International Journal of Pharmacy and Industrial Research (IJPIR)
IJPIR |Vol.14 | Issue 3 | Jul - Sept -2024
www.ijpir.com
DOI : https://doi.org/10.61096/ijpir.v14.iss3.2024.274-280
ISSN: 2231-3656
Print: 2231-3648

Research

Design and invitro characterization of alfuzosin HCL tablets for sublingual drug delivery system

Kotra Chandrasekhar Rangaiah*, Boddupalli Anitha, P. Sushma, S. Shailaja, N. Umarani

Department of Siddhartha Institute of Pharmacy, Hyderabad, Telangana, India

*Author for Correspondence: Kotra Chandrasekhar Rangaiah
Email: k.chandrasekhar@siddhartha.co.in

Published on: 25 Sept 2024

Published by:
DrSriram Publications

Abstract

Alfuzosin HCl (ALF) that is commonly used to treat benign prostatic hyperplasia (BPH), on the market. On the other hand, ALF-containing orally disintegrating tablets (ODTs) are not yet available for purchase. To make the selected medicinal molecule more soluble and to speed up its dissolving rate, this study developed sublingual tablets of ALF employing super disintegrating agents such as sodium starch glycollate, locust bean gum, and cross caramellose sodium. All of the formulations were prepared using the direct compression method with a 6-millimeter punch on an 8-station rotary tablet punching machine. All things considered, the mixtures displayed good flow properties including bulk density, tapped density, and angle of repose. All of the quality control evaluation parameters were met by the produced tablets, and they demonstrated good post compression properties according to the I.P limits. Optimal performance was achieved by the AF1 formulation, which exhibited the highest percentage of drug release (99.78%) in under 6 minutes. A super disintegrates containing ten milligrams of SSG is included in the AF1 formulation. According to the results of the permeability tests, ALF is an easily absorbed substance. Based on these results, the ODT method for ALF seems to be a good way to get patients to comply with treatment and get things rolling quickly.

Keywords: **Alfuzosin HCl,** Sodium starch glycollate, Locust bean gum and Cross caramellose sodium.

INTRODUCTION

The need for a quick pharmacological effect is what gave rise to the sublingual route of drug delivery. Patients of all ages can experience dysphasia, or trouble swallowing; however, those who are cognitively impaired,

resistant to medication, sick to their stomach, or on restricted liquid diets may find it particularly challenging to swallow these dosage forms. The region under the tongue has the highest porosity when the entire buccal cavity is considered[i]. There is usually a faster onset of effect when administered sublingually rather than orally because the absorption through the sublingual blood vessels usually happens before the hepatic first-pass metabolic processes. Sublingual tablets are usually small, flat, and lightly compressed so that they retain their softness. The tablet needs to dissolve in just a small amount of saliva for the active pharmaceutical ingredient (API) to be absorbed quickly. Developing systemic drug administration via the sublingual method was driven by the need for rapid pharmacological activity. With a medication absorption rate three to ten times greater than that of the oral route, the sublingual technique ranks second only to intradermal injection. Sublingual administration is the best option for drugs having a short half-life[ii]. There were some sublingual drug delivery formulations developed earlier such as Losartan potassium[iii], carvedilol[iv], rizatriptan benzoate[v], felodipine[vi], glimepiride[vii], perindopril[viii], ondansetron[ix].

Locust bean is a natural polymer. It is utilized in the development of several drug delivery systems such as tablets, capsules, beads, microspheres, gel and polymeric films. Hence we used locust bean gum in this research. Alfuzosin is a white to off-white crystalline powder. Soluble in water, sparingly soluble in alcohol, and practically insoluble in dichloromethane. ALF is used to treat the signs and symptoms of benign prostatic hyperplasia (BPH). Stored in closed container at room temperature, avoid direct sunlight[x]. In this study, we tried to formulate sublingual tablets of ALF HCl. The current work utilized super disintegrating agents including sodium starch glycollate, locust bean gum, and cross carmellose sodium to enhance the solubility and rate of dissolution of a specific pharmaceutical molecule.

MATERIALS & METHODS

Chemicals

Terbutaline sulfate was obtained as a gift sample from Natco Pharmaceuticals, Hyderabad, India. All other chemicals such as sodium starch glycolate, cross carmellose sodium, magnessium stearate, locust bean gum, microcrystalline cellulose, talc, sodium saccharine and mannitol were purchased from SD Fine Chemicals, Mumbai. All the reagents and chemicals used were of analytical grade.

METHODOLOGY

Determination of absorption maxima

A double beam UV/VIS spectrophotometer is used to obtain the UV spectra of a phosphate buffer with a pH of 6.8 buffer solution containing 10 µg/ml of the ALF has been made. The 200-400 range was used to scan the solution[xi].

Drug- excipient compatibility studies by FT-IR[xii]

The compatibility of the pure medicine and excipients might be ascertained by the use of FTIR spectra recorded on a Shimadzu FTIR spectrometer. The solid powder sample was ground with a mortar and KBr at a rate one hundred times the original amount in order to produce potassium bromide pellets by means of a KBr press. Afterwards, the powder that had been finely ground was placed into a die made of stainless steel and compressed between anvils of polished steel at a pressure of around 8t/in2. The spectra encompassed a wave number range of 4000 to 400 cm-1.

Formulation of Sublingual tablets of ALF[xiii]

The fast-dissolving sublingual tablets containing 10 mg of ALF were manufactured via direct compression, meaning that no granules were required for their production. According to the data shown in Table 1. Dry mixing, lubrication, compression, and sieving are the four steps that make up the direct compression method of making tablets. Each tablet contains several medical ingredients and 10 milligrams of ALF. It was found that the entire weight of the tablet was 150 mg[xiv].

Table 1: Composition of various tablet formulations

Ingredients	AF1	AF2	AF3	AF4	AF5	AF6	AF7	AF8	AF9
ALF (mg)	10	10	10	10	10	10	10	10	10
CCS (mg)	10	15	20	-	-	-	-	-	-
SSG (mg)	-	-	-	10	15	20	-	-	-
Locust bean gum (mg)	-	-	-	-	-	-	10	15	20
Mg Stearate(mg)	5	5	5	5	5	5	5	5	5

Talc(mg)	5	5	5	5	5	5	5	5	5
MCC (mg)	20	20	20	20	20	20	20	20	20
Mannitol	45	45	45	45	45	45	45	45	45
Sodium saccharin	10	10	10	10	10	10	10	10	10
Total wt. (mg)	150	150	150	150	150	150	150	150	150

Evaluation of Tablets[xv, xvi]

The formulated tablets were evaluated for the physicochemical parameters such as thickness, hardness, friability, weight variation test and uniformity of drug content.

***In -vitro* dissolution studies**

The in-vitro release investigations were conducted using a Lab India DS-800, a modified USP XXIII dissolving test device. In each test, a dissolving fluid of 500 milliliters of pH 6.8 phosphate buffer was utilized, along with a speed of 50 rpm and a temperature of 37ºC. To find out if ALF was present, we tested the absorbance of 5 ml samples of the dissolving liquid at 254 nm every two minutes. At regular intervals, five milliliters of the test medium were withdrawn and replaced with the same volume of pH 6.8 phosphate buffer for each test[xvii].

Release kinetics

Plotting the data from the in vitro dissolution investigation in several kinetics models allowed researchers to examine the sublingual tablets' in-vitro release kinetics[xviii].

Stability studies of the tablet

In this study, the selected formulation (AF1) was subjected to 12-week stability tests at 25◦C/60%RH and 40◦C/75%RH[xix]. We kept the selective packed formulations at 25°C with 60% relative humidity and 40°C with 75% relative humidity for 12 weeks. The medication content and the formulation's physical appearance were evaluated at set intervals. The formulations underwent additional scanning to search for possible alterations in the spectrum. Furthermore, studies on solubility in vitro were carried out[xx].

RESULTS AND DISCUSSION

Standard Calibration curve of TBS

Because of its high reproducibility, the UV spectrophotometric method was used to measure ALF at λmax 254 nm in a pH 6.8 phosphate buffer in this investigation. A correlation coefficient closer to 1 was observed for the standard curve in the concentration range of 0.1-0.6 µg/ml. A regression equation was generated with an R^2 value of 0.9983, which is y = 1.2809x + 0.0126.

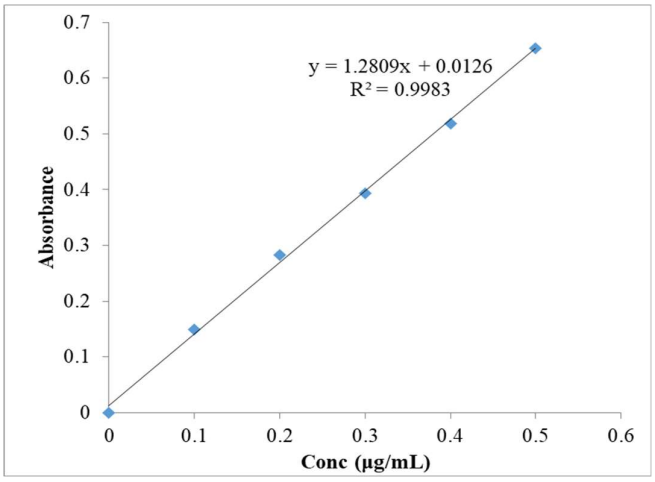

Fig 1: Standard graph of ALF in pH 6.8 Phosphate buffer

Evaluation Parameters for Sublingual Tablets of ALF

FTIR

The drug, polymer, and physical mixture were all graphed in FTIR; the physical combination shouldn't have any displacement of the functional peaks. It is very evident that the medicine and excipient did not interact.

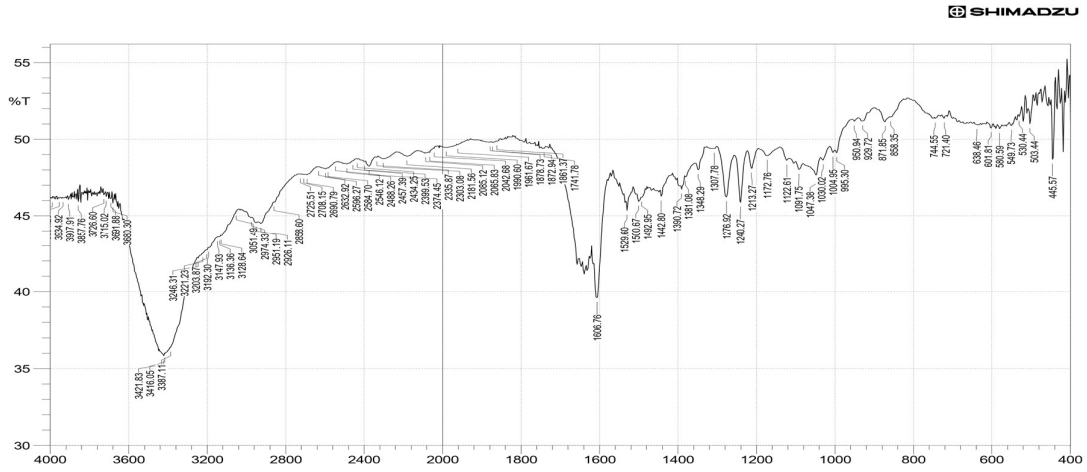

Fig 2: FTIR Spectrum of pure drug (ALF)

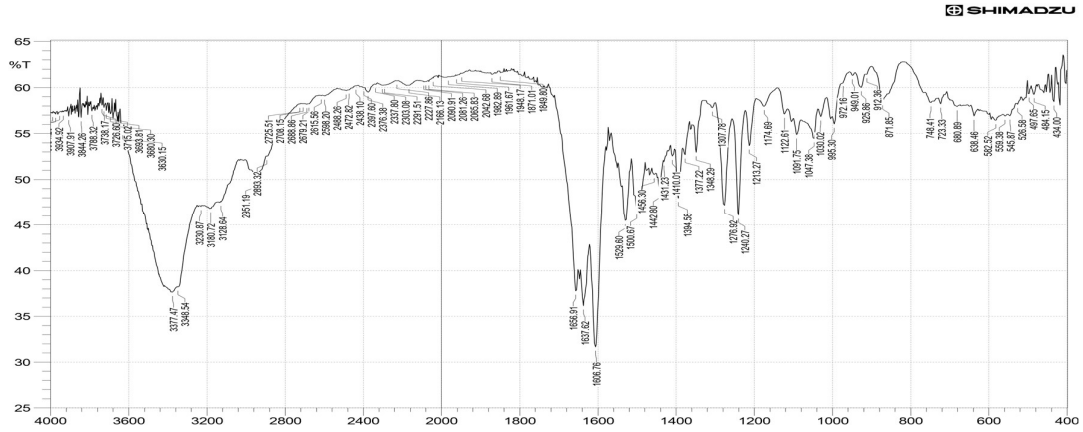

Fig 3: FTIR Spectrum of Optimized ALF sublingual tablet

N-H bending vibration, C-O stretch, C=C stretch, C-N stretch, and O-H bending were the prominent peaks seen in the infrared spectra of pure ALF, which ranged from 1390.72 cm-1 to 3246.31 cm-1. These peaks, which are recognized as ALF's distinctive peaks, were not altered when ALF's FT-IR spectra were examined with different excipients[xxi].

Pre-compression parameters

Powdered ALF and other excipients were tested for flow and derived properties, including bulk and tapped densities, angles of repose, Carr's index, and Hausner's ratio, before the fast-disintegrating sublingual tablets were made. The results, which met expectations, are shown in the table. The data was shown in the table 2. It was found that the angles of repose ranged from 19.11° to 27.75°. The bulk densities of the various formulations ranged from 0.56 to 0.65 (g/cc), whereas the tapped densities ranged from 0.67 to 0.75 (g/cc). The Carr's index of the prepared mixtures varies between 15.83% and 26.16%. The Hausner ratio can take on values between 1.161 and 1.335. Good flow properties and tablet-making potential were demonstrated by the results for the powder blends. In order to determine how the concentration of the super disintegrant affected the various physical properties of the manufactured tablets, nine pilot batches were made. From AF1 through AF3, the CCS concentration was adjusted between 10 and 20 mg, and from AF4 to AF6, the SSG content was adjusted between 10 and 20 mg. Between AF7 and AF9, the dosage of locust bean gum varied between 10 and 20 milligrams[xxii].

Table 2: Results of derived and flow properties of ALF physical mixture

F. Code	Bulk Density (gm/cm2)	Tap Density (gm/cm2)	Carr's Index (%)	Hausner ratio	Angle Of Repose(Ɵ)
AF1	0.65	0.72	15.83	1.161	27.75
AF2	0.62	0.75	24.51	1.294	25.66

AF3	0.61	0.71	19.72	1.217	24.22
AF4	0.59	0.73	26.16	1.335	23.11
AF5	0.61	0.69	20.04	1.222	21.95
AF6	0.56	0.67	24.29	1.29	23.17
AF7	0.59	0.67	18.93	1.205	21.4
AF8	0.62	0.75	22.81	1.294	19.11
AF9	0.58	0.68	22.13	1.254	21.97

All values are expressed as mean ± S.D, n = 3

Post compression Parameters

Hardness test

The table displays the results of a Monsanto toughness tester that was used to analyze the three tablets from each batch for hardness. Results showed that the tablet hardness, which varied from 2.85 to 3.43 kg/cm^2, was within the acceptable range for IP requirements. This ensures that every batch will perform admirably[xxiii].

Thickness

The three tablets from all of the batches were tested for thickness using a Vernier Caliper, according to the data in Table 3. The findings indicate that the thickness of the tablet varies between 2.84 and 3.29 mm[xxiv].

Weight variation test

Table 15 displays the results of a measurement of weight variation test that was conducted on each batch of tablets. The allowed limit is ±10%, because the average weight of the tablet is between 94.65 and 101.25 mg. The results of the tests showed that the tablet weights were within the acceptable range for the pharmacopoeia[xxv].

Table 3: Results of average weight, hardness, thickness, friability of all formulations ALF sublingual tablet

F. Code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Assay (%)
AF1	97.42	2.91	3.02	0.45	99.67
AF2	100.21	2.85	3.29	0.51	98.73
AF3	94.65	3.18	3.21	0.69	97.85
AF4	95.62	3.05	2.95	0.78	96.56
AF5	98.53	2.87	2.84	0.48	97.23
AF6	99.31	3.1	3.03	0.69	95.67
AF7	101.25	3.25	3.17	0.89	98.57
AF8	97.54	3.43	3.26	0.92	97.63
AF9	95.22	3.15	3.05	0.78	96.55

All values are expressed as mean ± S.D, n = 3

Friability

The statistics regarding the % friability of each batch's tablets is displayed in Table. A satisfactory mechanical toughness of tablets was shown by an average friability ranging from 0.45 to 0.92 percent, which was below the 1% official criterion of IP[xxvi].

Assay

Research using assay methods was performed on the pre-prepared mixes. All of the formulations showed drug content values ranging from 95.67% to 99.67%, according to the lab tests[xxvii].

In vitro disintegration time

The in vitro disintegration time of each batch's tablets was measured and the findings were displayed in a table. Results showed that the manufactured tablets had disintegration durations between 44.05 and 77.71 seconds[xxviii].

Table 4: Results of water absorption ratio, drug content, wetting time, disintegration of all formulations

F. Code	Water absorption ratio (%)	Drug Content (%)	Wetting time (Sec)	Disintegration time (Sec)
AF1	25.31	99.43	7.48	44.05
AF2	27.72	97.33	6.74	51.06

AF3	29.05	99.99	8.65	58.55
AF4	28.64	96.61	9.03	62.23
AF5	34.24	97.33	11.14	67.18
AF6	30.2	94.01	10.06	66.21
AF7	37.54	95.43	13.15	72.15
AF8	38.62	97.57	11.32	77.71
AF9	38.99	96.06	9.88	77

All values are expressed as mean ± S.D, n = 3

Drug content: The drug concentration was found to be between 94.01% and 99.99%. The results were presented in a table, and the results show that they may be reproduced with little variation from batch to batch[xxix].
Wetting time: Table contains a tabulation of the wetting time values. The range of the wetting time was 7.48 to 13.15 seconds.

In vitro Dissolution studies

In vitro dissolution tests were carried out using the paddle method with a USP dissolving device and 500 milliliters of pH 6.8 phosphate buffer. Almost eight minutes passed during the dissolving experiments. The fastest drug release rate (99.78%) within 6 minutes was observed in the AF1 formulations with 10 mg of super disintegrate cross carmellose sodium, as shown clearly in the tabular column. Consequently, it was found that sublingual tablets can be made using the super disintegrates approach. The AF1 formulation was considered to be the best.

Application of Release Rate Kinetics to Dissolution Data

Multiple models were employed to examine the drug release kinetics. In order to investigate the mechanism of the dosage form's drug release rate kinetics, the acquired data were fitted into the Higuchi, Korsmeyer-Peppas, zero-order, and first-order release models.

Stability Studies

For a duration of three months, an optimized formulation, AF-1, was the subject of stability investigations. Although there has been a small rise in assay, hardness, and friability, the overall look has not changed. At 25°C±2ºC/60% ± 5% RH and 40°C±2ºC/75% ± 5% RH, the dissolving profile of the optimum batch was calculated. The results showed that at each temperature, the percentage of drug released reduced marginally.

CONCLUSION

In this study, we tried to formulate ALF HCl tablets to be taken under the tongue. The current work utilized super disintegrating agents including sodium starch glycollate, locust bean gum, and cross carmellose sodium to enhance the solubility and rate of dissolution of a specific pharmaceutical molecule. Every single one of the recipes was made by compression using a rotary tablet punching machine that had eight stations and a 6mm punch. The bulk density, tapped density, and angle of repose were all well-represented by the combined formulations. The manufactured tablets fulfilled all I.P. limits for every quality control evaluation metric and showed good post-compression characteristics. Among all the formulations, AF1 showed the greatest percentage of drug release 99.78 percent in 6 minutes and is thus considered the best.

REFERENCES

1. Wilson JF. In the clinic: migraine. Ann Intern Med., 147(9): 2007.
2. Loder E. “Triptan therapy in migraine”, N Engl J Med. 363(1): 63-70, 2010.
3. Kumar D, Sharma A, Garg R. Formulation and Evaluation of Sublingual Tablet of Losartan Potassium. Asian Journal of Pharmaceutical Research and Development. 2018 Aug;6(4):54-66.
4. Siji C, Augusthy AR, Vipin KV. Formulation and evaluation of carvedilol sublingual tablet. Indo american journal of pharmaceutical sciences. 2018 Feb;5(2):1043-50
5. Singh H, Jaiswal P, Gupta S, Singh S. Formulation of rizatriptan benzoate sublingual tablets prepared by direct compression with different bioadhesive polymer: in vitro and ex vivo evaluation. Asian Journal of Pharmaceutical and Clinical Research. 2017 Sep:36-42
6. Hadi MA. Formulation and evaluation of sublingual tablets of felodipine for the treatment of hypertension. Indo american journal of pharmaceutical sciences. 2017 Dec;4(12):4781.
7. Al-Madhagi W, Albarakani AA, Alhag AK, Saeed ZA, Noman NM, Mohamed K. Formulation and Evaluation of New Glimepiride Sublingual Tablets. Journal of pharmaceutics. 2017;2017.

8. Bhanja SB, Ellaiah P, Roy HK, Samal BK, Tiwari S, Murthy KV. Formulation and evaluation of perindopril sublingual tablets. International Journal of Research in Pharmaceutical and Biomedical Sciences. 2011 Jul;2(3):1193-8.
9. Pawar PP, Ghorpade HS, Kokane BA. Sublingual route for systemic drug delivery. Journal of Drug Delivery and Therapeutics. 2018 Dec;8(6-s):340-3.
10. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 2092, Alfuzosin. Retrieved July 12, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/Alfuzosin.
11. Ritesh Patel, Patel H, Patel G, 'Optimization of Propanolol Hydrochloride Controlled Released Matrix Tablet Using Factorial Design, 2010, Article id- WMC 00914, Webmed Central Pharmaceutical Sciences.
12. Shinde Anilkumar J. Waghule Arun N. Paithane Amol, "Development and Characterization of Oral Fast Dissolving Tablet of Nifedipin Using Camphor as A Subliming Material." Research Journal of Pharmaceutical and Clinical Reseach. 2010; 1: 46-50.
13. Odou P, Barthelemy C, Robert H. Development of Midazolam Sublingual Tablets: In Vitro Study. Eur J Drug Metab Pharmacokinet. 1998;23(2):87-91.
14. Chetty DJ, Chen LL, Chien YW. Characterization Of Captopril Sublingual Permeation: Determination of Preferred Routes and Mechanisms. J Pharm Sci. 2001;90(11):1868-77.
15. Leon L, Herbert AL. Pharmaceutical Dosage Forms: Tablets. In: The Theory and Practice of Industrial Pharmacy. 3rd ed, New York: Lea and Febiger; 1991. p. 293-345.
16. Subrahmanyam CVS. Textbook of Physical Pharmaceutics 2nd edition. New Delhi: Vallabh Prakashan; 2003. p. 180-234.
17. Aburahma MH, El-Laithy HM, El-Said Hamza Y. Preparation And In Vitro/In Vivo Characterization of Porous Sublingual Tablets Containing Ternary Kneaded Solid System of Vinpocetine With B-Cyclodextrin and Hydroxy Acid. Sci Pharm. 2010; 78:363–79.
18. Bayrak Z, Tas C, Tasdemir U, Erol H, Ozkan CK, Savaser A, Ozkan Y. Formulation of Zolmitriptan Sublingual Tablets Prepared by Direct Compression with Different Polymers: In Vitro And In Vivo Evaluation. Eur J Pharm Biopharm. 2011; 78:499–505.
19. Martindale. The Complete Drug Reference. 37th Edition. London, Pharmaceutical Press, 2011; Vol 2: 1108-1109.
20. Gale G.D., Galloon S., Porter W.R., Sublingual Lorazepam: A Better Premedication. Br. J. Anaesth., 1983; 55(8): 761-765.
21. Yager J.Y., Seshia S.S., Sublingual Lorazepam in Childhood Serial Seizures. Am. J. Dis. Child., 1988; 142(9): 931-932
22. O'Boyle C.A., Barry H., Fox E., Mccreary C., Bewley A., Controlled Comparison of A New Sublingual Lormetazepam Formulation And I.V. Diazepam In Outpatient Minor Oral Surgery. Br. J. Anaesth., 1988; 60(4): 419-425.
23. Costas C.D., Coronado Quesada E., Rubio H., Simple-Blind Clinical Study With Sublingual Lorazepam Vs. Injectable Diazepam As Premedication In Colonoscopies. Acta Gastroenterol Latinoam., 1985; 15(1): 43-48. 9
24. Battrum D., Lorazepam Sublingual for The Nervous Dental Patient. J. Can. Dent. Assoc., 1988; 54(1): 41-42.
25. Caille G., Lacasse Y., Vezina M., Porter R., Shaar S., Darke A., A Novel Route for Benzodiazepine Administation: A Sublingual Formulation of Lorazepam, In: Advances in Neurotoxicology. Manzo L. Ed., Oxford And New York: Pergammon Press, 1980.
26. Moffat A.C. Absorption of Drugs through the Oral Mucosa. Top. Med. Chem 1971; 4: 21-29. 2.
27. Susanne B., Margareta D., Christer N. Invitro and Invivo Evaluation of a New Sublingual Tablet System for Rapid Oromucosal Absorption Using Fentanyl Citrate as the Active Substance. Eurp Jour Pharm Sci 2003; 20: 327-334.
28. Berner B., Birudaraj R., Shen S., Li X. Buccal Permeation of Buspirone: Mechanistic Studies on Transport Pathways. J. Pharm Sci. 2005; 94: 70-78.
29. Ishikawa T., Koizumi N., Mukai B. Pharmacokinetics of Acetaminophen from Rapidly Disintegrating Compressed Tablet Prepared Using Microcrystalline Cellulose and Spherical Sugar Granules. Chem Pharm Bull 2001; 49: 230-32.

.