IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
November 2021 Vol.:22, Issue:4

Formulation and Evaluation of Sertraline Hydrochloride Patch for Transdermal Drug Delivery System

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Ragini Verma[*1]

[1]*Doodhnath College of Pharmacy, Sakrar, Jhansi, Uttar Pradesh, India*

Submitted: 24 October 2021
Accepted: 30 October 2021
Published: 30 November 2021

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Sertraline Hydrochloride, Transdermal patch, Solvent casting technique, *In vitro* skin permeation

ABSTRACT

Objective: The present investigation aimed to prepare transdermal patches containing Sertraline Hydrochloride. The main was to minimize the dose of the drug for lesser side effects and increase the bioavailability of a drug. **Methods:** In the present study, a drug-loaded transdermal patch of Sertraline Hydrochloride was prepared by the solvent casting method with the help of polymers along with polyethylene glycol (PEG) 400 was used as the plasticizer. **Results:** The formulated transdermal patch by using sodium alginate, eudragit and HPMC K100M showed good physical properties. All prepared formulations indicated good physical stability. The results were best in *in-vitro* skin permeation through rat skin as compared to all other formulations prepared with a hydrophilic polymer containing permeation enhancer. The formulation, F1 is considered as the best formulation, since it shows maximum *in vitro* drug release as 99.321% at 6 hours. **Conclusion:** In conclusion, transdermal drug delivery system (TDDS) patches of Sertraline hydrochloride can be prepared using the polymer combinations, with plasticizer and enhancer. The release rate of the drug through patched increased simultaneously as the concentration of hydrophilic polymer was increased.

INTRODUCTION:

Transdermal drug delivery has been accepted as a potential non-invasive route of drug administration, with advantages of prolonged therapeutic action [1]. For decades, the utilization of skin as a route for delivering drugs has been an attractive alternative to conventional methods including injections and tablets. Its advantages include prolonged therapeutic action, decreased side effects, easy use, avoidance of pain, withdrawal in case of side effects, safety, better patient compliance,[2] avoidance of first-pass metabolism, and prevention of gastrointestinal degradation [3]. This method also tolerates reduced pharmacological dosing due to the shortened metabolization pathway to the transdermal route against the gastrointestinal pathway. The transdermal patch also allows stable dosing rather than the peaks and valleys in medication level connected with orally controlled medications. The route of oral administration has certain disadvantages for example damage of drugs by hepatic first pass through the metabolism and enzymatic degradation in the gastrointestinal tract. Constant intravenous administration at a programmed rate has been known as a superior mode of drug delivery not only to bypass the hepatic first-pass effect but also to sustain a constant, extended, and therapeutically effectual drug level in the body [4, 5].

Sertraline Hydrochloride is the hydrochloride salt of sertraline, a synthetic derivative of naphthalenamine with anti-serotoninergic and anti-depressant properties. Sertraline appears to selectively inhibit the neuronal uptake of serotonin, raising serotonin levels in the CNS. Sertraline hydrochloride is hydrochloride resulting from the reaction of equimolar amounts of sertraline and hydrogen chloride. A selective serotonin-reuptake inhibitor (SSRI), it is administered orally as an antidepressant for the treatment of depression, obsessive-compulsive disorder, panic disorder, and post-traumatic stress disorder. It has a role as a serotonin uptake inhibitor and an antidepressant.

The literature showed that this drug is being used in the treatment of depression but no scientific and research data is reported to treat depression using this drug in the form of transdermal patches. Our effort was to establish the transdermal patches containing Sertraline Hydrochloride and scientific data of this drug as cheap, common and affordable, effective, safe, readily available substitute antidepressant agent [6, 7].

MATERIALS AND METHODS:

MATERIALS:

Imipramine hydrochloride was a gifts sample from Harika Drugs Pvt. Ltd, Hyderabad, India and Hydroxy Propyl Methyl Cellulose (HPMC) K100M, Sodium alginate, Eudragit was purchased from Central Drug House Ltd., New Delhi, and Sodium phosphate monobasic dihydrate, Polyethylene glycol 400, Tween 80 LR was purchased from Merck, Mumbai, and S.D. Fine Chem Limited, India respectively.

METHODS:

Determination of Wavelength (λ_{max}): Sertraline hydrochloride drug 10 mg was accurately weighed and transferred into a 10 ml volumetric flask dissolved and volume make up with the ethanol. Take 0.1 ml solution from the stock and transfer it to 10ml volumetric flask and volume makeup with the help of ethanol then scan for determination of wavelength by double beam UV spectrophotometer [8].

Mass Spectroscopy Studies: Sample was sent to the Jubilant Chemsys Limited Noida, U.P. (INDIA), and a graph was shown in the results.

FTIR Studies: Sample was sent to the Jubilant Chemsys Limited Noida, U.P. (INDIA) and a graph was a show in the results.

Compatibility studies by HPLC:

Preparation of Mobile Phase: Mobile Phase was prepared by using ACN and Buffer in the ratio of 70:30 (v/v). Filter with the help of membrane filter (0.22µ) then sonicate it for 30 min.

Preparation of stock sample for compatibility studies: Stock sample was prepared by using a drug and each polymer in the ratio 50:50 w/w in 5 ml vials and adding 2 % of distilled water with constant mixing in triplets. Placed the prepared sample in stability chamber (at 40˚C ± 2˚C and 75% ± 5% RH), at room temperature and in freeze for 15 days.

Preparation of sample for compatibility studies: After 15 days weight accurately 10 mg of each sample from the stock in a 10 ml volumetric flask. Diluted and volume make up with the help of the mobile phase. Filter with the help of membrane filter then sonicates the sample for 30 min.

Chromatographic condition: Compatibility studies were performed with the help of the Shimadzu HPLC system using the C18 column under reversed-phase partition chromatographic conditions. The mobile phase flow rate was set at 1.0 ml/min. The injection volume of the sample was 20 µl. Detection was performed at 223nm wavelength. Run time was set for 15 min [9, 10].

Development of Analytical Method by Double Beam UV spectrophotometer:

Preparation of stock solution: Weight accurately 10 mg of the drug and transfer into 10 ml volumetric flask dissolved and volume make up with the phosphate buffer (pH 6.8).

Preparation of Phosphate Buffer pH 7.4 (100 ml): Weight accurately 1.42g of Sodium Dihydrogen Phosphate Dihydrate (Sodium Phosphate Monobasic Dihydrate) in 100 ml volumetric flask dissolved in distilled water and pH was adjusted with the help of acid and base then volume was made up with the distilled water.

Preparation of Calibration Sample: A calibration sample was prepared from the stock solution (i.e., 2,4,6,8.10 µg/ml). The absorbance was taken at 223nm that shows absorbance between UV Range (0.3-1.5).

Preparation of Validation Sample: For calculating the accuracy and precision Validation sample was also prepared from the stock solution in the triplicate (i.e., 3, 7, 9 µg/ml).

Validation of UV Analytical Method:

Linearity: Absorbance value and respective Conc. of calibration sample were plotted and least square linear regression was performed. The correlation coefficient was calculated as a measure of linearity [11].

Accuracy: Accuracy at each Conc. of validation sample was measured in terms of percent bias using formula.

$$\text{Percent bias} = \left[\frac{\text{Theroretical Conc.} - \text{Observed Conc.}}{\text{Theroretical Conc.}} \right] \times 100$$

Precision: Precision at each Conc. of validation sample was calculated in terms of relative standard deviation using the following formula [12].

$$\text{Relative Standard Deviation} = \left[\frac{\text{Standard Deviation}}{\text{Mean of calculated Conc.}}\right] \times 100$$

Stability study by HPLC Method:

Preparation of Mobile Phase: Mobile Phase was prepared by using ACN and Buffer in the ratio of 70:30 (v/v). Filter with the help of membrane filter (0.22µ) then sonicate it for 30 min.

Preparation of stock sample for drug stability studies: Weight accurately 50 mg of the drug in 50 ml volumetric flask in triplets, dissolved and volume make up with the help of phosphate buffer (pH – 7.4). Placed the sample in stability chamber (at 40˚C ± 2˚C and 75% ± 5% RH), at room temperature and in freeze for 15 days [13].

Preparation of sample for compatibility studies: After 15 days weight accurately 0.1 ml of the sample from all stock in 10 ml volumetric flask separately. Diluted and volume make up with the help of the mobile phase. Sonicate the sample for 30 min. Then analyze the sample with the help of HPLC.

Chromatographic condition: Compatibility studies were performed with the help of the Shimadzu HPLC system using the C18 column under reversed-phase partition chromatographic conditions. The mobile phase flow rate was set at 1.0 ml/min. The injection volume of the sample was 20 µl. Detection was performed at 223nm wavelength. Run time was set for 15 min [14].

Formulation of Sertraline Hydrochloride Patch for Transdermal Drug Delivery System by Solvent Casting Technique: Sertraline Hydrochloride Patch for Transdermal Drug Delivery System is preferably formulated using the solvent casting method, whereby the water-soluble ingredients are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally cast into the Petri plate and dried [15]. (Composition of Drug, Polymer, and other Excipients show below in Table 1 and Prepared Sertraline Hydrochloride Patch for Transdermal Drug Delivery System show below in Fig. 1)

Table No. 1: Formulation chart

S.N.	Drug (Mg)	Sodium Alginate (Mg)	Eudragit (mg)	HPMC E15 (Mg)	Glycerine (ml)	Tween 80 (ml)	PEG 400(ml)	Buffer	Water
1	160	160			0.2		0.4	q.s	q.s
2	160		160		0.2		0.4	q.s	q.s
3	160			160	0.2		0.4	q.s	q.s
4	160	80		80	0.2		0.4	q.s	q.s
5	160		80	80	0.2		0.4	q.s	q.s
6	160	160			0.2	0.5	0.4	q.s	q.s
7	160		160		0.2	0.5	0.4	q.s	q.s
8	160			160	0.2	0.5	0.4	q.s	q.s
9	160	80		80	0.2	0.5	0.4	q.s	q.s
19	160		80	80	0.2	0.5	0.4	q.s	q.s

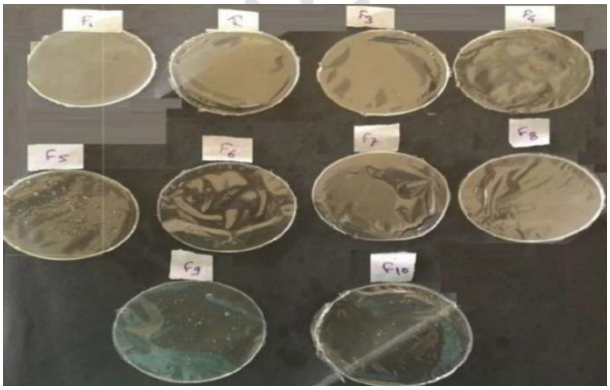


Fig. No. 1: Sertraline hydrochloride patch for transdermal drug delivery system

EVALUATION PARAMETER OF TRANSDERMAL DRUG DELIVERY SYSTEM:

Weight Variation: For evaluation of patch weight, three patches of every formulation are selected randomly and the individual weight of each 1x1cm patch was taken on a digital balance. The average weight was calculated.

Film thickness: The thickness of the film is measured by using a screw gauge with a least count of 0.01 mm at different places on the film. The thickness of the film was measured at three different places and the average thickness is the measure.

Surface pH: For determination of surface pH three patches of each formulation are allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of patches and allowing equilibration for 1 min. A mean of three reading is recorded [16, 17].

Folding endurance: Folding endurance of the film is determined by repeatedly folding one film at the same place till it broke, which was considered satisfactory to reveal good films properties. The number of times films could be folded at the same place without breaking gave the value of the folding endurance. This test was done on randomly selected three films from each formulation.

Drug content uniformity: This parameter was determined by dissolving film of 1 × 1cm diameter containing drug in 50 ml simulated salivary fluid with occasional shaking. Filtration was carried out to remove insoluble residue, 1 ml of the filtrate was diluted to 10 ml with simulated salivary fluid (pH 6.8). The absorbance was measured at specified nm using a UV spectrophotometer. The experiments were carried out in triplicate for the films of all formulations.

Tensile Strength: Tensile strength of the Transdermal Patch was determined by using a modified analytical balance strength machine. The sensitivity of the machine is one gram. It consists of 2 load cell grips. The lower one is fixed and the upper one is movable. The test patch of a specific size is fixed between these cell grips and force was gradually applied, till the patch breaks. The tensile strength of the patch was taken directly from the dial [18].

Percentage Moisture content: The Transdermal Patch is weighed accurately and kept in desiccators containing anhydrous calcium chloride. After three days, the patches were taken out and weighed [16]. The moisture content (%) was determined by the formula:

$$\% \text{ Moisture content} = [\text{Initial weight} - \text{Final weight}] / \text{Initial weight} \times 100$$

***In-vitro* Dissolution test:** The in vitro dissolution study is carried out in stimulated saliva solution pH 6.8 phosphate buffer using USP paddle (Type II) apparatus at 37±0.5°C. Samples are withdrawn at a regular time interval and analyzed by a UV-Visible spectrophotometer. In-vitro drug dissolution was performed using USP paddle apparatus. The studies were carried out at 37°C with a stirring speed of 50 rpm in 900 ml of pH 6.8 phosphate buffer dissolution medium. 5 ml of samples were withdrawn at predetermined time intervals of 1,2,3,4,5,6

minute and replaced with the same volume of buffer. The samples were collected and the absorbance was determined at 223 nm UV-visible spectrophotometer [19].

Skin Irritation Study: Skin irritation and sensitization testing was performed on healthy rats (average weight 200-250g). The dorsal surface (2cm2) of the rabbit is to be cleaned and remove the hair from the clean dorsal surface by shaving and cleaning the surface by using rectified spirit and the representative formulations can be applied over the skin. The patch is to be removed after 24 hr and the skin is to be observed and based on the severity of skin injury.

***In vitro* Skin Permeation Studies:** An *in vitro* permeation study can be carried out by using a diffusion cell. Full-thickness abdominal skin of male rats weighing 200 to 250g. Hair from the abdominal region is to be removed carefully, the dermal side of the skin is thoroughly cleaned with distilled water to remove any adhering tissues or blood vessels, equilibrated for an hour in dissolution medium or phosphate buffer pH 7.4 before starting the experiment, and is placed on a magnetic stirrer with a small magnetic needle for uniform distribution of the diffusant. The temperature of the cell is maintained at 32 ± 0.5°C using a thermostatically controlled heater. The isolated rat skin piece is to be mounted between the compartments of the diffusion cell, with the epidermis facing upward into the donor compartment. The sample volume of definite volume is to be removed from the receptor compartment at regular intervals, and an equal volume of fresh medium is to be replaced. Samples are to be filtered through a filtering medium and can be analyzed spectrophotometrically or HPLC [20].

RESULTS AND DISCUSSION:

Determination of Wave Length (λ_{max}): The wavelength of the Sertraline hydrochloride drug in Ethanol was found to be 248nm. (Spectra of Sertraline hydrochloride in Ethanol show below in Fig. 2)

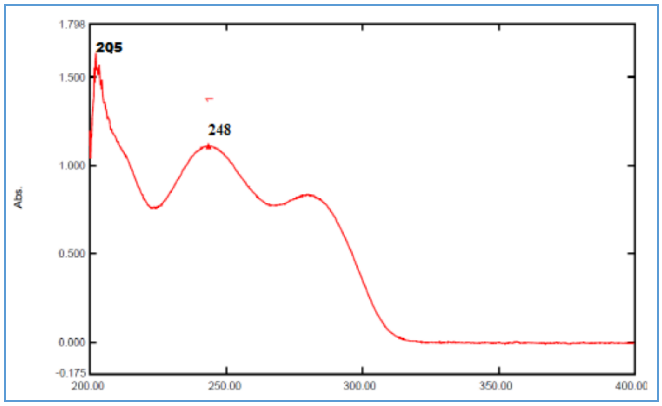


Fig. No. 2: Spectra of Sertraline hydrochloride drug in ethanol

Mass Spectroscopy Studies: The Spectroscopy was done, and the Mass of the Sertraline hydrochloride Drug was found to be 274. (Spectra of Mass Spectroscopy show below in Fig. 3)

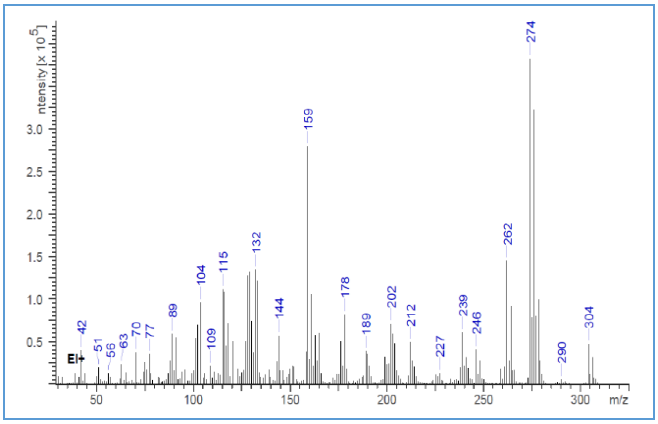


Fig. No. 3: Spectra of mass spectroscopy

FTIR Studies: FTIR Studies were done, and spectra are shown below. (Spectra of drug show in Fig. 4, Spectra of polymer show in Fig. 5, Compatibility Spectra of drug and polymer show in Fig. 6)

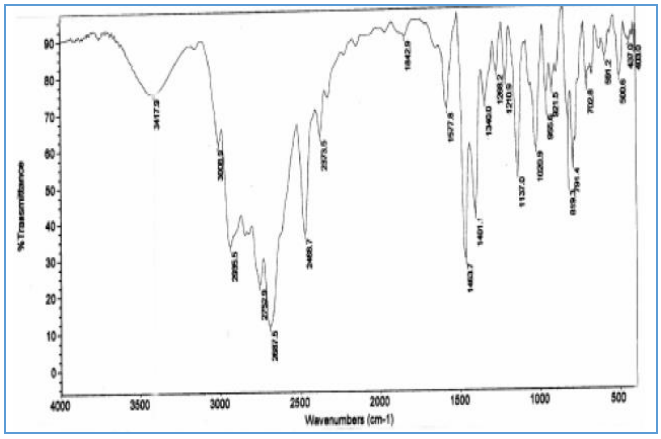


Fig. No. 4 FTIR Spectra of pure drug

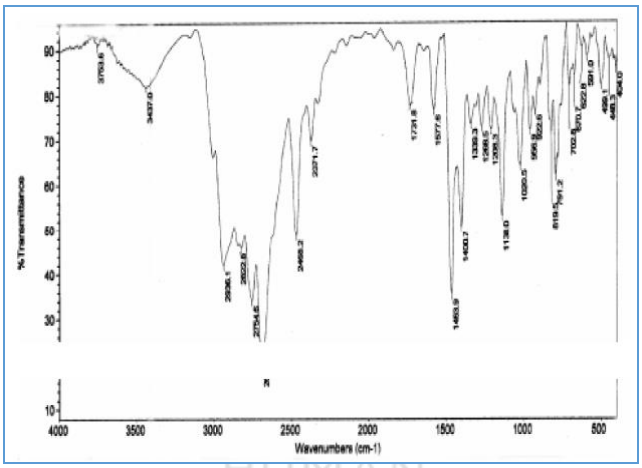


Fig. No. 5: FTIR spectra of drug and sodium alginate,

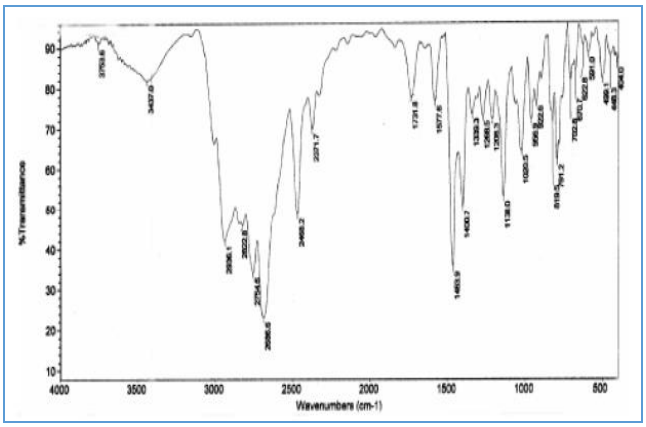


Fig. No. 6: Compatibility FTIR spectra of drug and eudragit

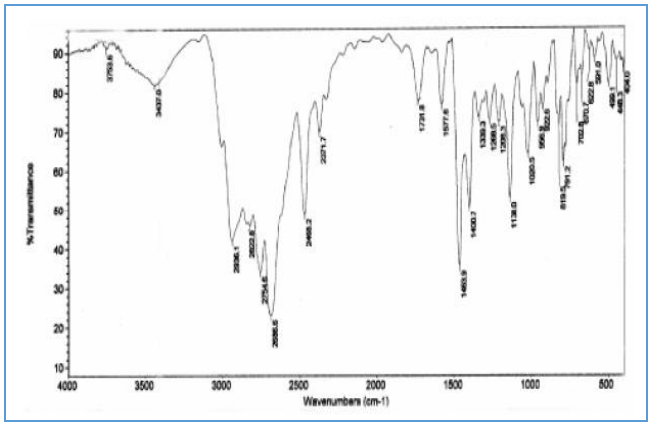


Fig. No. 7: Compatibility FTIR spectra of drug and HPMC E15

Compatibility Spectra of drug and polymer do not show a change in the drug and polymer peak and its value when compared with pure drug and polymer spectra that show compatibility for formulation**.**

Compatibility studies by HPLC

Compatibility studies of the drug with polymer were done and Spectra show below in Fig. 8, Fig. 9, and 10.

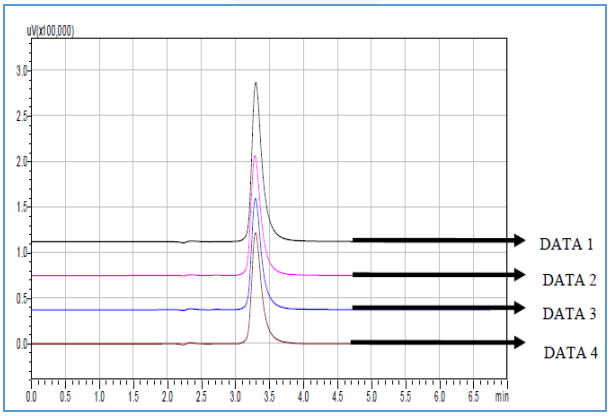


Fig. No. 8: Compatibility study of Sertraline hydrochloride drug with polymer sodium alginate (*DATA 1- Fresh, DATA 2- At Room, DATA 3- At Stability Chamber, DATA 4- At Freeze)

Compatibility spectra of dug with polymer sodium alginate do not show a change in area and RT in all conditions when compared with a fresh sample that shows the compatibility of drug and polymer.

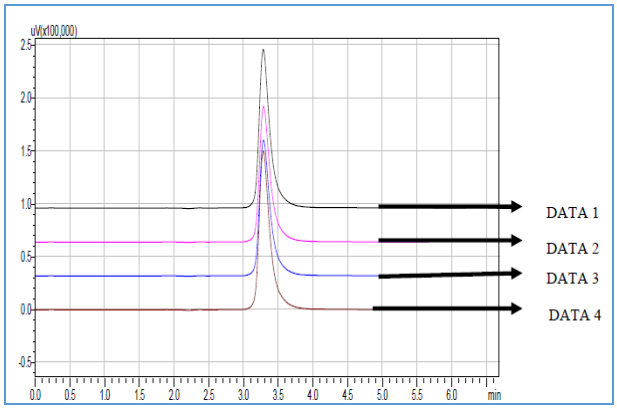


Fig. No. 9: Compatibility study of Sertraline hydrochloride drug with polymer eudragit (*DATA 1- Fresh, DATA 2- At Room, DATA 3- At Stability Chamber, DATA 4- At Freeze)

Compatibility spectra of dug with polymer eudragit do not show a change in area and RT in all conditions when compared with the fresh sample that shows the compatibility of drug and polymer.

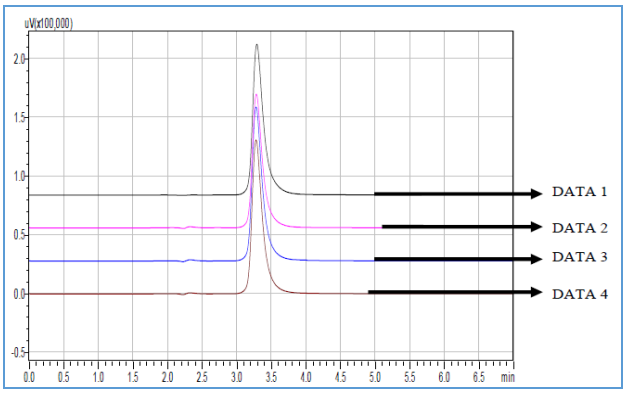


Fig. No. 10: Compatibility study of Sertraline hydrochloride drug with polymer HPMC E15 (*DATA 1- Fresh, DATA 2- At Room, DATA 3- At Stability Chamber, DATA 4-At Freeze)

Compatibility spectra of dug with polymer HPMC E15 do not show a change in area and RT in all conditions when compared with the fresh sample that shows the compatibility of drug and polymer.

Development of Analytical Method by Double Beam UV Spectrophotometer: The wavelength of Sertraline hydrochloride Drug in Phosphate Buffer (pH - 7.4) was found to be 274nm. (Spectra of Sertraline hydrochloride show below in Fig. 11)

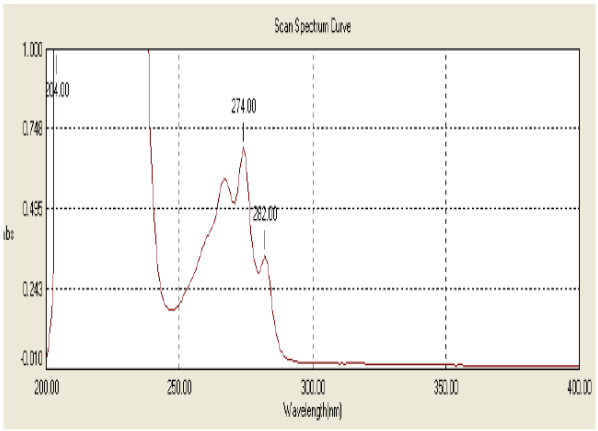


Fig. No. 11: Spectra of Sertraline hydrochloride drug in phosphate buffer (pH - 7.4)

UV Analytical Method: Calibration and Validation of the Sertraline hydrochloride drug was done. (Calibration Reading is shown below in Table 5.1, Intraday Calibration Data shown below in Table 2, Intraday Accuracy, precision S.D., etc. show below in Table. 5.3 and Calibration Graph show below in Fig. 5.10)

Table No. 2: Calibration reading

Calibration Samples(µg/ml)	Avg.
0	0
2	0.3289
4	0.5545
6	0.8633
8	1.1365
10	1.4411

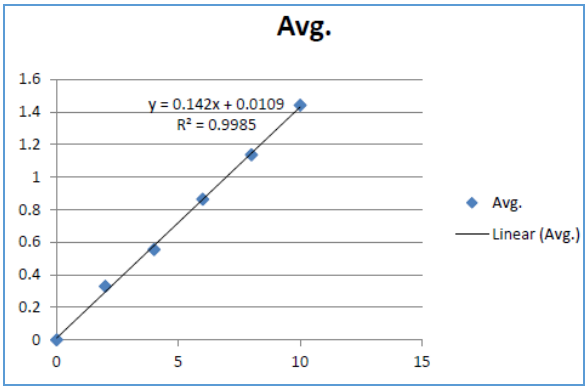


Fig. No. 12: Calibration curve of Sertraline hydrochloride drug in buffer pH – 7.4

Table No. 3 Intraday calibration data

Calibration Samples (µg/ml)	Abs. Day 1	Abs. Day2	Abs. Day3	Avg.
0	0	0	0	0
2	0.3173	0.318	0.3189	0.3189
4	0.5435	0.5465	0.5675	0.5525
6	0.834	0.8196	0.8213	0.8249
8	1.1315	1.133	1.143	1.135833333
10	1.422	1.3862	1.3541	1.387433333

Table No. 4: Intraday accuracy, precision, S.D., R.S.D., percent error data of validation samples at 274nm

Validation	Abs. Day 1	Abs. Day2	Abs. Day3	Avg. (x)	Amount	Avg. Amount	Accuracy (%)	SD	RSD	% Error
	0.4241	0.4171	0.4511	0.430766667	3.043035	3.0281095	100.9369818	0.019003	0.627567	0.936982
	0.4332	0.4212	0.4345	0.429633333	3.034577					
	0.4133	0.4123	0.4521	0.4259	3.006716					
7	0.9251	0.9648	0.9624	0.950766667	6.923632	6.8963516	98.51930822	0.03587	0.520123	-1.480
	0.9451	0.9167	0.9632	0.941666667	6.855721					
	0.9431	0.9221	0.9815	0.9489	6.909701					
9	1.3213	1.1146	1.2321	1.222666667	8.952736	9.0364842	100.4053805	0.072589	0.803291	0.405381
	1.2431	1.2431	1.2311	1.2391	9.075373					
	1.2345	1.232	1.2532	1.2399	9.081343					

Stability study by HPLC Method (After 15 days): A stability study of Sertraline hydrochloride was done. (Calibration Reading of fresh sample show below in Table 5 and Calibration Graph show in Fig. 13 Stability Spectra of the drug show below in Fig. 14)

Table No. 5: Calibration reading (Fresh)

CALIBRATION SAMPLES	AREA
10 (µg/ml)	1043776
20 (µg/ml)	2260273
30 (µg/ml)	3281013
40 (µg/ml)	4305214
50(µg/ml)	5448757

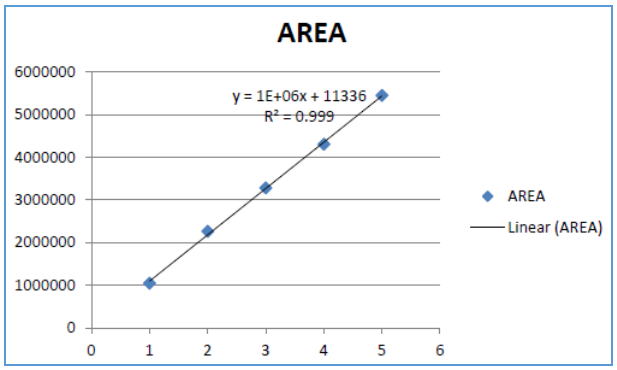


Fig. No. 13: Calibration curve of Sertraline hydrochloride drug

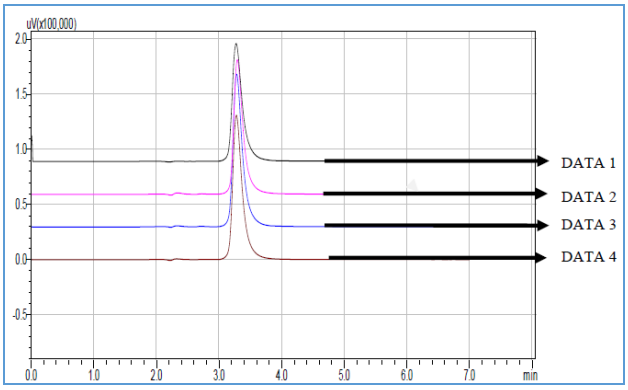


Fig. No. 14: Stability study of Sertraline hydrochloride drug (After 15 Days)(*DATA 1- Fresh, DATA 2- At Room, DATA 3- At Stability Chamber DATA 4-At Freeze)

No change was found in organoleptic properties and RT in all conditions after 15 days when compared with the fresh sample that shows the stability of the drug.

EVALUATION RESULTS OF TRANSDERMAL DRUG DELIVERY SYSTEM

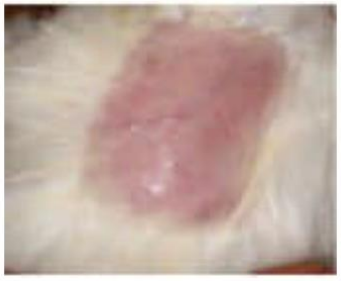
Evaluation of Sertraline Hydrochloride Patch for Transdermal Drug Delivery System was done. (Evaluation Data Show below in Table 6; Drug Release Profile Graph show in Fig. 15)

Table No. 6: Evaluation data of formulation F1.F2...F10

Formulation	Drug Content(%)	Weight Variation (mg)	Surface pH	Folding Endurance	Disintegration Time (In Sec.)	Tensile Strength(G)	Thickness (mm)	%Moisture Content
F1	99.1	17.76±0.11	7.4±0.02	4.78±0.52	95±0.002	141.2	0.15±0.01	1.4
F2	98.4	18.06±0.02	7.4±0.09	4.88±0.55	98±0.001	142.7	0.15±0.01	1.47
F3	99.3	18.83±0.50	7.37±0.02	4.56±0.54	95±0.001	140.5	0.16±0.01	1.27
F4	96.45	19.60±0.22	7.40±0.01	4.67±0.56	85±0.001	140.4	0.15±0.04	1.31
F5	97.17	18.53±0.90	7.36±0.04	5.51±0.57	94±0.003	143.8	0.15±0.02	2.14
F6	99.98	18.53±0.30	7.41±0.02	5.53±0.55	100±0.001	141.3	0.16±0.01	2.13
F7	93.66	19.06±0.55	7.41±0.01	5.63±0.52	104±0.002	141.8	0.15±0.01	1.18
F8	97.81	19.40±0.52	7.38±0.01	5.46±0.56	107±0.001	142.4	0.16±0.01	2.24
F9	91.6	19.63±0.45	7.39±0.01	5.52±0.57	111±0.002	142.5	0.16±0.01	1.18
F10	96.51	18.66±0.50	7.40±0.01	5.56±0.57	106±0.003	140.1	0.16±0.01	2.11

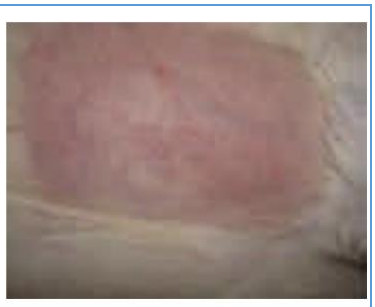
Skin Irritation study

No type of skin irritation effect was found on the rats' skin.



Rat skin after shaving the hair

Drug loaded transdermal patch pasted on the rat skin



Rat skin after removal of patch

In vitro skin permeation studies were found that the use of permeation enhancers increases the skin permeation of drugs.

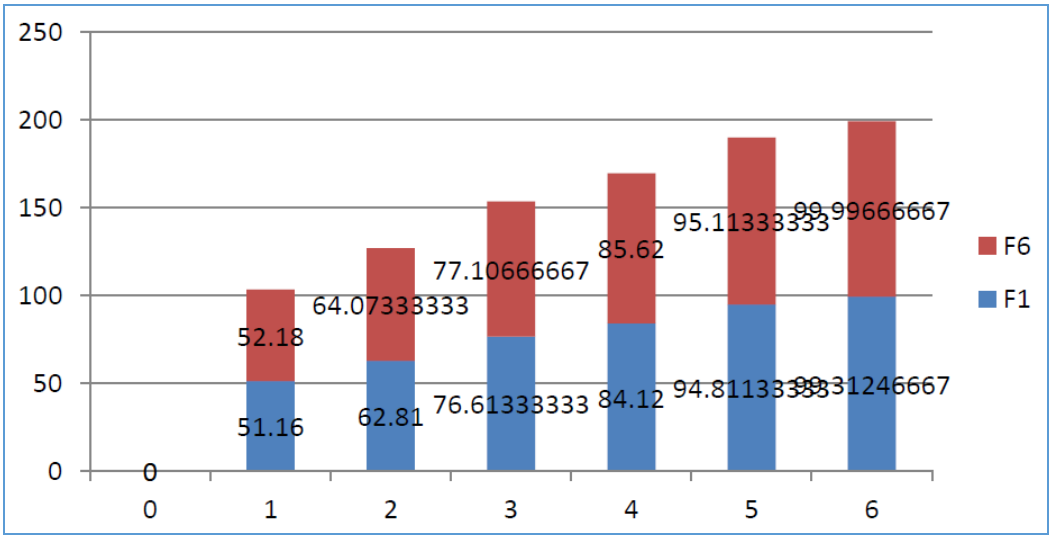


Fig. No. 15: In-Vitro Skin Permeation Profile of Sertraline hydrochloride (F1- without enhancer F6 - with enhancer)

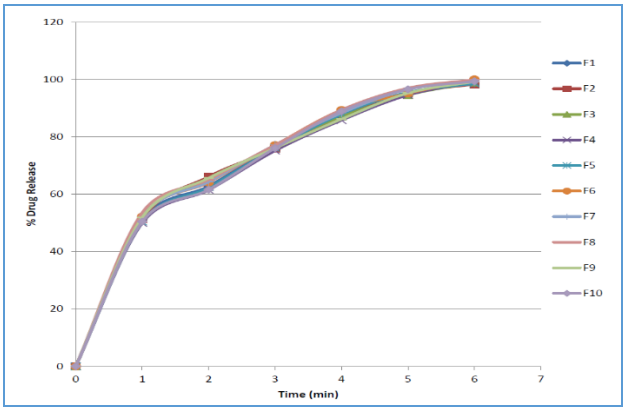


Fig. No. 16: Drug release profile

CONCLUSION:

Transdermal Patch of Sertraline hydrochloride was successfully prepared by solvent casting technique using Sodium alginate, Eudragit, HPMC E15 use as the Mucoadhesive Polymer, Tween 80 as Surfactant and Propylene Glycol 400 as Plasticizer. All the prepared formulations were evaluated for physical characteristics and Pharmaceutical Parameters. *In Vitro* Dissolution Profile of the drug, formulation F1 shows 99.312467 % Drug Release. But the use of penetration enhancer increases the dissolution profile then F6 shows 99.99667 %. So, in all prepared and evaluated formulations, F8 was found to be best for large-scale production. Sertraline Hydrochloride Patch for Transdermal Drug Delivery System was found to be an alternative to conventional dosage forms for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms.

REFERENCES:

1. Jianfang M.A., Chengxiao W., Huafei L. (2013) Design and evaluation of a monolithic drug-in-adhesive patch for Testosterone Based on Styrene–Isoprene–Styrene block copolymer. J Pharm Sci., 102 (7): 2221–2234.
2. Yang C., Peng Q., Xiaochang L. (2014) Novel chemical permeation enhancers for transdermal drug delivery. Asian J Pharma Sci., 9:51-64.
3. Eneko L., Rebecca EM Lutton, Woolfson A.D. (2016) Microneedle arrays as transdermal and intradermal drug delivery systems: Materials science, manufacture, and commercial development. Material Sci. Eng. R., 104:1–32.
4. Latha S, Selvamani P, Thirunavukkarasu C, kadambavadani R. Formulation development and comparison in the evaluation of a transdermal drugs delivery system for anti-emetic therapy. Int J Res Pharm Biomed Sci 2011;2:525-8.
5. Costa P, Ferreria DC, Morgado R, Sousa Lobo JM. Design and evaluation of the lorazepam transdermal delivery system. Drug Dev Ind Pharm 1997;23:939-44.
6. Apoorva, M., 2012. Formulation & Evaluation of Transdermal Patch of Sertraline. International Journal of Drug Development & Research 4, 220-226.
7. Ayarivan, P., 2011. Development and characterization of Eudragit based mucoadhesive Transdermal Patch of salbutamol sulfate. Saudi Pharmaceutical Journal 19, 207-214.
8. Deore V.A., Kumar R.S., P.S., G., 2013. Development and Statistical Optimization of Mucoadhesive Transdermal Patch of Indomethacin: In-vitro and Ex-vivo evaluation. International Journal of Advances in Pharmacy, Biology and Chemistry 2, 405-422.
9. Senthil Adimoolam, Navinchanda Chauhan Pratik, RavajibhaiYakinkumarSiroya, Patel JayantibhaiFalgunibeg, Vantoor, N.B., 2012. Formulation and Evaluation of Venlafaxine Hydrochloride Transdermal Buccal Patch. International Research Journal of Pharmacy 3, 282-286.
10. Patil Swapnil L., Mahaparale Paresh R., Shivnikar Madhavi A., Tiwari Shradha S., Pawar Ketan V., N., S.P., 2013. Transdermal Films an Innovative Drug Delivery System. International Journal of Research and Reviews in Pharmacy and Applied science 2, 482-496.
11. C, S.C., 2013. Formulation and Evaluation of Fumarate Transdermal Patch by Using Selected Polymers. Internation Journal of Pharmaceutical, Chemical and Biological Sciences 3, 854-860.
12. Saravanthi R.R., Rajalakshmi R., Krishna Moorthy S.B., Rupangada V., E., R.S., 2014. Mucoadhesive Transdermal Patch, An Innovative Drug Delivery System. International Journal of Pharm Tech Research 6, 1665-1678.
13. Panda B.P., Dey N.S., M.E.B., R., 2012. Development of Innovative Transdermal Film Dosage Forms: A Review. International Journal of Pharmaceutical Science and Nanotechnology 5, 1666-1674.
14. Bhimavarapu Rama Devi, NissankararaoDr. Srinath, Vaidya Swamynath V., Sandhyasree S., Shamili Swapna M., B., R.D., 2013. Development and In-vitro Evaluation of Mucoadhesive Transdermal Patch of Sertraline HCL. American Journal of Advanced Drug Delivery 1, 313-322.
15. Chinnala, 2015. Formulation and Evaluation of Transdermal Patch Containing Tizanidine Hydrochloride. International Journal of Pharma Research and Health Sciences 3, 621-635.
16. Mohamed Magdy I., Soliman Nadia A., H., A.-E.R.S., 2015. Development of A Novel Ketorolac Tromethamine Transdermal Patch. Journal of American Science 11, 27-37.
17. Desu Prasanna, Manoranjan, S., 2012. Formulation and Evaluation of Transdermal Patch of Zolmitriptan. International Research Journal of Pharmacy 3, 373-376.
18. Radha Madhavi B., Murthy Varanasi S.N., Rani Prameela A., Dileep, G.K., 2013. Transdermal Patch Drug Delivery System -An Innovative and Emerging Technology. Molecular Pharmaceutics & Organic Process Research 1, 1-6.
19. Sridhar Iswarya, Abha, D., 2013. Formulation and Characterization of Transdermal Patch of Ondansetron Hydrochloride. International Journal of Pharmaceutical Research and Development 5, 84-94.
20. Reddy P Srikanth et al. 2014. Design and Development of Transdermal Patches for Perindopril. Research Journal of Pharmaceutical, Biological and Chemical Sciences 5(2), 1525-1534.