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FORMULATION AND EVALUATION OF TRANSDERMAL PATCH CONTAINING ANTIHISTAMINIC DRUG BILASTINE

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ABSTRACT

The present investigation was aimed to formulate and evaluate Matrix- type Transdermal delivery system containing an antihistaminic drug, Bilastine with different polymer concentration by the solvent casting technique & explore the effect of polymers on the in-vitro drug release of Bilastine across skin Matrix. The present investigation aims to formulate and evaluate of medicated skin patches for the treatment of Urticaria. Skin patches were prepared by using hydroxyl propyl methyl cellulose HPMC K100 and Eudragit RS 100 as polymers, ethyl cellulose as plasticizer, PEG-4000 as permeation enhancers and chloroform as solvent. Prepared patches were subjected to different evaluation studies in which permeation studies were performed by using Franz diffusion cell apparatus, folding endurance, thickness, weight variation, percentage moisture uptake, etc. The results showed that F5 batch found were optimized i.e. thickness 0.11mm, weight variation about 2%, folding endurance about 103 folds, moisture uptake 1.03%, and showing drug assay about 97.57% with drug release in first hour 9.12 and cumulative drug release of 75.71%. The stability study proved that optimized batch was stable at accelerated stability conditions.

Keywords: Transdermal, Urticaria, Permeation enhancer, In-vitro permeation study

INTRODUCTION

Topical therapy is highly desirable in treating skin allaergies due to its localized effects, which results in minimal adverse systemic events and possibly improved adherence. However, the effectiveness of topical therapies is limited by minimal drug permeability through the skin plate. Skin allergies are a very

common condition in millions of people. The accounts for about half of all skin allaergies and are estimated to occur in over 10% of the population. Such allergies may be difficult to treat, and currently prescribed oral antihistaminic drug medications may cause side effects ranging from skin rashes to liver damage. Other treatment modalities include the use of topical medications. Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous allaergies (e.g. Urticaria) or the cutaneous manifestations of a general disease (e.g. Psoriasis) with the intent of the pharmacological or other effect of the drug to the surface of the skin or within the skin.

Transdermal is a topical drug delivery system. Trans means through and unguis means skin, so Transdermal drug delivery system is nothing but a system associated with drug delivery through the skin to achieve a targeted drug delivery system of the skin to treat skin fungal diseases. The hardness and impermeability of the skin makes it an unpromising route for drug delivery, however improvement in the topical delivery of compounds for the treatment of skin allergy (Urticaria) would reduce the need for systemic administration of drugs with its associated side effects. In addition, it may reduce the length of time required for treatment and help prevent relapse. Currently research on Transdermal drug delivery focuses on altering the, skin barrier by means of chemical, physical and mechanical means for drug penetration. Skin can suffer from a number of allaergies due to which they discolour (by use of certain systemic drugs), become brittle (by chronic use of detergents) or can cause chronic trauma leading to ingrowing of skins and thickened or infected skin which may lead to its avulsion from the skin bed. Preferably, skin allergies are treated topically to overcome inherent side effects of current treatments, for example pain and patient noncompliance associated with parenteral route and drug–drug interactions with the conventional oral therapy (e.g. concomitant use of fluconazole and atorvastatin increase the risk of myopathy/ rhabdomyolysis) [(1-7)].

MATERIALS AND METHODS

A) Materials

Bilastine was received a gift sample from Yarrow Chemicals Pvt. Ltd., Hydroxyl propyl methyl cellulose (HPMC K 100) and Eudragit RS 100 were obtained from Loba Chemicals Pvt. Ltd., Mumbai. All other chemicals and solvents were of analytical reagent grade.

B) Methods

1. **Development of standard calibration curve:**

Accurately weighed 50 mg of Bilastine was dissolved in 50 ml of Chloroform and from this 1 ml is diluted using phosphate buffer pH 6.4 in 100 ml volumetric flask to get the stock solution of 10 µg/ml concentration. From the stock solution 2, 4, 6, 8, 10 and 12 ml were withdrawn and further diluted to phosphate buffer pH 7.4 in 100 ml volumetric flasks to obtain a concentration range of 0.2-1.2µg/ml. The absorbance of the solutions was measured at 284 nm by using a UV-spectrophotometer. A graph of Concentration vs. Absorbance was plotted. [8-10]

2. Drug exicipient compatability studies:

The FTIR study performed to detect any doubtful interactions which affect stability of drug and excipients chosen for the preparation of patch, over the range of 4000-400 cm-1 in the Perkin Elmer FTIR spectrometer. [8-10]

3. Preparations of Medicated Skin Patch:

Skin patches are formulated by taking quantities of ingredients as mentioned in Table 1 using solvent casting method [11-15].

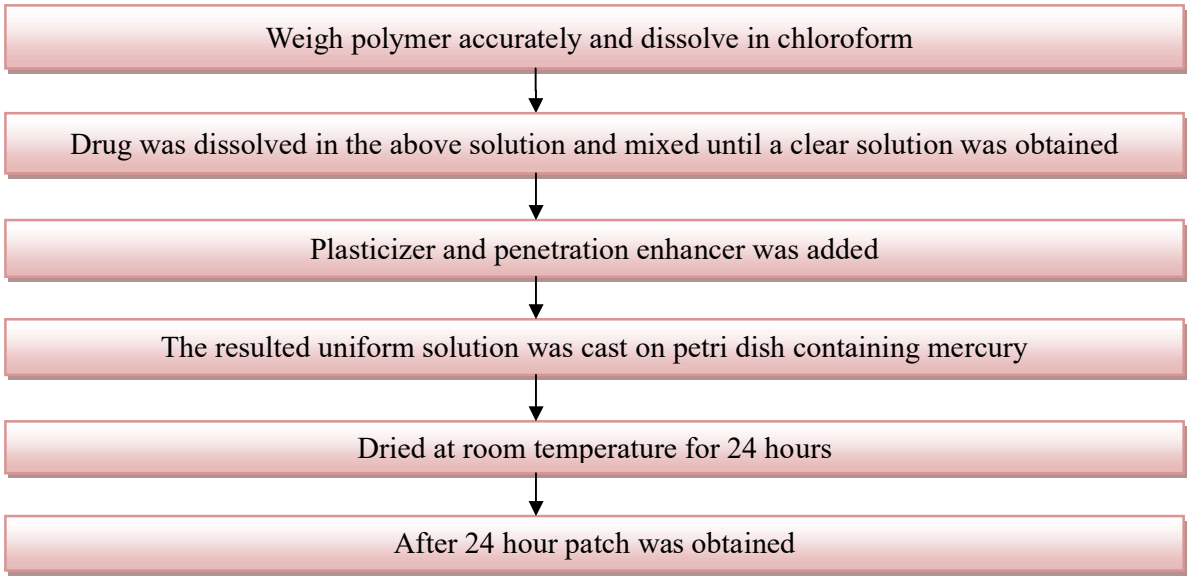

Table 1: Formulation Table

Formulation	API Bilastine	HPMC	PEG4000	Ethyl cellulose	Chloroform
F1	10mg	200mg	2mg	4mg	10ml
F2	10mg	250mg	4mg	6mg	10ml
F3	10mg	300mg	6mg	8mg	10ml
F4	10mg	350mg	8mg	10mg	10ml
F5	10mg	400mg	10mg	12mg	10ml
F6	10mg	450mg	12mg	14mg	10ml
F7	10mg	500mg	14mg	16mg	10ml
F8	10mg	500mg	16mg	10mg	10ml
F9	10mg	525mg	18mg	15mg	10ml

4. Evaluation of Medicated Skin Patch[16-21]:

i. Thickness

The thickness of patch was measured by using vernier caliper, with a least count of 0.01mm. The thickness uniformity was measured at three different sites and average of three readings was taken with standard deviation.

ii. Weight uniformity

Weight variation is studied by calculating the average weight of randomly selected individually weighed patches. The individual weight that evaluated from weight variation test should not be deviated significantly form average weight.

iii. Folding Endurance:

The folding endurance test of formulated patches was performed manually by folding the patch repeatedly at the same place (single point) till it broken. The number of times that the patch subjected to repeated folding at the same place without cracking/breaking indicates the folding endurance value. Folding endurance evaluation test involves the determination of folding capacity of the films that subjected to folding at the frequent extreme conditions which also an indicative of brittleness.

iv. Percentage moisture uptake:

Accurately weighed patches were placed in desiccators containing 100ml of saturated solution of potassium chloride, which maintains at 80-90% RH. After 3 days, the desiccated patches were taken out and subjected to weighing. The percentage moisture absorption was calculated using the formula:

$$\%\text{Moisture Uptake} = \frac{Final\ Wt. - Initial\ Wt.}{Initial\ Wt} \times 100$$

v. Drug assay

Weigh accurately portion of patch (equivalent to 100 mg of drug) and dissolved in 100 ml of phosphate buffer solution (6.4pH) in a 100ml volumetric flask. Place the flask on to the shaker for 24 hr to achieve the complete dissolution. Then obtained solution was filtered and the content was estimated spectrophotometrically at 284 nm by appropriate dilution.

vi. *In vitro* Transdermal permeation studies

Diffusion cell technique was used to determine the in vitro skin permeation of Bilastine from various formulated Transdermal patches. Diffusion cell composed of two compartments i.e., donar and receptor. Permeation studies was carried by placing the fabricated patch with prehydrated cellophane membrane in between receptor and donar compartment of the diffusion cell in which the receptor compartment was filled with 6.4 pH phosphate buffer. Transdermal patch was placed in such a way that the membrane

facing towards the donor compartment and the patch towards the receptor compartment containing buffer solution in which the receiver compartment was maintained at body temperature and was subjected to continuous stirring with the help of magnetic stirrer. At predetermined time intervals the samples to be analyzed are withdrawn and equal volume of pre-thremostated of fresh receptor fluid is replaced each time in order to maintain skin conditions. Then the samples were analyzed spectrophotometrically after appropriate dilution.

vii. Stability study

Optimized formulation was subjected to stability as per ICH guidelines at the following conditions. Samples were kept in stability chamber at following conditions for 3 months

1. 40 ± 2^0C and 75±5% RH (Accelerated temperature)
2. Room temperature

RESULTS AND DISCUSSION

Drug calibration:

The ultraviolet spectrum of Bilastine in Chloroform showed linearity in absorbance of Bilastine which was found to be at 284 nm. Results were showed in **Table 2 and Figure 1**.

Drug excipient compatibility study:

FTIR spectrum of drug and drug with excipients was obtained using Perkin Elmer and can be concluded that there were no interactions of drug and excipients. Spectrum was shown in **Figure 2 and 3**.

Preliminary evaluation:

All the formulations of transdermal patch showed thickness variation range from 0.11 to 0.18 mm as shown in **Table 3**. High thickness in batch F7 and F8 was found, it may be due to low solubility of polymer in solvent makes uneven distribution of polymer layer. Drug assay ranges 74 - 93% and weight ranges 294 – 299 mg. F9 batch showed highest drug assay of 92.57 % having thickness of 0.11 mm considered as optimized formula. Results of folding endurance, % moisture uptake are presented in **Table 3**.

***In-vitro* diffusion studies:**

% drug release of Bilastine with changes in concentration of polymers by were studied by diffusion test. Results mentioned in **Table 4 and Figure 4**.

Stability study

The stability study conducts by ICH (International Conference on Harmonization) guideline. It showed No significant change in properties of the optimized formulation & the drug release. Short term stability studies were performed in a Stability chamber over a period of 4 weeks (30 days) on the promising skin patch formulation F9. Sufficient number of patch formulation were packed in stability

container and kept in a Stability chamber at Temperature 400C & RH 75%. Samples were taken on 30 days for drug assay estimation; also the weight variation, folding endurance and in-vitro diffusion studies were performed to determine as shown in **Table 5**.

Table 1: Absorbance values of Bilastine on UV at 284 nm

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.14
3	4	0.172
4	6	0.24
5	8	0.285
6	10	0.297

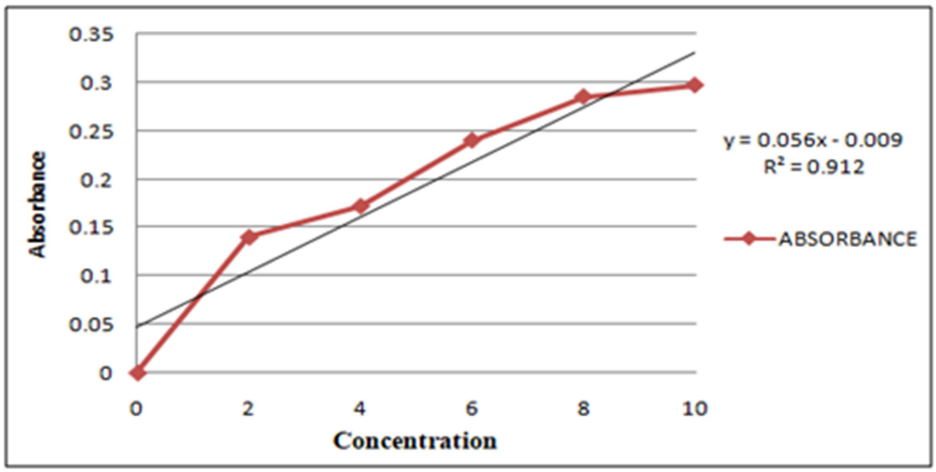

Figure 1: Calibration curve of Bilastine

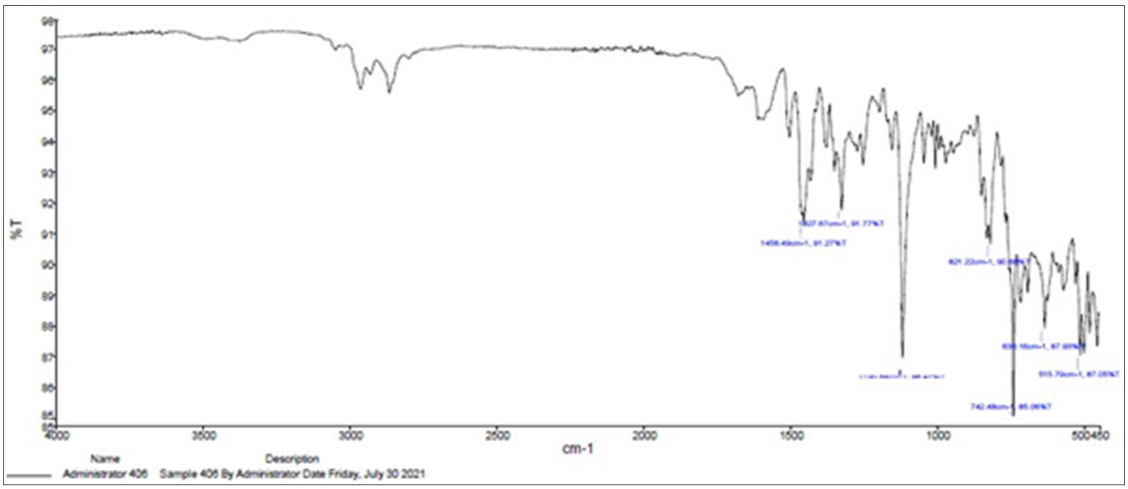

Figure 2: FTIR study of Bilastine

Table 2: Interpretation of Bilastine

Functional Group	Peak reported cm-1	Peak observed cm-1
O-H	3500-2500	3432
C=O	1710-1650	1663
C=N	1650-1550	1507
C-O	1250-1050	1119

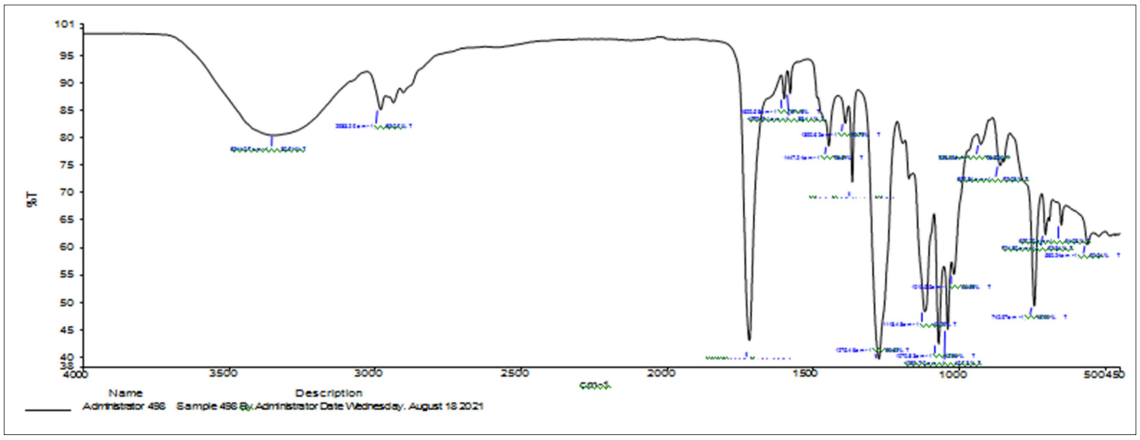

Figure 3: FTIR study of Drug and excipients

Table 3: Evaluation parameter of medicated skin patch

Batch code	Weight (mg)	Thickness (mm)	Folding endurance	Drug assay (%)	Moisture uptake (%)
F1	295	0.12	97	79.27%	1.27
F2	294	0.11	109	75.87%	1.39
F3	297	0.12	115	74.78%	1.45
F4	298	0.12	95	91.69%	1.72
F5	297	0.11	103	92.57%	1.06
F6	296	0.11	112	92.32%	1.68
F7	296	0.17	107	91.04%	1.81
F8	299	0.18	113	90.47%	1.93
F9	298	0.11	110	90.57%	1.54

Table 4: *In- vitro* drug diffusion study of all batches

Time (h)	% Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	8.37	8.9	8.7	7.4	9.12	10.27	11.44	12.84	11.15
2	14.08	14.78	12.9	17.5	17.12	13.25	17.15	17.58	15.10
3	19.87	19.85	19.8	20.25	25.36	19.41	21.83	22.18	19.20
4	26.15	28.12	27.9	29.1	32.14	22.88	26.54	25.87	23.22
5	32.18	32.1	29.1	38.9	40.12	27.48	29.71	30.28	29.52
6	39.17	39.52	38.9	47.3	49.8	32.88	36.38	37.62	35.12
7	47.14	49.15	47.3	59.82	55.36	40.28	44.05	44.87	34.56
8	59.9	62.1	59.82	64.5	61.24	46.15	50.33	51.94	52.66
9	67.14	68.2	64.5	69.7	68.32	53.48	53.14	57.24	52.34
10	69.67	70.18	66.7	70.8	70.71	55.38	58.51	61.78	55.18
11	70.47	72.86	68.37	71.61	73.87	58.32	62.73	63.57	58.18
12	72.67	74.18	69.7	72.81	75.71	60.38	64.51	65.78	62.18

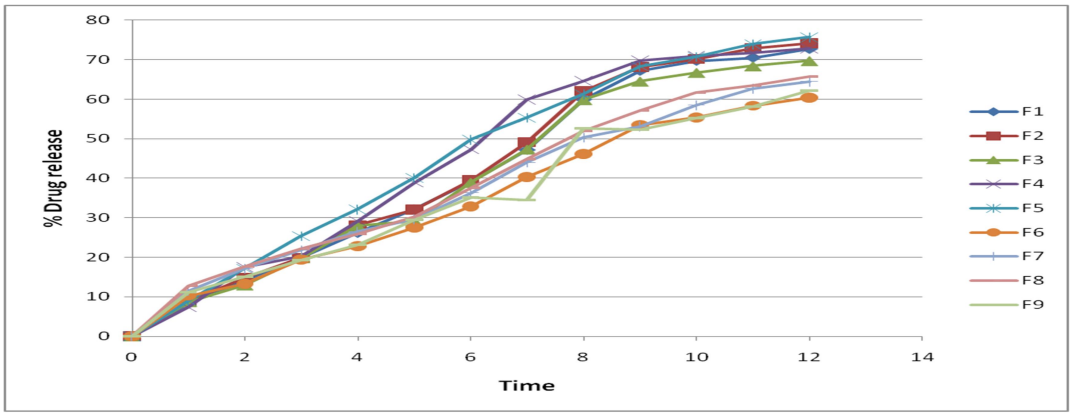

Figure 3: % Drug release of all formulations

Table 5: accelerated stability study

Batch Code	Weight (mg)	% diffusion at 12^{th} hr	Folding Endurance	Drug Assay (%)	Moisture Uptake (%)
F5 Before stability	297	75.71	103	92.57	1.06
F5 After Stability	297	75.30	110	91.99	1.10

CONCLUSION

The medicated skin patch of Bilastine was prepared successfully by using different concentration of polymer by solvent casting method. In the present work, Eudragit RS 100 and HPMC K 100 were used as polymers and ethyl cellulose were used as plasticizer for casting into patch to form adhesive type transdermal drug delivery system drug. All formulations showed good physicochemical properties such as thickness, weight variation, folding endurance, moisture uptake, moisture loss, drug content and % drug release from skin patches of antifungal drug i.e. Bilastine. Effect of polymers used has been checked on drug release for optimization. From these studies it has been understood that as the concentration of polymers increases, drug release was shown to be decreased. F9 batch shows better results as compare to other batches. The optimized batch was subjected to stability studies for a period of 1 month. The results indicated that there was no appreciable change in the values of in-vitro diffusion profile.

REFERENCES

[1] ChienYie. W, "Novel Drug Delivery System", 2nd edition., Revised and expanded, Marcel Dekker, Inc, New York, 2005.

[2] Debjit Bhowmik. Skin Drug Delivery System-A Novel Approaches For Drug Delivery System The Pharma Innovation, Jan 2013: 1(11).

[3] Ashutosh Badola. A Review: Transdermal Drug Delivery A New And Novel System. Asian Journal of Pharmaceutical Science & Technology, 2015: 5(4):227-233.

[4] David B Lebo. A Novel Transdermal Formulation (Skin Patch) for Delivery of CiclopiroxOlamine into the Skin and The Skin Folds, July 2014: 3(3).

[5] Kavyanjana R Nair. Skin Drug Delivery System-A Promising Route to Treat Skin Allaergies, International Journal of Scientific Engineering and Applied Science, March 2017:3(3).

[6] Nagoba S. N. Formulation and Evaluation of Medicated Skin Patches for the Treatment of Urticaria, International Journal of Pharmaceutical Science Invention, April 2018: 7(4I): 52-58.

[7] P. Nandini. A Review on Transdermal Drug Delivary System, World Journal

of Pharmacy and Pharmaceutical Sciences, 7(8): 260-269.

[8] Swami Avinash B., Dr. Nagoba S. N., 'Formulation and evaluation of liposomes containing erlotinib hydrochloride' Scholars Impact: International Multidisciplinary Multilingual Peer Reviewed Research Journal. Dec 2020; 7 (3): 294-301.

[9] Nagoba Shivappa N. and Shinde Nishiganda G.*et al*., "Formulation and Evaluation of Herbal Gel Containing Punica Ganatum'' International Journal of Innovative Science, Engineering & Technology, July 2019: 6 (7):36-51.

[10] Dr. Nagoba S. N., Bhalekar R. V., Swami A. B. et. al., "Formulation and Evaluation of Nanosponges Hydrogel for Topical Drug Delivery Containing Griseofulvin" International Journal of Medicine and Pharmaceutical Sciences (IJMPS). Apr 2020; 10 (2): 57–70.

[11] Rowe, Raymond C., Paul J. Sheskey, and Sian C. Owen, eds. Handbook of Pharmaceutical excipient. Pharmaceutical press London, 2006: Vol.6.

[12] Qvist MH, Hoeck U, Kreilgaard B, Madson F, Frokjaer S. Release of Chemical Penetration Enhancers From Drug-In-Adhesive Transdermal Patches, Int J Pharm, 2002; 231: 253–263.

[13] Shailesh T. Prajapati *et al*. Formulation and Evaluation of Transdermal Patch of Repaglinide, ISRN Pharmaceutics 2011, 1(1): 1-9.

[14] Kanabar Vishvesh B. Formulation and evaluation of transdermal patch of Cefdinir with various polymers, The Pharma Innovation Journal 2015; 4(6): 74-77.

[15] Ravi Shankar. Formulation and Evaluation of Ketoconazole Nanoemulsion Gel for Topical Delivery. American journal of pharmacopoeia research 2015; 5(5).

[16] Samyuktha Metta. Development and Evaluation of a Novel Transdermal Formulation (Skin Patch) for the Treatment of Urticaria, International Journal of Innovative Science and Research Technology, June – 2018: 3(6).

[17] Patel RP and Baria AH. Formulation and evaluation considerations of transdermal drug delivery system. International Journal of Pharmaceutical Research. 2011:3:1-9.

[18] Kaudewar K. D. and Nagoba Shivappa N. *et al*., "Formulation and Evaluation of Transdermal Patches Containing Antidiabetic Drug". International Journal of Innovative Science, Engineering & Technology, 2019, 6(7), 149- 164.

[19] Nagoba Shivappa N. and Sonkamble Pallavi S. *et al*., "Formulation and Evaluation of Herbal Gel Containing Solanum Nigrum Extract''

International Journal of Scientific Research in Science and Technology, 2019, 6(4), 83-91.

[20] Nagoba Shivappa N. *et al*., "Formulation and Evaluation of Transdermal Patches of Nicorandil, In World Journal of Pharmaceutical Research, 2018, 7(14), 543-555.

[21] Gaddime Sonali B. and Nagoba S.N. *et al*., "Formulation and Evaluation of Medicated Nail Patches for the Treatment of Onychomycosis" In International Journal of Pharmaceutical Science Invention 2018, 7(4), 52-58.