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FORMULATION AND EVALUATION OF MATRIX TYPE TRANSDERMAL PATCHES OF ATENOLOL AND STUDY THE EFFECT OF PERMEATION ENHANCER

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Abstract:
Transdermal drug delivery attaining much focus in the field of topical administration of dosage form for systematic circulation. The structure and composition of skin is major obstacle of this route which makes it impermeable for most of the substances. Its impermeability may be altered with the specific techniques like physical approaches or prodrug or uses of chemical enhancer. Atenolol is a selective β1 receptor blocker and effective in treatment of hypertension. The oral administration of its having short biological half life approximately 6 hours and due to extensive first pass metabolism only 45% reaches in the systemic circulation. Therefore need of a suitable type of dosage form of drug which is able to avoid the above subsidence for the systemic circulation.
The results showed Atenolol-HPMC-PVP patches having good physicochemical properties like appearance, weight variation, drug content, thickness, folding endurance. Moisture absorption and WVTR studied showed that patches were able to maintain their integrity. The cumulative in-vitro drug release was performed in phosphate buffer pH 7.4, in present study formulation HP1 exhibit 14.21±2.1 to 72.77±2.2, HP2 exhibit 17.35±1.8 to 76.32±2.8, HP3 exhibit 18.41±1.1 and HP4 exhibit 18.32±1.5 to 83.76±2.1 percent of release. In- vitro permeation studies were done on wistar rat skin. DMSO 1%w/w was used as permeation enhancer which significantly increased the cumulative permeated amount of atenlol. The permeation followed as HP1 exhibit 5.12±0.6 to 43.67±2.5, HP2 exhibit 6.03±0.3 to 51.83.HP3 exhibit 6.97±1.3 to 55.02±1.1, HP4 exhibit 8.48±1.5 to 57.53±1.5, HP5 exhibit 8.13±0.8 to 47.88±2.8, HP6 exhibit 10.15±0.9 to 55.58±2.3, HP7 exhibit 11.56±1.2 to 60.97±1.6 and HP8 exhibit 12.8±1.5 to 65.83±2.0 percent of release.
The method devised to prepare the patches was effective and reproducible. The patches formed were uniform with respect to physicochemical characteristics. In-vitro and In-vivo permeation of atenolol was better because of its hydrophilic nature exert an interaction with water soluble polymers resulted an increased drug release. The results showed that matrix type atenolol transdermal patches could be developed and administered via topical route over a prolonged period.
Keywords:*TDDS, Permeation enhancer, Systemic circulation, First pass metabolism, Atenolol,*

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INTRODUCTION:

Transdermal drug delivery attaining much focus in the field of topical administration of dosage form for systematically at a predetermined and reproducible rate over a prolonged period. The major obstacle of this route is the impermeability of the skin. In which stratum-corneum is the barrier to diminish the entry of medication in the optimum quantity to elicit the systemic action. For transporting the drug by means of this route having certain physicochemical qualities like low molecular size, lower daily dosage and having both hydrophilic as well as lipophilic properties [1]**.** In case of hydrophilic drug it becomes necessary to use of chemical permeation enhancer or any other technique like iontophoresis, electroporation, microoperation, sonophoresis etc [2] to cross the lipoidal barrier of stratum corneum. The major advantage of this route is steady infusion of drug, avoid first pass metabolism, ease of elimination in case of any toxicity, and avoid the gastric irritation. Hypertension is usually defined by the presence of chronic elevation of systemic arterial pressure above a certain threshold value. This is a progressive cardiovascular syndrome arising from complex and interrelated etiologies [3]**.** Atenolol is a selective β1 receptor blocker and effective in treatment of hypertension. Molecular weight of atenolol is 266.336[4] and the oral administration of it having short biological half life approximately 6 hours and due to hepatic activity only 45% reaches in the systemic circulation [5]therefore transdermal route is a suitable choice of delivery of drug for the systemic circulation.

MATERIAL AND METHODS:

Material: Atenolol was supplied as a gift sample from fourt's India, Chennai. HPMC, DMSO procured from S.D. fine chemical Ltd., Mumbai, India.PVP from BDH Ltd. Mumbai, India. All other chemicals used were of analytical grade.

Fabrication of Medicated Patches: The transdermal patches were prepared by solvent evaporation method. The polymers were weighed and dissolved in specified quantity of distilled water and mixed thoroughly. Calculated quantity of glycerin was added as plasticizer and DMSO as penetration enhancer and mixed thoroughly with the help of magnetic stirrer. 0.625% w/v of drug was dissolved in this dispersion and mixed thoroughly for 10 minutes. The resulted solution was poured in to a Petri dish and kept aside for the complete evaporation of solvent. After 24 hours the dried films were taken out and wrapped properly in aluminum foil and stored in a desiccator till the further characterization.

Table:1 Fabrication of the Atenolol matrix film of HPMC : PVP

Formulation code	Polymer 3% w/v HPMC:PVP	Drug % w/v Atenolol	Plasticizer % w/v Glycerol	Penetration enhancer % w/v Oleic acid	Solvent % w/v Distilled water
HP1	100 : 00	0.625	1	-	100
HP2	90 : 10	0.625	1	-	100
HP3	80 : 20	0.625	1	-	100
HP4	70 : 30	0.625	1	-	100
HP5	100 : 00	0.625	1	0.5	100
HP6	90 : 10	0.625	1	0.5	100
HP7	80 : 20	0.625	1	0.5	100
HP8	70 : 30	0.625	1	0.5	100

Evaluation of Patches:

Physical appearance: All the patches were visually inspected for color, clarity, flexibility, and smoothness. The results were depicted in **table-2** [6]**.**

Weight uniformity: six patches of a specified area were cut and measure the individual weight and average weight with the help of digital valance. The results were depicted in **table-2**[7]**.**

Drug content uniformity: The specified area of patch was dissolved in suitable solvent and shaken continuously for 24 hours. Then solution was filtered through filter media and after making a suitable dilution the solution is estimated spectrophotometrically. The results were depicted in **table-2**. [8,9]

Thickness: The patch thickness was measured by using screw gauze at six different places and the average thickness was calculated for three patches. The results were depicted in **table-2**. [10]**.**

Folding endurance: It performed manually and folds the prepared patches repeatedly until it has torn. The numbers of folding without tear is termed as folding endurance and provide information about mechanical support needed during handling and transportation of patches. The results were depicted in **table-2**. [11]

Moisture absorption test: Weighed films were kept in a desiccator at room temperature for 24 hours. These were then exposed to saturated solution of sodium chloride in order to maintain 74%RH and ammonium hydrogen phosphate to produce 93%RH until a constant weight is attained [12,13]. The results were depicted in **table-3** and graphically shown in **fig-1**.The percentage moisture uptake was calculated by formula:

$$\textbf{Percentage moisture uptake} = \frac{(\textbf{Final weight} - \textbf{Inital weight})}{(\textbf{Initial weight})} \textbf{x100}$$

Water vapor transmission rate: water vapor transmission rate was determined by placing saturated solution of potassium chloride in a desiccator and the whole assembly was kept for three days to achieve the humid condition above 84% RH. Glass vials of equal diameter were taken and to this filled one gram of fused calcium chloride. Then patches were fixed over the brim of vials with the help of adhesive like silicon adhesive grease and the vials were weighed accurately. These vials were then placed in the desiccator maintained at 84% RH. Weight gained due to water vapor transmission through the film obtained by weighing these vials every 24 hours for seven days [14]**.**The results were depicted in **table-4** and graphically shown in **fig-2.** The transmission rate was calculated by using formula:

$$\textbf{Transmission rate} = \frac{(\mathbf{W} \times \mathbf{L})}{(\mathbf{S})}$$

W= water transmitted in gram
L= Thickness of film
S= Exposed surface area

In-vitro **drug release:** The paddle over disc apparatus (USP apparatus V) was employed for assessment of release of drug from the prepared patches. The patch of definite weight was fixed over a glass plate with an adhesive. The glass plate was placed in dissolution medium and apparatus was equilibrated at 32±5^{0}C. The paddle was set at a distance of 2.5 cm from the glass plate and operated at a speed of 50 rpm. The sample withdrawn at appropriate interval and after suitable dilution the absorbance was determined spectrophotometrically [15]**.** The results of cumulative in-vitro release were shown in **fig.3**

In- vitro **skin permeation studies:** in vitro permeation study was performed by using franz diffusion cell. The receptor compartment was filled with dissolution medium phosphate buffer saline pH 7.4 and placed on magnetic stirrer with a magnetic bead for uniform distribution of medium. The temperature was maintained at 32±0.5^{0}C by using thermostat. The isolated rat skin was sandwiched between donor and receiver compartment of diffusion cell with the stratum-corneum facing towards donor compartment side. A sample of definite volume was withdrawn at regular interval from the receiver compartment and equal volume of phosphate buffer saline was replaced. Samples were to be filtered through filtering media and analyzed after suitable dilution the absorbance was spectrophotometrically. [16]**.**The results of cumulative in-vitro permeation were shown in **fig.4 and 5**.

RESULT :

Characterization for HPMC: PVP Patches -The results of physicochemical parameters like appearance, weight variation, drug content, thickness, and folding endurance were shown in **table -2.**

Table:2 Characterization for HPMC : PVP Patches

Physical property	Formulation Code			
	HP1	HP2	HP3	HP4
Appearance	Transparent, smooth, non-Sticky	Opaque, smooth, non-Sticky	Opaque, smooth, non-Sticky	Opaque, smooth, non-Sticky
Weight Variation	19.61±1.5	20.81±2.4	19.01±1.6	19.73±12.7
Drug Content	98.02±1.82	98.43±1.23	99.02±0.34	99.22±1.49
Thickness	0.11±0.026	0.10±0.016	0.12±0.02	0.09±0.015
Folding Endurance	>300	>300	>300	>300

Moisture absorption- The moisture absorption studied results were shown in **table-3,** and their graphical representation were shown in **fig:1**

Table:3 Moisture absorption by HPMC: PVP Patches

Code	75% RH			93% RH		
	Wt. of Patch (mg)	Moist. Abs. (mg)	% Moist. Abs.	Wt. of Patch (mg)	Moist. Abs. (mg)	% Moist. Abs.
HP1	20.21	2.32	11.47	19.63	3.17	16.14
HP2	19.98	2.14	10.71	19.88	3.29	16.54
HP3	19.91	2.51	12.60	19.21	3.31	17.23
HP4	20.13	2.53	12.56	19.51	3.47	17.78
HP5	19.78	2.31	11.67	19.25	3.21	16.67
HP6	19.95	2.43	12.18	19.32	3.25	16.82
HP7	19.33	2.76	14.27	19.53	3.19	16.33
HP8	19.93	2.75	13.79	19.41	3.33	17.56

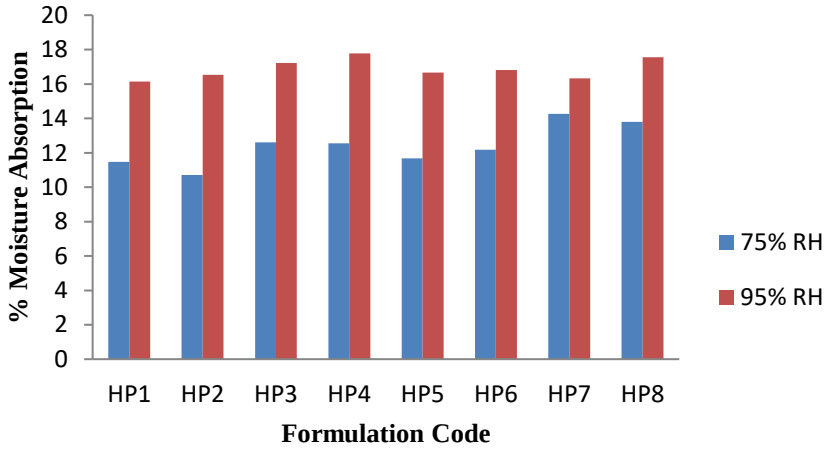

Fig:1 Moisture absorption Test

Water vapor transmission rate- The water vapor transmission rate results were showed in **table-4,** and their graphical representation were shown in **fig:2**

Table:4 WVTR by HPMC : PVP Patches

Code	Thickness (cm)	I day	II day	III day	IV day	V day	VI day	VII day	WVTR $\times 10^{-5}$ gm/cm/ 24hr
HP1	0.011	0.2747	0.2971	0.1920	0.1541	0.1431	0.1210	0.1150	4.2490
HP2	0.011	0.2971	0.2174	0.2830	0.1920	0.1541	0.1445	0.1220	4.8036
HP3	0.011	0.3346	0.2938	0.2570	0.2011	0.1771	0.1551	0.1450	5.1191
HP4	0.011	0.2971	0.3065	0.2830	0.2541	0.2130	0.1920	0.1650	5.0913
HP5	0.011	0.3187	0.2935	0.2410	0.2082	0.1710	0.1510	0.1400	5.0001
HP6	0.011	0.3567	0.3142	0.2751	0.2081	0.1852	0.1510	0.1390	5.3441
HP7	0.011	0.3567	0.3342	0.2937	0.2530	0.2112	0.1852	0.1710	5.9200
HP8	0.011	0.3571	0.3338	0.3037	0.2530	0.2312	0.1977	0.1720	6.0514

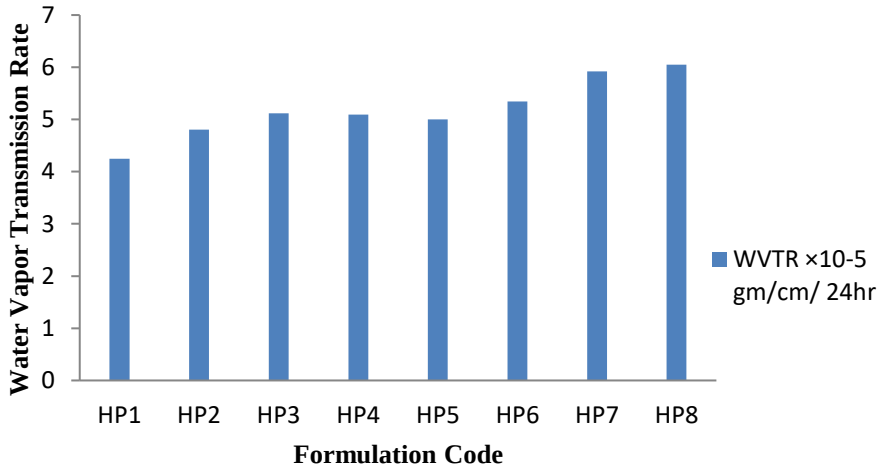

Fig:2 Water Vapor Transmission Rate

Cumulative in-vitro drug release-The cumulative in-vitro drug release was performed in phosphate buffer pH 7.4 and cumulative release of drug exhibited in **fig:3**

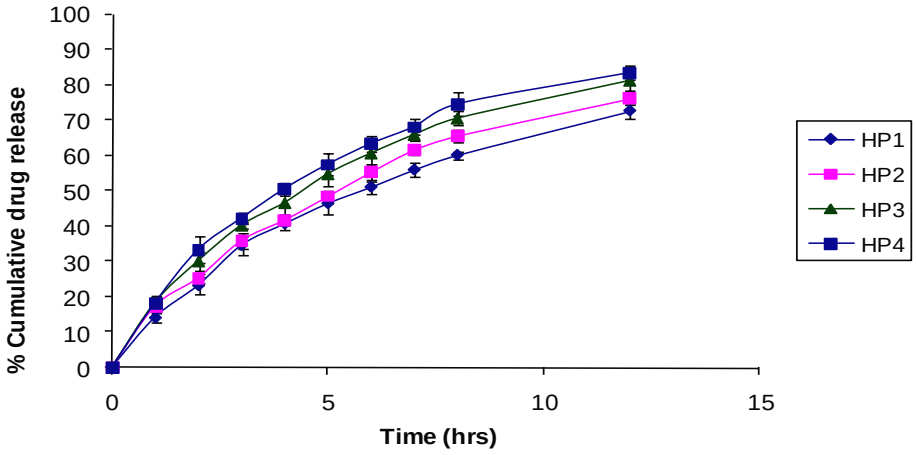

Fig:3 Percentage cumulative in-vitro release from HPMC:PVP patches

Cumulative in-vitro drug permeation and effect of permeation enhancer - The cumulative in-vitro permeation study was performed in phosphate buffer pH 7.4. The isolated rat skin was sandwiched between donor and receiver compartment of diffusion cell with the stratum-corneum facing towards donor compartment side. Cumulative in-vitro permeation and effect of enhancer were shown in **fig: 4 and 5** respectively.

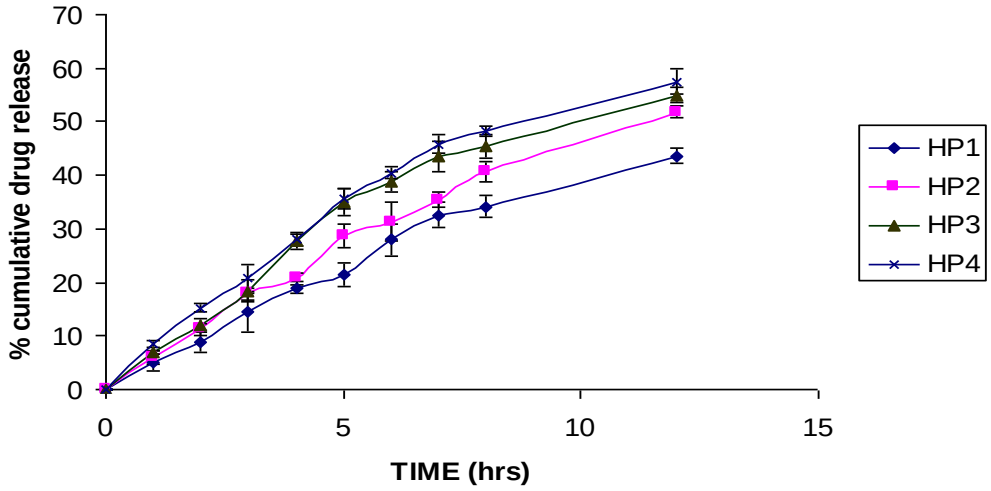

Fig:4 Percentage cumulative in-vitro permeation from HPMC:PVP patches

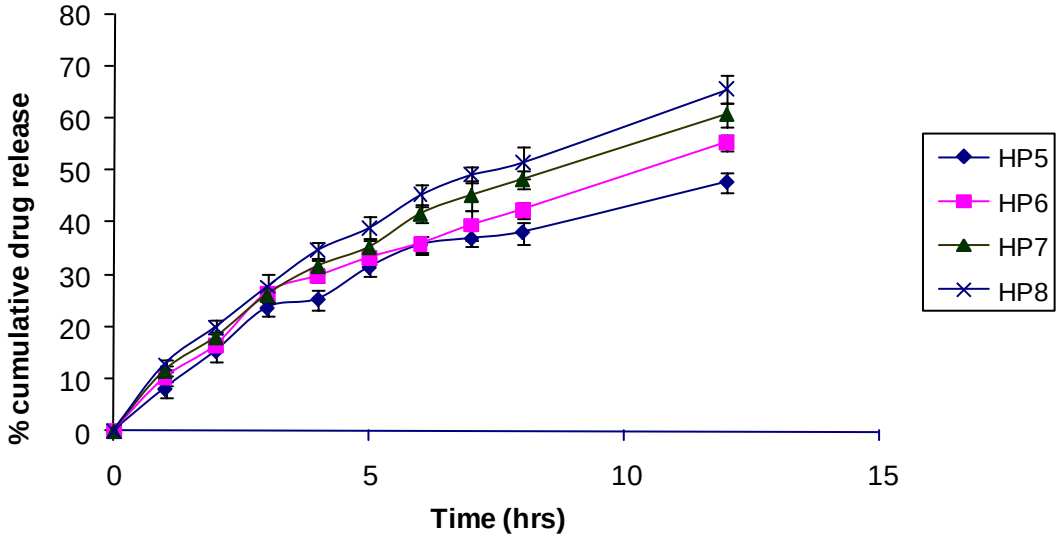

Fig:5 Effect of permeation enhancer on percentage cumulative in-vitro permeation from HPMC: PVP patches

DISCUSSION:

Characterization for HPMC: PVP Patches- Appearance offormulation HP1 which did not consist PVP was transparent, smooth and non-sticky, while all other formulation with PVP were opaque ,smooth and non-sticky. The weight of the patches were ranging from 19.01±1.6 to 20.81±2.4mg which were nearly almost same. Good uniformity of drug content was observed and it was ranges from 98.02±1.82 to 99.22±1.49. The results showed that the process employed for patch formulation had the minimum variability and efficient formulation techniques. Thickness of the patches was ranges from 0.09±0.015 to 0.12±0.02. The folding endurance of all the

patches were quite high >300 which indicate that patches have high mechanical strength and they would maintain their integrity on application of skin.

Moisture absorption-The moisture absorption studied were not show any uniform pattern at a specific relative humidity but at 93% RH absorption was higher than 75% RH and after three days all the patches were retain their shape although patches were sticky to touch.

Water vapor transmission rate-The water vapor transmission rate results were expressed that as the concentration of PVP increases relative to HPMC, the WVTR increases and ranging from 4.2490×10^{-5} gm/cm/ 24hr to 6.0514×10^{-5} gm/cm/ 24hr.

Cumulative in-vitro drug release-The cumulative in-vitro drug release was performed in phosphate buffer pH 7.4, in present study formulation HP1 exhibit 14.21±2.1 to 72.77±2.2, HP2 exhibit 17.35±1.8 to 76.32±2.8, HP3 exhibit 18.41±1.1 and HP4 exhibit 18.32±1.5 to 83.76±2.1 percent of release. The release studied showed that as the concentration of PVP increases the release rate were increases because of the PVP has the property to prevent crystallization of drug in polymer. An initial rapid release was observed due to direct exposure of matrix diffusion system to diffusion media and quick release of drug present at the surface.

Cumulative in-vitro drug permeation and effect of permeation enhancer - The in-vitro permeation studied indicates that permeation of drug varied from formulation batches according to the polymer and permeation enhancer utilized. The permeation followed as HP1 exhibit 5.12±0.6 to 43.67±2.5, HP2 exhibit 6.03±0.3 to 51.83.HP3 exhibit 6.97±1.3 to 55.02±1.1, HP4 exhibit 8.48±1.5 to 57.53±1.5,HP5 exhibit 8.13±0.8 to 47.88±2.8, HP6 exhibit 10.15±0.9 to 55.58±2.3, HP7 exhibit 11.56±1.2 to 60.97±1.6 and HP8 exhibit 12.8±1.5 to 65.83±2.0.The overall result showed that permeation was increased with an average enhancement ratio of 1.097.

CONCLUSION:

The method devised to prepare patches were effective and reproducible. The patches formed were uniform with respect to physicochemical characteristics. They showed no signs of interaction when subjected to FTIR analysis. The results showed none of the basic peak was disturbed. In-vitro and In-vivo permeation of atenolol was better because of its hydrophilic nature exert an interaction with water soluble polymers resulted an increased drug release. The results showed that atenolol could be administered via transdermal route over a prolonged period through the matrix type of TDDS.

Abbreviation:

HPMC- Hydroxypropyl methylcellulose
PVP- Polyvinylpyrrolidone
DMSO- Dimethyl sulfoxide
WVTR- Water vapor transmission rate
RH- Relative humidity

REFERENCES:

1- Negi Pankaj singh, Gananarajan G, Badola A., Kothiyal P., 2015, Formulation and evaluation of transdermal patch of atenolol, Indo American Journal of Pharmaceutical Sciences,2(12) 1609-1622
2- Bharkatiya M, Nemo R.k.,2019, Skin permeationenhancement technique, J young pharm.1(2):110-115
3- Ahad A, Hahad I Al-Jenoobi, Abdullah M AlMohizea, Naseem Akhtar, Mohammad Raish, Mohammad Aqil, 2015,Systemic delivery of β blockers via transdermal route for hypertension, Saudi pharmaceutical journal,23, 587-602.
4- Sarkar Vijay, Yadav kalash Chand, 2013, Formulation and evaluation of prolonged release transdermal drug delivery of atenolol for the treatment of hypertension, Current research in pharmaceutical sciences,03(04):132-137
5- Reddy B.V., Satynandan S., 2016,Preparation and characterization of Polymeric and Adhesivematrix diffusional transdermal drug delivery device of atenolol, Journal of Global Trends in Pharmaceutical Sciences,5(2);1706-1715
6- Vallmudi Pallav, Radhe G.V., Nadendla Rama Rao, 2017, Fabrication and characterization of glibenclamide transdermal patches, International Journal of Pharmaceutical Sciences Review and Research 47(1),31-35
7- Kharia A, Gilhorta R, Singhai A.K., 2019, Formulation and evaluation of transdermal patches for treatment of inflammation , International Journal of Pharmaceutical Sciences and Research, vol. 10 (5) 2375-2384
8- Tanwar H., Sachdeva R., 2016, Transdermal drug delivery: A review, IJPSR, vol7 (6), 2274-2290
9- Fathima S. A., Begum Shireen,Fatima S STransdermal drug delivery system, International Journal of Pharmaceutical and Clinical Research, 2017, 9(1), 35-43
10- Kriplani p, Sharma abhishek, chopra Bhawana , Dhingara Ashwani, Deswal Gupta, , 2018, Formulation of transdermal patches of diclofenac

sodium, Global Journal of Pharmacy and Pharmaceutical Sciences, vol.4, issue 5, 001-004

11- Singh Amandeep, Bali Alka, 2016, Formulation and characterization of transdermal patches for controlled delivery of Duloxetine hydrochloride, Journal of Analytical Science and Technology 7:25

12- Solunke R. S, Chaudhari P.D, 2016, Formulation and evaluation of glimepiride patches for transdermal drug delivery, Journl of biomedical and pharmaceutical research, vol.5, issue 6, 108-120

13- David S.R., Malek Nurafiqah, Mahadi Abdul Hanif, Chakravarthi Srikumar,Rajabalaya Rajan, 2018, Development of controlled release silicone adhesive based mupirocin patch demonstrates antibacterial activity on live rat skin against staphylococcus aureus, Drug design development and therapy, 12,481-494

14- Yadav Adhikrao vyankatrao , Urde mukund namdeo,2019, Formulation and evaluation of chitosan based transdermal patches of lornoxicam for prolonged drug release and to study the effect of permeation enhancer, Indian journal of pharmaceutical education and research, vol53, issue 1, 88-96

15- Kharat R. S., Bathe Ritesh Suresh , 2016, A comprehensive review on: Transdremal drug delivery system, Internation journal of biomedical and advance research 7(4) 147-159

16- Waghulde S., Naik P.P., Gorde N., Juvatkar P., Shirodkar P. Y.,Kale M.K., 2013,Development, recent invention and evaluation techniques of transdermal drug delivery, A review, International journal of pharmaceutical phytopharmacological research, 3(2):152-160.