International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.10 No.6, pp 545-552, 2017

Formulation and Evaluation of Fast Dissolving Buccal Films of Sumatriptan Succinate

T.Balakrishna*[1], S.Vidyadhara[1], T.E.G.K.Murthy[2], R.L.C.Sasidhar[1] and S.Vikas[1]

[1]ChebroluHanuamiah Institute of Pharmaceutical Sciences, Chandramoulipuram, Chowdavaram, Guntur-522019, INDIA
[2]Bapatla College of Pharmacy, Bapatla, A.P., India

Abstract : The aim of this workis to formulate and evaluate the Sumatriptan Succinate fast dissolving buccal films used for the treatment of Migraine. The designof developing fast dissolving drug delivery systems is to provide patient with more convenient means of drug administration and maximum drug dissolution in oral cavity and to bypassing the first metabolism, to increase the convenience and compliance by the pediatric and geriatric patients. In the present investigation, polyvinylalcohol (PVA) and polyvinylpyrrolidine (PVP) were used as film forming polymers. Solvent evaporation method was used for the preparation of fast dissolving buccalfilms. The films were prepared and evaluated for film thickness, folding endurance, dispersion test, drug content and dissolution. The In vitro dissolution studies were carried out using simulated salivary fluid (pH 6.8 phosphate buffer).Among all the formulations, Formulation S8 were released up to 99.8% of the drug from the film within 5 minutes of time which exhibits faster absorption and also shows desirable characteristics of the film.

Keywords : Buccal films, Sumatriptan Succinate, Polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), Solvent evaporation method.

Introduction:

Among all the routes of drug administration, the oral route is most advisable route in the designing the formulation of dosage form than drug delivery design by other routes of administration.[1,2] The oral mucosa is conveniently and easily accessible and therefore allows uncomplicated application of various dosage forms. Furthermore, the oral mucosa is robust against local stress or damage and shows fast cellular recovery. Active Substances can be administered locally to treat oral diseases such as periodontal disease, bacterial and fungal infections. A systemic action can be achieved via drug permeation through the mucosal epithelium. [3, 4] The concept of fast-dissolving drug delivery emerged from the desire to provide patient with more conventional means of taking their medication. Fast dissolving films recently have acquired great importance in the pharmaceutical industry due to their unique properties and specific advantages like no need of water for disintegration, accurate dosing, rapid onset of action, ease of transportability, ease of handling, pleasant taste and improved patient compliance.[5,6] Fast dissolving film is a type of drug delivery system, which when placed in the oral cavity it rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption, without chewing and intake of water.[7,8] This technology evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely

accepted form by consumers. This film has the potential to deliver the drug systemically through intragastric, sublingual or buccal route of administration and also has been used for local action. [9-11].

Now a day's migraine is a chronic, disorder, which usually begins in childhood, adolescence or early adult life, characterized by unilateral headache often accompanied by nausea and vomiting [12], gastrointestinal disturbance and extreme sensitivity to light and sound [13].Sumatriptan is a 5-HT1D (5-hydroxy tryptamine 1D)-receptor agonist, used in the treatment of migraine and cluster headache [14]. Sumatriptan succinate is the first member of a new class of antimigraine compounds that act as a specific and selective 5-hydroxytryptamine-1 receptor agonist [15]. The lower bioavailability of sumatriptan succinate is primarily because of presystemic first-pass metabolism and partly because of incomplete absorption [16].

Materials and Methods

Sumatriptan Succinate was procured as gift sample from M/S Aurobindo Pharmaceuticals, Hyderabad. Polyvinylalcohol (PVA) and polyvinylpyrrolidine (PVP) were commercially procured from M/S Yarrow Chem Products, Mumbai. Poly Ethylene Glycol (PEG) was procured commercially from Sisco research laboratories pvt, Ltd, Mumbai. Saccharin sodium was procurred commercially from High-Pure fine Chemicals, Chennai. All the materials used in the formulation were of pharmacopoeial standards.

Preparation of SumatriptanBuccal Film

Fast dissolving buccal films of Sumatriptan succinate were prepared by solvent evaporation method. Plasticizers like polyvinylalcohol and Polyvinylpyrrolidine were prepared in the form of aqueous solutions individually in 100ml beakers to attain clear solutions. Then the solution of Polyvinylpyrrolidine (PVP) was added to polyvinylalcohol (PVA) aqueous solution and stirred well to get homogenous solution which is marked as solution A. Accurate quantities of Sumatriptan succinate and saccharin sodium were weighed individually and dissolved in suitable quantity of Polyethylene glycol 200 (PEG 200) to get a drug and plasticizer solution which is marked as solution B. The solution B was added to aqueous solution A and mixed continuously. The obtained solution was drawn on the non adhesive base plate and dried under Infrared (IR) lamp for 24 hours. After drying the films were cut into suitable sizes. Various trials were conducted to carried out optimize formula for the preparation of Sumatriptan succinate buccal films. The various Compositions of Sumatriptanbuccal films were given in Table 1.

Table 1. Composition of various Sumatriptansuccinate buccal films

		Formulations								
SNO	**Ingredients Mg/10films**	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**
1.	Sumatriptan succinate	500	500	500	500	500	500	500	500	500
2.	Polyvinyl pyrrolidine	150	150	150	150	150	150	150	150	150
3.	Polyvinyl alcohol	150	175	200	225	250	250	250	250	250
4.	Poly ethylene glycol-200	150	125	100	75	50	75	100	175	150
5.	Sodium sacharine	10	10	10	10	10	10	10	10	10
6	water	5	5	5	5	5	5	5	5	5
	Total wt of the file(mg)	965	965	965	965	965	990	1015	1090	1065

Table 2: Evaluation of *Invitro* Dissolution Parameters for Sumatriptansuccinate Buccal Fast Dissolving Films

S.No	Formulation	T_{50} (min)	$DE_{5\%}$	First order		Hixon-crowell	
				K (min^{-1})	R^2	K ($mg^{1/3}$/min)	R^2
1	S1	3.0	19.8	0.156	0.946	0.0990	0.906
2	S2	3.2	19.6	0.234	0.954	0.1031	0.929
3	S3	3.5	22.8	0.267	0.914	0.076	0.932
4	S4	2.2	25.9	0.216	0.926	0.0690	0.924
5	S5	2.6	36.8	0.211	0.970	0.0710	0.963
6	S6	2.1	34.5	0.207	0.900	0.0806	0.931
7	S7	4.5	19.9	0.241	0.951	0.0752	0.921
8	S8	1.6	23.2	0.138	0.998	0.0760	0.988
9	S9	2.2	25.6	0.188	0.967	0.0712	0.928

Evaluation of Fast Dissolving Films

Film thickness

The filmthickness was measured by using screw gauge with a least count of 0.01 mm at different locations on the film. The filmthickness was measured at three different locations and the average weight wasdetermined. The obtained Results were given in table 2.

Folding endurance

Folding endurance was determined repeatedlyby folding a small strip of the film at the same place till number of times the film could be folded at the same place without cracking was noted as folding endurance. The film was folded at an angle of 180^0 at the same place till it broke or folded up to 100 times without breaking. The studies were performed in trice and the average mean was calculated.

Uniformity of Drug content

The content of drug uniformity of the filmswas tested by UV-visible Spectrophotometric method. The absorbance values weredetermined at a wavelength of 282 nm. The % drug content of various films was determined and given in the table 3.

Table 3: Evaluation of *Invitro* Dissolution Parameters for SumatriptanSuccinate Fas Buccal Dissolving Films

S. No	Formulation	Weight uniformity(mg)	Drug content (mg/film)	Film thickness (mm)	Dispersion test	Folding endurance (%)
1.	S1	101	48.259	0.034	Passed	96
2.	S2	100	48.543	0.034	Passed	99
3.	S3	102	48.895	0.034	Passed	105
4.	S4	102	47.698	0.032	Passed	65
5.	S5	101	48.2146	0.033	Passed	60
6.	S6	100	48.697	0.032	Passed	63
7.	S7	101	47.963	0.034	Passed	81
8.	S8	101	49.896	0.034	0.034	105
9.	S9	100	48.367	0.034	Passed	71

Dispersion test

A Film equivalent to 5mg of Sumatriptansuccinate was placed in 200ml of 6.8pH phosphate buffer and was stirred for 3 minutes. Then the resulting solution was passed through sieve number 22. The film passed the dispersion test only when no residue is left on the screen.

***In vitro* dissolution study by using Franz diffusion cell**

Invitro Dissolution studies were performed on all the film formulation by using an apparatus called Franz Diffusion Cell apparatus maintains a volume capacity of 15 ml was used for dissolution study. The film equivalent to 50mg of Sumatriptansuccinate was placed in between the two compartments of an apparatus and pipette 15 ml of 6.8 pH buffer (pH of saliva) was added to receptor compartment. cell is kept on magnetic stirrer and bead in the cell is maintained at a speed of 50 revolution per minute (RPM) and medium maintained at a temperature of nearly $32^0C \pm 0.5^0C$ and withdraw 1ml of samples at various time intervals and the samples were diluted with 6.8 pH phosphate buffer and measured the absorbance at 282 nm against 6.8 pH Buffer as Blank. The various dissolution profiles for films were given in shown in figure 1 The in vitro dissolution parameters were given in Table 3.

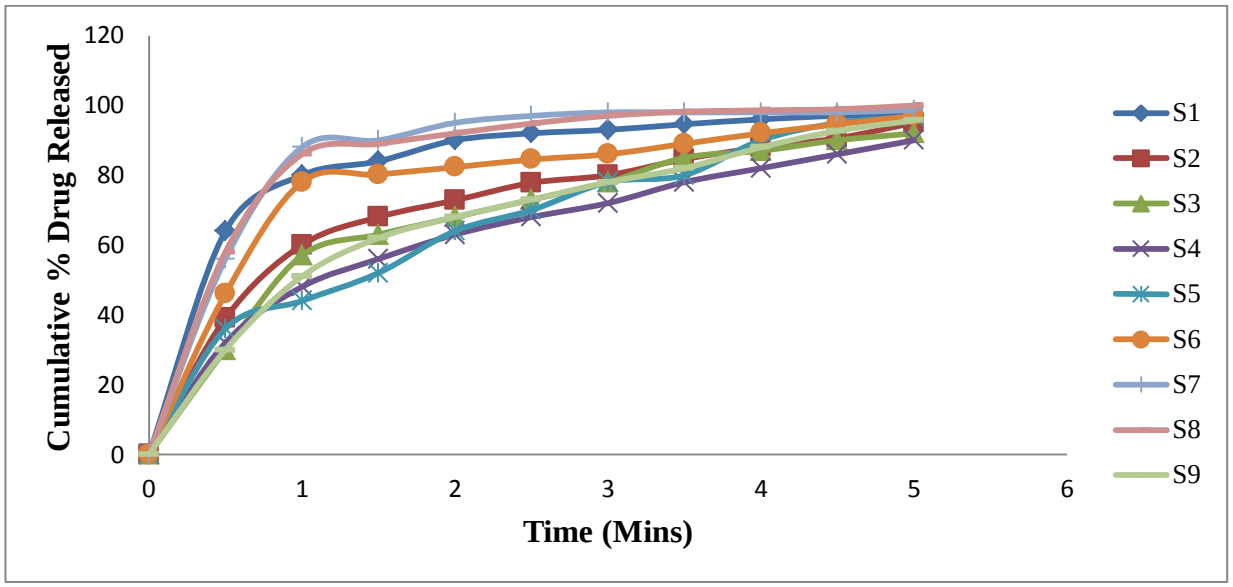

Figure 1: Drug Release Profiles for Sumatriptan Succinate Fast Buccal Dissolving Films

Evaluation of various dissolution parameters

Based on dissolution data obtained, various dissolution parameters were calculated such as T_{50}, T_{90}, $DE_{5\%}$ first order rate constant and Hixon–Crowell.

Characterization

Dissolution studies were performed on all the formulations, Among these, formulation S8 were further evaluated by Fourier transform infrared spectroscopy and differential scanning calorimetry.

Fourier transform infrared spectroscopy (FTIR)

The FTIR spectra of Sumatriptansuccinate and on optimized formulation S8 were obtained using Brucker FTIR spectrophotometer to study the interaction between drug and carrier in films. The samples were prepared in KBr discs (2 mg sample in 200 mg KBr) and the sampling range was 400-4000 cm^{-1} and the resolution was 4 cm^{-1}. The FTIR spectra were shown in Figures 2 to 3**.**

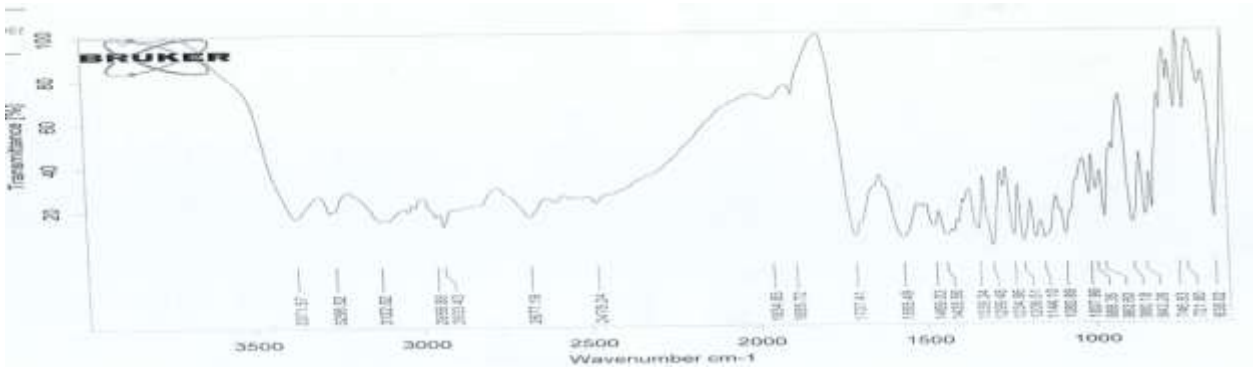

Figure 2: FTIR Spectrum of Sumatriptan Succinate Pure Drug

Figure 3:FTIR Spectrum of Optimised S8 Film Formulation

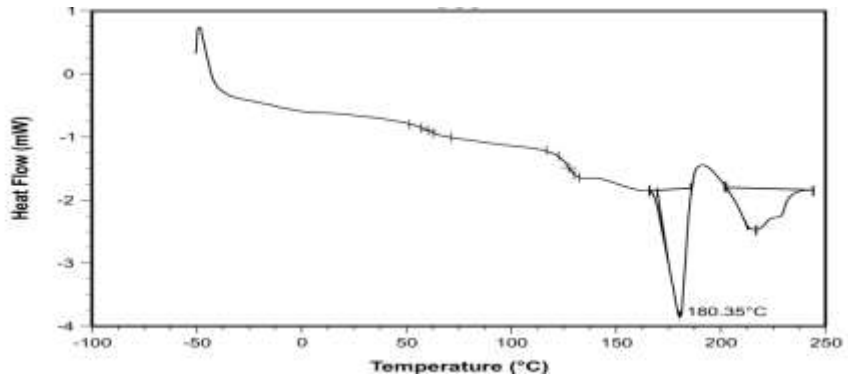

Figure 4: DSC of Pure Drugof Sumatriptan Succinate

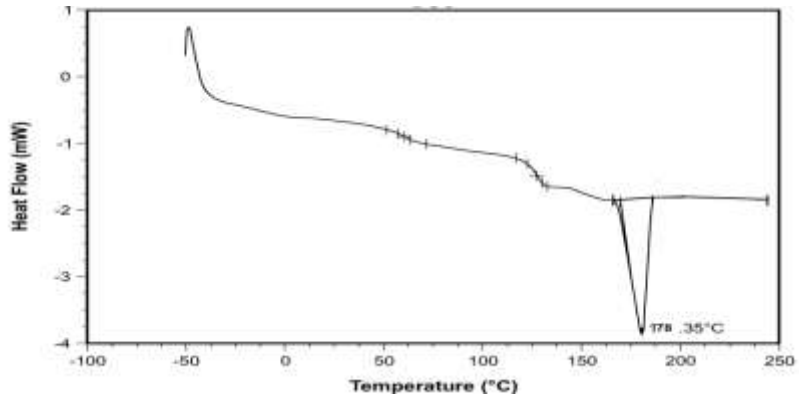

Figure 5: DSC of optimized formulation S8Sumatriptan Succinate fast dissolving Buccal Film

Differential Scanning Calorimetry:

Differential Scanning Calorimetry measurements were performed on sumatriptan succinate, and on optimized formulation S8 using differential scanning calorimeter (METTLER TOLEDO with eSTAR software). The samples were placed in a sealed aluminium crucible and evaluated with a heating rate of 20 º C/minat a temperature range of 25-250ºC. The thermograms were recorded and were shown in the figure 4-5.

Results and Discussion

The present investigation deals with the formulation and evaluation of fast dissolving buccal films of Sumatriptansuccinate which is used for the treatment of migraine in geriatrics and pedriatrics patients. The main focus on this study was to select the best combination of polymer and excipients to formulate Sumatriptansuccinate fast dissolving buccal films. Sumatriptansuccinate fast dissolving buccal films were prepared by solvent evaporation method using polyvinylpyrolidone (PVP) and polyvinylalcohol (PVA) were used at different concentrations as film forming polymers. Polyethyleneglycol (PEG 200) was used as plasticizer to make the pliableand flexible in nature. Saccharin Sodium was used as artificial sweetener in the formulation. The films wereprepared under identical conditions to minimize processing variables and evaluated for various physical properties such as thickness of a film, folding endurance, content ofdrug uniformity and dispersion test are used to ensure the stability of films. The composition of various fast dissolving buccal films of Sumatriptansuccinate was given in table 1.

The prepared films were further evaluated for thickness, folding endurance, dispersion test, drug content and invitro dissolution studies. The thickness of a film was found in the range of 0.31$\pm$0.003 to 0.34$\pm$0.003 mm. The optimized formulationS8film is having thickness 0.342mm. The folding endurance values of all prepared films ranged from 30 to 100 percent. The optimized formulationS8 film was found to have folding endurance of 100% which is highly beneficial or agreeable. The drug uniformity was found in the range of 47.963 $\pm$1.6 mg to 49.89$\pm$0.8 mg. The optimized formulationS8film was found to have 49.89 mg. The films were further subjected to dispersion test as per the Indian pharmacopoieal (IP)standard. All the prepared film formulations were found to disperse in 6.8 pH phosphate buffer within 3 minutes. No inert fibrous or insoluble materialwas left on the 22 mesh screenwhen the dispersion was passed through it. The prepared films were subjected tothickness of a film, drug content, folding endurance and dispersion test values obtained for various fast dissolving buccal films were given in table 3.

Fast dissolving buccal films of Sumatriptansuccinate were further subjected to In vitro dissolution studies by using Frantz diffusion cell with 15ml of 6.8 pH phosphate buffer as a medium which is maintained at a temperature 32^0C. The dissolution medium in the cell was maintained to rotate at 50rpm by using magnetic stirrer. The samples were withdrawn at various time intervals and were consequently diluted with 6.8 pH phosphate buffer and Absorbance values were noted at 282 nm by using ELICO Double beam spectrophotometer. The obtained dissolution profiles were given in Table 3 and were shown in figures 1 and 2. Formulations S1, S2, S3, S6, S7, S8 and S9 were found to release more than 90% of the drug within 5 minutes. The formulations S4 and S5 were failed to release 90 % of the drug in 5 minutes. The formulations S7 and S8 were found to be best suitable for fast dissolving and also these two films should possess all the physical characteristics required for the fast dissolving buccalfilm. The film formulations S7and S8 containing 30% of polyvinylpyrolidone(PVP)& 50 % of polyvinylalcohol(PVA) were found to exhibit best film forming properties with 100 % folding endurance value. These S7 and S8 formulations with 20 – 25 % of PEG were found to exhibit rapid dispersion in the dissolution media and dissolvedreadily in the same medium which indicated fast dissolving characteristics of the film. The drug release order from various Sumatriptansuccinate fast dissolving buccal films was given as S7>S8 >S1 >S6 >S2 >S3 >S9 >S4 >S5.The first order graphs for various fast dissolving buccal films were found to be linear with Co-relation coefficient values obtained were in the range of 0.914 to 0.998. It indicated that the drug release from the films was found to be concentration dependent.The Hixon Crowell Cube Root graphs for all theprepared buccal film formulations were found to be linear with R^2 values obtained in the range of 0.906 to 0.988. This indicated that the dissolution of the drug from the film was greatly dependent on weight uniformity of the film that undergoes dissolution per unit time. The in vitro dissolution parameters were given in Table 4.The prepared films wereto subjected to characterized by FTIR studies. The FTIR spectra of the commercial sample of Sumatriptansuccinate displayed bands at 3350 cm^{-1} due to N-H Stretch and 1735 cm^{-1} due to C=O Stretching. The FTIR spectra of Sumatriptansuccinate buccal film S8 exhibited characteristic bands at 3350 cm^{-1} due to N-H Stretch and 1735 cm^{-1} due to C=O Stretching. The IR

spectra of the film indicated that there are no interactions between drug and excipients used. Thus the spectra of optimized S8 film formulation should exhibited all the principle peaks present in thepure drug of Sumatriptansuccinate. Hence in indicates that there is no interaction between drug and excipients used in the formulation. The FTIR spectra of the pure drug Sumatriptansuccinate and optimized formulation S8 film were showed film properties. later DSC thermographic studies were carried out on Sumatriptansuccinate pure drug and formulation S8 film. The endothermic peak for pure Sumatriptansuccinate drug was obtained at 180.35^0C whereas for the S8 buccalfilm the broad endothermic peak was observed at 178.89^0c. The DSC thermogram for Sumatriptansuccinate and S8 formulation were shown in figure 4 and 5. The broad endothermic peak for S8 formulation was due to the formation of Sumatriptansuccinatec omplex with the film forming polymer used such polyvinylpyrolidone (PVP) and polyvinylalcohol (PVA)at higher concentrations in the film. Hence no interaction between drug and excipients were observed with DSC studies.

Conclusion

Fast dissolving buccal films of Sumatriptan Succinateprepared in the present study should exhibited good film properties as indicated by film thickness and folding endurancewas measured. All the filmsprepared were found to be stable uniform, flexible, pliable and 99% of drug was released from optimized filmS8 within 5 minutes of time.This was advisable for fast absorption. Hence fast dissolving buccalfilms of Sumatriptan Succinate were found to be suitable for exhibiting the better therapeutic effect in the treatment of migraine.

Acknowledgements

The authors express their gratitude to Aurobindo Pharmaceuticals, Hyderabad for providing the gift samples. The authors are thankful to the management of Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Guntur for providing the facilities to carry out the research work.

References

1. Vyas SP, Khar RK. Controlled oral administration. In: Controlled Drug Delivery Concepts and Advances. 1st ed. Delhi: Vallab Prakasham Publications; 2002.
2. Borsadia S, O'Halloran D, Osborne JL. Quick dissolving fi lms — A novel approach to drug delivery. Drug DelivTechnol 2003; 3:63-6.
3. Parakh SR, Gothoskar AV. Review of mouth dissolving tablet technologies. Pharm Technol 2003; 27:92-100.
4. Satishbabu BK, Shrinivasan BP. Preparation and evaluation of buccoadhesive fi lm of atenolol. Indian J Pharm Sci 2008; 20:175-9.
5. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. J Pharm Pharmacol 1998; 50:375-82.
6. Mishra R, Amin A. Formulation and characterization of rapidly dissolving fi lms of cetirizine hydrochloride using pullulan as a fi lm forming agent. India J Pharm Educ Res 2011; 45:75-6.
7. Prabhu P, Malli R, Koland M, Vijaynarayana K, D'Souza U, Harish N, et al. Formulation and evaluation of fast dissolving fi lms of levocitirizine di hydrochloride. Int J Pharm Investig 2011;1:99-104.
8. Tora GJ, Gorahowski SR. Principles of Anatomy and Physiology. Vol. 7. Wiley & Sons, Incorporated, John: HarpetToraToraGorahowski 1992; 770-4.
9. Yoshifumi G, Ryosei K. Preparation of fast dissolving fi lms for oral dosage from natural polysaccharides. Materials 2010;3: 4291-4296.
10. Rathi V, Senthil V, Kammili L, Hans R. A brief review on oral fi lm technology. Int J Res Ayurvedic Pharm 2011; 2:1138-47.
11. Barnhart SD, Sloboda MS. The future of dissolvable fi lms. Drug Delivery Technol 2007; 7:34-7.
12. Ravi S, Nurzalina K and Yusrida D. Chem. Pharm. Bull. **2011**; 59(8): 920—928.
13. Rita J. M, Pradip K. Ghosh, M, Umrethia and Rayasa S. R. Murthy. AAPS PharmSciTech.2006; 7(3).
14. Dixon C. M., Saynor D. A., Andrew P. D., Oxford J., Bradbury A., Tarbit M. H. Drug. Met.Dispos.1993; 21:761—769.

15. Femenia-Font A, C. Balaguer-Fernandez, V. Merino, V. Rodilla, and A. Lopez-Castellano. Eur. J. Pharm. Biopharm. 2005; 61: 50-55.
16. Dulery B. D, M.A. Petty, J. Schoun, M. David, and N.D. Huebert. J. Pharm. Biomed. Anal.1997; 15: 1009

*****