WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 8, Issue 4, 791-799 Research Article ISSN 2278 – 4357

FORMULATION AND EVALUATION OF FAST DISSOLVING SUBLINGUAL FILMS OF SERTRALINE HCL

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Article Received on
07 Feb. 2019,

Revised on 28 Feb. 2019,
Accepted on 21 Mar. 2019,

DOI: 10.20959/wjpps20194-13127

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ABSTRACT

The present study is aimed to prepare sublingual dosage forms of the seretraline Hcl with the purpose to achieve quick onset of action in management of antidepressant. Fast dissolving sublingual films of seretraline Hcl were thus prepared by solvent casting method water soluble polymer HPMC E15 was used as film forming polymer. poly ethylene glycol 400 and glycerin were used as plasticizer. Sucralose was added as a sweetener and peppermint oil as flavouring agent. The formulation prepared were evaluated for their uniformity of weight, surface pH, folding endurance, disintegration time, mucoadhesion time, tensile strength, %elongation, content uniformity and %drug release. The FTIR studies showed no interaction between drug and polymer. From the observation of evaluation results, it was concluded that formulation F3 containing PEG400 and glycerin for films prepared using HPMC E15was the best formulation among all other formulation. Films showed excellent stability when kept at RT as well as at 400ºc and 75% RH.

KEYWORDS: sertraline HCl, fast dissolving sublingual film, film forming polymer HPMC E15.

INTRODUCTION

The oral route is considered to be the ideal route for the administration of therapeutic substances. It is more acceptable from patients compliance aspects due to its low cost and ease of administration however, significant constraints are associated with oral route such as

hepatic first pass metabolism and drug degradation due to enzymes in it. Mostly the pediatric and geriatric patients find it difficult to take solid dosage forms because of fear about chocking. Fast dissolving tablets are used to resolve problems but it also associated the fear of chocking due to its size and shape. Mucosa layer can be considered as potential site for drug administration including mucosal linings of rectal, vaginal, occular, nasal and oral cavity. The oral cavity is highly acceptable by the patients because so many reasons like rich blood supply and short healing after damage, high mucosal permeability. In sublingual route the drug is placed under the tongue and allowed to dissolve. The barrier to drug absorption from this route is the epithelium of oral mucosa. Passive diffusion is the major mechanism for absorption of more drugs.

In this sublingual route of administration rapid absorption and higher blood vesseles due to high vascularisation of the region and Presence of saliva facilitates both drug dissolution and its subsquent permeation by keeping the oral mucosa moist.

Sertraline HCL is a selective serotonin reuptake inhibitor (SSRI) anti depressant and anxiolytic agent. The oral bioavailability of sertraline is about 45% because of extensive first pass metabolism in liver and gut wall. Sublingual routes of drug delivery offer distinct advantages over oral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of pre-systemic elimination within the GI tract these factors make the oral mucosal cavity a very attractive and feasable site for systemic drug delivery.

The aim of the study is to prepare fast dissolving sublingual film of sertraline HCL to achieve rapid onset of action as required during the antidepressant and anxiolytic activity. The fast dissolving sublingual films of sertraline HCL prevents its first pass metabolism. It also eliminates patient's fear of choking as well as need of liquid or water for oral administration of dosage form, also the patient will get rapid onset of action.

MATERIALS AND METHODS

Sertraline HCL was recieved as gift sample from KP LABS, Hydroxy propyl methyl cellulose was procured from otto laboratories, poly ethylene glycol procured from arihant traders and methanol were obtained from SDFCL, Glycerin was obtained from arihant traders, Sucralose was obtained from SDFCL, Citric acid was obtained from ADVENT, Pepperment oil obtained from MOLYCHEM.

Drug polymer compatibility studies

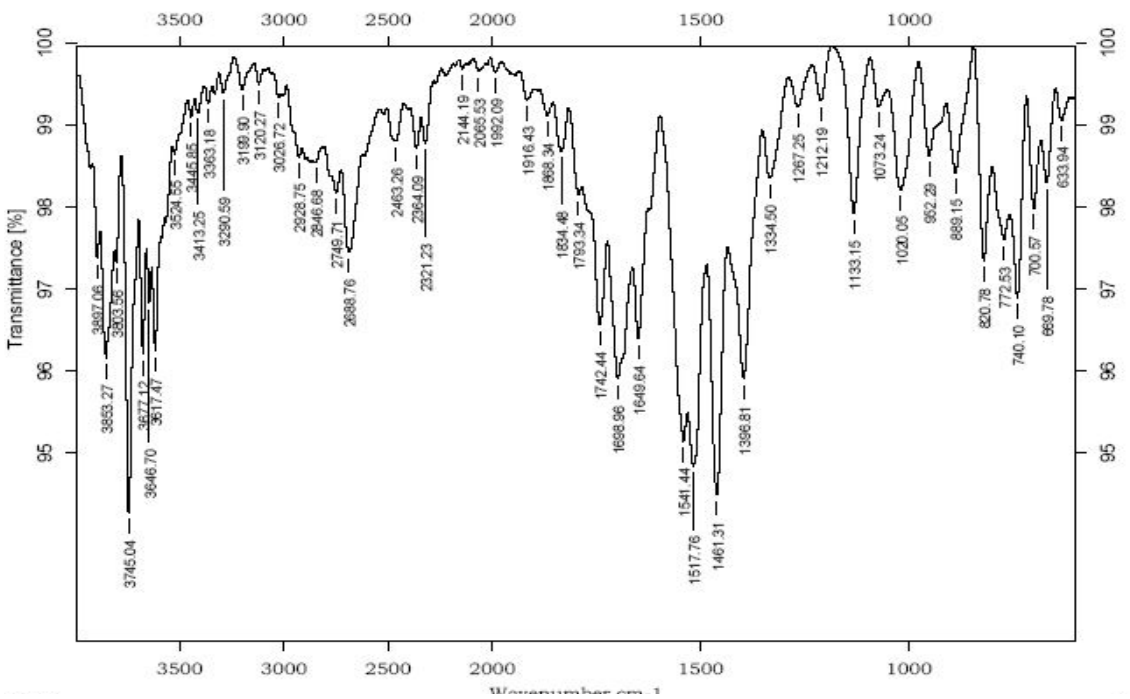
The interaction study between drug and polymer was carried out using FTIR. The KBr discs of drug and polymer in the ratio of 1:1 was prepared and spectra were obtained.

UV Spectrum Analysis of Sertraline HCL

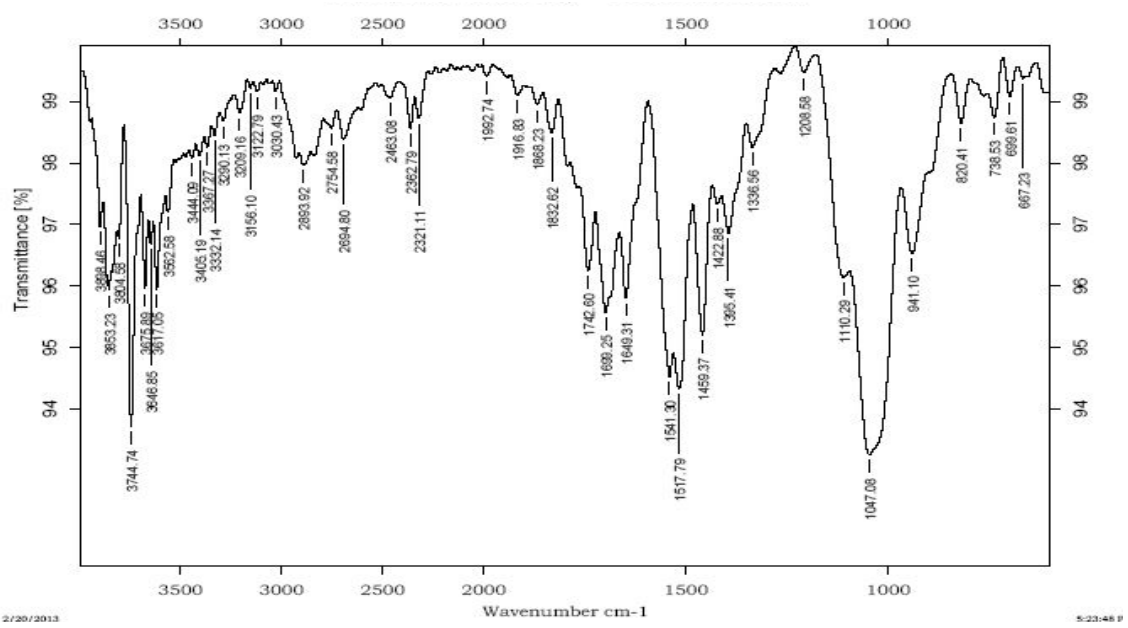
The solution of sertraline hcl in phosphate pH 6.8 was prepared and scanned in the range of 200-400 nm to get the maximum wave length and UV spectrum was obtained.

Standard plot of sertraline HCL in phosphate buffer pH 6.8

100 mg of sertraline was dissolved in 100ml of methanol (1000µg/ml) From the stock solution 10µg/ml was prepared in methanol and UV scan was taken between 200 to 400 nm. The absorption maximum was found to be 224 nm and was used for the further analytical studies. From the standard stock solution (1000µg/ml), appropriate aliquot were transferred to series of 10 ml volumetric flasks and made up to 10 ml with methanol so as to get concentration of 2,4,6,8,10 and 12 µg /ml. the absorbance of the solution were measured at 224 nm. This procedure was performed in triplicate to validate calibration curve.



FT-IR spectra for pure drug.



FT-IR spectra for pure drug + HPMCE15.

Method of preparation of Fast dissolving sublingual films of sertraline HCL

Films were prepared using solvent casting method. The aqueous solution I was prepared by dissolving HPMC E15 in cold water and keeping it aside for 4 hrs to remove the air bubbles. Solution II was prepared by dissolving sucralose, peppermint oil and plasticizers i.e. polyethylene glycol 400 and glycerin. Solution I was then added to solution II it was then casted on to petri plates and dried at RT for 24 hrs After drying, films were carefully removed from plates, cut in to required size (2X2) cm the samples were then evaluated for various tests.

Thickness

The thickness of each film was measured by using digital vernier calipers at five different positions of the patch and the average was calculated.

Weight uniformity of patches

Three patches of size 2×2cm were weighed and the weight variation was calculated.

Folding Endurance

The folding endurance of each film was determined by repeatedly folding the film at the same place till it was broken or folded up to 300 times, which is considered satisfactory to reveal good film properties.

Composition of sertraline HCL sublingual films

S.NO	INGREDIENTS	F1	F2	F3	F4	F5	F6
1	SERTRALINE HCL(mg)	113	113	113	113	113	113
2	HPMC E15(mg)	500	500	500	500	500	500
3	PEG400(ml)	1.0	1.0	1.0	1.5	1.5	1.5
4	GLYCERENE(ml)	0.1	0.2	0.3	0.1	0.2	0.3
5	SUCRALOSE (mg)	50	50	50	50	50	50
6	PEPPERMENT OIL(ml)	0.3	0.3	0.3	0.3	0.3	0.3
7	CITRIC ACID (mg)	70	70	70	70	70	70
8	WATER(ml)	10	10	10	10	10	10

Surface pH

The oral film was slightly wetted with the help of water. Then the ph of film was measured by bringing the electrode in contact with the surface of the oral film. This study was performed for six batches of each film formulation and mean± S.D was calculated.

Percentage elongation

It was determined by the increase in the length of the film just before the breaking of the film. The formula used for calculating % Elongation is as shown below:

%Elongation = [Final length - Initial length] /Initial length X 100.

Drug content uniformity

The film of 2×2cm^2 was cut and dissolved in phosphate buffer pH 6.8 and volume made to 100 ml in volumetric flask. Then 1 ml was withdrawn from this solution and made to 10 ml the absorbance of this solution was measured at 224 nm using UV visible spectrophotometer and the concentration was calculated by correcting the dilution factor, the drug content was calculated and the test was performed in the triplicates and the standard deviation was calculated.

Formulation code	Thickness(mm)	Weight(mg)	Folding endurance	% elongation
F1	0.10±0.020	55.66±0.57	298±0.5	15 ±1
F2	0.13±0.005	34.66±0.57	210±1	10.33±0.57
F3	0.11±0.011	51.66±0.57	310±0.9	14.33±1.15
F4	0.09±0.005	32.33±0.57	172±2	12 ±1
F5	0.16±0.010	51.33±1.15	210±1.5	14.66±0.57
F6	0.15±0.005	49.66±0.57	330±1	13.33±0.57

Disintegration time

In vitro disintegration time was measured visually in a beaker containing 25 ml phosphate buffer P^H 6.8 and swirling the media every 10 seconds. The disintegration time was noted as the time when the film starts to break.

In vitro dissolution

Dissolution study of film was performed in USP type 2 apparatus using 300 ml phosphate buffer P^H 6.8 at 50 rpm speed and 37±0.5º c temperature. The samples were withdrawn at the time intervals of 30 sec and analyzed spectro photometrically.

Formulation code	Surface pH	Disintegration time (sec)	Drug content
F1	6.0±1	20.33±0.57	95.9%
F2	5.9±0.057	23±1	92.2%
F3	6.8±0.057	23±1	99.8%
F4	6.3±0.060	23.66±1.1	93%
F5	6.5±0.057	28±1	94.2%
F6	6.7±0.057	35±1	94.9%

Stability studies

The optimized batch F3 was packed in a butter paper covered with aluminium foil and was isothermally stressed to study the stability under accelerated temperature and relative humidity conditions carried out 40ºc /75% RH,25ºc/60%RH and 25ºc/40%RH for period of 3 months. Test samples were withdrawn every month and were subjected to various tests, including visual inspections of the film, disintegration time and cumulative percent of drug release.

RESULTS AND DISCUSSION

In the present study, fast dissolving sublingual film formulations of setraline HCL were prepared by solvent costing method using HPMC E15 as film forming polymer, glycerine and polyethylene glycol 400 as plasticizers in various ratios, Sucralose as sweetener and peppermint oil as flavoring agent. The effect of different concentration of plasticizers on tensile strength of film formulations was studied.

Fast dissolving sublingual films of sertraline HCL were evaluated for the various evaluation parameters. The films were prepared by using varying concentrations of different plasticizers with constant concentration of film forming polymer. All the prepared films were transparent, non-sticky, flexible and good in appearance.

The slight difference in the thickness of films could be attributed to the uneven surface of the plate. The individual weight of the films was measured and weight variation was calculated. The slight different in the weight could be proportionately related to the variation in the film thickness. The pH of all the formulations was found in the range of 5.9to 6.8. This shows that all the films prepared were of neutral pH.

All the films showed good folding endurance and most of them showed folding endurance of more than 290.The tensile strength of formulation F1 was found to be highest with the highest % elongation. The disintegration time of the films was found to be in the range of 20-35 sec. The higher disintegration time of could be attributed to higher concentration of the film forming polymer as well as the muco adhesive nature of this polymer.

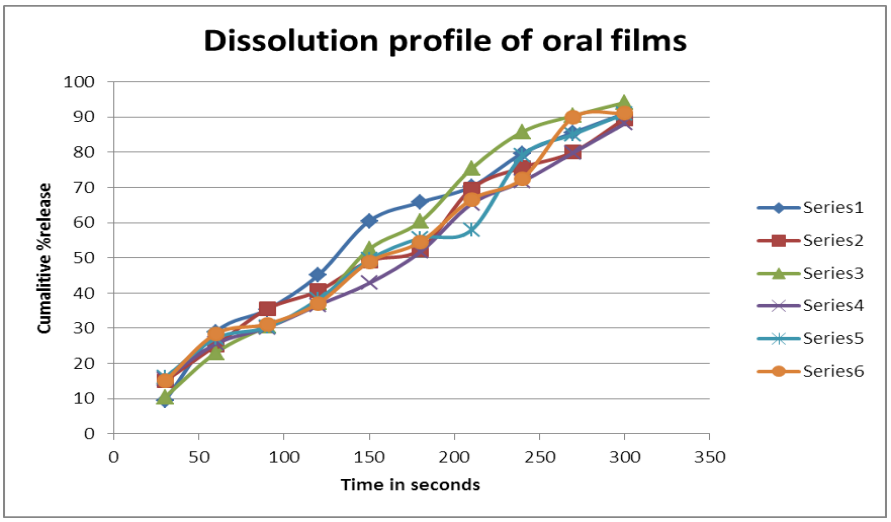
The formulations F1, F2, F3, F4, F5 and F6 showed better drug content of above 90%. The reason of slight variation in the drug content of the prepared film can be attributed to the different in the thickness of the film. Almost total amount of drug was found to be released from the formulations within 270-300 sec i.e. 4 – 5 min. Formulations F1, F3, F5 and F6 showed the best drug release of more than 90% within 5 min. thus from drug content and drug release evaluation data, it could be said that three formulations F1, F3and F6 shows better drug content as well as drug release profile.

The films showed good stability at both RT and accelerated conditions for the period of 45 days. There was no significant change in mechanical properties, drug content and drug release of the film. This shows that the film will remain stable to the wear and tear that occurs during its handling and transportation.

CONCLUSION

The results of the studies indicated that HPMC E15 could be used as a film forming polymer for the formulation of sublingual film of Sertraline HCL. All the films prepared using HPMC E15 showed acceptable mechanical properties. The in vitro disintegration time of all the formulation batches was found to be within 20-35sec. On the basis of tensile strength, drug content and in vitro dissolution, formulation F3 was found to be the promising formulation showing better strength and good drug release profile. Also this formulation was stable for a period of 45 days with no significant change in drug content and drug release profile. Thus it could be said that the fast dissolving sublingual film of sertraline HCL could be a better

option for acute treatment of migraine attacks compared to the available conventional dosage forms.



***In-vitro* dissolution of formulations in simulated salivary fluid pH 6.8.**

REFERENCES

1. Alims, vijender, "Formulation and Evaluation of fast dissolving oral films of diazepam". Journal of pharmacovigilance, 2016; 4(3): 1 of 5.
2. Shruti C Prabhu, sarvesh D parsekar, "A Review on fast dissolving sublingual films for systemic drug delivery". Int J of Pharmaceutical and Chemical Science, 2014; 3(2): 501.
3. Bhupinder bhyan, Sarita Jangra, "Orally fast dissolving films: Innovations in formulation and technology". Int J of pharmaceutical sciences review and research, 2011; 9(2): 50.
4. Rajni Bala, pravin pawar,"A new approach to oral drug delivery system ".Int J of pharmaceutical Investigation, 2013; 3(2): 67-76.
5. Pavan kumar Kothapuvaru, swati rawat,"Preparation of fast dissolving oral films on new generation Anti-migraine drugs by solvent casting method". Int J of Current Research, 2016; 8(5).
6. Amit kumar bind, G.Gnanarjan,"A Review: Sublingual route for systemic drug delivery". Int J of drug research and technology, 2013; 3(2): 31-36.
7. Dr.Suresh V. Chennapati,"Formulation and Evaluation of oral thin film contining Amlodipine bysylate, 2014.
8. Mahlingan K, Mohd nazish,"Fast dissolving sublingual film - A Review". Indian Journal of novel drug delivery, 2016; 8(2): 54-61.
9. Parmar D, Patel U, "Orally fast dissolving films as dominant dosage form for quick release ". Int J Pharmaceutical research and Bio-Sci, 2012; 1(3): 27-41.

10. Varsha S.Nair,R B.Saudagar,"A Review on fast dissolving sublingual films for systemic drug delivery". World J of Pharmacy and Pharmaceutical sciences, 2015; V(4)03: 342-361.
11. Amit R.Kayastha, Smita S, "A Review on: Fast dissolving sublingual film". Indian J of Pharmacy and technology, 2017; 9(2).
12. Asish Dev, Sameer S.Mundke, "Critical aspects in sublingual route of drug delivery". Pharmaceutical and biol ogical evaluation, 2016; 3(1): 42-49.
13. Muhammad Irfan, Quratulain Bukhtar, "Orally disintegrating films: A modern expansion in drug delivery system". Saudi: Pharmaceutical J, 2016; V 24(5): 537-546.
14. Patel priti, Patel jaymin, "A Review on fast dissolving sublingual film". An Int peer Raviewed Pharmaceutical J that Encourages Innovations and Creativities, 2015; V(5)3: 79-285.
15. B.P.Panda, N.S. Dey and M.E.B. Rao, "Development of Innovative orally fast disintegration of dosage form of review". Int J of Pharmaceutical Science and Nanotechnology, 2012; 5(2).
16. Prachi pandey, Sonan chauhan,"Fast dissolving sublingual film of Zolmitriptan: A Novel treatment approach for migraine attacks". Indian J OF Pharmaceutical research and Education, 2014; 48.