;
Revision Date: 11-01-2022;
Accepted Date: 04-06-2022.

DOI: 10.5530/ijper.56.3s.149

Correspondence:
Prof. Manan Patel
Assistant Professor,
Department of Pharmaceutics,
SAL Institute of Pharmacy,
Ahmedabad, Gujarat, INDIA.
E-mail: mananpatel1875@gmail.com

www.ijper.org

MATERIALS AND METHODS

Sublingual tablets were compressed by using Eletriptan Hydrobromide as a API, Kyron T-314(Disintegrant), PVP K-30 (Binder), Stevia (Sweetener), Neusilin US 2 and Mannitol (Diluent) and Talc and Magnesium stearate. Eletriptan Hydrobromide was supplied by Cadila Pharmaceuticals Ltd. Neusilin US 2 was provided by Gangwal Chemicals and Kyron T-314 was gifted by Corel Pharma.

Drug-excipient compatibility studies by Fourier transform infrared and differential scanning calorimetry (FTIR &DSC)

Compatibility studies were carried out by FTIR and DSC to find out any interaction between drug and excipients. The FTIR spectroscopy study of pure Eletriptan Hydrobromide was done using Shimadzu 8400S and characterization of the drug and excipients was carried out using DSC study.

METHODS

Direct compression

Direct compression is a simpler and cost-effective method appropriate for powders, which possess good flow properties. Sublingual tablets of Eletriptan Hydrobromide (EH) were prepared by direct compression method. All the materials were passed through a sieve (80 mesh).EH was blended with the excipients (sweetening agent, dry binder, superdisintegrant, alkalizing agent and diluent) except the lubricant and glidant for 10 min. Afterward the lubricant and glidant were added to the blend and mixed for 5 min and then compressed with the help of rotary die press into sublingual tablets.[9]

Selection of excipients

In the selection of excipients, preliminary batches were prepared using different superdisintegrants (crospovidone, croscarmellos sodium, sodium starch glycolate and Kyron T-314), alkalizing agent (Sodium bi carbonate and di-sodium hydrogen phosphate) and sweetener (stevia in different concentration) along with other excipients like Mg stearate, talc and PVP.

Optimization of sublingual tablet of Eletriptan Hydrobromide by using 3^2 Full Factorial design

A pharmaceutical product of desired quality can be obtained by optimizing the different formulation factors affecting it at different levels using experimental design. Therefore, 3^2 full factorial design was employed for optimization of sublingual tablet of Eletriptan hydrochloride. The two selected factors were concentration of superdisintegrants (X_1) and concentration of alkalizing agent (X_2). Each factor was checked at three levels (-1, 0, +1). The dependent variables were disintegration time (Y_1) and % drug release (Y_2) at 15 min. Design Expert 11 software was used to obtain correlation between the independent variables and dependent variables. The composition of batches formulated are shown in Table 1.

Formulation of batches according to 3^2 full factorial design

All the batches were formulated according to 3^2 full factorial design and is shown in Table 2.

Evaluation Parameters

The sublingual tablets were evaluated for the following parameters.

Pre-compression parameters

All the pre-compression parameters like angle of repose, bulk density, tapped density, Carr's index and Hausner ratio were evaluated and compared with standard optimized data for the selection of a formulation method. From the results obtained it was shown that powder mixture has good flow property and compressibility. Therefore, direct compression method was selected as a method of choice for formulation development.[10]

Post Compression parameters

The final tablets were evaluated for the following post compression parameters

Disintegration time (DT)

Disintegration test was carried out as per United State Pharmacopeia.

Wetting time (WT)

Wetting time test is not a standard test in USP but it provides concerned evaluation of sublingual tablet. The

Table 1: Formulation of batches according to 3^2 Full Factorial design.

Independent variables					
X_1			X_2		
Concentration of superdisintegrant (Kyron T-314)(mg)			Concentration of alkalizing agent ($NaHCO_3$)(mg)		
-1	0	+1	-1	0	+1
0.5	2	3.5	0	20	40
Dependent variables					
Y_1			Y_2		
Disintegration time (sec)			% Drug release (in 15 min)		

Table 2: Formulation of batches from B1 to B9.									
Ingredients(mg)	**B1**	**B2**	**B3**	**B4**	**B5**	**B6**	**B7**	**B8**	**B9**
API	20	20	20	20	20	20	20	20	20
Kyron T-314	0.5	2	3.5	0.5	2	3.5	0.5	2	3.5
PVP k30	1	1	1	1	1	1	1	1	1
Sodium bicarbonate	0	0	0	20	20	20	40	40	40
Mannitol	50	49	48	36.5	35.5	34.5	23.5	22.5	21
Neusilin US2	25	24.5	24	18.5	18	17.5	11.5	11	11
Stevia	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mg.stearate	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1
Total weight	100	100	100	100	100	100	100	100	100

time required by moisture to enter the tablet is measured and it presents the time needed to release the drug in presence of small quantity of saliva. The tablet is placed in the middle of two layers of absorbent paper which is fixed into a rectangular plastic dish (11 cm × 7.5 cm). The paper is completely wetted with distilled water and the excess of water is removed from the dish. The time needed by water to diffuse into tablet from the wetted paper is noted using a stopwatch.[11]

Weight variation

20 tablets are selected at randomly, individual weight and the average weight of tablet is noted. None of the tablets must deviated from the average weight by more than ±7.5%.[11]

Hardness Test

The hardness of tablet was measured by Schleuniger hardness tester. The hardness of sublingual tablet is important factor, as it should be optimum neither more hard nor soft.[11]

Friability

Twenty tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted, and reweighed.[11]

Dissolution

USP Dissolution rate Test Apparatus type-II was used to carried out dissolution study. In Dissolution apparatus 500ml of Phosphate buffer pH 6.8, and maintained at 37°C±0.5°C at 50 rpm was used. 5ml aliquots were periodically withdrawn and replaced with same volume of fresh Phosphate buffer pH 6.8. The samples were then analysed at 219 nm by UV spectrophotometry.[11,12]

Taste masking[13,14]

Taste masking was carried out by A.S.E analytics by using artificial sensory system which helps in studying palatability applying chemical sensors and multivariate statistics. In the technique chemical sensors are used which contains chemical sensing membrane electrodes which are sensitive to ions that are found in the structure of drug after they are dissolved in distilled water. Sample preparations: unit dose was dissolved in 100mL of single distilled water. To maintain uniformity placebos were measured in equivalent dosage. For measurements chemical sensors were immersed in the sample beaker and continuous readings were recorded after every 10 sec interval for a total duration of 6 min by multichannel voltmeter in standard laboratory conditions. Data processing was done by taking average of last three readings at the end of 3min, 5min and 6min for multivariate data processing.

The palatability reported is on the basis of the distance in the chemo metrics space between a placebo and the same formulation of API. The formulated products are either close to the placebo or midway between the placebos and API.

Ex-vivo permeation studies

Ex-vivo permeation studies were carried out with modified Franz's diffusion cells.[7,15] Phosphate buffer 6.8 was used for the studies and maintained temperature at 37°C.[8,16] Goat oral mucosal membrane was used as a permeation barrier. Samples were collected at predetermined time intervals (0, 3, 6, 9, 12, 15, 18, 24,30) min.[17,18] All Samples were analyzed for drug content by UV spectrophotometer at 219 nm. All permeation studies were carried out in triplicate.[19,20]

RESULTS AND DISCUSSION

FTIR Study

As depicted from FTIR spectra obtained of pure drug and drug along with various critical excipients in Figure 1 and 2, it was observed that the characteristic

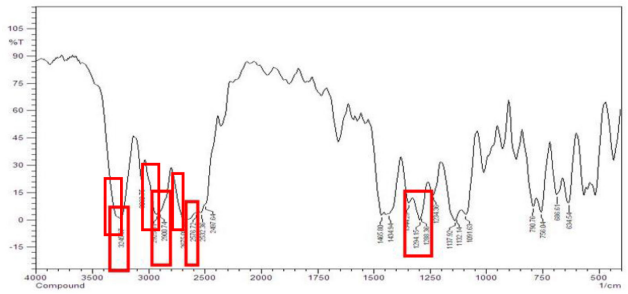


Figure 1: FTIR of Pure Drug.

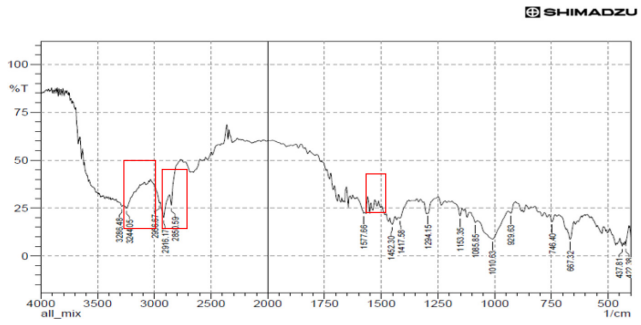


Figure 2: FTIR of Pure Drug with all excipients.

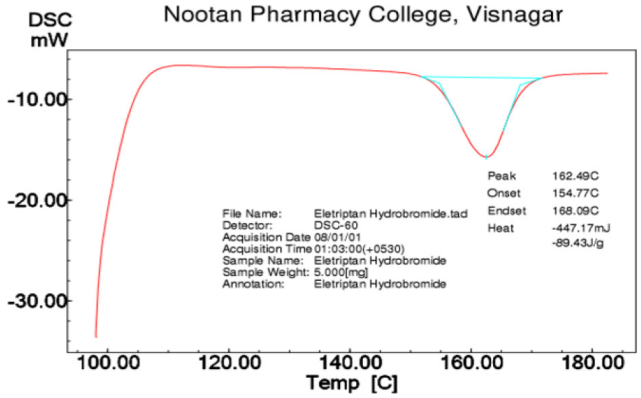


Figure 3: DSC of Pure Eletriptan Hydrobromide.

peaks of the functional group of Eletriptan Hydrobromide did not change in the FTIR obtained for mixture of drug and excipients (Figure 2). So, by this, conclude that there is no incompatibility between drug and various excipients.

DSC study

Overlay of DSC of pure drug and the physical mixture of drug with excipients clearly shows no interaction as the drug peak is unchanged and no shifting is seen. The melting point range of EHas shown in Figure 3 and 4 was found to be in range of 160-165°C which is comparable with the reported range of drug (164°C-169°C).

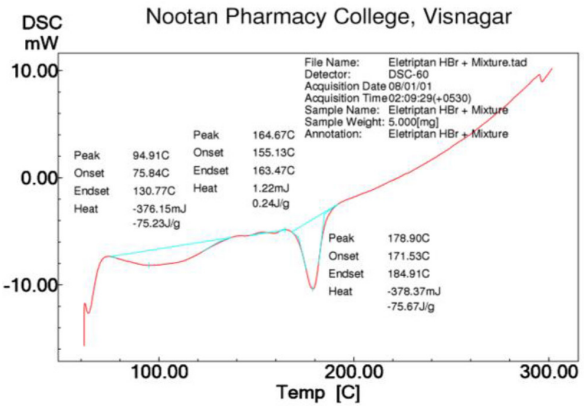


Figure 4: DSC of Pure Drug with all the excipients.

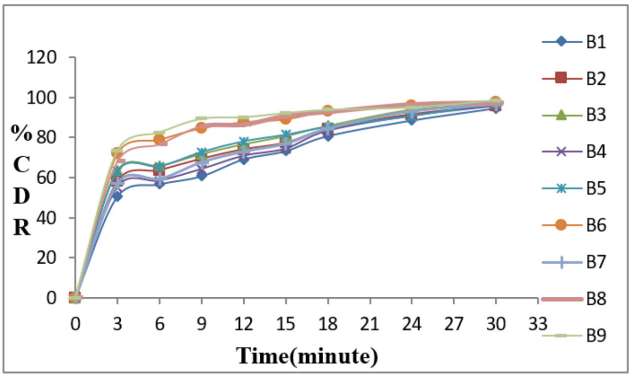


Figure 5: Drug Release of B1 to B9 Batches.

Result of Preliminary studies

Proper disintegration time of tablet was not obtained by using Crospovidone, Croscarmellose sodium and sodium starch glycolate as superdisintegrant so Kyron T-314 was used in further batches and best result was obtained. Moreover, From the result of dilution studies we concluded that combination of mannitol and Neusilin US2 give proper hardness and disintegration. Di-sodium hydrogen phosphate was avoided because of its hygroscopic nature. While, Sodium bicarbonate was selected as alkalizing agent because of its non-hygroscopicity and it gave desired pH range.

Result of Pre and Post compression parameters

All the pre and Post compression parameters are given in Table 3.

In-vitro release study

The prepared tablet were subjected to drug release studies and it can be seen from the Figure 5 that the batch B9 showed the highest drug release at 15 min of 92.23%. It can be concluded from above observation that at 3.5% concentration of Kyron T-314 better disintegration of tablet is achieved. As the concentration of Kyron T-314

Table 3: Pre and Post Compression Characterization.									
Pre compression parameters									
Parameters	**B1**	**B2**	**B3**	**B4**	**B5**	**B6**	**B7**	**B8**	**B9**
Angle of repose	32.53	32.59	32.6	33.1	33.4	33.9	34.4	34.8	35.4
Carr's index	11.09	11.16	12.29	12.61	12.77	12.80	13.10	13.91	14.61
Hausner's ratio	1.12	1.13	1.14	1.14	1.15	1.15	1.15	1.16	1.17
Post compression parameters									
Appearance	**White colored 100mg tablets**								
Weight variation(mg)	99± 1.4	98± 1.3	101± 1.6	100± 1.1	98± 1.0	102± 1.4	100± 1.2	99± 1.3	100± 1.0
Hardness(kg/cm^2)	8.53 ±0.15	8.33± 0.11	8.23± 0.11	6.3± 0.2	6±0.1	5.83± 0.15	5.5± 0.1	5.33± 0.11	5.2± 0.10
Thickness(mm)	2.82± 0.015	2.83± 0.005	2.85± 0.01	2.92± 0.011	2.95± 0.015	2.96± 0.015	3.03± 0.01	3.03± 0.005	3.04± 0.011
Friability(%)	0.33± 0.02	0.352± 0.027	0.368± 0.028	0.409± 0.017	0.429± 0.009	0.470± 0.016	0.572± 0.006	0.593± 0.007	0.639± 0.018
Content Uniformity (mg)	98.9 ± 0.52	99.26 ±0.76	99.03 ±0.49	98.8± 0.96	98.86 ±0.70	101.3 ±0.5	98.63 ±0.75	100.36± 0.96	102.13± 0.35
DT (sec)	49	25	17	41	18	10	34	15	9
Wetting time(sec)	25	16	10	15	12	10	14	10	08
%CDR at 15 mins	73.29± 0.54	77.25± 0.36	80.71± 0.55	74.35± 0.55	81.32± 0.35	89.13± 0.21	76.81 ±0.34	90.61± 0.35	92.23± 0.35

Average ±SD n=3

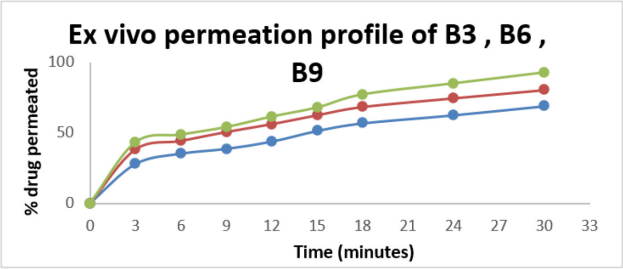


Figure 6: *Ex-vivo* permeation study of batch B3, B6 and B9.

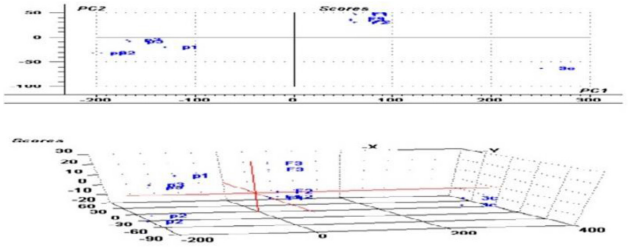


Figure 7: 2D and 3D graph represents Taste masking study.

increase there is a decrease in disintegration time and increase in the amount of the drug release.

Ex-vivo permeation studies

The prepared tablets were subjected *to ex-vivo* permeation studies and it can be seen from the Figure 6 that the batch B9 showed highest permeation of 93.17% across the semi-permeable membrane. It can be concluded that at 40% concentration of Sodium bicarbonate better alkalization of tablets is achieved. However, increasing the concentration of the alkalizing agent, there is an increase in the permeation of drug across the membrane. The % drug permeated across membrane is directly proportional to the concentration of alkalizing agent

Taste masking Study

In the Figure 7 shows, 2-dimension plot, 3c is 10^{-2} Molar Concentration of API. All formulations are midway between Placebos and API. The first dimension has 92% variance, second has 6% variance – it is given here as X-expl (explained x variance) and in 3-dimension plot shows that F3 is closer to its respective placebos than F1 and F2. Here the third dimension has 1% variance. Formulation 1, 2 and 3 had concentration of stevia as 0.5mg, 1mg, and 1.5 mg respectively while the placebos had same concentration of stevia excluding the API.

Generation of full and reduced model for 3^2 full factorial design

Data transformation of 3^2 full factorial design with the values of dependent variables and independent response are given in Table 4 and the summary of result of full and reduced model regression analysis is given in Table 5.

Table 4: Data transformation of 3^2 full factorial design with the values of dependent variables and independent responses.

Batches	Real values		Responses	
	concentration of Kyron T-314(mg) X1	Concentration of alkalizing agent(mg) X2	Disintegration Time(sec)Y1	%Drug release at 15 mins Y2
B1	0.5	0	49	73.29
B2	2	0	25	77.25
B3	3.5	0	17	80.71
B4	0.5	20	41	74.35
B5	2	20	18	81.32
B6	3.5	20	10	89.13
B7	0.5	40	34	76.81
B8	2	40	15	90.61
B9	3.5	40	9	92.23

The best result was found in B9 batch in which tablet disintegrates in 9 sec and 92.23% drug release achieved within 15 min.

Generation of full and reduced model for 3^2 full factorial design

The summary of result obtained from the full and reduced model regression analysis is given in Table 5. From the analysis of the multiple regression, for the Response Y1, it was shown that the coefficients of variables X1 and X2 having negative and positive sign respectively, which determines that as the concentration of Kyron T-314and increases, disintegration time decreases. It can be concluded that the factor X_1 is having more significant effect than X_2 on response Y_1. On other side, values of X_1 and X_2 both are positive which shows that as the concentration of Kyron T-314 and Sodium bicarbonate increases, there is increase in the drug release. The higher value of X_1 indicates that X_1 has more effect on response Y_2 compared to X_2. Hence it is concluded that the concentration Kyron T-314 affects the disintegration time and the concentration of Kyron T-314 and Sodium bi-carbonate affects the cumulative drug release in the formulation.

Statistical analysis of disintegration time(Y1)

The polynomial equation was generated using Design Expert

$$Y_1 = 18.11 + (-14.66)\,X1 + (-5.5)\,X2 + (7.33)\,X11 + (1.75)\,X12$$

The contour plot defines that, with increase in the concentration of Kyron T-314 and Sodium bicarbonate there was decrease in the disintegration time. Statistical analysis shows that effect of X_2 variable is less effective than the X_1 variable. However, X1 and X2 are significant variables with *p* value less than 0.05.

Statistical analysis of % drug release at 15 min (Y_2)

Design Expert 11.0.0.5 was used to generate the polynomial equation.

Table 5: Summary of result of full and reduced model regression analysis.

Y1 (Disintegration Time)							
Response Y1	b0	b1	b2	b11	b22	b12	R2
Coefficient	18.11	-14.66	-5.5	7.33	1.83	1.75	0.998
P value	0.0003	<0.0001	0.0008	0.0018	0.0767	0.0372	
Equations							
Full Model	18.11 + (-14.66)X1 + (-5.5)X2 + (7.33)X11 +(1.83)X22 + (1.75)X12						
Reduced Model	18.11 + (-14.66)X1 + (-5.5)X2 + (7.33)X11+ (1.75)X12						
Y2 (Cumulative %Drug release)							
Response Y2	b0	b1	b2	b11	b22	b12	R2
Coefficient	82.92	6.27	4.73	-1.97	0.21	2	0.949
P value	0.036	0.0101	0.0218	0.36	0.91	0.22	
Equations							
Full Model	82.92 + (6.27)X1 + (4.73)X2 + (-1.97)X11 + (0.21)X22 + (2)X12						
Reduced Model	63.667 + (6.27)X1 + (4.73)X2						

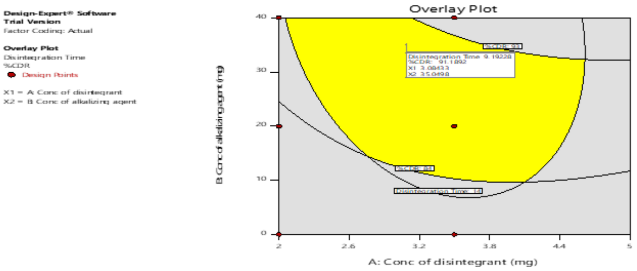


Figure 8: Overlay plot of response Y1 and Y2.

Table 6: Formulation of check point batch.

Sr.no	Excipient	Quantity(mg)
1	API	20
2	Kyron T-314	3.04
3	PVP k30	1
4	Sodium bicarbonate	35.05
5	Mannitol	25
6	Neusilin US2	12.5
7	Stevia	1.5
8	Mg.stearate	1
9	Talc	1

$$Y_2 = 63.667 + (6.27)\ X1 + (4.73)\ X2$$

As there is increase in concentration of Sodium bicarbonate, there is increase in the drug release of drug which can be seen in the contour plot. From the equation, the effect of X_1 variable is more significant than the effect of X_2 variable which is indicated by that the co-efficient of X_2 (concentration of Sodium bicarbonate) is less than the co-efficient if X_1 (concentration of Kyron T-314)

Optimization of formulation

In the Figure 8 we can see the optimized area of the response. The significance of yellow region indicates that any combination of the independent variables with the yellow region will give the desired results. Moreover, response Y1(Disintegration time) was set in the range of 6 to 14 sec response Y2(% Drug release at 15 min) was set in the range of 84 to 93%. As seen in the plot result of check point batch is very near to optimized batch and it found to be at X1=1 and X2=1.

Formulation of check point batch (B10)

The check point batch is formulated according to overlay plot (Figure 8). The coloured region of the overlay plot will give the combination of independent variables using which desired results for the dependent response can be obtained. Table 6 shows formulation of check point batch.

There are different pre-compression and post-compression parameters are evaluated and results are given in Table 7.

The comparison of predicted and experimental value for dependent responses is given in Table 8.

In-vitro drug release and permeation of check point batch was found to be 91.33% at 15 min and 92.07% at 30 min respectively which was found comparable with batch B9.

Table 7: Results of Check point batch.

Sr.no	Parameters	Observation
1	Appearance	White 100 mg tablets
2	Angle of Repose	35.3
3	Carr's index(%)	14.51
4	Hausner'sratio(%)	1.17
5	Weight variation(mg)	99
6	Hardness(kg/cm^2)	5.3
7	Friability(%)	0.621
8	Content uniformity(%)	98.6
9	Disintegration time(sec)	10
10	Wetting time(sec)	8
11	In-vitro dissolution(%) at 15 min	91.33
12	Ex-vivopermeation (%) at 30 min	92.07

Table 8: Comparison of Experimental and Predicted results.

Response	Check point Batch	
	Experimental	Predicted
Disintegration Time(sec)	10	10
Drug release at 15 min	91.33	91.08

Table 9: Short term stability study.

Number of weeks	Disintegration time (sec)	% Drug release at 15 min
0	9	92.23
1	9	92.27
2	10	92.24
3	10	91.98
4	11	91.89

Short term stability study of the optimized formulation

Short term stability study was carried out at specified condition (35°C ± 5°C and 75% ± 5%) and evaluated

for its parameters to check it's stability after one month. The optimized formulation (B9) was packed in blister pack. After one month the tablet was evaluated for drug content, disintegration time, hardness, thickness, diameter and *in-vitro* drug release. All outcome results are given in Table 9.

CONCLUSION

Thus, it can be concluded from the results obtained for the current research that the sublingual tablet of Eletriptan Hydrobromide can be formulated as it offers advantages of reduction in the time for the onset of action, bypass first pass metabolism and this will cause an increase in bioavailability of drug in the systemic circulation over conventional tablets or film-coated tablets.

ACKNOWLEDGEMENT

The authors are thankful to Dr. Mahesh T. Chhabria, Principal, L. M. College of Pharmacy for all the help and support. Authors would also like to ackowledge Cadila Pharmaceuticals for providing the gift sample of drug and Gangwal Chemicals for gifting Neusilin US2 and helped us to carry out this research work in a smooth way.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

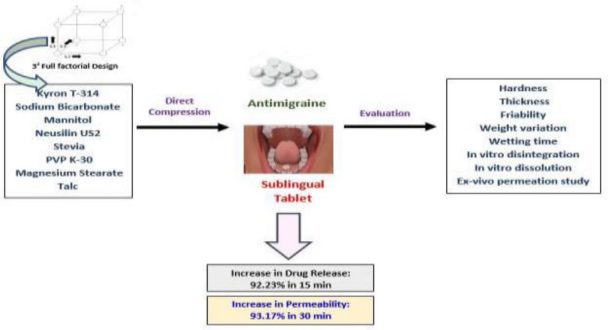
ABBREVIATIONS

PVP: Polyvinylpyrrolidone, **FTIR:** Fourier Transform Infrared Spectroscopy, **DSC:** Differential Scanning Calorimetry, **EH:** Eletriptan Hydrobromide, **DT:** Disintegration time, **WT:** Wetting time, **UV:** Ultraviolet, **API:** Active Pharmaceutical Ingredient, **USP:** United States Pharmacopeia, **DOE:** Design of Experiments, **CPP:** Critical Process parameters.

REFERENCES

1. Elrington G. Harley St. Migraine: Diagnosis and treatment. J Neurol Neurosurg Psychiatry. 2002;72:10-5.
2. Weatherall MW. The diagnosis and treatment of chronic migraine. Ther Adv Chronic Dis. 2015;6(3):115-23. doi: 10.1177/2040622315579627, PMID 25954496.
3. Elio A, Piero B, Paolo C. *et al*. Current and emerging evidence-based treatment options in chronic migraine: A narrative review. J Headache Pain. 2019;20(1).
4. Belsey JD. The clinical and financial impact of oral triptans - an updated meta-analysis. J Med Econ. 2002;5(1-4):79-89. doi: 10.3111/200505079089.
5. Capi M, Curto M, Lionetto L, De Andrés F, Gentile G, Negro A, *et al*. Eletriptan in the management of acute migraine: An update on the evidence for efficacy, safety, and consistent response. Ther Adv Neurol Disord. 2016;9(5):414-23. doi: 10.1177/1756285616650619, PMID 27582896.
6. Pawar PP, Ghorpade HS, Kokane BA. Sublingual route for systemic drug Delivery. J Drug Delivery Ther. 2018;8(6-s):340-3. doi: 10.22270/jddt.v8i6-s.2097.
7. Kumar B, Suryaprakash R. Formulation and *in-vitro* Evaluation of mucoadhesive Buccal tablets of anti-migraine Drug. Inventive Rapid NDDS. 2015;4.
8. Pingale AP, Katti S. Formulation and evaluation of fast disintegrating tablet of eletriptan hydrobromide. Res J Pharm Technol. 2014;7:792-7.
9. Sah S, Badola A, Kothiyal P. Sublingual tablets: An overview. Indian J. IJPBR. 2016;4(2):20-6. doi: 10.30750/ijpbr.4.2.3.
10. Kumar MK, Nagaraju K, Bhanja S, Sudhakar M. Formulation and evaluation of sublingual tablets of terazosin hydrochloride. Int J Pharm Sci Res. 2014;5(2):417-27.
11. Prajapati PH, Oza M, Patel C. Formulation and evaluation of sublingual tablet of paroxetine hydrochloride. Int J Pharm. 2013;3(2):1019-36.
12. Bozal-Palabiyik B, Uslu B, Ozkan Y, Ozkan SA. *In-vitro* drug dissolution studies in medicinal compounds. Curr Med Chem. 2018;25(33):4020-36. doi: 10.2174/0929867325666180322145335, PMID 29577852.
13. Lorenz JK, Reo JP, Hendl O, Worthington JH, Petrossian VD. Evaluation of a taste sensor instrument (electronic tongue) for use in formulation development. Int J Pharm. 2009;367(1-2):65-72. doi: 10.1016/j.ijpharm.2008.09.042, PMID 18951963.
14. Jain H, Panchal R, Pradhan P. *et al*. Electronic tongue: A new taste Sensor. Int J Pharm Sci Rev Res. 2010;5(2):91-6.
15. Padalkar R, Damle M. Formulation, development and evaluation of novel mouth dissolving drug Delivery system of eletriptan hydrobromide. World J Pharm Pharm Sci. 2016;5(9):1590-604.
16. Silva-Abreu M, Espinoza L, Halbaut L, Espina M, García M, Calpena A. Comparative study of ex vivo transmucosal permeation of pioglitazone nanoparticles for the treatment of Alzheimer's disease. Polymers. 2018;10(3):316. doi: 10.3390/polym10030316.
17. Pinto S, Pintado ME, Sarmento B. *In vivo, ex vivo* and *in vitro* Assessment of Buccal Permeation of Drugs from Delivery Systems. Expert Opin Drug Deliv. 2020;17(1):33-48. doi: 10.1080/17425247.2020.1699913, PMID 31786958.
18. Patel VF, Liu F, Brown MB. Modeling the oral cavity: *In vitro* and *in vivo* evaluations of buccal drug Delivery systems. J Control Release. 2012;161(3):746-56. doi: 10.1016/j.jconrel.2012.05.026, PMID 22626941.
19. Senel S, Hincal AA. Drug permeation enhancement via buccal route: Possibilities and limitations. J Control Release. 2001;72(1-3):133-44. doi: 10.1016/s0168-3659(01)00269-3, PMID 11389992.
20. Sattar M, Hadgraft J, Lane ME. Preparation, characterization and buccal permeation of naratriptan. Int J Pharm. 2015;493(1-2):146-51. doi: 10.1016/j.ijpharm.2015.07.035, PMID 26196276.

PICTORIAL ABSTRACT



SUMMARY

The present study involves the formulation and development of sublingual tablet of Eletriptan Hydrobromide. The marketed formulation of Eletriptan Hydrobromide is film coated tablet which having slow onset of action and directly exposed to extensive first pass metabolism. The present formulation was carried out to achieve faster onset of action and avoid first pass metabolism. FTIR and DSC study showed the drug is pure and there is no interaction between the drug and the other excipients. All excipients were selected carefully like alkalizing agent and super disintegrants to achieve optimum alkalization and better disintegration time. Direct compression method was used for the tablet's formulation.

The tablets containing the drug were formulated by applying the DOE using design Expert. However, Critical process parameters (CPP) were considered to obtain the better result of reduction in disintegration time and increase the drug release. The design applied to formulate tablets was 3^2full factorial design which yielded 9 possible combinations as seen in table and all these possible combinations were evaluated for both pre-compression and post compression parameters as shown in table and it was found that factorial batch B9 showed the best disintegration time of 9 sec and 92.97% of drug release in 15 min.

Concentration of Sodium bicarbonate was taken 0, 20 and 40% for experimental study. From the result of permeation, it was found that maximum permeation enhancement was obtained when the concentration of sodium bicarbonate was 40%. It shows the drug remains in unionized form.

Check point was prepared from overlay plot and that was showing similar result as optimized batch, and after that stability study was also carried out after 1 month which did not show any changes in result.

About Authors

Mr.Manan Patel, Assistant Professor at Sal Institute of Pharmacy. He has more than 2 years of teaching Experience. He has completed his B.Pharm and M.Pharm from L.M. College of Pharmacy.

Dr. Radhika Pandya, Assistant Professor at L. M. College of Pharmacy. She has about 11 years of teaching experience. Her area of interest is working on dissolution enhancement techniques and development of novel drug delivery systems. Application of QbD approach in product development is her expertise. She has done M.Pharm from L. M. College of Pharmacy and Ph.D from Nirma University. She has about 6 publications to her credit

Cite this article: Patel M, Pandya R. Formulation and Evaluation of Oral Trans-mucosal Delivery System of Eletriptan Hydrobromide. Indian J of Pharmaceutical Education and Research. 2022;56(3s):s413-s421.