WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 11, 1212-1226. Research Article ISSN 2277–7105

FORULATION AND EVALUATION OF TRANSDERMAL PATCH FOR THE TREATMENT OF FUNGAL NAIL INFECTION

***Sangeeta Manjhi and Bishesar Sahu**

Rungta Institute of Pharmaceutical Sciences and Research, Kohka- Kurud, Bhilai, 490024, Chhattisgarh, India.

Article Received on
04 April 2025,

Revised on 25 April 2025,
Accepted on 15 May 2025

DOI: 10.20959/wjpr202511-36854

***Corresponding Author**
Sangeeta Manjhi
Rungta Institute of Pharmaceutical Sciences and Research, Kohka-Kurud, Bhilai, 490024, Chhattisgarh, India.

ABSTRACT

Onychomycosis, a fungal infection affecting the toenails or fingernails, presents treatment challenges due to limited nail blood supply and the adverse effects of systemic antifungal drugs. This study aimed to develop and evaluate tavaborole-loaded transdermal patches as an alternative treatment using the solvent casting method. Hydroxypropyl methylcellulose (HPMC) and polyvinyl pyrrolidone K30 (PVP K30) were employed as film-forming polymers, while polyethylene glycol 400 (PEG 400) functioned as both a plasticizer and penetration enhancer. The formulated patches were assessed for their physicochemical properties, including thickness, weight uniformity, moisture content, folding endurance, tensile strength, elongation percentage, and drug content. The results demonstrated uniformity, flexibility, and adequate mechanical strength, ensuring effective drug delivery. The adhesive patch system facilitated sustained drug release and enhanced ungual penetration, offering a promising, patient-friendly alternative to conventional treatments for onychomycosis.

KEYWORDS: Onychomycosis, Transdermal patch, Tavaborole, Physiochemical evaluation.

1) INTRODUCTION

Onychomycosis is a fungus that can affect either the toe or fingernails. The limited blood supply to the afflicted nails and the recognized adverse effects of antifungal drugs have complicated systemic therapy for onychomycosis.[1] Onychomycosis is also known as nail fungus or fungal nail infection. It is commonly referred to as tinea unguium, derived from the Latin term for “fungus” (tinea) and “nail” (unguium).[2] Up to 90% of cases are caused by

dermatophytes like Trichophyton mentagrophytes and Trichophyton rubrum are responsible, although other fungi such as yeast or molds, can also be responsible.[3]

Transdermal drug delivery system (TDDS) are considered patient-friendly due to their non-invasive nature, the fact that they do not require professional administration, reduced gastrointestinal side effects, and improved patient adherence. Transdermal drug delivery system enhance bioavailability, efficacy and drug translocation, avoiding peptic first pass metabolism.[4]

The adhesive patch is one of the new therapies that provides advantages including improved nail hydration, which promotes drug diffusion through the nail, and regulated or sustained drug release over an extended length of time with a single dose. A drug in-adhesive patch is made up of active chemical, additives, an adhesive, a backing layer, and a release membrane. The adhesive layer that holds the medication and or active components in this kind of patch comes into direct contact with the nail surface. Therefore, it is essential to choose the right adhesive.[5] Topical therapies can be enhanced by using formulation that are easy to apply, promote ungual drug absorption, and remain in touch with nail plates for an extended length of time by constantly releasing medication.[6]

Fig 1.1: - Transdermal Drug Delivery System.

The goal of this research is to formulate and evaluate a transdermal patch for the effective treatment of fungal infections. The study aims to develop a controlled drug delivery system

that enhances bioavailability, ensures sustained drug release, and improves patient compliance. By utilizing transdermal patches, the research seeks to overcome limitations associated with conventional antifungal treatments, such as poor nail penetration, systemic side effects, and frequent dosing requirements. Additionally, the study focuses on evaluating key parameters, including drug permeability, adhesion properties, and release kinetics, to ensure the efficacy and stability of the formulation. Ultimately, the objective is to provide a more efficient, patient-friendly, and non-invasive approach to treating fungal infections.[1]

Type of transdermal patches

1. Single layer drug in matrix
2. Multi layer drug in matrix
3. Reservoir type patches
4. Matrix type patches
5. Vapour type patches[7]

Tavaborole is the newest class of topical antifungal treatment are a new class of drugs called oxaboroles, which contains boron. It has been discovered that boron has a unique ability to attach functional group at certain enzyme target location, making them inaccessible and reducing their functionality. In July 2014, tavaborole became the first synthetic in this class of medication to get Food and Drug Administration (FDA) clearance.[8] Tavaborole is used to treat a variety of skin diseases and exhibits antimycotic action against several types of candida.[7,9]

2) METHODOLOGY

2.1 Material

Tavaborole was kindly provided as a gift sample by Life Bioscience. HPMC (Hydroxypropyl Methyl Cellulose), Polyvinyl Pyrrolidone K30 (PVP K30), Polyethylene Glycol 400 (PEG 400), methanol, and acetone was purchased from Loba Chemie Pvt.Ltd.

Table 1: Ingredient table of Tavaborole loaded Patch.

S.No.	Ingredients	Activity
1	Tavaborole	Active ingredient (Drug)
2	HPMC	Thickening agent
3	Polyvinyl Pyrrolidone K30	Binding agent, Stabilizer
4	Polyethylene Glycol 400	Penetration enhancer
5	Methanol: Acetone	Solvent

3) Pre formulation test

3.1 pH of Tavaborole: - The pH of Tavaborole was measured by dissolving an appropriate amount of the drug in distilled water and recording the pH using a calibrated digital pH meter. The measurement was performed at 25 ± 2°C. The observed pH value was 6.66.[18]

Fig 3.1: - pH of Tavaborole.

3.2 Solubility of Tavaborole

3.2.1 Solubility in Water: - The solubility of Tavaborole was tested in distilled water. An excess amount of the drug was added to water and stirred at room temperature (25 ± 2°C). Tavaborole was found to be slightly soluble in water.[19]

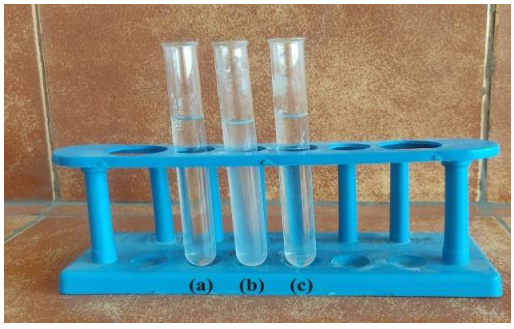

Fig 3.2: - Solubility of Tavaborole.

(a) Water, (b) Methanol, (c) Ethanol

3.2.2 Solubility in Methanol: -The solubility of Tavaborole was examined in methanol. Upon stirring at room temperature (25 ± 2°C), Tavaborole was observed to be freely soluble in methanol.

3.2.3 Solubility in Ethanol: - The solubility of Tavaborole was assessed in ethanol (absolute). The drug showed freely soluble behavior in ethanol when stirred at 25 ± 2°C.

3.3 Melting point of Tavaborole: - Tavaborole exhibited a melting point of **132°C**, indicating its thermal stability under standard conditions. This value aligns with its crystalline nature and confirms its purity.[20]

Fig 3.3: - Melting point of Tavaborole.

4.1 METHOD

1. Tavaborole loaded transdermal patch was prepared using the solvent casting method utilized film forming polymer such as hydroxypropyl methyl cellulose (HPMC) and polyvinyl pyrrolidone k30 (PVP K30) along with a plasticizer and the penetration enhancer polyethylene glycol 400 (PEG 400).
2. The detailed composition of the tavaborole transdermal patch is provided in table 2.
3. Add ethanol and acetone, respectively, in a beaker at a ratio of 3:1.

Fig 4.1: - Solvent mixture of methanol and acetone

4. After that, leave them in a magnetic stirrer machine for few minutes.

Fig 4.2: - Solvent mixture under magnetic stirrer.

5. The polymer HPMC and polyvinyl pyrrolidone were precisely weighed and separately dispersed in a mixture of acetone and methanol in a 3:2 ratio.

Fig 4.3: - Hydroxypropyl Methyl Cellulose.

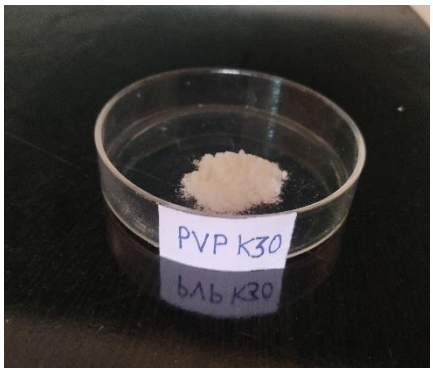

Fig 4.4: - Polyvinyl Pyrrolidone K30.

Fig 4.5: - Mixing polymer using magnetic stirrer.

6. Once the polymers were dissolve, the drug was added to the polymeric solution, followed by the incorporation of polyethylene glycol 400 (PEG 400) as a plasticizer and penetration enhancer.

Fig 4.6:- Add API (Tavaborole)

Fig 4.7: - After API adding PEG 400.

7. The solution was thoroughly mixed using a magnetic stirrer.
8. The entire solution was the poured carefully into a glass petri dish.

Fig 4.8: - Solution pour in petri dish.

9. The solvent acetone and methanol were subsequently removed by heating it to 580^0 under reduced pressure.

Fig 4.9: - Dried film of Tavaborole.

10. Afterward, the dried film was removed and store in self-sealing plastic envelopes, then kept in desiccators until the evaluation tests were conducted.

Table 2: Composition of the Tavaborole Transdermal patch.

Ingredients	Formulation			
	F1	F2	F3	F4
Tavaborole (mg)	50	40	50	60
Polyvinyl Pyrrolidone K3O (mg)	150	100	200	250
HPMC (mg)	500	200	300	600
Polyethylene Glycol 400 (mg)	0.25	0.15	0.25	0.50
Methanol (ml)	18	18	18	18
Acetone (ml)	12	10	12	12

5) Evaluation parameters

5.1 Physiochemical evaluation

5.1.1 Analytical characterization and identification of a drug using uv spectroscopy, and preparation of standard calibration curve by uv spectroscopy

After precisely weighing 15 mg of tavaborole, the volume was increased to 50 ml with methanol, producing a stock solution with a concentration of 100µg/ml. Various volumes of the stock solution were pipetted into 10-milliliter volumetric flasks in order to create a standard calibration curve. Each flask received a final volume of 10 ml after methanol was added, producing levels of 1, 2, 3, and 4,5 µg/ml. A UV spectrophotometer was used to test the absorbance of these solutions.[10]

5.1.2 Thickness

Transdermal film thickness is measured at several location on the film using a traveling microscope, dial gauge, screw gauge, or micrometre.[11]

5.1.3 Uniformity of weight

Ten randomly chosen separately, and the average weight is determined in order to study weight fluctuation. The average weight and the individual weight shouldn't differ all that much.[12]

5.1.4 Moisture content

The developed film were marked weighed separately, and stored for 24 hours at room temperature in a desiccator filled with activated silica. The film were repeatedly weighed separately until their weight remained consistent. Calculate the percentage of moisture absorption using the following formula.[13,14]

Percentage moisture content = $\frac{Initial\ weight - Final\ weight}{Final\ weight} \times 100$

5.1.5 Folding Endurance

Determining folding endurance entails figuring out how well the patches fold. Folding endurance is measured by folding the patch repeatedly in the same spot unit it breaks ten times. The folding endurance value is the number of times the patch could be folded in the same spot without breaking.[15]

5.1.6 Tensile Strength Determination and Percentage Elongation Break Test

The transdermal patch's tensile strength is ascertained using the pulley system. Two tiny catches were used to pull the patch in the other way, progressively increasing the strain until the patch broke. The unit of measurement for the tensile strength was kg/cm2.The length immediately preceding the break point was noted in order to calculate the percentage elongation break, which was then calculated using the formula below.[16]

Elongation percentage = $\frac{(L1-L2)}{L2} \times 100$

5.1.7 Drug content determination

A precisely weighed piece of film is taken and dissolved in 100 milliliters of the solution that contains the day. This solution is continually swirled in a magnetic stirrer for twenty-four hours. Prior to filtering, the whole solution is sonicated, and the drug content is determined spectrophotometrically using an appropriate dilution.[17]

6) RESULT AND DISCUSSION

6.1 Physical Characterization

Table 3: - Physical Description of Tavaborole.

Characterization	Description	
	As per IP	As per drug sample
Color	White to off white	White to off white
Appearance	White crystalline powder	White crystalline powder
Surface texture	Smooth	Smooth
Odor	Odourless	Odourless

6.1 Analytical characterization and identification of a drug using uv spectros

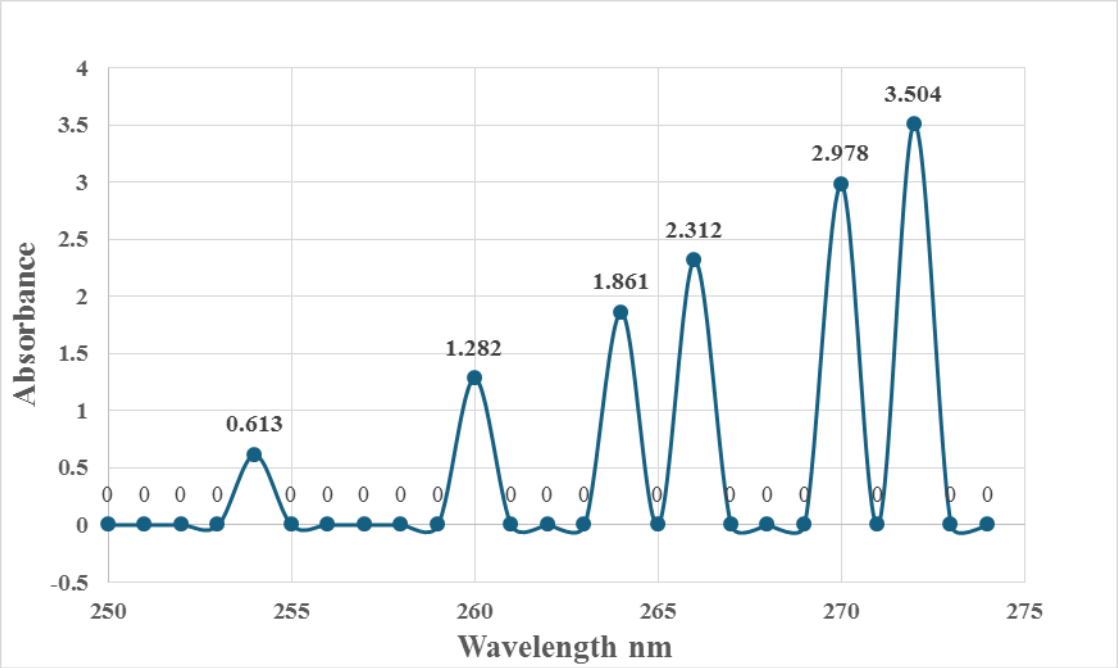

Fig 6.1: - UV spectroscopy curve of Tavaborole.

Table 4: Concentration and Absorption of Tavaborole.

S.No.	Concentration (µg/mL)	Absorption
1.	1	0.613
2.	2	1.282
3.	3	1.861
4.	4	2.312
5.	5	2.978
6.	6	3.504

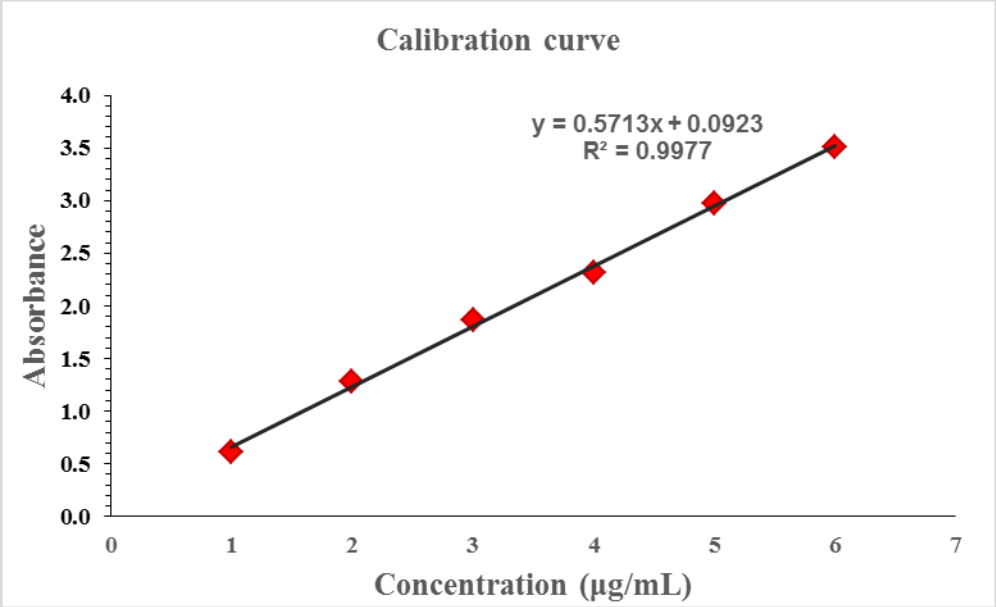

Fig 6.2: - Calibration curve of Tavaborole.

6.3 Thickness

The patches were observed to range in thickness from 0.130±0.005 to 0.185±0.008 mm. This demonstrated that the patches are obviously consistent in thickness. In Table 5, the thickness parameter findings for each formulation are displayed.

6.4 Uniformity of weight

All prepared patches were found to weigh between 85.30±3.10 and 92.10±2.75. This indicates that their weights are comparable. The weight uniformity findings for each formulation are displayed in Table 5.

6.5 Moisture Content

The moisture content for each formulation has been shown to be between 1.90±0.12 and 3.10±0.18. The weight uniformity findings for each formulation are shown in Table 5.

6.6 Folding Endurance

The patches' folding durability ranged from 118 to 140. The patch formulation F2 had the lowest folding endurance (118), whereas F3 had the greatest (140).

Table 5: -Tavaborole transdermal patches' physiochemical characteristics (thickness, moisture content, folding durability, and weight homogeneity).

Formulation	Thickness(mm) (n=3)	Weight uniformity(mg) (n=3)	Moisture content (%)	Folding Endurance (n=3)
F1	0.130±0.005	85.30±3.10	1.90±0.12	120±3.8
F2	0.145±0.007	78.60±2.95	2.20±0.14	118±3.5
F3	0.160±0.006	92.10±2.75	2.75±0.15	140±4.2
F4	0.185±0.008	88.50±3.20	3.10±0.18	130±4.0

Data represented as the standard deviation (SD) and mean value (n=3)

6.7 Tensile Strength Determination and Percentage Elongation Break Test

The tensile strength for each formulation was determined to be between 1.83±0.12 and 2.50±0.16 kg/cm2. The percentage elongation for each formulation was determined to be between 12.5±1.2 and 18.2±1.7.

Table 6: -Tensile Strength and Percentage Elongation data of Tavaborole transdermal patches.

Formulation	**Tensile Strength** (kg/cm2)	Percentage(%) Elongation
F1	1.83±0.12	12.5±1.2
F2	2.05±0.15	14.8±1.5
F3	2.50±0.18	18.2±1.7
F4	2.20±0.16	16.5±1.6

6.8 Drug content determination

Drug content analysis was performed on all Tavaborole formulations using PBS (pH7.4) as the medium, and the results are displayed in Table 7.

Table 7: Drug content data of Tavaborole transdermal patches.

Formulation	Percent drug content (%)
F1	82.5
F2	79.3
F3	90.4
F4	85.2

Drug content was determined. F3 has a drug level of 90.4%, while F1 has a lower drug content of 82.5%.

7) CONCLUSION

The present study aimed to develop and evaluate tavaborole-loaded transdermal patches using the solvent casting method, incorporating HPMC and PVP K30 as film-forming polymers. PEG 400 was included as both a plasticizer and a penetration enhancer to facilitate

drug diffusion across the nail plate. The patches were successfully formulated and systematically assessed for thickness, weight uniformity, moisture content, folding endurance, tensile strength, percentage elongation, and drug content to determine their suitability for transdermal drug delivery.

The physicochemical evaluation confirmed that all formulations exhibited consistent thickness (0.130±0.005 mm to 0.185±0.008 mm), ensuring uniform patch formation. Weight uniformity analysis showed minimal variation among formulations, with weights ranging from 85.30±3.10 mg to 92.10±2.75 mg, indicating reliable reproducibility. Moisture content values ranged from 1.90±0.12% to 3.10±0.18%, ensuring patch stability and resistance to brittleness. Folding endurance values (118–140 folds) confirmed that the patches possessed good flexibility and durability, allowing them to withstand repeated handling without breaking.

The mechanical properties were assessed through tensile strength and percentage elongation tests. The tensile strength ranged from 1.83±0.12 kg/cm² to 2.50±0.18 kg/cm², confirming adequate mechanical resistance to prevent tearing during application. The percentage elongation varied from 12.5±1.2% to 18.2±1.7%, demonstrating the patches' flexibility and ability to adhere effectively to the nail surface.

Drug content analysis revealed effective drug incorporation, with values ranging from 79.3% to 90.4%, indicating satisfactory drug loading. Among all formulations, F3 exhibited the highest drug content (90.4%), suggesting superior drug entrapment and uniform distribution within the polymeric matrix, which enhances potential therapeutic efficacy.

Overall, the findings demonstrate that tavaborole-loaded transdermal patches offer a promising alternative for the treatment of onychomycosis. The transdermal drug delivery system (TDDS) provides advantages such as enhanced bioavailability, sustained drug release, reduced gastrointestinal side effects, and improved patient compliance. The adhesive nature of the patch ensures prolonged drug contact with the nail plate, promoting better penetration and therapeutic effectiveness. Based on superior drug content, tensile strength, and flexibility, F3 emerged as the most promising formulation for further development and potential clinical application.

8) ACKNOWLEDGEMENT

The author sincerely appreciates Rungta Institute of Pharmaceutical Sciences and Research, kohka-kurud, Bhilai (Chhattisgarh) for providing the necessary facilities and resources for this research. Special thanks to Mr. Bishesar Sahu for his valuable guidance and support.

9) REFERENCE

1. ELHASSAN, GAMAL OSMAN. "PREPARATION AND CHARACTERIZATION OF ITRACONAZOLE TRANSDERMAL PATCHES CONTAINING SINGLE-PHASE EMULGEL."
2. Asz-Sigall, Daniel, Antonella Tosti, and Roberto Arenas. "Tinea unguium: diagnosis and treatment in practice." Mycopathologia, 2017; 182: 95-100.
3. Tuncay Tanrıverdi, Sakine, et al. "Terbinafine hydrochloride loaded liposome film formulation for treatment of onychomycosis: in vitro and in vivo evaluation." Journal of liposome research, 2016; 26.2: 163-173.
4. Bird, David, and Nuggehalli M. Ravindra. "Transdermal drug delivery and patches—An overview." Medical Devices & Sensors, 2020; 3.6: e10069.
5. Etebari, F., Khorram, M., Setoodeh, P., Zomorodian, K., Enjavi, Y., & Zareshahrabadi, Z. (2023). Formulation development and characterization of an antifungal nail patch based on Pistacia atlantica gum for transungual treatment of onychomycosis. Journal of Drug Delivery Science and Technology, 88: 104967.
6. Kushwaha, A., Murthy, R. N., Murthy, S. N., Elkeeb, R., Hui, X., & Maibach, H. I. (2015). Emerging therapies for the treatment of ungual onychomycosis. Drug development and industrial pharmacy, 41(10): 1575-1581.
7. Joshi, S., Banyal, M., & Faruk, A. (2020). Formulation and evaluation of clotrimazole loaded transdermal patch. World Journal of Pharmaceutical Research, 9(10): 790-803.
8. Jinna, Sphoorthi, and Justin Finch. "Spotlight on tavaborole for the treatment of onychomycosis." Drug design, development and therapy, 2015; 6185-6190.
9. Elewski, Boni E., and Antonella Tosti. "Tavaborole for the treatment of onychomycosis." Expert opinion on pharmacotherapy, 2014; 15.10: 1439-1448.
10. Siddiqui, M. R., AlOthman, Z. A., & Rahman, N. (2017). Analytical techniques in pharmaceutical analysis: A review. Arabian Journal of chemistry, 10: S1409-S1421.
11. Parivesh, Sakalle, Dwivedi Sumeet, and Dwivedi Abhishek. "Design, evaluation, parameters and marketed products of transdermal patches: A review." J Pharm Res, 2010; 3.2: 235-240.

12. Alam, M. I., Alam, N., Singh, V., Alam, M. S., Ali, M. S., Anwer, T., & Safhi, M. M. (2013). Type, preparation and evaluation of transdermal patch: a review. World journal of pharmacy and pharmaceutical sciences, 2(4): 2199-2233.
13. Kumar, Sahoo Sunit, Baurahari Behury, and Patil Sachinkumar. "Formulation and evaluation of transdermal patch of Stavudine." Dhaka University journal of Pharmaceutical sciences, 2013; 12.1: 63-69.
14. Patel, D., and K. Kavitha. "Formulation and evaluation aspects of transdermal drug delivery system." International journal of pharmaceutical sciences review and research, 2011; 6: 1-12.
15. Bhatia, Chakshu, Monika Sachdeva, and Meenakshi Bajpai. "Formulation and evaluation of transdermal patch of pregabalin." International Journal of Pharmaceutical Sciences and Research, 2012; 3.2: 569.
16. Pawar, Nandini V., and Aney J. Samuel. "FORMULATION AND EVALUATION OF ECONAZOLE LOADED TRANSDERMAL PATCH FOR ITS ANTIFUNGAL ACTIVITY AGAINST TINEA PEDIS." METHODOLOGY, 3: 4.
17. Patel, R. P., Patel, G., Patel, H., & Baria, A. (2009). Formulation and evaluation of transdermal patch of aceclofenac. Research Journal of Pharmaceutical Dosage Forms and Technology, 1(2): 108-115.
18. Pudipeddi, Madhu, et al. "Measurement of surface pH of pharmaceutical solids: a critical evaluation of indicator dye-sorption method and its comparison with slurry pH method." Journal of pharmaceutical sciences, 2008; 97.5: 1831-1842.
19. Mantri, R. V., and R. Sanghvi. "Solubility of pharmaceutical solids." Developing Solid Oral Dosage Forms. Academic Press, 2017; 3-22.
20. Young, J. C. "True melting point determination." Chem Educator, 2013; 18: 203-208.