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Formulation and evaluation of salbutamol sulphate sublingual tablets

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ABSTRACT

Salbutamol sulfate is a selective B2 bronchodilator which is used in the treatment of asthma. Conventional Salbutamol tablets available in the market are not suitable where quick onset of action is required. Salbutamol sulfate sublingual tablets were prepared by using mannitol, Aspartame, aerosil, magnesium steartate, talc and natural super disintegrants like karaya gum, locust bean gum, gellan gum by direct compression method.F6 formulation of locust bean gum was seleted as best formulation. It was shown less disintegration time of 12 seconds. It was observed that less disintegration time was observed when locust bean gum was used as natural super disintegrant, may be due to swelling at faster rate upon contact with water and elimination of lump formation after disintegration when compared with gum karaya and gellan gum. F6 formulation was found to be the best as this formulation shown less disintegration time and possessing good tabletting properties. The bioavailability of salbutamol sulfate is 44%. Bioavailability also can be increased using natural superdisintegrants. Sublingual absorption avoids first pass metabolism.

Keywords: Saluabutamol Sulphate, Sublingual, First Pass Metabolism.

INTRODUCTION

Tablets Sublingual meaning literally ‘under the tongue’ refers to a method of administering substances via the mouth in such a way that the substances are rapidly absorbed via the blood vessels under the tongue rather than viathe digestive tract. The routes of absorption via the highly vascularised buccal mucosa allow the substance a more direct access to the blood circulation, thus providing direct systemic administration medically, sublingual drug administration is applied in the field of cardiovascular drugs, steroids, some barbiturates and enzymes. It has been a developing field in the administration of many vitamins and minerals which are found to be readily and thoroughly absorbed by this method [1].

There is considerable evidence that most sublingual substances are absorbed by simple diffusion;

The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes. The sublingual dosage formoffers fast release of drug from the formulation and it reaches the systemic circulation directly, which bypasses the metabolism of the salbutamol in the liver and offers a fast relive form the anginal pain, hypertension which will be worth in such conditions [2].

MATERIAL AND METHODS

Salbutamol sulphate (A.P.I) and gelllan gum were obtained from yarrow chemicals, Mumbai. Locust bean gum, karaya gum were obtained from S.D. Fine chemicals. Mannitol, Talc and Magnesium stearate, aspertamate, aerosols were obtained from S.D. Fine Chemicals. Pvt Ltd, Mumbai, India. All chemicals and solvents used were of analytical grade.

Table 1: Formulation of sublingual tablets

S.no	Ingredients (Mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1.	Salbutamol	2	2	2	2	2	2	2	2	2	2	2	2
2.	Gum karaya	10	12	14	16	-	-	-	-	-	-	-	-
3.	Gellan gum	-	-	-	-	20	22	24	26	-	-	-	-
4.	Locust bean gum	-	-	-	-	-	-	-	-	10	15	20	25
5.	Mannitol	78	76	74	72	68	66	64	62	78	76	74	72
6.	Aspartame	4	4	4	4	4	4	4	4	4	4	4	4
7.	Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
8.	Talc	2	2	2	2	2	2	2	2	2	2	2	2
9.	Aerosil	2	2	2	2	2	2	2	2	2	2	2	2
10.	Total Wt.	100	100	100	100	100	100	100	100	100	100	100	100

METHODOLOGY

Formulation of sublingual tablets: Salbutamol sulphate sublingual tablets were prepared by the direct compression method using different excipients. The excipients used were mannitol, aerosol (antiglident), Aspartame (sweetening agent), Magnesium stearate , Talc were used as lubricants, Locust bean gum, karaya gum, gelllan gum (super disintegrants). Different concentrations of excipients were used to prepare different formulations of sublingual tablets. Compositions of various formulations are shown in Table 1. All the ingredients of the sublingual tablets of Salbutamol sulphatewere weighed and mixed in mortar with the help of pestle. Then the blended material was slightly compressed on the 8mm punch.

Evaluation

Pre-compression studies of formulated sublingual tablets of Salbutamol sulphate

The following parameters were evaluated

Bulk density, Tapped density, Compressibility index, Hausner's Ratio

Post-compression studies formulated sublingual tablets of Salbutamol sulphate

The following parameters were evaluation Hardness, Thickness, Friability, Content uniformity.

In-vitro disintegration time

The USP device to rest disintegration was six glass tubes are “3 long, open at the top and held against 10” screen at the bottom and of the basket rack assembly. One tabletis placed in each tube and the basket rack is poisoned in 1 litre beaker of buffer at37+2°C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.[8]

Invitro release studies

In-vitro drug release of Salbutamol sulfate sublingual anti-asthmatic tablets were determined using USP Dissolution Apparatus II (Paddle type) (Electrolab TDT-08L).the dissolution test was performed using 900ml 6.8 pH buffer at 37°C+0.5°C. The speed of rotation of paddle was set at 50rpm. 5ml samples were withdrawn at time points of 1,2,3,4,5,10,15,20,25,and 30 min and same volume was replaced with fresh media. Absorbance of solution was checked by UV spectrophotometer (ELICO-164double beam spectrophotometer, Hyderabad, India) at a wavelength of 205nm and drug release was determined from standard curve.[9]

Accelerated stability studies

The optimized formulation was subjected to stability studies at 40°C+75%RH for period of three months. Each tablet was individually wrapped in aluminium foil and packed in ambered colored bottle and put at above specified condition in a heating humidity chamber for three months. For every one month tablets were analyzed for the hardness, friability disintegration time, drug content

and in-vitro drug release. Theresults are obtained within the limits.[10]

RESULTS AND DISCUSSION

Drug-Excipient compatibility studies

The drug polymer and polymer-polymer interaction was studied by the FTIR spectrometer using Shimadzu 8400-S, Japan. Two percent (w/w) of the sample with respect to a potassium bromide disc was mixed with dry KBr. The mixture was grind into a fine powder using an agate mortar and then compressed into a KBr disc in a hydraulic press at a pressure of 1000psi. Each KBr disc was scanned 16 times at 2 mm/sec at a resolution of 4 cm-1 using cosine apodization. The characteristic peaks were recorded.

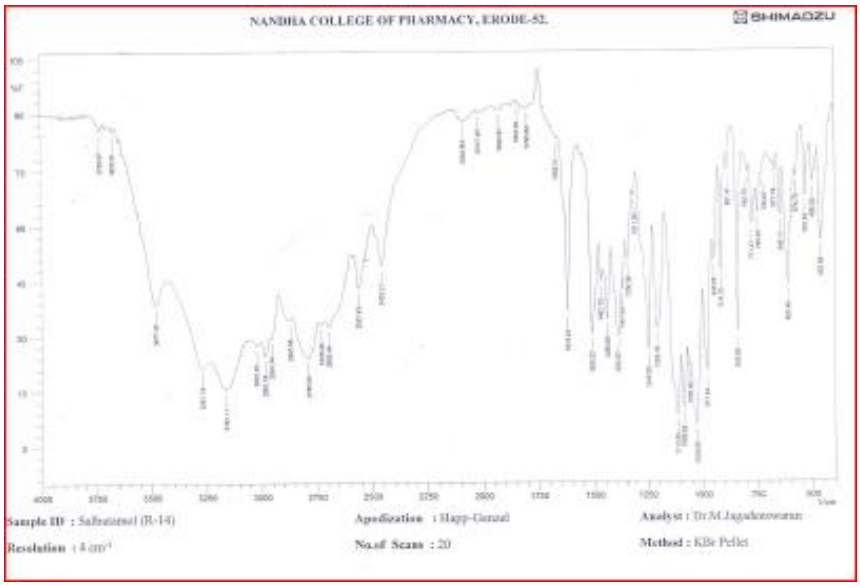

Figure No: 1 FTIR Spectra of Salbutamol sulphate

Table No: 3 FTIR Spectra of Salbutamol sulphate

S.No	Functional group present	Type of vibration	Reference peak (cm-1)	Observed peak (cm-1)
1	Phenolic	O-H stretch	1200	1205.43
2	Alcholic	O-H stretch	1350-1260	1056.92
3	20 amine	N-H stretch	1650-1550	1669.34
4		C-CH3	2972-2953	2954.74

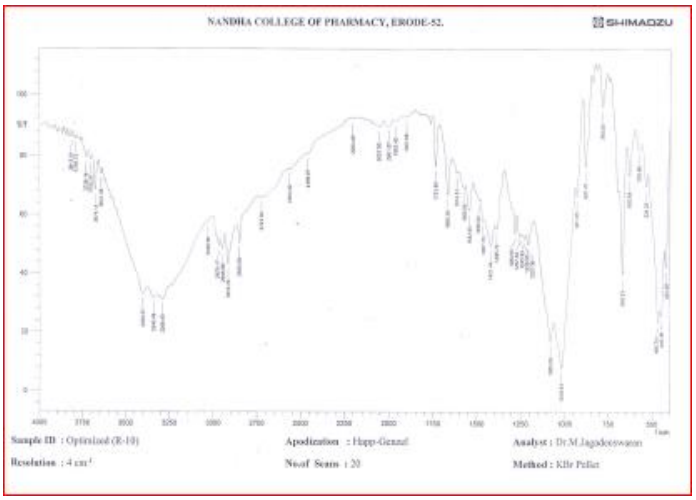

Figure No:2 FTIR spectra of Optimized formulation

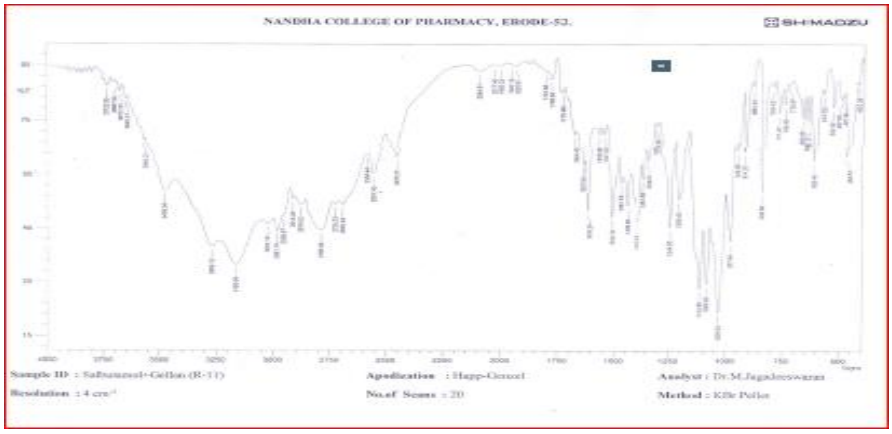

Figure No: 3 FTIR spectra of Salbutamol sulfate+ Gellan gum

PRECOMPRESSION PARAMETERS

The hardness of the tablets was found to be 3.1±0.3-3.8±0.4 (kg/cm²) and friability was foundto be below 1% indicating good mechanical resistance. The thickness of the tablets was found to be 2.9±0.3-2.0±0.1 (mm). All the tablets passed weight variation test, as percentage weight variation was within the pharmacopoeial limits i.e.±7.5% and the values were found to be in the range of 101±0.54-94±0.65 (mg).

The most important parameter that needs to be optimized in the development of sublingual tablets is the disintegration time of tablets. In the present study disintegration time of all batches were found in the range of 17±0.59-49±0.1 (sec) fulfilling the official requirements(less than 1 min) for disintegrating tablets.

F6 formulation of gellan gum was selected as best formulation. It as it shown less disintegration time of 17 seconds. It was observed that less disintegration time was observed when Gellan gum was used as natural super disintegrant, may be due to swelling at fasterrate upon contact with water and elimination of lump formation after disintegration when compared with gum karaya and gellan gum.

Table No: 4 Pre-compression parameters of sublingual Tablets

Formulation Code	Bulk density	Tapped density	Carr's Index	Hausner's ratio	Angle of repose
F1	0.40±0.13	0.46±0.17	13±0.22	1.12±0.54	23±0.24
F2	0.42±0.12	0.49±0.15	10±0.32	1.12±0.43	22±0.25
F3	0.43±0.15	0.50±0.12	14±0.43	1.12±0.75	24±0.45
F4	0.49±0.10	0.53±0.14	12±0.61	1.12±0.65	20±0.54
F5	0.53±0.11	0.57±0.13	11±0.32	1.11±0.64	24±0.25
F6	0.39±0.14	0.45±0.15	10±0.42	1.10±0.72	20±0.24
F7	0.50±0.13	0.66±0.24	17±0.71	1.12±0.45	22±0.56
F8	0.56±0.24	0.70±0.15	16±0.21	1.12±0.51	24±0.12
F9	0.59±0.34	0.71±0.14	18±0.32	1.10±0.56	22±0.13
F10	0.79±0.43	0.64±0.41	19±0.14	1.11±0.54	23±0.12
F11	0.54±0.31	0.40±0.15	15±0.22	1.12±0.46	24±0.02
F12	0.86±0.42	0.56±0.32	14±0.12	1.12±0.41	22±0.14

Table No: 5 Post-compression parameters of sublingual Tablets

S. No.	Formulation code	Hardness (Kg/cm2)	Thickness (mm)	Friability (%)	Disintegration time(sec)	Weight Variation (mg)
1	F1	3.2±0.1	2.0±0.3	0.55±0.4	41±0.5	101±0.54
2	F2	3.6±0.4	2.1±0.4	0.53±0.2	42±0.2	98±0.45
3	F3	3.3±0.3	2.±0.5	0.64±0.1	46±0.3	97±0.65
4	F4	3.5±0.2	2.3±0.3	0.71±0.5	44±0.1	96±0.32

5	F5	3.1±0.3	2.4±0.2	0.86±0.6	30±0.4	94±0.65
6	F6	3.3±0.6	2.1±0.3	0.56±0.7	17±0.5	100±0.54
7	F7	3.2±0.8	2.6±0.5	0.64±0.8	46±0.2	98±0.64
8	F8	3.4±0.7	2.1±0.6	0.61±0.9	44±0.4	99±0.62
9	F9	3.5±0.5	2.5±0.2	0.69±0.4	48±0.1	95±0.54
10	F10	3.8±0.4	2.9±0.3	0.79±0.2	28±0.4	94±0.76
11	F11	3.3±0.6	2.1±0.1	0.46±0.5	29±0.5	100±0.65
12	F12	3.5±0.9	2.3±0.4	0.58±0.3	30±0.1	96±0.65

Invitro drug release

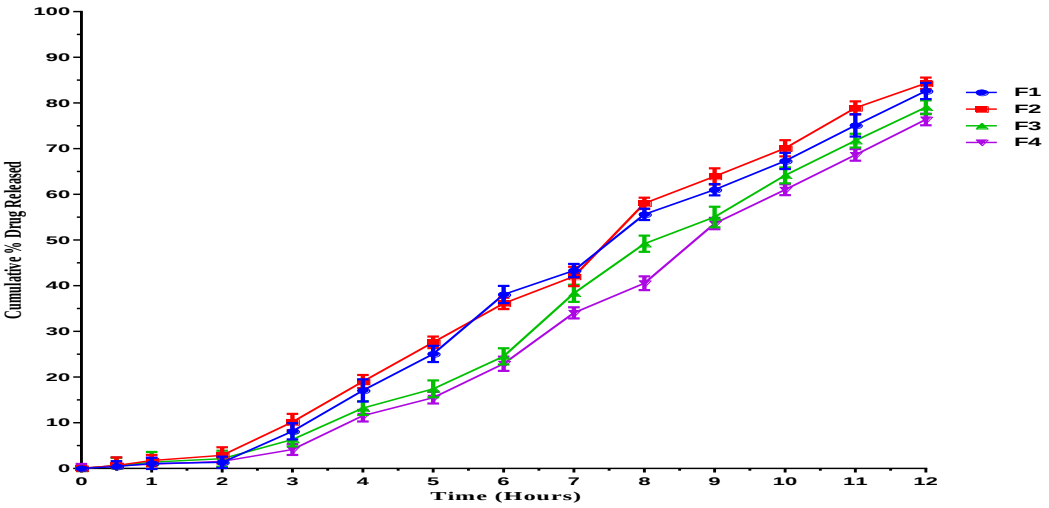

Figure No.6 Invitro drug release of salbutamol sulfate from F1-F4

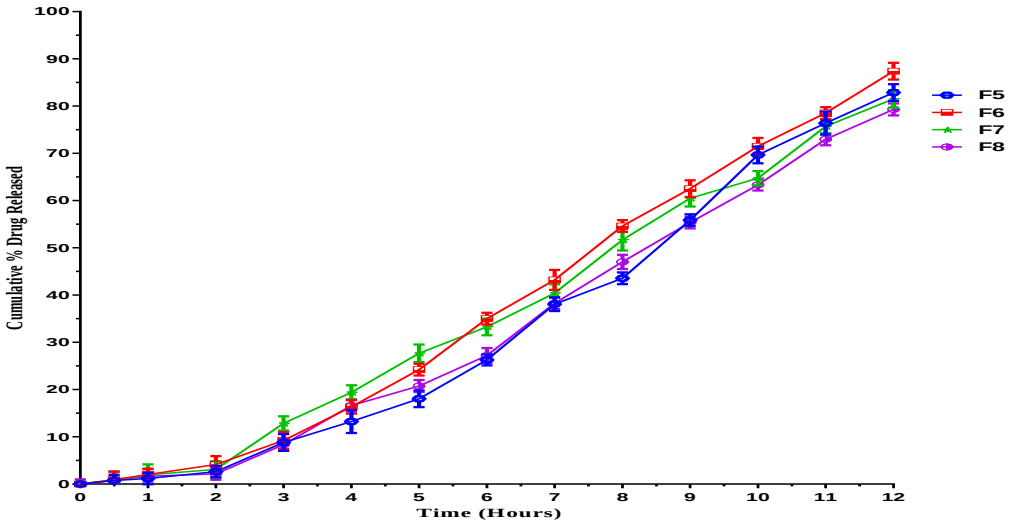

Figure No.7 Invitro drug release of salbutamol sulfate from F6-F8

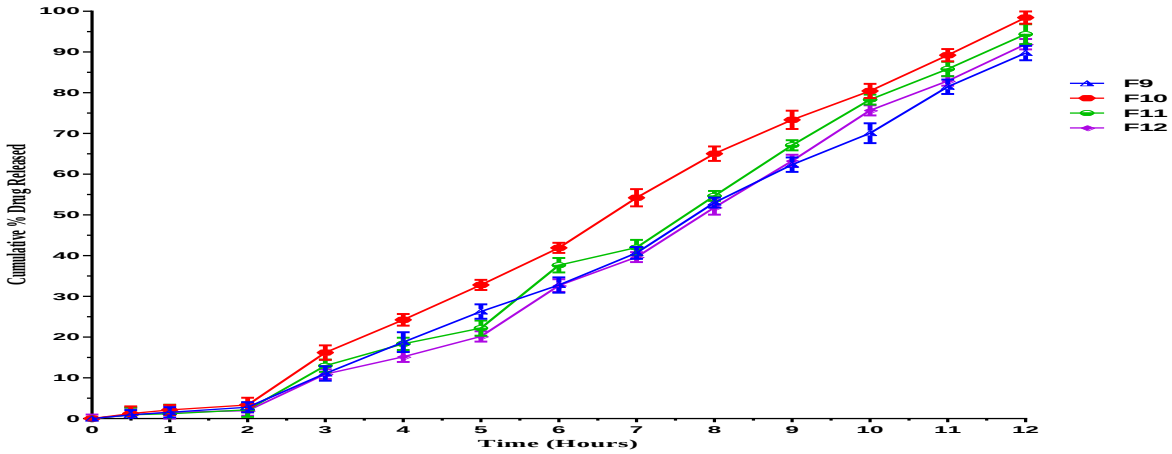

Figure No.8 Invitro drug release of salbutamol sulfate from F9-F10

CONCLUSIONS

The concept of sublingual tablets containing salbutamol sulfate offers a suitable and practical approach in serving the desired objective of asthma. The excipients used in the formulation were inexpensive and are easily available. Most of the excipients used in formulation are water-soluble and hence have better-patient acceptability. The present work of optimized formulation of a sublingual tablet containing Salbutamol was successful in terms of reducing manufacturing difficulties, cost and providing a better patient compliance with effective medication. It has been observed from the above study that excipients like mannitol, aspartame, aerosil etc. were ideal excipients and effective for formulating sublingual tablets. F6formulation was considered to be the best among all other batches since it exhibited a good dissolution profile, disintegration time, uniformity of drug content and further good stability and In vitro absorption profile. Disintegration time of F6 formulation was found to be 15sec. In the present study, it was revealed that use of natural super disintegrates can produce tablets that provide less than 1min Disintegration Time and less than 10 min t 90% .Formulation F6 was subjected to further stability studies. Stability study was carried out at 45°C and 75% RH according to the ICH guidelines. The samples were analyzed at intervals of first month for the drug content and dissolution profile and disintegration time. The results indicated that there was no significant variation in the formulations.

SUMMARY

The present work is an attempt to formulate and evaluate sublingual tablets of salbutamol sulfate using natural superdisintegrants. This dosage form is associated with many advantages like quick onset of action and it bypasses the liver. Especially, in case of management of asthma. Sublingual tablets provide effective and easier way of medication. Compared to commonly used tablets, capsules and other oral dosage forms, sublingual absorption is generally much faster and more efficient. Sublingual dosages are convenient for young children, the elderly and patients with swallowing difficulties, and in situations where potable liquids are not available. Peak blood levels of most products administered sublingually are achieved within 10-15 minutes, which is generally much faster than when those same drugs are ingested orally. The percent of each dose absorbed is generally higher than that achieved by means of oral ingestion.Various types of sublingual dosage forms are available in market like tablets, films and sprays. Sublingual absorption is efficient. The percent of each dose absorbed is generally higher than that achieved by means of oral ingestion. Salbutamol sulfate sublingual tablets drug release appears to be a safe, well-tolerated option for treating early and advanced asthma. This medication has a wide spectrum of use in treating asthma. Asthma is a common long-term inflammatory disease of the airways of the lungs. It is characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. Symptoms include episodes of wheezing, coughing, chest tightness, and shortness of breath. These episodes may occur a few times a day or a few times per week. Depending on the person, they may become worse at night or with exercise Rapidly, sublingual tablets can be prepared by the existing direct compression method using salbutamol

sulfate drug with natural superdisintegrants in the range of concentrations such as Gum karaya F1-F4 (10-16%), Gellan gum (20-26%) and Locust bean gum (10-25%).

REFERENCES

[1]. NareshB.Rajgor, Manish Patel, Viral M. Shah, VH Bhaskar, Ganesh C.Rajput,'Preparation and Characterization of Terbutaline Sulphate Microsphere'., 2(5), 2010, 450-459

[2]. KuldeepMalodia, Anil Kumar, Sunil Kumar and PankajRakha' Formulation and evaluation of extended release tablets of salbutamol sulphate'. 5(1), 2013, 177.

[3]. SardarmalYadav, Shiv Garg, Ashish Kumar Pareek, Pradeep Kumar and Manoj kumar'Formulation and optimization of sublingual tablet of Ramipril', Journal of Chemical and Pharmaceutical research. 7(8), 2015, 1078.

[4]. NandvishalV.Deore, Vinod M. Thakare, Bharat W.Tekade, Vijay R. Patil, 'Formulation and evaluation ofTerbutaline sulphate pulsatile drug delivery system', 1(3), 2012, 1004-1015.

[5]. Sudhir R lliger, Ashwini S. Joshi, BhautikV.Patel. 'Formulation and In-vitro Evaluation of Sublingual Tablets of Ondansetron Hydrochloride using CoprocessedExcipients', Indian Journal of Pharmaceutical Education and Research. 2014, 9.

[6]. Shalin P.Thakker, Sudhir R lliger, Ashwini S. Joshi, BhautikV.Patel(2014)'Formulation and In-vitro Evaluation of Sublingual Tablets of Ondansetron Hydrochloride using CoprocessedExcipients',Indian Journal of Pharmaceutical Education and Research., 2014, 9.

[7]. AshwiniRajendra,ShivakumarS,SridharBk, 'Preparation and Evaluation of Extended Release Matrix Tablets of Diltiazem Using Blends of Tamarind Xyloglucan with Gellan gum and sodium carboxy methyl cellulose',Scholars Research Library., 3(4), 2011, 383.

[8]. ShivGarg, Ashish Kumar Pareek, Pradeep Kumar and Manoj kumar'Formulation and optimization of sublingual tablet of Ramipril', Journal of Chemical and Pharmaceutical research, 7(8), 2015, 1081.

[9]. Ashish Kumar Pareek, Pradeep Kumar and Manoj kumar'Formulation and optimization of sublingual tablet of Ramipril',Journal of Chemical and Pharmaceutical research., 7(8), 2015, 1081

[10]. Manoj kumar'Formulation and optimization of sublingual tablet of Ramipril', Journal of Chemical and Pharmaceutical research., 7(8), 2015, 1082.