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Research

Design and Evaluation Of Esomeprazole Medical Trans-dermal Drug Delivery Patches

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Abstract

The goal of the present research work is to formulate, development and characterization oftransdermal systems used to treat gastro-esophageal, peptic-ulcer disease, and Zollinger–Ellison syndrome. Formulations were prepared by employing combination of HPMCK15M, PVPK30, and EC in various ratios.From the research, various conclusions were drawn. The patches showed good thickness, tensile strength and content uniformity of drug. The used polymers (HPMCK15M, PVPK30, and EC in various ratios) employed to design transdermal patches in different proportion. Invitro release from transdermal patches showed extended release of drug for 24 hours. The Esomeprazole penetration from formulated transdermal patches was found tofollow diffusion mechanism and obeys zero order release. So we can conclude that transdermal delivery system would be used as drugcarrier for Esomeprazole.

Keywords: Transdermal Drug Delivery System, Esomeprazole, Physicochemical evaluation.

INTRODUCTION

To provide continuous drug infusion through an intact skin, various transdermal systems have been designed for topical application and it control the delivery of drug and its permeation via the skin tissue. Historically, developments related to TDDS have been incremental, concentrating on overcoming issue related with the skin barrier properties, minimizing skin irritation and improving the outlook related with passive patch systems. TDDS defined as self-contained, discrete dosage form applied to the unharmed skin then it deliver the drug, via skin at controlled manner in the systemic circulation. Transdermal drug delivery via the skin provides a suitable route of administration for a various clinicalindications. A pharmaceutical scientist focuses on the development of transdermal drug delivery over the last 25 years. The skin offers a large and easily penetrable surface for drug delivery. Transdermal routes, from that of other routes are quite non-invasive, like simple adhesion of a "Patch" similar as that of application of a Band-Aid. A transdermal drug delivery systems transfer a precise dose of drug through the skin and into systemic circulation.

Preparation of calibration curve for Esomeprazole

Esomeprazole was dissolved in 10 ml methanol and volume is made up to 100 ml in volumetric flask with PBS pH 7.4. From stock solution 1 ml was pipette out (100 µg/ml)then further diluted to get solutions having concentrations 2µg/ml to 24 µg/ml. Absorbance of these solutions were measured using UV Spectrophotometer at 220 nmwith PBS pH 7.4 as a blank. The calibration curve was produced for entire range from2 to 10 µg/ml.

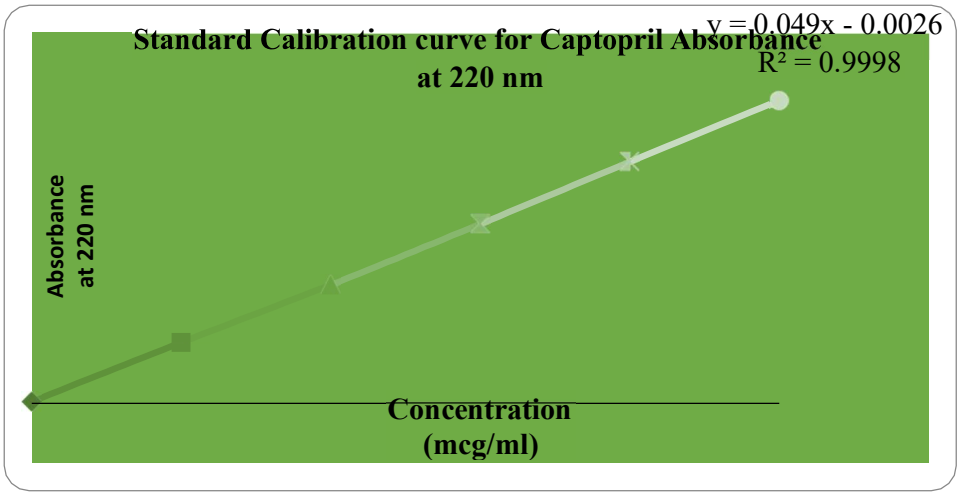


Fig 1: Standard curve for Esomeprazole

Compatibility study

FTIR absorption spectra of Esomeprazole, polymers (HPMCK15M, PVPK30, and EC) anddry sample of drug was directly placed after mixing and triturating. Also combined mixture of Esomeprazole and polymer was recorded by using FTIR spectrophotometer (Bruker FTIR).

Preparations of transdermal patches

The transdermal patches of composition listed in table no.5.3 were prepared by solutioncasting technique employing a glass substrate (Bangles wrapped with aluminum foil).Membrane type transdermal systems with Esomeprazole prepared using HPMC alone and by employing various proportions of HPMCK15M, PVPK30, and Ethyl Cellulose. Thepolymers was accurately weigh and dissolved in a suitable solvent mixed until clear solution formed with magnetic stirrer then added Esomeprazole to the uniform polymeric solution and mixed completely to form uniform solution. PEG400 and dibutyl phthalateadded as a plasticizer. DMSO and tween-80 were used as a penetration enhancer. The polymer solution was poured into bangles placed in a suitable level, hard rigid surface and patches were dried at a room temperature in a dust free environment for 24 hrs. aninverted funnel was covered over the bangles to avoid fast evaporation of the solvent[50-57]. Patches of 3.14 cm2 were prepared by cutting and packed in an aluminum foil and kept in a desiccator.

Table 1: Composition of Esomeprazole transdermal patches

Formulation	F1	F2	F3	F4	F5	F6	F7
Drug (mg)	65	65	65	65	65	65	65
HPMCK15M(mg)	500	450	400	300	-	-	-
PVPK30 (mg)	-	50	100	200	400	300	200
EC (mg)	-	-	-	-	100	200	300
PEG-400*(ml)	0.18	0.18	0.18	0.18	-	-	-
Dibutyl phthalate*(ml)	-	-	-	-	0.2	0.2	0.2
Tween 80 (ml)	0.14	0.14	0.14	0.14	-	-	-
DMSO* (ml)	-	-	-	-	0.11	0.11	0.11
DCM/Methanol (ml)	12	12	12	12	-	-	-
Chloroform (ml)	-	-	-	-	5	5	5

Research envisaged

Thickness of patches

The thickness of Patches was measured by digital vernier calipers with least count 0.001mm at three different sites average of three reading was taken with standard deviation.

Weight variation

The three disks of 3.14 cm2 was cut and weighed on electronic balance for weight variation test. The test was done to check the uniformity of weight and thus check the batch- to- batch variation.

Drug content

Accurately weighed patches were individually dissolved in minimum quantity ofmethanol and made volume up to 100 ml with PBS pH 7.4 solutions; 10 ml was transferred to flask and made volume 100 ml. The absorbance was recorded at 243 nm.The blank solution was made in the same manner except the patches without drug wereused.

Percentage Moisture content

The films were weighed & placed in desiccators containing calcium chloride at 400c ina dryer for at least 24 hrs or more until it gives a constant weight. The % of moisture content was the difference between constant weight taken and the initial weight and asreported with percentage by weight moisture content.

Swelling index

The patches of 3.14 cm2 were weighed and added into petri dish which contains 10 mldouble distilled water and were permeated to absorb moisture at a fix time interval check the increase weight of the patches. Continue this process till same weight observed until weight remaining the same over a period of time. Swelling index (% S)was determined by applying the formula.

S (percentage) = Wt – Wo / Wo x 100

Where, S percent swelling, Wt patch weight at time t.Wo patch weight at time zero.

Folding endurance

This was obtained by constantly folding one patch at the same place without breaking gave the value of folding endurance. This test performed to check folding ability of transdermal patches also indicate brittleness of patches, more brittle patch when foldingendurance value less.

Percentage Elongation

A film strip (4 x 1cm) was cut on a glass plate with a sharp blade. The %
elongation break is to be determined by observing the length just before the breakingpoint with formula by pointer on the graph paper.

Percent elongation = IB – Io / Io × 100Where-

Io = Original film length.

IB = Length of film at break when stress is applied.

Tensile Strength

The tensile strength of the patches was found by the apparatus designed as shown in fig The design of instrument such that, it had one wooden frame that horizontally placed having fixed scale. On the top of frame two clips were attached to hold patchesthat under study. From two clips one clips fixed and other moved. Instrument also has pulley to hold weight a patch, weight applied to one end of pulley and other end attachedto the fixed clip. During the test wooden platform not dislocate from the original place so platform was fixed carefully to avoid dislocation. Three patches were cut for study having 3.14 cm2 sizes. Thickness and breadth of patches were noted at three sizesand calculated average value. Rate of stress changes was maintained constant with theaddition of 0.5gm per 2 minutes. The elongation was observed and the total weights taken were used for calculation. Formula for tensile strength.

Fig 2: Assembly for tensile strength

***In-vitro* permeation studies**

The permeation studies were done according to the approved protocol by the animal ethics committee IAEC (IAEC NO: NIPS/05/29/2016) at the pharmacology department, NIPS, Bhopal. For in-vitro evaluation of TDDS, albino rat was selected because of its easy availability and suitability. In this work franz diffusion cell was used. The Franz diffusion cell was designed from borosilicate glass generally comprisetwo compartments, one containing the active compartment (donor compartment) and the other containing receptor solution (receptor compartment) separated with barrier i.e. skin membrane .The cell consist of sampling port and temperature regulating jacket.The outlet and inlet was connected with latex tube so the jacket has stagnant water inside at 370ºC. The volume of receptor cell was 25 ml and effective surface area available for permeation was 3.14cm^2. The two compartment of the cell fixed with strong clips[62-69]. A Teflon bead of 12mm was used to stir the receptor solution using magnetic stirrer.

Fig 3: Franz diffusion cell

Stability studies

Stability studies were performed at the different storage condition 25ºC• }20 ºC temp.,60%• }5% RH and 40 ºC• }20 ºC temperature, 75%• }5% RH, for 90 days on optimized formulation batches (F4&F5). The parameters studied for stability studies are thickness, drug content, assay, moisture content and uptake and in vitro drug permeation.

RESULTS AND DISCUSSION

Appearance and color of drug

The Esomeprazole sample shows white color in powder form.

Melting Point

The Esomeprazole M.P. was observed 106 ^{0}C.

Solubility

The drug solubility in a given vehicle determines the active concentration at which the drug could be presented on the skin surface. Hence, a good solubility in a chosen vehicleensures the transfer of the drug via delivery systems.

Freely soluble- DMSO, Methylene chloride, Methanol
Sparingly soluble- 95% Ethanol, Isopropanol
Slightly soluble- Ethyl ether

Partition Coefficient

The drug without sufficient lipophilicity encounters difficulty in crossing the lipid bilayer.However, when the lipophilicity becomes too prominent, the drug may form a reservoir within these layers. Hence, a balance of hydrophilicity and lipophilicity is desirable in thestructure of drug and octanol-phosphate buffer saline partition coefficient is thought be good indicator. We found a partition coefficient value of 3.859 ± 0.02.

SPECTROSCOPIC STUDIES
Characterization of Esomeprazole

FTIR spectra of Esomeprazole

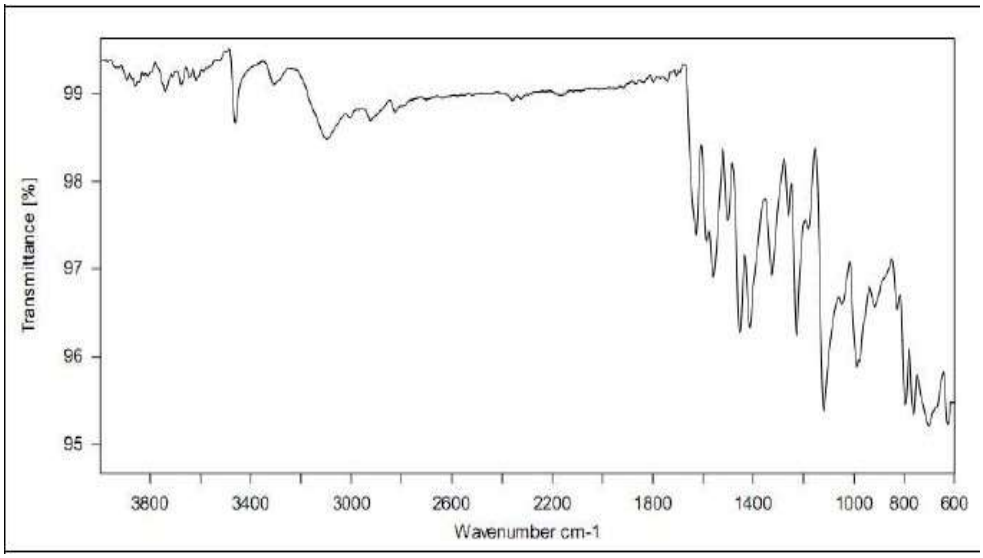


Fig 4: Standard calibration curve of Esomeprazole in PBS pH 7.4

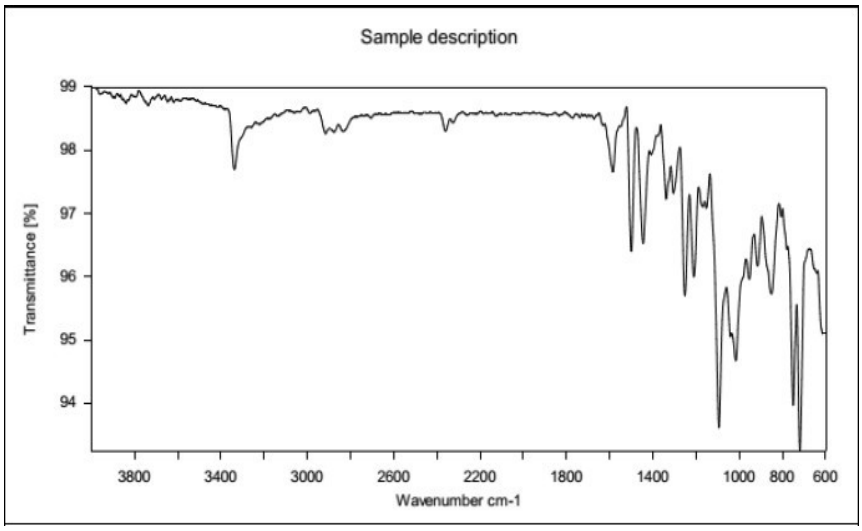


Fig 5: FTIR Spectra of Esomeprazole TDDS Formulation

The compatibility studies were performed to find out interaction of drug with the polymerthat is used in the formulation of TDDS. The FT-IR spectrum of the drug and polymer did not show presence of any additional peaks for new functional groups. These results suggestcompatibility between drug and polymer.

Drug-Polymers Interaction Study

The interaction studies were carried out to find out interaction of drug with the polymer used in the preparation of TDDS. The FT-IR spectrum of the drug and polymer did not show presence of any additional peaks for new functional groups. These results suggest compatibility between drug and polymer.

Formulations of Transdermal Patches

Seven formulations of Esomeprazole Patches compose with different polymers HPMCK15M,PVP K30, Ethyl cellulose, Chloroform, Methanol, Dichloro methane were used as a castingsolvent. PEG400 and dibutyl phthalate used to give plasticity to patches and DMSO, Tween80 are used to enhance penetration of drug through transdermal systems. The polymeric solution was poured into bangles placed in a suitable level, hard rigid surface and patcheswere dried at a room temperature in a dust free environment for 24 hrs. an inverted funnelwas covered over the bangles to avoid fast evaporation of the solvent. Patches of 3.14 cm2were prepared by cutting and packed in an aluminum foil and kept in a desiccator. The prepared transdermal therapeutic

Formulated Transdermal patches of Esomeprazole

Fig 6: Matrix type transdermal patch

Physicochemical Evaluation data of Transdermal Patches ofEsomeprazole

nulationCode	ckness(mm)	Weight variation(mg)	% DrugContent	Folding endurance	Tensile strength Kg/mm^2
F1	0.12±0.01	0.150±0.01	95.92±3.1	57±12.04	2.45±0.81
F2	0.19±0.02	0.148±0.05	96.59±3.2	36.6±21.0	2.80±0.80
F3	0.14±0.004	0.155±0.04	97.51±2.1	38±18.20	2.40±0.70
F4	0.17±0.008	0.160±0.01	99.65±2.2	60±24.33	3.85±1.80
F5	0.35±0.09	0.149±0.05	98.36±2.12	58±22.03	3.92 ±1.84
F6	0.37±0.003	0.156±0.01	97.71±1.11	57±10.41	2.81±1.84
F7	0.35±0.003	0.153±0.02	98.71±1.12	59±10.41	2.93 ±1.78

Physicochemical Evaluation data of Transdermal Patches ofEsomeprazole

FormulationCode	% Elongation	% MoistureContent	% Moistureuptake	Swellingindex
F1	24.43±2.51	1.85±0.35	4.87±3.13	24.17±1.38
F2	23.80±2.12	2.6±0.77	3.6±3.7	25.75±0.72
F3	25.75±2.61	3.1±1.29	5.3±1.22	25.50±2.12
F4	26.25±4.12	3.2±1.82	4.7±0.85	23.41±0.74
F5	28.04±4.71	3.23±2.1	5.7±1.45	22.82±1.25
F6	25.26±4.19	2.7±0.98	4.76±1.06	24.18±1.37
F7	24.25±4.18	2.8±0.97	4.77±1.05	25.19±1.36

***In-vitro* Drug Permeation Kinetics**

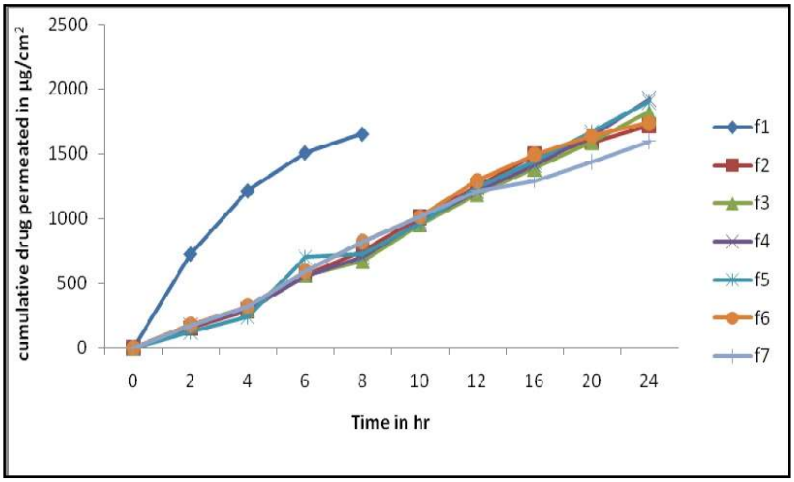
Time(hrs)	F1	F2	F3	F4	F5	F6	F7
2	35.18	7.53	8.58	8.43	5.87	8.84	8.43
4	58.75	14.03	14.47	14.42	11.70	15.55	15.55
6	73.02	27.26	27.31	27.02	33.95	28.78	28.78
8	80.00	36.47	32.65	33.99	35.26	39.72	39.72
10		48.85	46.19	47.46	46.45	49.07	49.07
12		60.39	57.40	58.69	60.05	62.60	58.69
16		72.38	67.03	68.46	69.64	72.25	62.60
20		76.92	76.92	79.27	80.58	79.27	69.64
24		83.23	88.29	93.00	92.05	84.15	77.15

***In-vitro* Drug Permeation of Esomeprazole Data Batches F1-F7**

Cumulative drug permeated in (µg/cm^2)						
F1	F2	F3	F4	F5	F6	F7
728	155	177	174	122	182	174
1216	290	299	298	242	321	321
1511	564	565	559	702	595	595
1656	754	675	703	729	822	821
_	1011	956	982	961	1015	1015
_	1250	1188	1214	1243	1295	1214
_	1498	1387	1417	1441	1495	1295
_	1592	1592	1640	1668	1640	1441
_	1722	1827	1925	1905	1741	1597

Invitro drug release was studied for all patches of Esomeprazole transdermal patches.The studies were performed upto 24 hours for all the patches.The cumulative percentage release of formulation (F1,F2,F3,F4,F5,F6,F7) were found to be (80%,83.23%,88.29%,93%,92.05%, 84.15%,77.15%) out of these, F4 has maximum released. The optimized formulation F4 has high amount drug release due to good compatibility between the drug and polymers.

In vitro Drug permeation of Esomeprazole Formulations



Kinetic values for drug release from transdermaltherapeutic system

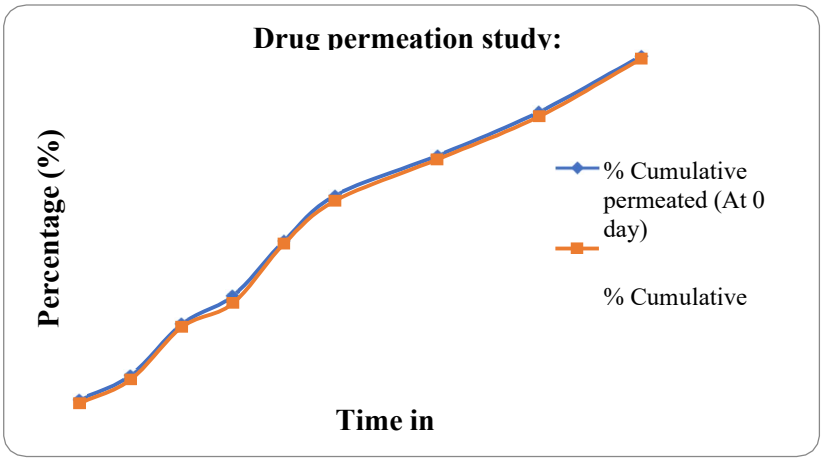
Sr.No	Zero Order	First Order	Higuchiplot	Korsmeyer- Peppas		Best FitModel
	(r^2)	(r^2)	(r^2)	(r^2)	(n)	__
F1	0.926	0.991	0.941	0.893	0.11	Zero order
F2	0.985	0.973	0.989	0.890	0.12	Higuchi matrix
F3	0.995	0.909	0.995	0.927	0.12	Zero order
F4	0.994	0.852	0.995	0.926	0.12	Higuchimatrix
F5	0.916	0.882	0.988	0.906	0.28	Higuchimatrix
F6	0.992	0.974	0.990	0.981	0.22	Zero order
F7	0.988	0.933	0.983	0.870	0.11	Zero order

Optimized formula follows zero order release

Stability Study

Present studies were performed to check the formulation stability of optimized batches F4and F5 at accelerated conditions of temperature and humidity at an interval of three month.

Drug Permeation study of F4



SUMMARY & CONCLUSION

Eventually, based on results of various evaluation parameters like thickness,strength, elongation, better compatibility and stability the transdermal matrix patches wassuccessfully designed and developed by trial and error method. Formulations were prepared by employing combination of HPMCK15M, PVPK30, and EC in various ratios.From the research, various conclusions were drawn. The patches showed good thickness, tensile strength and content uniformity of drug. The used polymers (HPMCK15M, PVPK30, and EC in various ratios) employed to design transdermal patches in different proportion. Invitro release from transdermal patches showed extended release of drug for 24 hours. From the result of present experimental investigation, the formulation F4 showed good results on evaluation studies. Hence F4 formulationwere the Optimized formulation. The Esomeprazole penetration from formulated transdermal patches was found tofollow diffusion mechanism and obeys zero order release. So we can conclude that transdermal delivery system would be used as drugcarrier for Esomeprazole.

REFERENCES

1. Girish Chopda, Transdermal Drug Delivery Systems: A Review. pharmainfo. net, 12th January 2006, page No –2 to 11.
2. Sankar V, Johnson DB, Sivanand V, Ravichandran V, Raghuraman S, Velrajan G, Palaniappan R, Rajasekar S, Chandrasekaran AK. Design and evaluation of nifedipine transdermal patches. Indian journal of pharmaceutical sciences. 2003;65(5):510-5.
3. Kusum Devi V, Saisivam S, Maria GR, Deepti PU. Design and evaluation of matrix diffusion controlled transdermal patches of verapamil hydrochloride. Drug development and industrial pharmacy. 2003 Jan 1;29(5):495-503. https://www.tandfonline.com/doi/abs/10.1081/DDC-120018638
4. Lewis S, Pandey S, Udupa N. Design and evaluation of matrix type and membrane controlled transdermal delivery systems of nicotine suitable for use in smoking cessation. Indian journal of pharmaceutical sciences. 2006 Mar 1;68(2). https://go.gale.com/ps/i.do?id=GALE%7CA146854934&sid=googleScholar&v=2.1&it=r&linkaccess=abs&issn=0250474X&p=AONE&sw=w
5. Bagyalakshmi J, Sheriff S, John S, Ravi TK, Manna PK, Manavalan R. Transdermal delivery of ampicillin sodium patch made from volatile vehicle. Indian journal of pharmaceutical sciences. 2004;66(1):103-5.
6. Swarnalate S. Transdermal formulation and evaluation of tiomolol maleate, Pharmacy on line. The international journal of pharmacy. 2006;2.
7. Panigrahi L, Ghosal SK. Formulation and evaluation of pseudolatex transdermal drug delivery system of terbutaline sulphate. Indian journal of pharmaceutical sciences. 2002;64(1):79-82.
8. Manvi FV, Dandagi PM, Gadad AP, Mastiholimath VS, Jagadeesh T. Formulation of atransdermal drug delivery system of ketotifen fumarate. Indian journal of pharmaceutical sciences. 2003;65(3):239-43.
9. Jain S, Sapre R, Umamaheswari RB, Jain NK. Protransfersomes for effective transdermal delivery of norgestrel preparation and in vitro characterization. Indian journal of pharmaceutical sciences. 2003;65(2):152-60.
10. Sankar V, Johnson DB, Sivanand V, Ravichandran V, Raghuraman S, Velrajan G, Palaniappan R, Rajasekar S, Chandrasekaran AK. Design and evaluation of nifedipine transdermal patches. Indian journal of pharmaceutical sciences. 2003;65(5):510-5.