EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 1
312-318
Year: 2016

FORMULATION AND IN-VITRO EVALUATION OF ORALLY-DISSOLVING MONTELUKAST SODIUM THIN FILM

Akelesh T*, Nimisha MP, Sam Johnson Udaya Chander J, Venkatanarayanan R, Senthil Kumar C

Department of Pharmaceutics, R.V. S College of Pharmaceutical Sciences, Sulur - 641402, Coimbatore, Tamil Nadu, India.

***Author for Correspondence: Akelesh T.**

Department of Pharmaceutics, R.V. S College of Pharmaceutical Sciences, Sulur - 641402, Coimbatore, Tamil Nadu, India.

Article Received on 18/11/2015 **Article Revised on 10/12/2015** **Article Accepted on 01/01/2016**

ABSTRACT

Montelukast sodium is a leukotriene receptor antagonist (LTRA) is indicated for the prophylactic therapy of mild-to-moderate asthma and to relieve symptoms of seasonal allergies. The oral thin film is a dosage form which, when placed in the oral cavity, quickly gets hydrated and then disintegrates to release the drug. The purpose of the present study is to formulate oral thin film of Montelukast sodium by solvent casting method using hydrophilic polymers like HPMC, methyl cellulose and sodium CMC with PEG400 as plasticizer. Mannitol was used as the sweetening agent and it also helps in disintegration. Menthol used as the flavouring agent. The compatibility of the drug in the formulation was confirmed by FT-IR studies. By varying concentration of polymers, nine formulations (F1-F9) were formulated. The prepared oral thin films were evaluated for physical appearance, weight variation, thickness, surface pH, folding endurance, drug content, moisture absorption, disintegration time and *in-vitro* dissolution studies. The prepared films were clear, transparent and had smooth surface. *In-vitro* dissolution studies revealed higher drug release from formulation F7, releases 98.94% at the end of 300 seconds and considered as the best formulation. The stability studies were carried out, which does not show any significant changes after three months.

KEYWORDS: Oral thin film, Montelukast Sodium, HPMC, Sodium CMC, Methyl cellulose, Solvent casting.

1. INTRODUCTION

The most common and convenient route for the administration of drug molecule is the oral route. Tablets and capsules are the most popular oral dosage forms used, that include conventional and controlled- release tablets as well as hard and soft gelatin capsules; however, many patients have difficulty in swallowing tablets and hard gelatine capsules and therefore do not take medication as prescribed by the physicians. Paediatric and geriatric patients in particular experienced the greatest difficulty in swallowing tablets as well as people who are ill and supine in bed and those patients who are busy travelling without having water. In order to overcome these difficulties of the traditional oral solid dosage forms, fast-dissolving drug delivery systems have been developed.

The fast dissolving drug delivery system was developed during the late 1970s as an alternative to tablets, capsules and syrups for paediatric and geriatric patients who experience difficulties in swallowing the oral solid dosage forms. The fast dissolving oral drug delivery systems will dissolve or disperse quickly in seconds to few minutes after placement in the mouth without water, can avoid the problem of swallowing of tablet. They offer substantial advantage over ordinary tablets, are more convenient to administer in as much as drinking water is not required, and enhance the potential for improved compliance in patients who have difficulty in taking tablets. The fast dissolving systems include tablets, wafers, films, granules and powders.

The oral medicated thin film can be defined as a “dosage form that employs a water- dissolving polymer which allows the dosage form to quickly hydrate, adhere, and dissolve when placed on the tongue or in the oral cavity to provide rapid local or systemic drug delivery”. Oral thin films have the postage stamp size which contains active pharmaceutical ingredients and excipients. Efficacy of the API is improved as it dissolves in the oral cavity.

Oral films disintegrate rapidly within few seconds when it comes in contact with saliva without need of water. These are useful for the geriatric and paediatric patients and also for the patients suffering from emesis, diarrhoea, allergic attacks, cough, mental disorders, bedridden patients etc. Oral films are also used for local effects like local anaesthetics for oral ulcers, toothaches, cold scars. Generally the shelf life of film is 2-3 years it depends on the API added to the film.

Ideal features of the oral thin film

- Do not require water to swallow and should dissolve or disintegrate in the mouth in few seconds.
- Compatible with taste masking and other excipients.
- Leave minimal or no residue in the mouth after oral administration.
- Resistant to environmental conditions such as humidity and temperature.
- They are adaptable to the existing processing and packaging machinery.
- Processing and packaging can be done at low cost.
- Should have excellent mucoadhesion.

Advantages of oral thin film

- Oral cavity has larger surface area which leads to rapid dissolution and disintegration of the oral dosage form.
- Oral thin films are solid unit dosage form, so provide accurate dosing and great precision.
- No risk of chocking.
- Due to pregastric absorption the bioavailability of drug is improved and fewer doses are required which improve the patient compliance.
- Oral thin film does not require water to swallow so it has better acceptability for the dysphagic patients.
- Provide good mouth feel.
- Oral films are flexible and less fragile so it can easily transport, handled and stored.
- It avoid first pass metabolism as it directly absorb from oral cavity via mucosa and enter in to the systemic circulation, hence the dose and side effect are reduced.
- Fast dissolving films disintegrate immediately within seconds when placed on tongue without the need of water and release the medicament.
- Stability of the dosage form is enhanced.

Disadvantages of oral thin film

- High dose cannot be incorporated.
- Drug should have low dose.
- Oral films have expensive packaging.
- This dosage form is moisture sensitive.

2. MATERIALS

Montelukast sodium was received as a gift sample. The polymers HPMC, Methyl cellulose and Sodium CMC were obtained from SD fine-chem. Ltd, Mumbai, and PEG 400 received from Himedia Laboratories Pvt. Ltd, Mumbai.

2.1. Compatibility studies of drug and polymer

The drug-excipients interaction study was carried out by using Infrared Spectroscopy. FTIR study was carried out to check compatibility of drugs with excipients. IR spectrum of drug and optimized formulation were determined on Fourier Transform Infrared spectrophotometer using KBr pellet method.

3. METHOD

3.1 Preparation of Montelukast sodium oral thin film.

The oral thin films of Montelukast sodium were prepared by solvent casting method, using the film forming polymers, SodiumCMC, Methyl cellulose and HPMC.

The accurately weighed amount of polymer was dispersed in three fourth volume of distilled water, with continuous stirring. The calculated amount of the Montelukast sodium was incorporated in to the polymeric solutions. Calculated amount of mannitol, menthol were added to the polymeric solution and then poly ethylene glycol was added, the final volume was adjusted up to 10 ml with distilled water. PEG 400 was used as the plasticizer, mannitol as sweetening agent and menthol as the flavouring agent. The solution kept aside for sometime without disturbance. And the resulting bubble free viscous solution was casted on to a petridish. The area of the petridish was 63.58cm^2. These petridishes kept in the hot air oven at 40^{0}C for 24 hours. The films were cut in to size of 2×2 cm^2 containing 5 mg of Montelukast sodium.

Table.1: Formulation Batches of Montelukast sodium oral thin film.

Ingredients	Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Montelukast sodium (mg)	9.45	79.45	79.45	79.45	79.45	79.45	79.45	79.45	79.45
SodiumCMC (mg)	100	200	300	-	-	-	-	-	-
Methylcellulose (mg)	-	-	-	100	200	300	-	-	-
HPMC (mg)	-	-	-	-	-	-	100	200	300
PEG 400 (ml)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Mannitol (mg)	5	5	5	5	5	5	5	5	5
Menthol	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Water up to(ml)	10	10	10	10	10	10	10	10	10

4. EVALUATION

4.1 Physical appearance and surface texture[7, 8]: The physical appearance was checked visually and surface texture was evaluated by touch or feel of the film.

4.2 Weight uniformity test: The formulated oral thin films were cut at different regions, and each films having area 4cm^2 weighed separately using an electronic balance. Average weight was calculated.

4.3 Thickness of film[8]: Film thickness of 3 films was measured with the help of screw guage. The film was placed between the two jaws and the thickness of each film was measured. And mean value calculated.

4.4 Surface pH[8,14]: The formulated films evaluated for the surface pH, the film was placed in a petridish and was moistened with 0.5ml of distilled water and kept for 30sec. The pH was noted by bringing the electrode of the pH meter in contact with the surface of the formulation.

4.5 Folding endurance[8]: The folding endurance of the formulated oral thin film was measured manually. A film of area 4cm^2 was cut and repeatedly folded at the same place till it gets broke. The number of times the film can be folded at the same place without any breaking gave the value of folding endurance.

4.6 Percentage moisture absorption[14]: The films were weighed individually and kept in a dessicator containing 100ml of saturated solution of aluminium chloride and 75±5%RH was maintained. After three days, the films were taken out and reweighed. The percentage moisture absorption was calculated using the following formula

% moisture absorption= (final weight-initial weight/initial weight) ×100

4.7 Tensile strength[14,34]: Tensile strength is the maximum stress applied to a point at which the film breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the film as given in the equation below,

Tensile strength = Break force/ cross sectional area of the sample.

4.8 Content uniformity[14]: The drug content of the films from every batch was estimated. From each batch of oral thin film, the films of area 4cm^2 was cut, and dissolved in100ml of buffer using magnetic stirrer for one hour. The drug concentration was then evaluated spectrophotometrically at λ_{max} of 341nm. The experiment was repeated three more times to validate the results.

4.9 In vitro disintegration time[15]

The in vitro disintegration time is determined visually, a glass petridish was filled with 10 ml of phosphate buffer (pH 6.8), and the film (4cm^{2}area) was carefully placed in the centre. The set up was kept undisturbed. The time at which the film starts to break or disintegrate was noted. The test was performed three times on each formulation and the mean value determined.

4.10 In vitro dissolution studies[14]

The dissolution studies were carried out for determining the drug release from the oral thin films. The dissolution

Drug – Polymer compatibility studies

studies of the films were carried out by using USP type1 (basket apparatus) with 300 ml of phosphate buffer pH 6.8, temperature maintained at 37±0.5^{0}C. Medium was stirred at 50 rpm. 5 ml samples were withdrawn at every 50 seconds of intervals, replacing the same amount with fresh medium. Amount of drug in the withdrawn samples was determined by UV spectrophotometrically at 341 nm.

5. RESULTS AND DISCUSSION

5.1 PRELIMINARY SCREENING

Drug

Physical appearance: The drug was found to be odourless and off white powder.

UV scanning of Montelukast sodium in pH 6.8 buffer

The prepared solution of Montelukast sodium in pH 6.8 phosphate buffer solution was scanned by UV spectrophotometer. From the UV spectrum of Montelukast sodium, it was concluded that the drug has λ_{max} of 341nm.

Standard curve of Montelukast sodium in pH 6.8 phosphate buffer

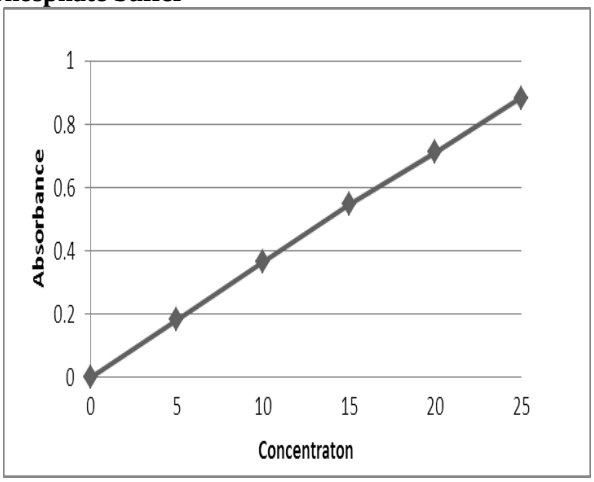

Fig: 1. Standard calibration curve of Montelukast sodium in phosphate buffer 6.8

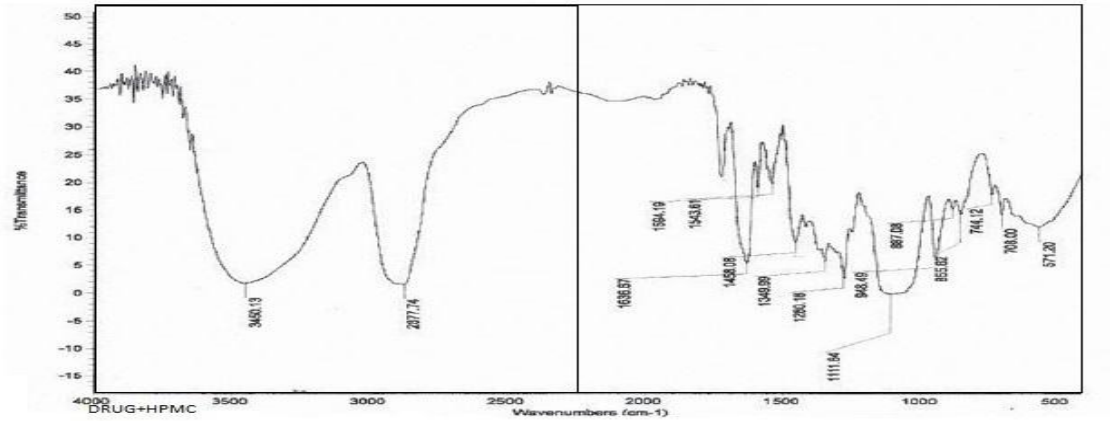

Fig: 2. FT IR spectrum of optimised formulation (F7)

The drug polymer interaction was checked by the IR spectrum of the optimised formulation with the IR spectrum of the drug. The chief absorption bands of drug are present in the montelukast sodium excipients mixture with same degree of sharpness and position; it indicates that there is absence of physical and chemical interactions among both active component and the excipients.

Table.2: IR Spectral data of drug and polymer (F7 formulation)

Group responsible	Frequency of drug	Frequency of formulation(cm^{-1})
O-H	3432.12	3450.13
C-H	2966.00	2977.74
C=O	1636.43	1636.57
C-N	1265.02	1280.16

5.2 EVALUATION

Physical appearance and surface texture

All the films were found to be transparent and the surfaces of the films were smooth in nature. It was concluded that the films were elegant.

Weight uniformity test

The drug loaded films were tested for uniformity of weight. The weight of the films ranges from 10.26±0.016-26.14±0.012. The weight of the films was increased with increasing the concentration of the polymers.

Thickness

Drug loaded oral thin films were tested for thickness using micrometer screw guage. From the results it inferred that the formulation F7 has least thickness.

The thickness of the oral thin films was increased with increasing the concentration of the polymers.

Folding endurance

The drug loaded oral thin films were tested for folding endurance, which measures the ability of the film to withstand rupturing. The results inferred that the formulation F9 have highest folding endurance.

Tensile strength

The formulated oral thin films were tested for tensile strength. The results inferred that the tensile strength of the film increases with increasing the polymer concentration.

Drug content

Test for drug content uniformity was carried out. The drug content for the formulation was found to be in the range of 98.82±0.6% to 99.66±0.27%, which showed that there was uniform distribution of the drug in the oral thin films of all formulations within the limits.

Percentage moisture absorption

Prepared oral thin films were tested for the moisture absorption. The polymers used are hydrophilic in nature. The results inferred that on increasing the amount of hydrophilic polymers the moisture absorption also increased.

Surface pH: The prepared formulations were tested for surface pH. The surface pH of the formulations ranges from 6.62±0.048 to 6.9±0.02, which is close to the salivary pH and hence no irritation was expected.

Disintegration time Disintegration time of formulations was found in the range of 28-86 seconds.

Table.3: Evaluation of Montelukast sodium oral thin film

Formulations	Appearance	Weight of films	Thickness of films	Folding endurance	Tensile strength	Surface pH	% moisture absorption
F1	Transparent	11.12 ±0.01	0.08 ±0.016	210 ±0.01	1.41 ±0.02	6.72 ±0.04	1.54 ±0.012
F2	Transparent	17.13 ±0.01	0.11 ±0.014	252 ±0.02	1.61 ±0.018	6.78 ±0.02	2.12 ±0.01
F3	Transparent	24.18 ±0.01	0.17 ±0.014	285 ±0.024	1.82 ±0.02	6.9 ±0.02	2.64 ±0.01
F4	Transparent	10.26 ±.0.016	0.068 ±0.012	238 ±0.01	1.14 ±0.03	6.62 ±0.048	1.49 ±0.05
F5	Transparent	16.45 ±0.01	0.096 ±0.01	262 ±0.014	1.45 ±0.06	6.65 ±0.07	2.1 ±0.01
F6	Transparent	22.11 ±0.01	0.162 ±0.012	288 ±0.01	1.75 ±0.04	6.7 ±0.02	2.68 ±0.02
F7	Transparent	12.25 ±0.01	0.06 ±0.012	255 ±0.02	1.43 ±0.01	6.8 ±0.04	1.51 ±0.02
F8	Transparent	18.21 ±.0.01	0.09 ±0.012	274 ±0.018	1.67 ±0.01	6.82 ±0.04	2.01 ±0.01
F9	Transparent	26.14 ±0.012	0.15 ±0.016	297 ±0.02	1.86 ±0.016	6.86 ±0.05	2.75 ±0.02

Table.4: Drug content and Invitro disintegration time of Oral thin films

Formulation	Drug content (%)	Disintegration time(seconds)
F1	99.02±0.3	38±1.52
F2	98.84±0.2	64±1.41
F3	98.92±0.3	86±1.41
F4	98.91±0.43	41.±2.16
F5	98.87±0.4	68±1.63
F6	98.82±0.6	80±2.16
F7	99.66±0.27	28±0.81
F8	99.02±0.4	56±2.16
F9	98.96±0.22	74±0.4

In Vitro Drug Release Study

Dissolution studies of all batches were carried out using phosphate buffer (pH 6.8) as dissolution medium.

Table.5: In-vitro Drug Release Study

Time in seconds	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	**0**	0	0
50	31.22	24.84	18.26	28.96	24.74	21.52	**34.49**	25.72	22.05
100	45.32	38.72	32.65	46.95	37.89	34.05	**48.62**	41.02	38.70
150	54.92	51.27	46.98	56.12	52.92	50.48	**62.14**	56.11	52.06
200	75.54	70.06	62.86	76.86	74.10	68.94	**78.61**	72.23	69.51
250	86.62	82.15	81.89	85.94	83.01	81.36	**89.42**	87.26	84.34
300	97.32	94.4	92.78	96.92	94.13	93.89	**98.94**	97.12	95.88

In-vitro drug release studies were carried out in USP basket type apparatus using phosphate buffer pH 6.8. Dissolution studies of formulations F1, F2 and F3 showed that the films containing sodium CMC have drug release of 97.32%, 94.4% and 92.78% at the end of 300 seconds. The formulations F4, F5 and F6 showed the drug release of 96.92%, 94.13% and 93.89% at the end of 300 seconds respectively. The dissolution studies of formulations F7, F8 and F9 showed that the films containing HPMC have drug release of 98.94%, 97.12% and 95.88% at the end of 300 seconds. The dissolution rate is increases with decrease in disintegration time. The formulation F7 showed more drug release compared to other formulations. The disintegration time of F7 formulation was 28 seconds, at the end of 300 seconds the drug was more released from F7 formulation, 98.94%. Hence the formulation F7 was selected as the best formulation.

DISSOLUTION KINETICS

Table.6: R^2 values for applied Dissolution Models

S.no	Kinetic models	r^2 values
1	Zero order	0.958
2	First order	0.825
3	Higuchi	0.988
4	Korsmeyer-Peppas	0.908

The dissolution kinetics of optimized batch was applied to various dissolution models such as Zero order, First order, Higuchi, Korsmeyer-Peppas. The best fitted model gives the highest r^2 value and least slope value. From the result of Dissolution kinetic studies, it was concluded that the optimized batch follows the Zero order kinetic model as it had highest r^2 value with Higuchi mechanism.

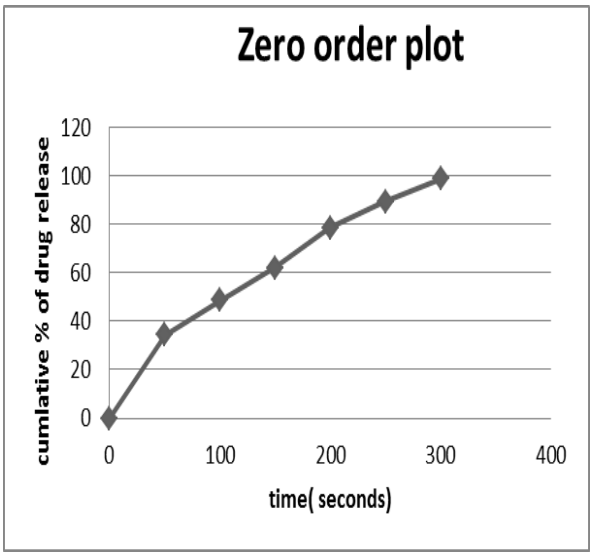

Fig.3: Zero order release kinetics for the formulation F7

Stability studies of the optimized formulation

The stability study of the optimized formulation of montelukast sodium oral thin film was carried out and analyzed for its physical appearance, drug content, moisture absorption, surface pH, in-vitro disintegration time and in-vitro drug release. The stability studies were carried out for three months according to ICH guidelines.

Table.7: Physical appearance, drug content, moisture absorption, surface pH, in-vitro disintegration time of formulation F7 after stability studies

S.No.	Parameter	Stability study			
		Initial	30th day	60th day	90th day
		$40^0 \pm 2^0$C and 75±5% RH	$40^0 \pm 2^0$C and 75±5% RH	$40^0 \pm 2^0$C and 75±5% RH	$40^0 \pm 2^0$C and 75±5% RH
1	Physical appearance	Transparent	Transparent	Transparent	Transparent
2	Surface pH	6.8	6.8	6.8	6.8
3	Percentage moisture absorption	1.51	1.56	1.61	1.66
4	Drug content	99.66%	99.41%	99.22%	99.08%
5	In vitro disintegration time(sec)	28	28	30	29

Table.8: In-vitro drug release under stability study of the formulation F7

Time (Seconds)	Percentage of cumulative drug release			
	Initial	30th day	60th day	90th day
50	32.49	32.28	32.04	31.86
100	46.62	46.51	45.96	45.28
150	56.14	55.92	55.28	54.13
200	78.61	78.22	77.84	77.32
250	91.42	91.28	91.06	90.88
300	98.94	98.82	98.71	98.34

The stability study carried out on selected formulation stored at 40^0C±2^0C at 75±5% RH for three months. The formulation was analyzed for its physical appearance, drug content, moisture absorption, surface pH, and disintegration time and In-vitro drug release at 30 days of interval. The study showed that there was no significant change in the drug content, In-vitro disintegration time and In-vitro drug release studies. And hence the optimised film found to be stable.

6. CONCLUSION

In the present investigation study an attempt has been made to formulate oral thin film of montelukast sodium. The oral thin film of montelukast sodium was successfully formulated by solvent casting method using

HPMC, methyl cellulose and sodium CMC. And the formulation F7 showed drug release of 98.94% at the end of 300 seconds. The drug release follows zero order kinetics and which showed better stability when stored under 40±2^{0}C and 75±5% RH for 3 months. All the physicochemical parameters were satisfied for F7 formulation.

REFERENCES

1. Jain N K. Advances in controlled and novel drug delivery. New Delhi, CBS publishers, 2001; 209-211.
2. M.D. Nehal Siddiqui, Garima Garg, Pramod Kumar Sharma. A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents. Advances in biological research, 2011; 5(6): 291-303.
3. Tapash K. Ghosh, William R. Pfister. Drug delivery to the oral cavity molecules to market. Drugs and the Pharmaceutical Sciences, 145.
4. Parul Saini, Anoop Kumar, Pankaj Sharma, Sharad Visht. Fast Disintegrating Oral Films: A Recent Trend of Drug Delivery. Int J of Drug Development and Research, 2012; 4(4): 80-94.
5. Priyanka Nagar, Iti Chuhan, Mohd Yasir. Insights into polymers: Film Formers in Mouth Dissolving Films. Drug Invention Today, 2011; 3(12): 280-9.
6. S. Jeganath, Y. Venkata Kiran Kumar, G. H. Srinivasa Rao, D. Thirupathaiah, V. Lakshmi Narayana. Fast Dissolving System-A review. Int J of Research in Pharmaceutical and Nano Sciences, 2013; 2(1): 25.43.
7. Aggarval Jyoti, Singh Gurpreet, Saini Seema, Rana A C. Fast dissolving films: A novel approach to drug delivery. Int research J of Pharmacy, 2011; 2(12): 69-74.
8. Yogyatha S Pathare, Vishakha S Hastak, Amrutha N Bajaj. Polymers used for fast disintegrating oral films: A review. Int.J of Pharmaceutical Sciences Review and Research, Jul-Aug, 2013, 21(1): 169-78.
9. Patel Jitendra C, KR Patel, NM Patel. Review On Fast Dissolving Film. International Journal of Advanced Pharmaceutics, 2013; 3(1): 44-50.
10. Rajesh RoshanRai, Pavithra Chirra1, Venkataramudu Thanda. Fast Dissolving Tablets: A Novel Approch to Drug Delivery – A Review. Int J of Preclinical and Pharmaceutical Research, 2012; 3(1): 23-32.
11. Tejvir Kaur, Bhawandeep Gill, Sandeep Kumar, G. D.Gupta. Mouth Dissolving tablets: A Novel Approach to Drug Delivery. Int J of Current Pharmaceutical Research, 2011; 3(1): 1-7.
12. R. Gowri, N. Narayanan, S. Revathy, P. Prabhavathy, G. Preethy Mol, G. Rekha. Melt In Mouth Films-An Effective Alternative Drug Delivery System. Int J of Biological & Pharmaceutical Research, 2013; 4(9): 645-50.
13. Nishi Thakur, Mayank Bansal, Neha Sharma, Ghanshyam Yadav and Pragati Khare. Overview - A Novel Approach of Fast Dissolving Films and Their Patents. Advances in Biological Research, 2013; 7 (2): 50-8.
14. Naziya Khatoon, N.G. Raghavendra Rao, B. Mahipal Reddy. Over view on Fast Dissolving Oral Films. Int J of Chemistry and Pharmaceutical Sciences, 2013; 1(1): 63-75.
15. Ravi Saurabh, Rishabha Malviya, Pramod Kumar Sharma. Trends in buccal film: Formulation characteristics, recent studies and patents. European J of Applied Sciences, 2011; 3(3): 93-101.
16. Ajoy Bera, Ashish Mukherjee. A Detailed Study of Mouth Dissolving Drug Delivery System. Acta Chim. Pharm. Indica, 2013; 3(1): 65-93.
17. Ravneet Kaur, Rajni Bala. Exploration of Different Polymers and Optimization of Concentration of Plasticizer in the Formulation of Oral Fast Dissolving Strips. Int J of pharmaceutical research and bio sciences, 2012; 1(4): 94-101.
18. Ganesh R. Kulkarni, Dr. Moreshwar. P. Patil. Design and In-Vitro Evaluation of Mouth Dissolving Film Containing Amlodipne Besylate. World J of Pharmacy and Pharmaceutical Sciences, 2014; Vol 3(10): 925-45.
19. Montelukast sodium. Pharmacopeial Forum, Jan-Feb, 2010; 36(1).
20. Kanika Dhote, Vinod Dhote, Subhendu Mishra. Oral thin films: an overview. Asian J of Pharmaceutical Education and Research, 2015; 4(2): 1-29.
21. Raymond C Rowe, Paul J Sheskey, Sian C Owen. Hand book of pharmaceutical excipients, 5th, edition. Pharmaceutical press publishers, 2007.
22. Kapoor D, Vyas RB, Lad C, Patel M, Tyagi BL. Fabrication And Characterization Of Oral Thin Films Of Leukotrine Receptor Antagonist (LTRA). J of Drug Delivery & Therapeutics, 2015; 5(2): 77-82.
23. Manavalan Ramaswamy. Physical Pharmaceutics. Vignesh publisher, 2007; 267-312.
24. Leon Lachman, Herbert A. Leiberman, Joseph L. Kanig. The Theory and Practice of Industrial Pharmacy, 3rd edition. Vargese Publishing House, 365-368.
25. Chi L. Li, Luigi G. Martini, James L. Ford, Matthew Roberts. The use of Hypromellose in oral drug delivery. J of Pharmacy and Pharmacology, 2005: 533-46.