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Fabrication, Optimization, and Evaluation of Transdermal Patch: As an Alternative and Effective Transdermal Delivery System for Grainsetron HCl

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Abstract

Aim: This study aimed to formulate and evaluate grainsetron HCl transdermal patches to reduce the problems associated with oral delivery of the drug and enhancement of drug permeation through the skin. ***Methods:*** Grainsetron HCl loaded transdermal patch were prepared by solvent evaporation method. Six formulations were prepared based on the two independent variables, type of surfactant and Phospholipid: Edge activator ratio and were evaluated for their vesicle size, PDI, and entrapment efficiency. The optimized formulations were incorporated into transdermal patches, which were evaluated for physicochemical properties *ex-vivo* permeation, skin irritancy, and stability studies. ***Result:*** *Ex-vivo* skin permeation study of optimized formulation NEB3 plot of cumulative amount of drug release versus time generate for Permeation studies. From this plot, permeation kinetic parameters such as permeation flux, permeability coefficient and enhancement ratio were calculated. The results showed that NEB3 with 30% w/w had a flux of 174.25±1.04 and released 65.21% in 720 minutes. The results of the in-vivo skin irritation study indicate that the optimized batch NEB3 did not cause significant irritation on rat skin for up to 14 days and was safely used for up to 24 hours. The stability of the optimized formulation (NEB3) was assessed at various temperatures over a period of 30 days. The optimized formulation was assessed for various parameters such as appearance, weight variation, folding endurance, tensile strength, and drug content. The evaluation showed no significant changes in the formulation under room, oven, and cold temperatures. ***Conclusion:*** The study concluded that transdermal patches of Grainsetron HCl could be used as a potential approach with effective transdermal delivery for the management of chemotherapy induced vomiting.

Keywords: Grainsetron HCl, Optimization, Transdermal delivery; *ex-vivo* study & stability study.

INTRODUCTION

TDDS has become one of the most widely investigated routes of non-invasive drug delivery into the body through the skin, unlike conventionally used direct administration routes that make use of needle-based injections. TDDS has significantly influenced the delivery of various therapeutic agents, especially in pain management, hormonal therapy, and treatment of diseases of the cardiovascular and central nervous systems [1-2]. Granisetron, a selective serotonin receptor antagonist, suppresses nausea and vomiting brought on by chemotherapy and radiation by competitively blocking serotonin's action at 5-HT3 receptors [3]. The current study generated a matrix-type transdermal therapeutic system has been created using different ratios of hydrophilic and hydrophobic polymers along with Granisetron HCl. The current investigation aimed to decrease dosing frequency and enhance the absorption of the antiemetic drug used for chemotherapy-induced vomiting, utilizing the solvent evaporation technique.

MATERIALS AND METHODS

Grainsetron hydrochloride was procured from Niksan Pharmaceutical Pvt. Ltd, Ancleshwer (India), Gujarat as a gift sample. Carbopol 934P and ethylcellulose was purchased from Renkem laboratory.

Formulation of transdermal patch

Transdermal patches of Granisetron Hydrochloride were prepared by solvent evaporation technique. The matrix-type transdermal patches containing Granisetron Hydrochloride were prepared

using different ratios of ethyl cellulose and carbopol 934P. Polymers in different ratios were dissolved in methanol then drug was added slowly to the polymeric solution. To the mixture, Propylene glycol (0.2 ml) as plasticizer and Span 80 (0.1 ml) as permeation enhancer were added and mixed. The dispersion was poured within a glass bangle in a glass plate previously lubricated with Light liquid paraffin. The plate was kept aside for drying at room temperature for 24 hrs. Inverted funnel was placed over the glass plates to prevent the current of air. After drying, the patches were peeled from glass plates, wrapped in aluminum foil and preserved in desiccator for further studies. Compositions of different formulations NEB1 to NEB6 are represented in Table.1 and photographs are shown below:

Table 1: Different formulation compositions of Granisetron Hydrochloride transdermal patches

Formulations	Granisetron Hydrochloride (mg)	EC: CP (mg)	Span 80 (ml)	Propylene glycol (ml)
NEB1	11	200:200	0.1	0.2
NEB2	11	133:267	0.1	0.2
NEB3	11	100:300	0.1	0.2
NEB4	11	267:133	0.1	0.2
NEB5	11	300:100	0.1	0.2
NEB6	11	320:80	0.1	0.2

Preliminary screening

Various evaluation parameter like appearance, Tensile strength, % elongation, Drug content etc. was determined as per standard procedure [4].

***Ex-Vivo* diffusion Study of Final Optimized Transdermal Patch (NEB3)**

For this study previously sacrificed with ether wistar rats skin was collected, first of hair from the skin was removed then skin wash with phosphate buffer solution and finally covered with aluminum foil and stored at 3-5 ^{o}C in a freezer for permeation study. Before permeation study, skin was taking outside and dips into buffer solution for 24 hrs and 30 minutes before permeation study dip into 0.1 N saline solution. For the diffusion study skin was remove and mounted between the donor and receptor compartment of the diffusion cell in such a way the dermal side of skin was facing receptor compartment. The drug loaded transdermal patch placed over the membrane and receptor compartment filled with 13 mL of pH 6.8 buffer. The temperature of diffusion medium maintained at 32 ± 2^{o}C. This whole assembly kept on a magnetic stirrer and solution in the receiver compartment constantly and continuously stirred using magnetic bead. The samples were withdrawn (2 ml, each time) at different time interval and an equal amount of pH 6.8 buffer replaced each time, absorbance of the sample measured using UV 302 nm for NEB3 [5]. The amount of drug permeated per square centimeter at each time interval was calculated and plotted against time. The regression analysis of steady state data and release rate was calculated.

Regression Analysis of *Ex-vivo* Drug Release Study

The drug permeation data subjected to various kinetic equations to understand the mechanism as well as order of drug release. From the obtained graph, transdermal flux was calculated from the slope of cumulative drug release curve and permeation coefficients (cm/hr) measured by dividing the flux with initial concentration of drug (mg/cm^2). From the back extrapolation Lag time was calculated. Diffusion coefficient (D/h^2) and permeability coefficient (Kp) also calculated from the data of *ex-vivo* studies using given equations, respectively (D/h^2=1/6×Tlag, Jss = (dq/dt).1/A, Kp = Jss/Cs). To study the effect of concentration of NEB on the permeation of drug through the skin enhancement ratio was calculated using following formula.

Enhancement ratio = permeability of coefficient with enhancer/ permeability of coefficient without enhancer

This study was performed in triplicate, average results were recorded, and obtained results were express as mean ± S.D. To study the impact of both the independent factors on the selected dependent factors two-way analysis of variance (ANOVA) at a significance level of $p<0.05$ was perform (Pichayakorn W etal 2012). To express effect of both the variables, surface plots such as contour plots and 3D plots with their polynomial equations were generate with the help of Design expert software 9.0.

Drug Release Kinetic In order to investigate the mechanism and pattern of drug release from NEB3 Patch, the release data analyzed with the zero-order equation (Qt=Qt0+k0), first-order equation (lnQt = ln Q0+k1t,), higuchi equation (Q= kH t½) and hixon-crowell equation (Mt=M0-KH (t) ½).

***In - vivo* Skin Irritation Study of Transdermal Matrix Patch**

Skin irritation studies designed to detect irritation under conditions of maximal stress and during the assessment of transdermal drug products. Study performed on 18 wistar rats for 14 days. Skin irritation study performed on three groups (each group have 6 rats), namely

Group 1 assigned as a control group apply with natural skin irritant, 0.9 % w/v saline,

Group 2 apply with placebo patch,

Group 3 apply with final optimized patch.

Patch applied on the backside of hairless skin of rats for 23 ± 1 h upto 14 days to the same skin site. After 24 hrs if any type of irritation found then patch should be applied on other site. Each day skin was examined for any type of major and minor skin reactions as mention below scale of 0 to 7 numbers, which is same as given in authorized book.

0 = no evidence of irritation
1 = minimal erythema, barely perceptible
2 = definite erythema, readily visible; minimal edema or minimal popular response
3 = erythema and papules
4 = definite edema
5 = erythema, edema, and papules
6 = vesicular eruption
7 = strong reaction spreading beyond test site
Individual daily results should be note down and mention in the table with each day which type of skin reaction occur [6].

Stability studies of optimized formulation (NEB3)

The purpose of stability study is to provide evidence on the quality of a drug substance or drug product which varies with time under the influence of a variety of environmental factors such as temperature, humidity and light. Optimized formulation (NEB3) was selected for stability studies on the biases of physiochemical characteristics and drug content of formulation. The satisfactory formulation was sealed in an aluminum foil and stored at room temperature, an oven and refrigerator condition for 1 month [7].

RESULT AND DISCUSSION

The patches' thickness was adjusted between 0.031 and 0.056 mm. indicates that the film's thickness increased linearly with polymer concentration. A low standard deviation in the measurements of film thickness guaranteed the homogeneity of the solvent-evaporation-prepared patch. The patches' weight ranged from 0.054 gm to 0.154 gm. The movie demonstrates how weight increased linearly with polymer content. A low standard deviation value in the measurements of the film weight guaranteed the homogeneity of the solvent-evaporated patch. It was discovered that the tensile strength ranged from 0.72 to 0.58. The best tensile strength was demonstrated by formulation NEB3. It was discovered that the % elongation fell between 15.34% and 31.2%. Out of all the patches, the formulation NEB3 exhibited the lowest percentage of elongation at 15.34% (fig 5). Manual folding endurance testing revealed that formulation NEB3 had the highest folding endurance (157.8 folds), whereas formulation NEB6 had the lowest folding endurance (82 folds). The findings show that when films are applied, they have a maximum folding endurance and remain intact even when the skin folds normally. Information about the stability of the formulations is provided by the studies on moisture content. According to the observation of percentage moisture absorption, formulation NEB3 13.5 had the largest moisture absorption, whereas formulation NEB6 (1.813) had the lowest moisture uptake. At 80–90% relative humidity, it was discovered that the hydrophilic polymer Carbopol had a greater capacity to absorb water than the lipophilic polymer. This finding was explained by the hygroscopic characteristic of Carbopol. On the other hand, moisture absorbed did not alter film strength or integrity. Moisture uptake gives information about the stability of formulations. According to the moisture loss study observation, formulation NEB3 12.75 had the largest % moisture loss, while formulation NEB6 5.34 had the lowest percentage moisture loss. Because of their hygroscopic nature, it was discovered that the formulations' moisture contents increased as the concentrations of the hydrophilic polymer (Carbopol 934P) and the lipophilic polymer (EC) decreased. However, the formulations' low moisture content kept the patches from becoming completely dry and brittle. According to the water vapor transmission rate (WVTR) values in gm/hr cm^2, formulation NEB6 had the highest water vapour transmission rate (0.0048) after 24 hours, whereas formulation NEB2 had the lowest water vapour transmission rate (0.00374). Within 72 hours, the same outcomes were observed. The casting solvent's vaporization rate, which may or may not depend on its boiling point and vapour pressure during the polymer's desolvation, could be the cause of the variance in WVTR. The aforesaid finding was shown in Table 7. Granisetron HCl transdermal patches had a drug content that ranged from 81.2 % to 98.182 %, according to the drug content observation (table 2). As per physiochemical screening NEB3 formulation was selected as optimized formulation.

Table 2: Physiochemical Screening of Patches

F. Code	Thickness (mm)	Wt. variation	Tensile strength	%elongation	Folding endurance	%moisture absorption	%moisture loss	WVTR studies (gm/ hr cm^2)	
								After 24hrs	After 72 hrs
NEB1	0.044	0.104	0.72	15.25%	133.6	7.072	10.33	0.00292	0.00388
NEB2	0.047	0.134	0.69	20.63%	145.6	9.232	10.12	0.00265	0.00374
NEB3	0.031	0.154	0.76	15.34%	157.8	13.53	12.75	0.0034	0.0048
NEB4	0.040	0.054	0.72	23.76%	111.6	5.54	6.26	0.0038	0.0052
NEB5	0.047	0.073	0.62	31.2%	93.6	2.88	5.78	0.0044	0.0072
NEB6	0.056	0.055	0.58	29.46%	81	1.83	5.34	0.0048	0.00844

Ex-vivo skin permeation study of optimized formulation NEB3 plot of cumulative amount of drug release versus time generate for Permeation studies and represent in Fig 1 & table 3. From this plot, permeation kinetic parameters such as permeation flux, permeability coefficient and enhancement ratio were calculated (table 4).

Table 3: *Ex-vitro* skin permeation study of optimized formulation (NEB3)

Time (min)	% Cumulative drug release
0	0
30	12.6
60	18.22
120	28.25
240	42.14
360	50.09
480	56.26
720	65.21

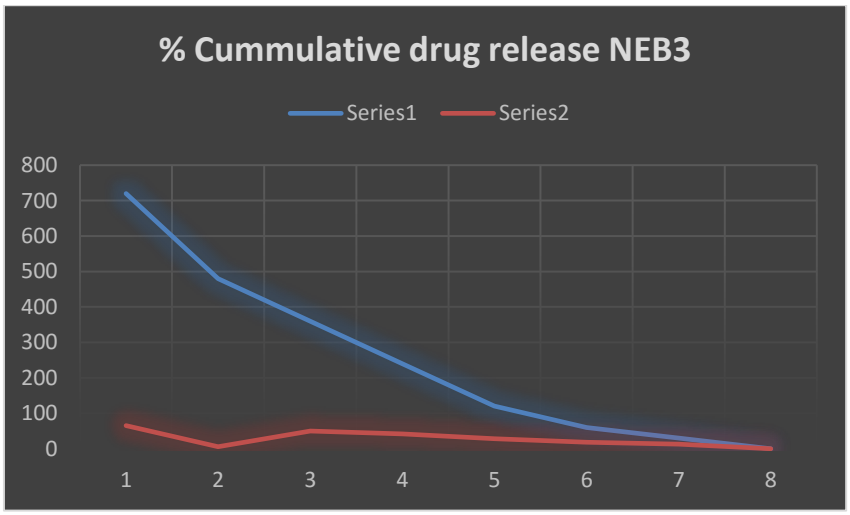


Fig. 1: Cumulative drug release study

Table 4: Permeation Kinetic parameters of NEB3

BatchCode	ransdermalFluxJss (µg/cm²/hr)	Lag time(h)	Permeability Coefficient (Kp)	DiffusionCoefficient(D) (cm/h×10^{-8})	ancement Ratio
NEB3	174.25±1.04	1.30±0.13	1.710×10^{-5}±2.01	0.0286±0.02	1.331±0.06

The results showed that NEB3 with 30% w/w had a flux of 174.25±1.04 and released 65.21% in 720 minutes. Drug penetration increases with greater drug concentration because unsaturated fatty acids alter the structure of the stratum corneum, enhancing the diffusion of drug molecules through the epidermal layers. Thus, adding PEG as a plasticizer in transdermal matrix patches containing drugs could enhance both physical strength and drug release characteristics. The medication release rate is influenced by the choice of polymer and its concentration. Drug release from the polymeric matrix is triggered by the influx of water into the matrix, leading to polymer swelling and regulated drug release over a specific duration. The drug release data from the final optimized batch was analyzed using various kinetic models to investigate the mechanism of drug release from the patch and through the skin. The regression coefficient indicates that drug release from the patch follows a zero-order pattern, with continuous controlled release for up to 16 hours (table 5). The correlation coefficient (R2) of Higuchi's model was shown to be 0.992, indicating diffusion took place. The drug release mechanism begins with the expansion of the polymer matrix, followed by the diffusion of the drug from the matrix, therefore adhering more successfully to Higuchi's and Korsmeyer-Peppas models.

Table 5: Correlation coefficient of different kinetic models for *ex-vivo* permeation study

Release Kinetic	Correlation coefficient(R^2) NEB3
Zero order	0.886
First order	0.960
Higuchi	0.992

The study found that saline solution, being a skin irritant, caused modest redness after 10 days and clear redness and noticeable swelling after 12 days. Both the placebo and optimized batch did not show any irritation for up to 10 days. After that, a slight erythema with light redness was observed at the application site.

The results of the *in-vivo* skin irritation study indicate that the optimized batch NEB3 did not cause significant irritation on rat skin for up to 14 days and was safely used for up to 24 hours. Photographs of the optimized batch NEB3 before and after the *in-vivo* skin irritation study are presented in Table 6-8 & Figure 2.

Table 6: Skin Irritation study of Group (Group with0.9%w/v Saline)

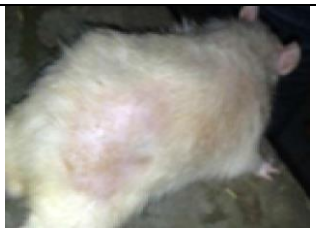
Sr. No.	Skin Irritation Symptom	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14
1	0	-	-	-	-	-	-	p	p	p	p	p	p	p	p
2	1	-	-	-	-	-	-	-	-	-	p	p	p	p	p
3	2	-	-	-	-	-	-	-	-	-	-	-	p	p	p
4	3	-	-	-	-	-	-	-	-	-	-	-	-	p	p
5	4	-	-	-	-	-	-	-	-	-	-	-	-	-	p
6	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	7	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 7: Skin Irritation study of Group (Applied with Placebo Patch of NEB3)

Sr. No.	Skin Irritation Symptom	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14
1	0	-	-	-	-	-	-	-	-	-	-	P	p	P	p
2	1	-	-	-	-	-	-	-	-	-	-	-	P	P	p
3	2	-	-	-	-	-	-	-	-	-	-	-	-	P	p
4	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	7	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 8: Skin Irritation Study of Group (Applied Patch of NEB3)

Sr. No.	Skin Irritation Symptom	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14
1	0	-	-	-	-	-	-	-	-	P	P	P	P	P	p
2	1	-	-	-	-	-	-	-	-	-	-	P	P	P	p
3	2	-	-	-	-	-	-	-	-	-	-	-	P	P	p
4	3	-	-	-	-	-	-	-	-	-	-	-	-	-	P
5	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	7	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Batches	D1	D14
Group 0.9% w/v Saline		
NEB3(Plecebo)		

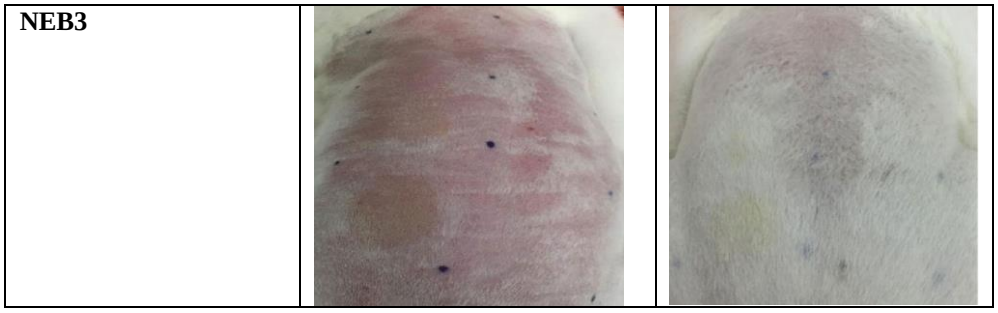


Fig. 2: Primary irritation study

Stability in pharmaceutics refers to a pharmaceutical product's capacity to retain its qualities within defined limitations over its stated shelf life. Defining the shelf life of a drug involves conducting investigations and testing as per a predetermined timetable to gather data on the chemical, physical, and microbiological stability of the drug. The stability of the optimized formulation (NEB3) was assessed at various temperatures over a period of 30 days. The optimized formulation was assessed for various parameters such as appearance, weight variation, folding endurance, tensile strength, and drug content. The evaluation showed no significant changes in the formulation under room, oven, and cold temperatures. This data is presented in table 9 and figure 3.

Table 9: Stability studies of optimized formulation (NEB3) at different temperature after 30 days

S. No.	Parameters	At Room temperature	Oven temperature	Cold temperature
1.	Appearance	No change	Slightly change	No change
2.	Weight variation	0.154 ±0.47	0.148±0.43	0.151±0.83
3.	Folding endurance	157.6±1.27	154.6±1.22	156.6±1.86
4.	Tensile strength	15.34±0.48	14.32±0.079	15.01±0.55
5.	Drug content	96.182±0.37	92.102±0.24	97.21±0.26

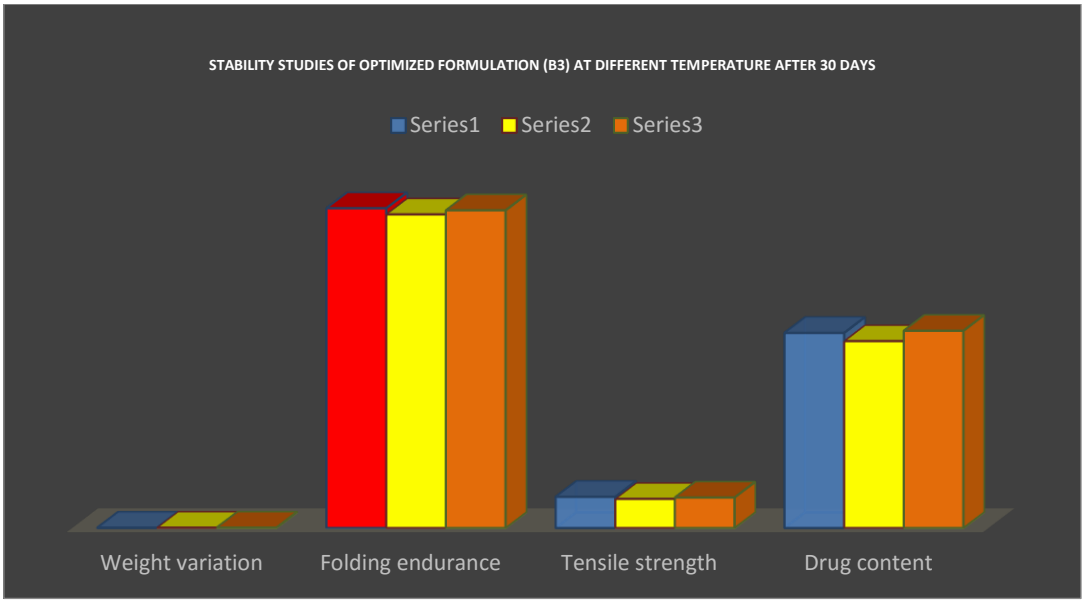


Fig. 3: Stability studies of optimized formulation (NEB3) at different temperature after 30 days

CONCLUSION

The *ex-vivo* drug release experiments of the improved formulation NEB3 showed that only 65.21% of the medication penetrated through rat skin within 720 minutes. This suggested an opportunity to incorporate a permeation enhancer in the formulation to enhance the drug's penetration rate through the rat skin. The stability analysis of the optimized formulation showed no significant changes under room, oven, and cold temperatures. In the future, pharmacokinetic investigations can be extended to include *in-vivo* studies on higher animals and controlled clinical trials on human subjects. The primary goals in developing the transdermal system were to increase patient compliance, decrease the frequency of administration, and lengthen the duration of drug release.

REFERENCES

1. Asbill CS, Michniak BB. Percutaneous penetration enhancers: Local versus transdermal activity. Pharm Sci Technolo Today. 2000; 3:36–41.
2. Balaji P, Thirumal M, Gowri R, Divya V, Ramaswamy V. Design and evaluation of matrix type of transdermal patches of methotrexate. Int J Pharm Chem Biol Sci. 2012; 2:464–71.
3. Yaaqoob Alhammadi *et al.*, Granisetron: An Overview of Its Pharmacology, Clinical Efficacy, and Safety. Anaesthesia & Surgery.4:3:1.
4. Pandit V, Khanum A, Bhaskaran S, Banu V. Formulation and evaluation of transdermal films for the treatment of overactive bladder. Int J Pharm Tech Res. 2009; 1:799–804.
5. Sachan R, Bajpai M. Transdermal drug delivery system: a review. Int J Res Dev Pharm Life Sci. 2013; 3:748–765.
6. Parivesh S, Sumeet D, Abhishek D. Design, evaluation, parameters and marketed products of transdermal patches: a review. J Pharma Res. 2010; 3:235–240.
7. Gannu R, Vishnu YV, Kishan V, Rao YM. Development of nitrendipine transdermal patches: in vitro and ex vivo characterization. Curr Drug Deliv. 2007; 4:69–76.
8. Himesh soni. Formulation and Development of Hydrogel Based System for Effective Delivery of Rutin. IJAP;5(1), (2013),5-13.