RESEARCH PAPER

Development And Evaluation Of Biperiden Hcl Sublingual Film

Hitesh A. Prajapati[1], Shivam D. Parekh[2], Suraj R. Chauhan[3], Gazala Y. Ansari[4], Bhumi A. Raval[5], Jitendra O. Bhangale[6]

[1-2]Student, Smt. N. M. Padalia Pharmacy College, Navapura, Ahmedabad, Gujarat, India 382210
[3]Associate Professor, Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat, 382210, India
[4]Assistant Professor, Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat, 382210, India
[5]Professor, Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat, 382210, India; https://orcid.org/my-orcid?orcid=0009-0000-5129-1977
[6]Professor and Principal, Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat, 382210, India; https://orcid.org/0000-0002-2049-3610

Corresponding Author: Dr. Jitendra O. Bhangale
*Email: jitu2586@gmail.com Mobile: +91-7405285680

Abstract

The present study aimed to develop and evaluate sublingual films of Biperiden HCl to enhance patient compliance and improve bioavailability by bypassing first-pass metabolism. Biperiden HCl, a BCS class I drug with limited oral bioavailability was selected as a suitable candidate for rapid drug delivery. Sublingual films were prepared using the solvent casting method employing polymers such as polyvinyl alcohol (PVA), along with excipients including polyethylene glycol 400, croscarmellose sodium, and aspartame. The prepared films were evaluated for physicochemical and performance parameters, including thickness, weight variation, folding endurance, surface pH, drug content, disintegration time, and in vitro drug release. The films exhibited uniform thickness acceptable weight variation, and high folding endurance indicating good mechanical strength. Surface pH values were close to physiological conditions, suggesting minimal irritation. Drug content ranged from 98.47% to 99.51%, confirming uniform drug distribution. Among all formulations, batch B8 demonstrated optimal performance with highest folding endurance 302.33 ± 1.53, fastest disintegration time 11.92 ± 1.39 sec, and maximum drug release 99.18% within 12 minutes. Stability studies indicated no significant changes in physicochemical properties and drug release profile over one month under accelerated conditions. In conclusion, the developed sublingual films of Biperiden HCl, particularly batch B8, showed promising characteristics for rapid drug release and improved bioavailability. This formulation approach can serve as an effective alternative to conventional oral dosage forms, especially for patients with swallowing difficulties.

***Keywords*:** Sublingual films, Biperiden HCl, Polyvinyl alcohol.

How To Cite This Article: Prajapati Ha, Parekh Sd, Chauhan Sr, Ansari Gy, Raval Ba, Bhangale Jo. Development And Evaluation Of Biperiden Hcl Sublingual Film. Int J Drug Deliv Technol. 2026;16(27s):1068-1073. Doi: 10.25258/ijddt.16.27s.122

INTRODUCTION

Conventional dose forms are the best option, elderly and pediatric patients cannot take them since they have trouble swallowing pills and capsules. The drug Biperiden HCl is used to treat Parkinson's disease by reducing rigidity and improving muscular control. It has a dose of 2 mg orally 3 to 4 times a day and is classified as BCS class I, meaning it has high permeability and solubility. Its half-life of up to 18.4 hours allows for minimal interruption of a stable plasma concentration. Despite these factors, the bioavailability of Biperiden HCl is only 33%, and it takes 1.5 hours for peak plasma concentrations to be reached. Taking into account every requirement, it was an ideal match for Sublingual Films.[1,2] In order to improve patient compliance, an attempt is being made in the current study to formulate Sublingual Films of Biperiden HCl that will dissolve within the oral cavity in an instant of seconds and absorb the drug from the mouth and GIT. Additionally, the drug's will go directly into systemic circulation will improve its bioavailability.[3,4] So main objective was to development and evaluation of biperiden HCl sublingual film.

MATERIALS

HPMC E5, Polyvinyl Alcohol, Polyethylene glycol 400, Croscarmellose sodium, Aspartame were received from Chemdyes Corporation, Rajkot, Gujarat. while Methanol, was received from Finar Chemicals Pvt. Ltd. Ahmedabad.

METHOD: Sublingual Film of Biperiden HCl were prepared by using Solvent Casting method. In solvent casting method initially, the water-soluble polymers are dissolved in water and methanol at 1,000 rpm and can be heated up to 60 °C. All the other excipients like colors, flavouring agent, sweetening agent, etc., are dissolved separately. Then both the solutions obtained are mixed thoroughly stirring at 1,000 rpm. The obtained solution is incorporated with the API dissolved in suitable solvent. The entrapped air is removed by sonicating the prepared solution. The resulting solution is cast as a Film and allowed to dry, which is then cut into pieces of the desired size.[5,6] The Films were prepared by using ingredients with concentrations as mentioned in table 1.

Table 1: Formulation of sublingual films of Biperiden HCl

Ingredients	Formulation code								
	B1	B2	B3	B4	B5	B6	B7	B8	B9
Biperiden HCl (mg)	132.6	132.6	132.6	132.6	132.6	132.6	132.6	132.6	132.6
PVA (mg)	40	45	50	40	45	50	40	45	50
CCS (mg)	3	3	3	4.5	4.5	4.5	6	6	6
Aspartame (mg)	5	5	5	5	5	5	5	5	5
PEG 400 (ml)	10	10	10	10	10	10	10	10	10
Water (ml)	5	5	5	5	5	5	5	5	5
Methanol (ml)	5	5	5	5	5	5	5	5	5

Determination of Melting point of Biperiden HCl: Melting point of Biperiden HCl was measured by melting point apparatus. Minimum amount of drug was placed in a thin-walled capillary tube closed at one end. This capillary was then mounted in a melting point apparatus with thermometer and then their temperature range over which Biperiden HCl melts is measured. The readings were taken in triplicate.[7,8]

Estimation of Biperiden HCl by UV spectroscopy method:

Biperiden HCl 10 mg was dissolved in 100 ml of phosphate buffer (pH 6.8) to produce the standard stock solution, which has a concentration of 100 ppm. The working solution was prepared by diluting the stock solution with pipette output of 1, 2, 3, 4, and 5 ml, respectively, into a 10 ml volumetric flask. It was possible to reach concentrations of 10, 20, 30, 40, and 50 ppm. Working solution absorbance was determined in triplicate using λmax at 254 nm and phosphate buffer (pH 6.8) as a blank.[7,8]

Evaluation Parameters of Sublingual Film[9-12]

Physical Appearance: Stickiness, Surface appearance, and film clarity of the prepared batches were examined.

Weight variation: Ten randomly chosen films were weighed on an analytical balance, and the average weight of each film was obtained. It is preferred that the weight of the film remain somewhat consistent. Making sure a film has the right amount of excipients and API is helpful.

Thickness of Films: By using micrometer screw gauge the thickness of the film was measured at five different places; an average of these five values was calculated. This is essential to ascertain uniformity in the thickness of the film this is directly related to the accuracy of dose in the film.

Folding Endurance: By folding the film repeatedly in the same location until it breaks, folding endurance is measured. The total number of folds the film can withstand without breaking is used to compute the folding endurance value.

Surface pH: Developed Petridish was centered around the film. After that, 0.5 ml of phosphate buffer was added to it, and it was left for 30 seconds. After that, pH was measured using an electrode and allowing for equilibrium to be reached.

***In-vitro* Disintegration Time**: In a petridish with 10 ml of pH 6.8 phosphate buffer, a film was placed on stainless steel wire mesh, and the amount of time it took for the film to break was recorded. Three readings on average were taken into account.

Drug Content: After dissolving the film in 10 ml of pH 6.8 phosphate buffer, it was filtered. Using a double beam UV visible spectrophotometer set at 254 nm, the drug content was evaluated. The concentration was then determined using the calibration curve.

***In vitro* Drug release**: USP type II Dissolution apparatus was used for *in vitro* dissolution studies. It was filled to capacity with 500 cc of pH 6.8 phosphate buffer and kept at 37 ± 5 ˚C with 50 rpm. The film was placed on a watch glass, correctly clamped, and covered with nylon wire mesh. After that, this unit was placed into the dissolving flask. At various times, 5 ml of water were eliminated and replaced with an equal volume of fresh buffer solution. The samples were examined using a UV Visible Spectrophotometer at a wavelength of 254 nm.

Stability Studies: The optimized batch was put into the Stability Chamber for a month at 40˚C ± 2˚C and 75% ± 5% relative humidity after being covered in aluminum foil in accordance with ICH guidelines. After a month was complete, the films were removed and evaluated according to every criterion.

RESULTS AND DISCUSSION

Melting point of Biperiden HCl

Melting point determination is one of the popular techniques used to identify drug using melting point apparatus and melting point of Biperiden HCl was found in the range of 98 to 102 ˚C. Reported melting point of Biperiden HCl is 101 ˚C and is thus similar to the melting point of Biperiden HCl.

Estimation of drug by UV overlay spectra

The absorbance of the prepared working solutions was assessed at their maximum wavelength of 254 nm, using a UV-Visible Spectrophotometer, with a blank solution of phosphate buffer at pH 6.8 as reference.

A calibration curve for the prepared working solutions of Biperiden HCl was generated by graphing concentration against absorbance, as depicted in Fig 1 Table 2 displays a regression analysis derived from the Biperiden HCl calibration curve. The displayed calibration curve of Biperiden HCl gives the regression equation y = 0.0236x + 0.066, which shows a

correlation coefficient of 0.9981. Based on the reported λmax of 254 nm, it can be concluded that that drug was Biperiden HCl.

Table 2: Absorbance of different concentration of Biperiden HCl in 0.1 N HCl

Sr. No.	Concentration (ppm)	Absorbance			Mean Absorbance ± S. D.
		I	II	III	
1	10	0.289	0.287	0.289	0.288 ± 0.001
2	20	0.562	0.569	0.561	0.564 ± 0.004
3	30	0.765	0.768	0.769	0.767 ± 0.002
4	40	0.998	0.998	0.999	0.998 ± 0.001
5	50	1.249	1.251	1.252	1.251 ± 0.002

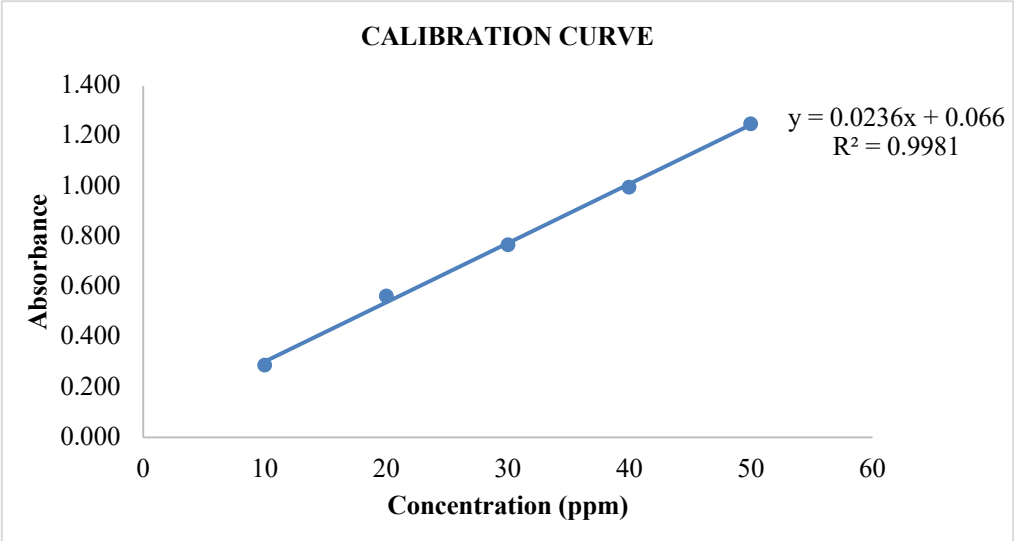

Fig 1: Calibration curve of Biperiden HCl in phosphate buffer at pH 6.8

Evaluation Parameters of Sublingual Film

From physical appearance parameters it was seen that batches were non sticky, smooth and transparent in appearance. The evaluation data of the developed subungual films (B1–B9) demonstrate satisfactory physicochemical characteristics with acceptable reproducibility (n = 3), indicating robustness of the formulation approach. The thickness of all batches ranged from 0.28 ± 0.28 mm to 0.34 ± 0.34 mm, confirming uniform film casting with minimal variation. Weight variation values (129.44 ± 1.05 mg to 188.44 ± 0.90 mg) were within acceptable limits, suggesting consistency in polymer distribution and solvent evaporation. Folding endurance, an indicator of mechanical strength and flexibility, varied significantly among batches (197.00 ± 1.73 to 302.33 ± 1.53). B6 and B8 exhibited the highest folding endurance (>300), indicating superior mechanical integrity, which is essential for handling and application under the nail. Surface pH of all formulations was found to be in the range of 6.62 ± 0.01 to 6.76 ± 0.01, which is close to the physiological pH of the nail bed, suggesting minimal risk of irritation upon application. The in-vitro disintegration time showed notable variation across formulations, ranging from 11.92 ± 1.39 sec to 47.98 ± 1.29 sec. Among all batches, B8 demonstrated the fastest disintegration 11.92 sec, indicating rapid film hydration and drug release potential, whereas B3 showed comparatively slower disintegration. Drug content across all batches was found to be uniform 98.47 ± 0.17% to 99.51 ± 0.42%, indicating efficient drug incorporation and homogeneity of the formulation. Overall, batch B8 emerged as the optimized formulation, exhibiting an optimal balance of mechanical strength, fastest disintegration time, acceptable surface pH, and high drug content uniformity. These findings suggest that B8 is a promising candidate for effective subungual drug delivery with enhanced performance characteristics. The Weight variation, Thickness, Folding endurance, Surface pH, in vitro Disintegration time and Drug Content data are mentioned in Table 3.

Table 3: Weight variation, Thickness, Folding endurance, Surface pH, in vitro Disintegration time and Drug Content data

Batch	Thickness (mm ± S.D.)	Weight variation (mg ± S.D.)	Folding Endurance	Surface pH	*In-vitro* Disintegration time (sec ± S.D.)	Drug Content (%)
B1	0.28 ± 0.28	129.44 ± 1.05	220.67 ± 1.53	6.76 ± 0.01	45.95 ± 1.27	99.51 ± 0.42

B2	0.29 ± 0.29	140.48 ± 1.10	234.67 ± 1.53	6.73 ± 0.01	44.79 ± 1.47	99.36 ± 0.20
B3	0.31 ± 0.31	152.44 ± 1.20	197.00 ± 1.73	6.71 ± 0.01	47.98 ± 1.29	98.86 ± 0.49
B4	0.30 ± 0.30	144.27 ± 1.02	261.67 ± 1.53	6.72 ± 0.01	38.96 ± 1.48	98.65 ± 0.23
B5	0.31 ± 0.31	157.28 ± 0.84	247.67 ± 1.15	6.69 ± 0.01	41.74 ± 1.47	98.47 ± 0.17
B6	0.32 ± 0.32	169.09 ± 0.98	300.00 ± 1.73	6.66 ± 0.01	20.75 ± 1.20	99.01 ± 0.59
B7	0.31 ± 0.31	161.53 ± 1.07	264.67 ± 0.58	6.68 ± 0.01	34.87 ± 1.32	99.02 ± 0.61
B8	0.33 ± 0.33	174.48 ± 0.95	302.33 ± 1.53	6.65 ± 0.01	11.92 ± 1.39	99.38 ± 0.26
B9	0.34 ± 0.34	188.44 ± 0.90	283.33 ± 0.58	6.62 ± 0.01	29.82 ± 1.34	98.91 ± 0.31

(n=3)

% Cumulative Drug Release study

The in vitro drug release profiles of subungual films (B1–B9) demonstrated a time-dependent increase in cumulative drug release over 12 minutes, indicating efficient hydration and diffusion behaviour of the formulated films. All batches exhibited rapid initial drug release within the first 2 minutes (21.92–48.35%), which may be attributed to surface-associated drug and quick polymer swelling. This was followed by a release phase up to 12 minutes. Among the formulations, batch B8 showed the highest drug release at all time points, reaching 99.18% within 12 minutes, indicating superior drug diffusion and rapid disintegration characteristics. Similarly, B6 (97.36%) and B4 (94.68%) also demonstrated high release profiles, suggesting effective polymer matrix erosion and drug liberation. In contrast, B3 exhibited comparatively slower drug release (88.36% at 12 minutes), correlating with its longer disintegration time observed earlier. The slower release may be due to higher polymer density or stronger matrix integrity, which retards drug diffusion. B1 and B2 also showed moderate release profiles (90.36% and 91.26%, respectively), indicating balanced release behaviour. The enhanced performance of B8 can be attributed to its optimized composition, which likely promotes rapid hydration, reduced diffusional resistance, and efficient drug dispersion within the polymeric matrix. Overall, the release kinetics suggest that most formulations follow a fast-release pattern suitable for subungual delivery, with B8 identified as the best-performing batch due to its maximum and rapid drug release as mentioned in Fig 2. These findings further support the selection of batch B8 as the optimized formulation, offering a desirable combination of rapid disintegration and maximum drug availability for effective therapeutic action.

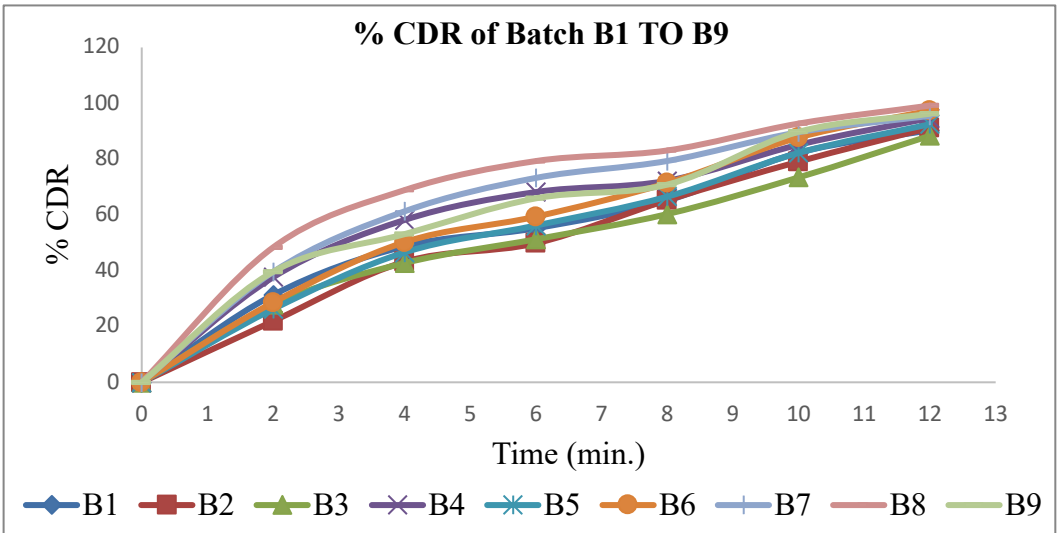

Fig 2: % CDR vs Time of batch B1 to B9

STABILITY STUDY

The comparison of different parameters and In *Vitro* Drug Release of Optimized batch and after 1 months are presented in Table 4 and Fig 3 respectively.

Table 4: Result of the Stability study

Parameters	**Optimized batch (B8)**	**Optimized batch after 1 month**
Thickness (mm)	0.33 ± 0.33	0.33 ± 0.33
Folding endurance	302.33 ± 1.53	299.67 ± 1.53
In vitro disintegration time (sec.)	11.92 ± 1.39	12.38 ± 1.02
Drug Content (%)	99.38 ± 0.26	98.00 ± 0.65

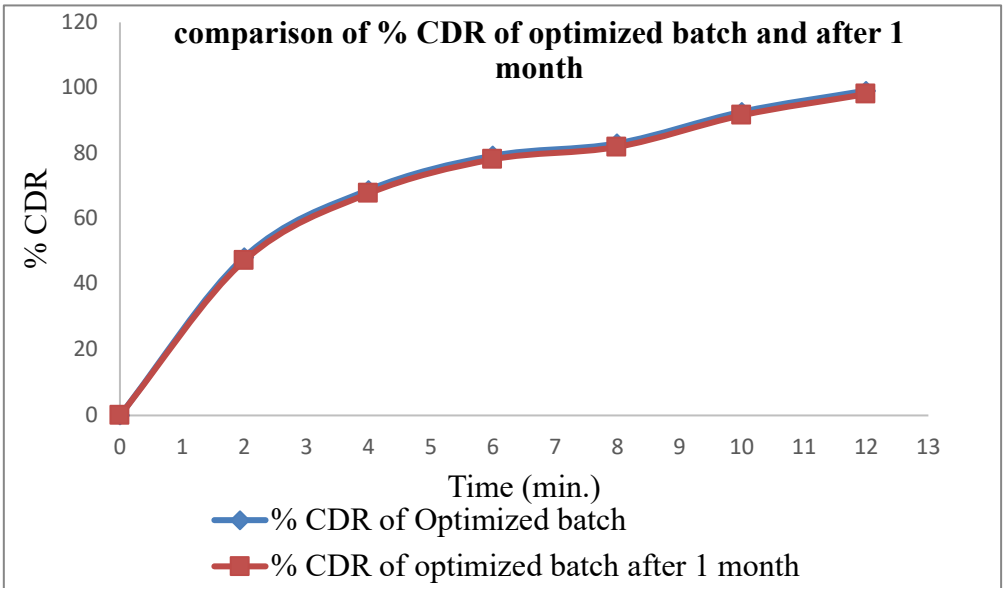

Fig 3: Comparison of % CDR of Optimized batch and Stability batch

CONCLUSION

The present investigation focused on the formulation and evaluation of sublingual films of Biperiden HCl to overcome the limitations associated with conventional oral dosage forms, particularly low bioavailability and difficulty in swallowing among geriatric and Parkinson's patients. The films were prepared using the solvent casting method with polyvinyl alcohol as the primary film-forming polymer, along with suitable plasticizers and superdisintegrants to enhance flexibility and rapid drug release. Preformulation studies confirmed the identity and purity of Biperiden HCl. All batches showed uniform thickness, acceptable weight variation, and good mechanical strength, with folding endurance ranging from 197 to 302. Surface pH values were close to physiological conditions, indicating suitability for sublingual administration. Drug content across all batches was found to be uniform, confirming homogeneity. The in vitro disintegration time varied among batches, with B8 exhibiting the fastest disintegration. Drug release studies demonstrated rapid and efficient release, with batch B8 achieving 99.18% drug release within 12 minutes. Stability studies of the optimized batch indicated no significant changes in physicochemical properties or drug release profile under accelerated conditions. The formulation effectively addresses the limitations of conventional oral therapy by enabling rapid onset of action and improved bioavailability through sublingual absorption. Overall, the developed sublingual film system represents a promising and patient-friendly alternative for the management of Parkinson's disease.

ACKNOWLEDGEMENT

The authors are grateful to Smt. N. M. Padalia Pharmacy College, Ahmedabad, for encouragement and for providing the necessary facilities to carry out this research work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Mahboob MGH, Riaz T, Jamshaid M, Bashir I and Zulfiqar S, "Oral Films: A Comprehensive Review." *International current pharmaceutical journal.* **2016**, *5(12)*: 111-117.
2. Patel NK and Pancholi SS, "An overview on: Sublingual route for systemic drug delivery." *International Journal of Pharmaceutical and Bio-Medical Science.* **2012**, *3(2)*: 913- 923.
3. Bind AK, Gnanarajan G and Kothiyal P, "A review: Sublingual route for systemic drug delivery." *International Journal of Drug Research and Technology.* **2013**, *3(2)*: 31-36.
4. Hooda R, Tripathi M and Kapoor K, "A review on oral mucosal drug delivery system." *The Pharma Innovation.* **2012**, *1(1)*: 13-19.
5. Vaishali AS, Anushree AH and Sneha BG, "Formulation development of oral fast-dissolving sublingual film of Resveratrol." *International Journal of Pharmaceutical Sciences and Research*, **2023**, *14(5)*: 2447-2466.
6. Satyajit S, Ami M, Asit RS, Asha K and Vikash D, "Formulation and evaluation of sublingual film of Asenapine maleate by using 3^2 full factorial design." *Aegaeum Journal*. **2020**, *8(4)*: 80-95.
7. Amit D, Vikram S, Divya J, Geeta R, "Solubility enhancement of Biperidin HCl by complexation with hydroxypropyl β-cyclodextrin." *Journal of Applied Pharmaceutical Research.* **2015,** *3(2)*: 27-29.
8. Malleswara RP, Sudhakar Babu AMS, Navya SK, Teja Rameswarapu NSV, K. L. N. Mallikharjunarao KLN and Prasanna KD, "Formulation development and invitro evaluation of immediate release tablets of biperiden HCl cyclodextrin complexes." *International Journal of*

Research in Pharmaceutical and Nano Sciences. **2013**, *2(6)*: 757 - 767.

9. Rita NW, Farheen A and Pranita K, "Formulation and evaluation of fast dissolving sublingual film of Paroxetine hydrochloride for treatment of depression." *Asian Journal of Pharmaceutical and Clinical Research*. **2019**, *12(10)*: 126-132
10. Sachin G, Sonali S, Omprakash B, Sandeep S and Mahesh B, "Formulation and Evaluation of Oral Fast Dissolving Sublingual Film of Propranolol HCl." *International Journal of Pharma Research and Health Sciences*. **2018**, *6(2)*: 2369-2373.
11. Kailas KM, Remeth JD, Vishwajeet SG, Vijay DH, Bhimrao KR, Nikhil SD, "Taste Masked Oral Fast Dissolving Sublingual Strips of Rizatriptan Benzoate for Migraine Therapy." *Marmara Pharmaceutical Journal.* **2017**, *21(2)*: 235-242.
12. Upendra CG, Pooja PP and Pravin DC, "Development of Fast Dissolving Sublingual Wafers by Using Film Former: Optimization and Characterization." *Journal of Chemical and Pharmaceutical Research.* **2017**, *9(4)*: 82-91.