FORMULATION AND *IN-VITRO* EVALUATION OF TRANSDERMAL FILMS OF AN ANTI HYPERTENSIVE DRUG

Gudapa Reddy Rajareddy^{1*}, Valluru Rajashekar², Jayanthi³, Saleem Shaik⁴, K.A Sridhar⁵
East West College of Pharmacy, Rajiv Gandhi University of Health Sciences, Bangalore, Karnataka, India
Email: rajareddy1989@gmail.com

Article Received on: 13/03/13 Revised on: 21/04/13 Approved for publication: 17/05/13

DOI: 10.7897/2230-8407.04615

IRJP is an official publication of Moksha Publishing House. Website: www.mokshaph.com

© All rights reserved.

ABSTRACT

In the present study was made to develop a suitable matrix type transdermal patch of Candesartan Cilexetil, using blends of two different types of polymeric combinations viz. HPMC K100 and Eudragit RL100 prepared formulations were subjected to various physiochemical evaluation tests like moisture content loss, moisture absorption, flatness to study the stability of the formulations, *in vitro* dissolution was performed to determine the amount of Candesartan present in the patches. Drug excipient interaction studies were carried out using Fourier transform infrared (FTIR) spectroscopy technique. The *in vitro* release of the drug from the formulations was studied using commercial semi permeable membrane. All the formulations were found to be suitable for formulating in terms of physiochemical characteristics and there was no notification in significant interaction between the drug and polymer used. *In vitro* dissolution data showed that formulation of F11 showed faster release of drug than the F14 formulations during dissolution studies. Skin irritation studies revealed that the batch containing HPMCK100-Eudragit RL100 has no erythema and edema. Based on the observation, we can reveal that HPMCK100- eudragit RL100 polymers are better suited for the development of Candesartan cilexetil transdermal patches.

Keywords: Candesartan cilexetil; Matrix type transdermal patches; Eudragit RL100; HPMC K100.

INTRODUCTION

Transdermal drug delivery systems (TDDS) are defined as discrete dosage forms containing drugs which when coming intact with skin delivers the drug into the adjacent tissue & systemic circulation^{1,2}. The motto of pharmaceutical research is to overcome the hurdles coming in fixing the effective therapeutic level and inhibiting the undesired side effects³. To deliver the right amount of medicine at the right target site becomes complicated if each medication were to be delivered in an optimal and preferred manner to the individual patient⁴. The transdermal products are to avail the maximum amount of dose via the skin to the systemic circulation and simultaneously avoiding the retention and metabolism of drug in dermis⁵.

In the present days TDDS is one of the prominent methods in drug application. A large numbers of drugs are being formulated by this route. Transdermal drug delivery systems are also known as patches.

Advantages of Transdermal Drug Delivery systems⁶ are as follows, Avoidance of first pass metabolism, avoidance of gastro intestinal incompatibility, predictable extended duration of activity, minimizing undesirable side effects, provide utilization of drugs with short biological half lives and narrow therapeutic window.

Disadvantages Transdermal Drug Delivery systems^{7,8} are skin irritation or contact dermatitis at the site of application also causes edema, itching etc. The aim of the study is to achieve the objective of systemic medication through topical application and release of drug via skin by developing transdermal drug delivery system.

Candesartan is an angiotensin II receptor antagonist and is widely used in the management of hypertension to reduce cardiovascular mortality in patient with left ventricular dysfunction following myocardial infarction, and in the management hypertension to reduce cardiovascular mortality in patients with left ventricular dysfunction following myocardial infarction, and in the management of heart failure. It acts selectively at the AT₁ receptor subtype.

By blocking the rennin-angiotension II mediated effects including vasoconstriction. Sodium and water retention enhanced sympathetic activity and cardiovascular cellular growth⁹. Candesartan is a potent and highly selective angiotensin II receptor type I antagonist that lowers blood pressure in hypertensive patients. The drug is rapidly absorbed following administration¹⁰.

MATERIALS AND METHODS

Candesartan pure drug gift sample from Aurobindo Pharma Ltd, Hyderabad, India. HPMC K100 Central drug house, New Delhi Eudragit RL100 India Fine chemicals, Mumbai Methanol Karnataka Fine chem, Bangalore Isopropyl alcohol Thermo fisher scientific India pvt ltd Mumbai and all other materials used were of pharmacopoeial grade.

Methods

The section is instantiated and materialized by a set of methods, techniques and tools. It covers procedure, pre and post formulation characterization of TDDS.

Preformulation studies

The study involves the development of analytical technique and the curve of linearity, revise of solubility profile of the CAN, and the incompatibility profile between the drug and the polymer of choice.

Development of analytical method-by UV spectroscopy

The UV spectroscopic analytical method was developed to characterize and estimate the drug in and out of dosage form throughout the entire work. The principle involved in the method was absorption of UV light by the drug moiety. The method was developed using Shimadzu 1800 as the system and UV Probe as the software.

Curve of Linearity

For development of analytical curve the drug was dissolved in phosphate buffer pH 7.4 to get a concentration of 1mg/ml

solution. The further dilutions of the same were made with phosphate buffer pH 7.4 to get a range of concentrations 5, 10, 15, 20, 25 and 30 mcg/ml respectively and analysed by UV-Spectroscopy.

Solubility

The solubility profile of CAN was determined as described by Ooya with slight modification. The sample (100mg) was added to the screw capped vials each containing fixed volume (20mL) of various solvent and stirred at 150 rpm by magnetic at $37 \pm 2^\circ\text{C}$. The solvent of choice was water, phosphate buffer 7.4, and methanol. The samples were taken at 24 hrs, centrifuge, and filtered through 0.2 μm filter (Millipore, USA) and analyzed for respective drug content by UV Spectroscopy. The study was carried thrice for each solvent system.

Incompatibility study

The drug polymer interaction study was carried out by Fourier-Transfer infra red spectrum analysis. The FTIR spectra's of dry samples maintained at isothermal stress conditions were recorded on Shimadzu FTIR 8400S. The KBr pellet method was employed as FTIR sampling technique. The samples – pure drug and the physical blend of drug and polymers stored at isothermal stress condition were mixed with KBr (IR grade) at ratio of 1:5 by weight. Thin layered pellets were prepared by subjecting samples to hydraulic press 10,000-12,000 kg/cm² pressure. The analysis was carried in the frequency range between 4,000-400 cm⁻¹ with 4cm⁻¹ resolution. The results were the mean of 6 scans.

Formulation of transdermal patches of Candesartan cilexetil (CAN)

Transdermal patches of candesartancilexetil were prepared by solvent evaporation technique for the formulation shown. The required amount of polymers was accurately weighed and dissolved in the solvent 15ml of methanol and kept aside to form a clear solution. DBT (30%) was used as a plasticizer and different permeation enhancer DMSO (10%). 16mg of CAN (drug) was dissolved in the above solution and mixed till it dissolves and form a clear solution. The resulted uniform solution was poured in a Petri plate and dried. A funnel was placed over the Petri plate to prevent fast evaporation of the solvent. After 24hrs the dried films were taken out and stored in desiccators for further studies.

Evaluation of transdermal patches

Weight uniformity of patches

Three patches of the size 2cm diameter were weighed individually using digital balance and the average weights were calculated.

Folding endurance

The folding endurance was determined by repeatedly folding endurance the film at the same place until it broke. The number of times the film could be folded at the same place without breaking was consider as folding endurance value^{11, 12, 13}.

Percentage moisture content

The 3 patches of each batch was weighed individually and kept in a desiccators containing fused calcium chloride at room temperature for 24 hrs.¹⁴ The liners were again weighed and the percentage moisture content was calculated using the formula:

$$\text{Moisture content (\%)} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

Percentage moisture uptake

The weighed release liners of each batch (n=3) were kept in desiccators at room temperature for 24 hrs and then exposed to 80-90% relative humidity using a saturated solution of potassium chloride for 24hrs.¹⁴ Finally, the films were weighed and the percent moisture uptake was calculated using the formula.

$$\text{Moisture content (\%)} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Patch thickness

The thickness of patches were determined by selecting randomly patches and using digital vernier caliper, the film was measured at three different places and mean value was calculated¹⁴.

Drug content

1cm² area of the film was cut and each dissolved in sufficient quantity of methanol. The volume was made up to 10ml. 1ml was then withdrawn from this solution and diluted to 10ml. The absorbance was then measured at 256nm. From the absorbance and the dilution factor, the drug content in the film was calculated^{15, 16}.

In vitro diffusion studies

The diffusion study was carried out by using Franz diffusion cell. In this method cellophane membrane is used as the model membrane. The membrane was placed between the donor compartment and the reservoir compartment (phosphate buffer PH 7.4). The patch was placed on the membrane and the compartments clamped together. The receptor compartment (27ml capacity) was filled with phosphate buffer PH 7.4 and hydrodynamics in the receptor compartment was maintained by stirring with a magnetic bead at 100 rpm. 5ml of sample withdrawn and replaced with receptor medium. 5ml sample was diluted up to 10ml with phosphate buffer 7.4 to get concentration in between 2-12 $\mu\text{g/ml}$ and assayed spectrophotometrically at 256nm and amount of drug release at various time intervals was calculated.

RESULTS & DISCUSSION

The physicochemical evaluation study of the formulated patches, reveals that the range weights of the patches are 175.11mg to 615.34mg and the percentage (%) deviation is ± 1.0 to 1.8 % which is in the acceptable range. The results of thickness of the patches formulated are in between 0.23 mm to 0.27 mm and the folding endurance is 200. The drug content for the candesartan transdermal patches formulated with HPMC K100 & Eudragit RL100 indicates in between 92.47% to 98.71%. The results of *in vitro* diffusion study shows that, an increase in polymers concentration increases the diffusion rate and also the combination of Eudragit RL100 and HPMC K100 polymers shows increase in diffusion rate which are formulated with 30 % DBT. The data is enlisted successively between 80.335 ± 2.45 – 90.674 ± 0.130 , 79.552 ± 1.742 – 86.752 ± 1.79 , 88.818 ± 0.156 – 95.360 ± 0.158 , in HPMC K100, Eudragit RL100 & combination of HPMC K100 & Eudragit RL100 respectively. The diffusion data values were fitted in different models like Zero order, First order, Higuchi and Peppas to study the diffusion pattern of drug along with its kinetics. The regression co-efficient values of the compounds are enlisted in tables 5, 6, 7, 8.

Table 1: Formulation of Candesartan cilexetil transdermal patches

Formulations	Drug (mg)	HPMC K100 (mg)	Eudragit RL100 (mg)	Plasticizer (%)	Permeation enhancer (%)	Solvent 15ml
F1	16	100	-	DBT (30%)	DMSO (10%)	Methanol +IPA
F2	16	200	-	DBT (30%)	DMSO (10%)	Methanol +IPA
F3	16	300	-	DBT (30%)	DMSO (10%)	Methanol +IPA
F4	16	400	-	DBT (30%)	DMSO (10%)	Methanol +IPA
F5	16	500	-	DBT (30%)	DMSO (10%)	Methanol +IPA
F6	16	-	100	DBT (30%)	DMSO (10%)	Methanol
F7	16	-	200	DBT (30%)	DMSO (10%)	Methanol
F8	16	-	300	DBT (30%)	DMSO (10%)	Methanol
F9	16	-	400	DBT (30%)	DMSO (10%)	Methanol
F10	16	-	500	DBT (30%)	DMSO (10%)	Methanol
F11	16	400	100	DBT (30%)	DMSO (10%)	Methanol +IPA
F12	16	300	200	DBT (30%)	DMSO (10%)	Methanol +IPA
F13	16	200	300	DBT (30%)	DMSO (10%)	Methanol +IPA
F14	16	100	400	DBT (30%)	DMSO (10%)	Methanol +IPA

Table 2: Thickness of Candesartan cilexetil transdermal patches at different locations

Formulations	Thickness (mm) of liners at different location				
	Left	Right	Top	Bottom	Center
F1	0.26 ± 0.005	0.25 ± 0.01	0.25 ± 0.005	0.24 ± 0.011	0.26 ± 0.005
F2	0.25 ± 0.005	0.24 ± 0.005	0.24 ± 0.005	0.25 ± 0.005	0.24 ± 0.005
F3	0.25 ± 0.015	0.24 ± 0.005	0.24 ± 0.005	0.25 ± 0.011	0.24 ± 0.005
F4	0.26 ± 0.01	0.25 ± 0.00	0.25 ± 0.015	0.25 ± 0.005	0.25 ± 0.015
F5	0.27 ± 0.01	0.25 ± 0.005	0.25 ± 0.015	0.24 ± 0.005	0.24 ± 0.011
F6	0.25 ± 0.005	0.25 ± 0.01	0.24 ± 0.005	0.24 ± 0.011	0.23 ± 0.005
F7	0.26 ± 0.005	0.24 ± 0.005	0.24 ± 0.005	0.25 ± 0.005	0.26 ± 0.005
F8	0.25 ± 0.015	0.24 ± 0.005	0.26 ± 0.005	0.24 ± 0.011	0.25 ± 0.005
F9	0.26 ± 0.01	0.25 ± 0.00	0.25 ± 0.015	0.25 ± 0.005	0.25 ± 0.015
F10	0.27 ± 0.01	0.25 ± 0.005	0.25 ± 0.015	0.24 ± 0.005	0.24 ± 0.011
F11	0.26 ± 0.005	0.25 ± 0.01	0.25 ± 0.005	0.24 ± 0.011	0.25 ± 0.005
F12	0.25 ± 0.005	0.24 ± 0.005	0.24 ± 0.005	0.25 ± 0.005	0.26 ± 0.005
F13	0.25 ± 0.015	0.24 ± 0.005	0.24 ± 0.005	0.25 ± 0.011	0.25 ± 0.005
F14	0.26 ± 0.01	0.25 ± 0.00	0.25 ± 0.015	0.25 ± 0.005	0.24 ± 0.015

Table 3: Physicochemical evaluations of Candesartan cilexetil transdermal patches

Formulation	Weight variation (mg)	Folding Endurance	Drug content
F1	177.50±1.85	200±0.57	92.97±0.50
F2	285.42±1.02	200±1.14	98.71±0.57
F3	372.50±1.009	200±0.66	97.25±0.52
F4	487.57±1.02	200±0.57	94.4±0.74
F5	615.34±1.01	200±0.57	95.63±0.57
F6	175.11±1.03	200±0.57	92.72±2.15
F7	305.32±1.02	200±0.56	94.18±0.70
F8	427.52±1.01	200±1.01	95.34±0.72
F9	510.10±1.03	200±1.01	94.87±1.01
F10	610.62±1.01	200±0.57	95.83±0.57
F11	612.50±1.03	200±0.57	94.63±2.15
F12	613.75±1.02	200±0.56	93.98±0.70
F13	610.24±1.01	200±1.01	92.47±0.72
F14	615.41±1.03	200±1.01	95.67±1.01

Table 4: Moisture content & uptake recovered for candesartan patches

Formulation	%Moisture absorption	%Moisture loss
F1	8.05± 0.57	5.9±0.32
F2	5.35±0.27	3.55±0.29
F3	6.17±0.74	2.76±0.41
F4	6.87±0.70	2.32±0.66
F5	6.25±0.55	3.35±0.33
F6	9.05±0.70	2.61±0.79
F7	6.96±0.51	2.35±0.16
F8	8.45±0.36	1.28±0.87
F9	7.84±0.79	4.97±0.68
F10	6.57±0.55	1.63±0.33
F11	7.02±0.70	2.47±0.79
F12	6.59±0.51	4.26±0.16
F13	5.74±0.36	2.59±0.87
F14	6.45±0.79	1.64±0.68

Table 5: *In-vitro* Permeability of CAN from F1-F5 formulations

Time (hrs)	Percentage Cumulative Drug Permeability				
	F1	F2	F3	F4	F5
1	11.079 ± 1.78	9.2928 ± 1.26	13.760 ± 1.3	17.036 ± 1.11	7.22 ± 1.86
2	15.216 ± 1.23	14.290 ± 0.68	19.585 ± 0.92	23.766 ± 0.45	14.274 ± 1.2
3	19.441 ± 2.34	22.574 ± 1.34	27.207 ± 1.2	30.561 ± 1.11	21.612 ± 1.93
4	26.380 ± 0.54	30.473 ± 1.89	32.083 ± 0.12	36.419 ± 0.62	29.134 ± 1.79
5	35.581 ± 3.12	37.709 ± 3.64	37.720 ± 2.91	42.850 ± 1.94	35.615 ± 2.65
6	41.361 ± 2.87	44.604 ± 1.75	43.633 ± 2.11	49.017 ± 2.17	43.723 ± 0.98
7	47.958 ± 3.56	50.991 ± 2.00	49.524 ± 1.98	55.702 ± 1.84	51.052 ± 2.13
8	55.183 ± 2.17	57.301 ± 0.97	55.338 ± 2.45	62.067 ± 1.89	58.074 ± 1.28
9	61.306 ± 2.91	63.777 ± 3.12	61.615 ± 1.23	68.300 ± 0.68	66.017 ± 2.91
10	67.538 ± 2.11	69.822 ± 2.87	68.708 ± 2.34	74.643 ± 1.34	74.347 ± 2.11
11	73.881 ± 1.98	76.220 ± 3.56	76.430 ± 0.54	81.096 ± 1.89	83.063 ± 1.98
12	80.335 ± 2.45	83.027 ± 2.17	83.644 ± 2.87	87.362 ± 1.75	90.674 ± 2.45

Table 6: *In-vitro* Permeability of CAN from F6-F10 formulations

Time (hrs)	% CDR ± SD				
	F6	F7	F8	F9	F10
1	3.0380 ± 1.25	5.1230 ± 1.29	6.910 ± 0.97	7.803 ± 0.37	10.186 ± 0.62
2	10.153 ± 1.58	12.326 ± 0.91	13.848 ± 0.27	14.907 ± 0.61	17.136 ± 0.92
3	16.992 ± 1.79	21.581 ± 1.87	24.218 ± 0.34	25.442 ± 1.21	26.810 ± 0.28
4	25.067 ± 2.37	28.289 ± 0.91	30.120 ± 1.42	32.403 ± 1.84	33.584 ± 1.32
5	32.944 ± 1.76	35.007 ± 0.81	36.408 ± 1.96	39.320 ± 0.62	40.258 ± 1.51
6	40.401 ± 0.91	41.030 ± 1.27	42.784 ± 1.26	45.784 ± 0.55	47.020 ± 1.61
7	46.921 ± 0.83	47.924 ± 1.98	48.895 ± 2.71	52.822 ± 1.62	54.113 ± 2.34
8	53.716 ± 2.87	54.610 ± 2.71	56.121 ± 1.70	59.298 ± 1.74	60.644 ± 2.14
9	60.191 ± 1.96	60.975 ± 0.28	62.839 ± 1.79	65.343 ± 0.91	67.936 ± 1.42
10	66.535 ± 1.26	67.207 ± 1.32	70.076 ± 2.37	72.039 ± 0.81	74.907 ± 1.26
11	72.988 ± 2.71	74.444 ± 1.61	76.694 ± 1.76	78.901 ± 2.71	82.045 ± 2.71
12	79.552 ± 1.70	81.659 ± 2.34	83.722 ± 0.83	85.630 ± 1.32	86.752 ± 1.79

Table 7: *In-vitro* Permeability of CAN from F11-F14 formulations

Time (hrs)	% CDR ± SD			
	F11	F12	F13	F14
1	7.8036 ± 0.31	10.1864 ± 0.67	5.12300 ± 0.21	6.31439 ± 0.91
2	16.9928 ± 0.69	16.8383 ± 0.49	13.8157 ± 0.54	15.2278 ± 0.15
3	24.3397 ± 1.23	26.1599 ± 1.97	22.4533 ± 1.27	25.5752 ± 0.82
4	32.2162 ± 1.47	32.8229 ± 1.87	29.8665 ± 1.82	31.6977 ± 1.69
5	40.2691 ± 1.54	39.6845 ± 1.92	36.8053 ± 1.73	38.8019 ± 1.82
6	46.3033 ± 2.74	46.6894 ± 2.31	43.6447 ± 1.0	45.8069 ± 2.67
7	53.9922 ± 2.87	54.0805 ± 2.78	51.1682 ± 1.84	52.6023 ± 1.85
8	61.8246 ± 2.78	61.5598 ± 1.94	58.5372 ± 2.58	59.9713 ± 1.95
9	69.7451 ± 1.25	68.4765 ± 1.79	66.5350 ± 1.86	67.3734 ± 2.0
10	77.9966 ± 1.58	75.2608 ± 1.95	74.9189 ± 1.46	74.4556 ± 1.64
11	87.4727 ± 1.79	83.6447 ± 1.87	83.3910 ± 1.79	81.7032 ± 1.97
12	95.3601 ± 1.95	91.2233 ± 2.54	90.492 ± 2.86	88.8185 ± 2.86

Table 8: Release kinetic data of CAN containing matrix type of F1-F14

Formulation Code	Mathematical Models		
	Zero order (r ²)	First order (r ²)	Higuchi (r ²)
F1	0.7908	0.8787	0.9081
F2	0.7673	0.9457	0.9058
F3	0.7759	0.9788	0.9162
F4	0.7238	0.9675	0.9027
F5	0.7294	0.9855	0.8649
F6	0.7922	0.8873	0.8998
F7	0.7845	0.8661	0.9055
F8	0.7676	0.9343	0.9011
F9	0.7443	0.9035	0.8964
F10	0.7242	0.9432	0.8852
F11	0.6954	0.9927	0.8517
F12	0.7157	0.9844	0.8742
F13	0.7254	0.9076	0.8651
F14	0.7272	0.9440	0.8794

The FTIR spectrum of candesartan along with selected polymers was taken and the characterization was taken and the characteristic peaks were shown in Figures 1,2, 3,4.

The DSC curve of candesartan showed a single sharp endothermic peak at 126.7^oc corresponding to its melting point. The intensity (or height) of the endothermic peak of candesartan-Eudragit RL 100 and HPMC K100 at 197.5^oc and indicating interaction of candesartan with Eudragit RL 100 and HPMC K100 were shown in Figure 6.

XRD of candesartan exhibited diffraction peak indicating its nature. In combination with polymers with drug exhibited little changes in the diffraction peak of the candesartan observed conformity were shown in Figure 7.

CONCLUSION

Hypertension being a very common disorders leading to preventable death had been treated with different classes of drugs in form of several dosages. Oral being the popular route of administration for these antihypertensive has come across several demerits; hepatic first pass metabolism being the major leading to under dose therapy. To overcome the above major demerit the current dissertation focused at transdermal drug delivery system with main objective of "Design and Development of Matrix Type Transdermal Drug Delivery" followed by its physicochemical characterization as further intention. For the study Candesartan cilexetil was considered as the drug of choice as it gets metabolized at higher rate with patient variance.

The matrix type transdermal drug delivery system of Candesartan cilexetil was successful designed and developed by trial and error method. As a part of further objective the analytical method was successfully developed by UV spectroscopy and was found feasible as an application tool. The components of the matrix drug delivery system were compatible with each other ensuring their stability as intact and that of the system.

The permeability enhancers DMSO and DBT enhanced the diffusion permeability for Candesartan cilexetil by the in vitro release profile was purely diffusion controlled oriented obeying the law of first order kinetics which states the release of drug is dependent on the concentration available.

In whole we feel that the DBT had a better impact on permeability of drug through skin at 5% concentration but the nature of it to cause irreversible skin damage oriented the focus towards DMSO. The DMSO is expected to provide the patient compliance by enhancing the permeability of Candesartan cilexetil thereby providing better bioavailability with controlled diffusion flow of drug throughout a day.

With this we put an end to the work stating the matrix type transdermal drug delivery system of Candesartan cilexetil

with DMSO as penetrating enhancer improve the bioavailability of drug by delivering the molecule directly to blood stream by process of controlled diffusion and hence patient compliance is predicted.

ACKNOWLEDGEMENT

The authors are grateful to the East West College of pharmacy, Bangalore, for their all necessary facilities and encouragement assistance by them.

REFERENCES

1. Jayaraj kumar. K and Suneetha. K. C. Brief view on delivery of antihypertensive drugs through transdermal patches. *J Int Tech Pharm Sci.* 2010; 1 (7): 305-319.
2. Debjit Bhowmik and Chiranjib. Recent advances in transdermal drug delivery system. *Int J Pharm Tech Res.*2010; 2(1): 68-77.
3. Prabhu Prabhakara and Marina Koland. Preparation and evaluation of Transdermal patches of Papaverine hydrochloride. *Int J Res Pharm Sci* 2010; 1(3): 259-266.
4. Dipen M. Patel and Kavitha K. Formulation and evaluation aspects of transdermal drug delivery system. 2011; 6 (2).
5. Ting Li, Changshun Ren. Optimized preparation and evaluation of Indomethacin transdermal patch. *Asian J Pharm Sci.* 2007; 2 (6): 249-259.
6. Ramkanth S and Alagusundaram M. Design and characterization of matrix type transdermal drug delivery system using metoprolol tartrate. *Int j Adv Pharm Res.* 2010.
7. Gattani S. G and Jadhav R.T. Formulation and evaluation of transdermal films of diclofenac sodium, *Int j Pharm Tech Res.* 2009; 1(4): 1507-1511.
8. MghanF. Wilkosz and Robin H. Bonger. *Transdermal Drug Delivery. Part I: Current status.* U. S. Pharmacist. 28 (4): 38-42.
9. *Transdermal Drug Delivery Technology Revisited. Recent Advances Latest Reviews*2010; 5(2):1-6.
10. Chopda G. *Transdermal Drug Delivery systems, A Review.* Pharmainfo.net. 2010.
11. Kajal ghosal, Rajan R and Nanda A. Effects of Chemical Enhancers on the Release of Glipizide through matrix Patch. *Int J ChemTech Res.* 2009; 1(4): 1128-1130.
12. Ji-Hui Zhaoa, Ji-Hua Fub and Shu-Ming Wang. A novel transdermal patch incorporating isosorbide dinitrate with bisoprolol In vitro and in vivo characterization. *Int J Pharm.* 2007; 33(7): 88–101. <http://dx.doi.org/10.1016/j.ijpharm.2006.12.030>
13. Vishnu M Patel, Bhupendra G Prajapati, and Madhabhai M Patel. Effect of Hydrophilic Polymers on Buccoadhesive Eudragit Patches of Propranolol Hydrochloride Using Factorial Design. *AAPS PharmSciTech.* 2007; 8 (2).
14. Meenakshi B, Rajesh Kumar N, Mahip B. Development and characterization of transdermal patches of metoprolol tartrate. *Asian J Pharm Clin Res* 2010;3(2):130-4.
15. V, Sumanth M H, Suman L, Vinay T, Srinivasrao D and Jayaraj Kumar K. Development and Physicochemical, *In-Vitro* Evaluation of Antihypertensive Transdermal Patches. *J Pharm Sci Res.* 2010; 12(3): 171-177.
16. Padmalatha H, Vidyasagar G. Quantitative estimation of candesartan by uv spectrophotometry. *Indian J Pharm Tech.* 2011; 3 (2): 2653-2658.

Cite this article as:

Gudapa Reddy Rajareddy, Valluru Rajashekar, Jayanthi, Saleem Shaik, KA Sridhar. Formulation and in-vitro evaluation of transdermal films of an anti hypertensive drug. *Int. Res. J. Pharm.* 2013; 4(5):66-71