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Research

Design fabrication and characterization of ethyl cellulose based transdermal patches encompass atenolol for improved *Invitro* skin permeation

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Abstract

As far as the transdermal drug delivery is concern, various penetration enhancers are used for the drug diffusion through skin. In matrix dispersion type systems, the drug is dispersed in the solvent along with the polymers and solvent allowed to evaporate forming a homogeneous drug-polymer matrix.Matrix type systems were developed in the present research. an attempt has been made to develop a matrix-type transdermal therapeutic system comprising of Atenolol with different concentration of various polymers alone using solvent evaporation technique. The physicochemical compatibility of the drug and the polymers was studied by infrared spectroscopy. The results obtained showed no physical-chemical incompatibility between the drug and the polymers. F1formulation has been selected as the best formulation among all the other formulations. The *in vitro* drug diffusion studies from the formulation were found to be sustained release. All the evaluation parameters obtained from the best formulation were found to be satisfactory. The data obtained from the *in vitro* release studies were fitted to various kinetic models like zero order, first order, Higuchi model and peppas model. From the kinetic data it was found that drug release follows peppas modelrelease by diffusion technique from the polymer.

Keywords: Transdermal drug delivery, ethyl cellulose, Atenolol, solvent evaporation Technique

INTRODUCTION

The idea of delivering drugs through skin is old, as the use is reported back in 16th century B.C. Today the transdermal drug delivery is well accepted for delivering drug to systemic circulation.Until recently, the use of transdermal patches for pharmaceuticals has been limited because only a few drugs have proven effective delivered through the skin typically cardiac drugs such as nitroglycerin and hormones such as

estrogen.Transdermal therapeutic systems are defined as self-contained discrete dosage forms which, when applied to the intact skin, deliver the drug(s), through the skin, at controlled rate to the systemic circulation.

The first Transdermal drug delivery (TDD) system, Transderm-Scop developed in 1980, contained the drug Scopolamine for treatment of motion sickness. The Transdermal device is a membrane-moderated system[1-9]. The membrane in this system is a microporous polypropylene film. The drug reservoir is a solution of the drug in a mixture of mineral oil and polyisobutylene. This study release is maintained over a one-day period.Non-medicated patch markets include thermal and cold patches, nutrient patches, skin care patches (a category that consists of two major sub-categories therapeutic and cosmetic), aroma patches, and weight loss patches, and patches that measure sunlight exposure.

To achieve and to maintain a plasma drug concentration above the minimum therapeutic drug level, the barrier properties of the skin must be overcome before the effective transdermal controlled delivery of drugs can be successfully accomplished, the following approaches have been shown to be potentially promising for accomplishing the goals of reducing skin barrier properties and enhancing the transdermal permeation of drugs[10-16].Generally, methods to enhance transdermal drug permeation can be grouped into two categories: Chemical methods and Physical methods.

MATERIALS AND METHODS

The materials used in this current research work are procured from reliable sources of Atenolol, SURA LABS, Dilsukhnagar, Ethyl HPMC, Eudragit, PEG-400 are procured from Merck Specialities Pvt Ltd.All other reagents and chemicals used in this research work has been purchased from the reliable sources.

Construction of calibration curve

A 100mg of Atenolol was accurately weighed and was first dissolved in 35ml methanol solution. The solution was then diluted using phosphate buffer (pH-7.4) to 100 ml. (stock solution-I).It was further diluted with phosphate buffer pH – 7.4 to get solutions in concentration range of 5,10,15,20 and 25 µg /ml[17-24]. The absorbances of these solutions were determined spectrophotometrically at 270 nm.

Preparation of blank patches

Polymers of single or in combination were accurately weighed and dissolved in respective solvent and then casted in a Petri-dish with mercury as the plain surface[25-32]. The films were allowed to dry overnight at room temperature.

Formulation of drug incorporated transdermal patches

The matrix-type transdermal patches containing Atenolol were prepared using different concentrations of Ethyl Cellulose,HPMC and Eudragit RSPO polymers. The polymers in different concentrations were dissolved in the respective solvents as mentioned in the table 1. Then the drug was added slowly in the polymeric solution and stirred on the magnetic stirrer to obtain a uniform solution. Dibutyl phthalate was used as plasticizers[33-41]. Then the solution was poured on the Petri dish having surface area of 78 cm2 and dried at the room temperature.

Table 1: Formulation of Atenolol patches

Ingredients	Formulation Chart								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Atenolol	25	25	25	25	25	25	25	25	25
Ethyl Cellulose	25	50	100	-	-	-	-	-	-
HPMC	-	-	-	25	50	100	-	-	-
Eudragit RSPO	-	-	-	-	-	-	25	50	100
PEG-400 (ml)	10	10	10	10	10	10	10	10	10
Chloroform	15	15	15	15	15	15	15	15	15
Dimethylsulphoxide (ml)	2	2	2	2	2	2	2	2	2
Dibutyl phthalate* (ml)	7	7	7	7	7	7	7	7	7

Evaluation parameters of patches

Thickness

The thickness of patches was measured by digital Verniers calipers with least count 0.001mm. The thickness uniformity was measured at five different sites and average of five readings was taken with standard deviation.

Folding endurance

The folding endurance was measured manually for the prepared patches. A strip of patch (4x3 cm) was cut evenly and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gave the exact value of folding endurance.

Weight variation

The three disks of 2*1 cm^2 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 Determination

The prepared drug contained patches specified surface area (2 cm^2) were cut and dissolved in (5% of methanol contained) 100ml of pH 7.4 phosphate buffer, and vigorously shaked for 12hrs, and then sonicated for 15 minutes, centrifuged at 5000 rpm for 30 min.

Flatness

A transdermal patch should possess a smooth surface and should not constrict with time. This can be demonstrated with flatness study. For flatness determination, one strip is cut from the centre and two from each side of patches[42-45].

***Invitro* drug diffussion study**

The *in vitro* study of drug permeation through the semi permeable membrane was performed using a Franz type glass diffusion cell. The modified cell having higher capacity (25 ml) is used to maintain sink condition. This membrane was mounted between the donor and receptor compartment of a diffusion cell[46]. The transdermal patch was placed on the membrane and covered with aluminum foil. The receptor compartment of the diffusion cell was filled with isotonic phosphate buffer of pH 7.4. The hydrodynamics in the receptor compartment were maintained by stirring with a magnetic bead at constant rpm and the temperature was maintained at 37±0.5ºC. The diffusion was carried out for 12 h and 1 ml sample was withdrawn at an interval of 1 hour. The receptor phase was replenished with an equal volume of phosphate buffer at each sample withdrawal. The samples were analyzed for drug content spectrophotometrically at 270 nm

Drug release kinetics

Diffusion data of above two methods was fitted in Zero order, first order and Higuchi equations has been exploited

Compatibility study

FTIR

The infrared spectrum of the pure Atenolol sample was recorded and the spectral analysis was done[47]. The dry sample of drug was directly placed after mixing and triturating with dry potassium bromide.

RESULTS AND DISCUSSION

Calibration curve of Atenolol

Initially the drug was tested by UV to know their significant absorption maximum which can be used for the diffusion study of the drug as denoted in the figure 1.

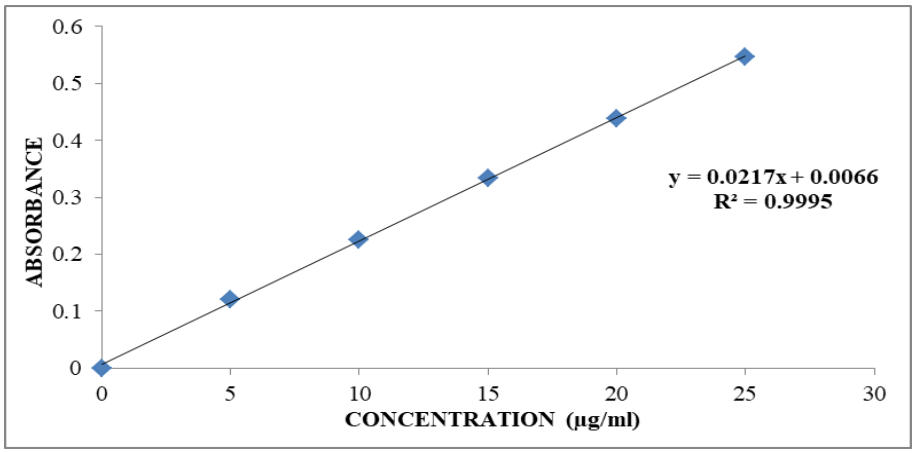

Fig 1: Standard calibration curve of Atenolol

Evaluation of Patches

The formulations F1 to F9 were varying in thickness when compared to other formulations which is due to the variation in the polymer concentration. Which shows the increase in polymer concentration increases the thickness of patch. For all other formulations it was found to be in between 0.041±0.007to 0.051±0.004 mm.All formulations from F1 to F9 shows weight variation in between 70 ±9.58 to 79 ±6.85 mg.Folding endurance from formulations F1 to F9 was found to be in between 81 ± 0.15 to 89 ± 2.15 which can withstand the folding of the skin as represented in the figure 2.All formulations showed % drug content from 95.1 ± 2.61 to 99.74 ± 1.57.

***Invitro* diffusion study**

All the formulation *in vitro* diffusion study was carried out by using Franz type diffusion cell under specific condition such as temp maintained at 32 ± 0.5 ºC. The diffusion was carried out for 12 h and 5 ml sample was withdrawn at an interval of 1 hour as shown in the figure 2,3&4.The formulations F4 to F6 were prepared by different concentrations of HPMC (25, 50 and 100mg) in 2*2 cm^2patch the drug release or drug permeation from the patch was dependence on the concentration of polymer in the matrix. The 50mg (F5) concentration of polymer was showed maximum drug release 95.64 within 11 hours.The 50mg(F8) concentration of polymer was showed maximum drug released at 12 hours 86.78%. Out of all the formulations the F1 has shown a good parameter and passes all the test.

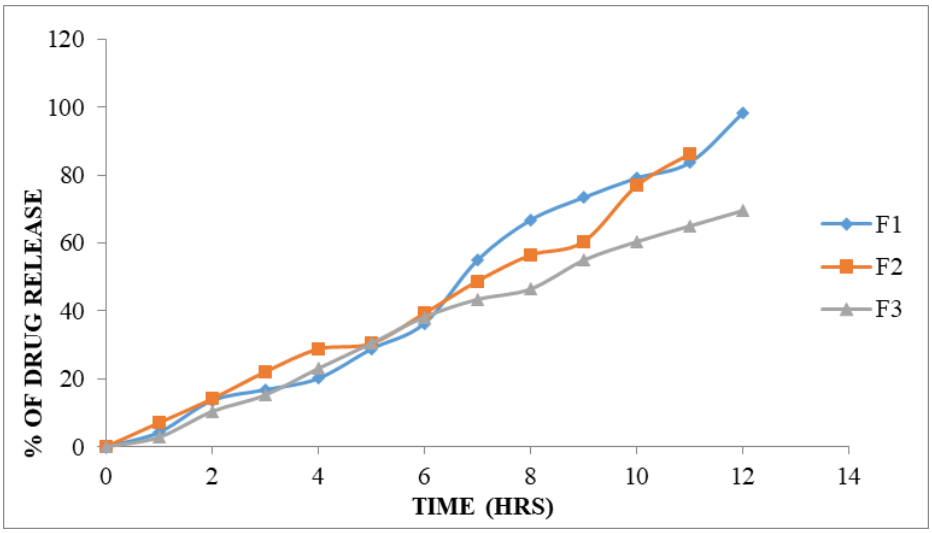

Fig 2: Cumulative % drug permeation of Atenolol patch (F1, F2 and F3)

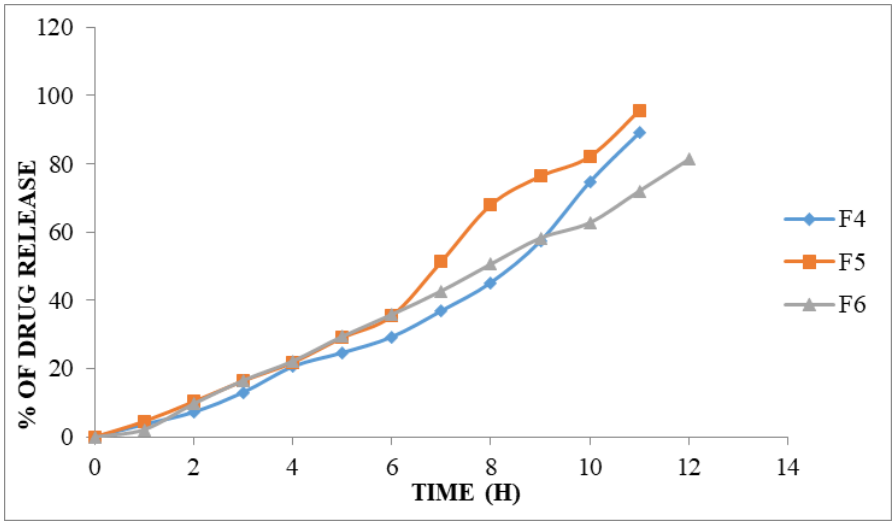

Fig 3: Cumulative % drug permeation of Atenolol patch (F4, F5 and F6)

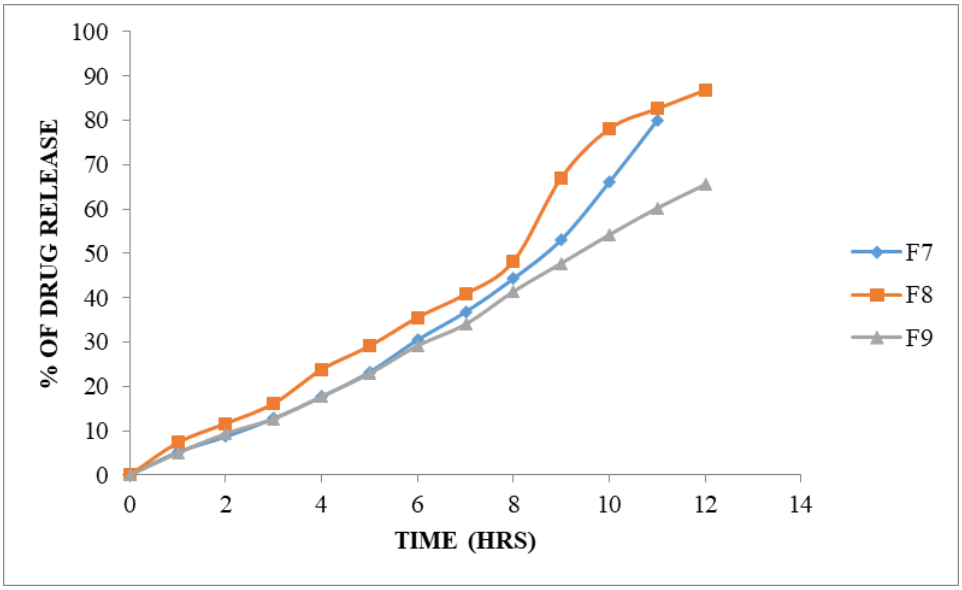

Fig 4: Cumulative % drug permeation of Atenolol patch (F7, F8 and F9)

Pharmacokinetic models for Atenolol

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model. From the kinetic data it was found that drug release follows peppas model release by diffusion technique from the polymer as represented in the figure 5.

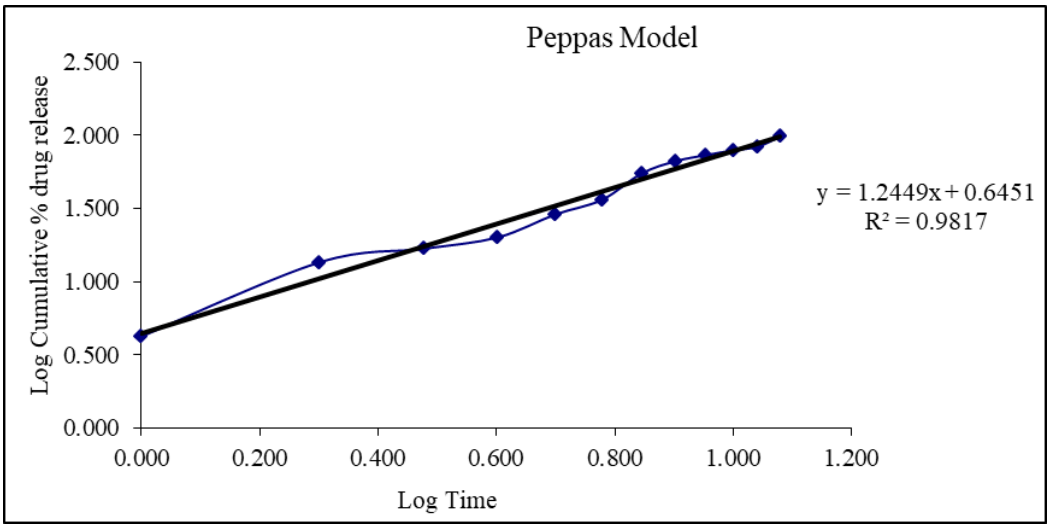

Fig 5: Graph of peppas release kinetics

Compatibility studies
FTIR

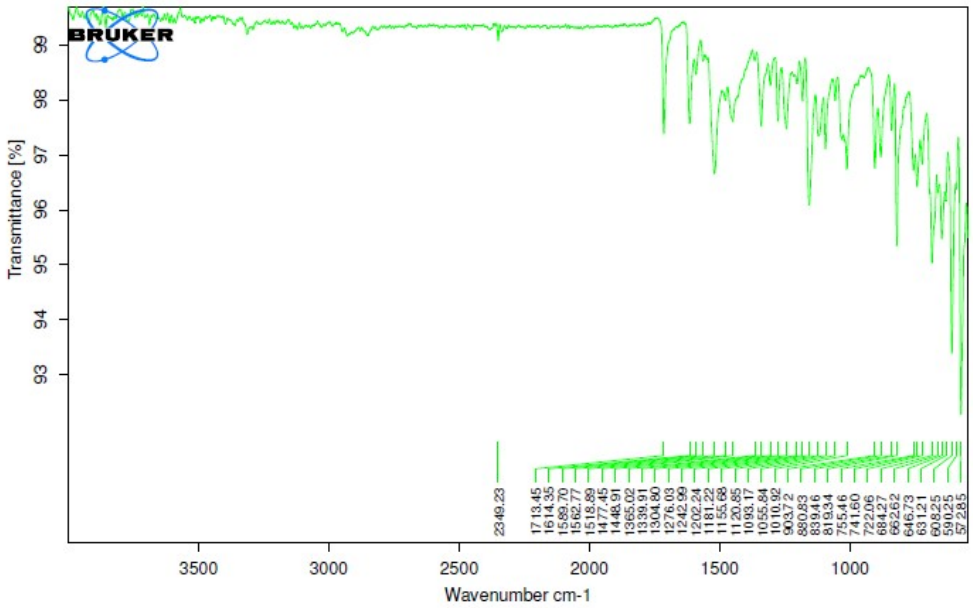

Fig 6: FTIR Spectrum of pure Atenolol drug

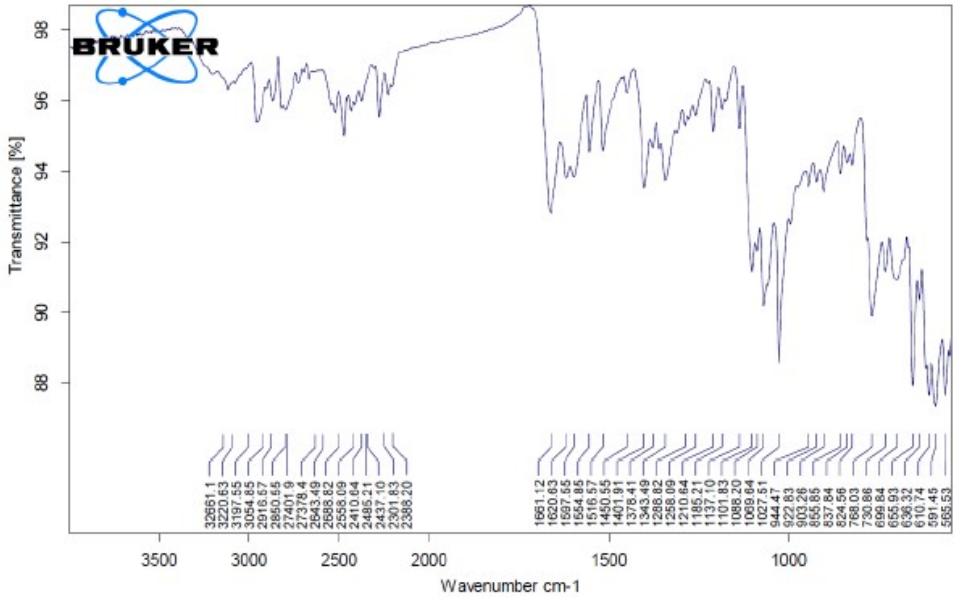

Fig 7: FTIR of Optimized formulation

The compatibility studies of the drug with excipients indicate no characteristic visual changes and no additional peaks were observed during FT-IR studies as shown in the figure 6 &7.

CONCLUSION

Current research investigation an attempt has been made to design and develop the formulation of Atenolol patches using different types of polymers by solvent evaporation technique and mercury substrate method. The drug used isthe best studied for therapy in treating high blood pressure.Atenolol was successfully formulated as controlled release transdermal patches, which prevents the frequency of administration and gives good patient compliance.From the experimental results obtained, F1formulation has been selected as the best formulation among all the other formulations. The *invitro* drug diffusion studies from the formulation were found to be sustained release. All the evaluation parameters obtained from the best formulation were found to be satisfactory.The data obtained from the *invitro* release studies were fitted to various kinetic models like zero

order, first order, Higuchi model and Pappas model. From the kinetic data it was found that drug release follows peppas model release by diffusion technique from the polymer.Based on the observations, it can be concluded that the attempt of formulation and evaluation of theAtenolol patches was found to be successful in the release of the drug for an extended period of 12hrs. Hence it can be concluded that atenolol transdermal patch can be successfully prepared by solvent evaporation method.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Wilson KJW, Waugh A, editors. Ross and Wilson: anatomy and physiology in health and illness. 8th ed. Churchill Livingstone; 1996. p. 360-6.
2. Franz TJ. Transdermal delivery in treatise on controlled drug delivery. 3rd ed. New York: Marcel Dekker Inc; 1991.
3. Benson HAE. Transdermal drug delivery: penetration enhancement techniques. Curr Drug Deliv. 2005;2(1):23-33. doi: 10.2174/1567201052772915, PMID 16305405.
4. Honeywell-Nguyen PL, Bouwstra JokeA. Vesicles as a tool for transdermal and Dermal Delivery. Drug Discov Today Technol. 2005;2(1):67-74. doi: 10.1016/j.ddtec.2005.05.003, PMID 24981757.
5. Gannu R, Vishnu YV, Kishan V, Rao YM. Development of nitrendipine transdermal patches: in vitro and ex-vivo characterization. Curr Drug Deliv. 2007;4(1):69-76. doi: 10.2174/156720107779314767, PMID 17269919.
6. Gupta JRD, Irchiayya RN.Garud. Formulation and evaluation of matrix type transdermal patches of glibenclamide. Int J Pharm Sci Dev Res. 2009;1(1):46-50.
7. Walters KA, Roberts ms. Dermatological and transdermal formulations. p. 204-41.
8. Oh SY, Jeong SY, Park TG, Lee JH. Enhanced transdermal delivery of AZT (zidovudine) using iontophoresis and penetration enhancer. J Control Release. 1998 February 12;51(2-3):161-8. doi: 10.1016/s0168-3659(97)00162-4, PMID 9685913.
9. Pathan IB, Setty C. Chemical penetration enhancers for transdermal drug delivery systems. Trop J Pharm Res. April 2009;8(2):173-9. doi: 10.4314/tjpr.v8i2.44527.
10. Tiwary AK, Sapra B, Jain S. Innovations in transdermal drug delivery: formulations and techniques. Recent Pat Drug Deliv Formul. 2007;1(1):23-36. doi: 10.2174/187221107779814087, PMID 19075872.
11. Malvey S, Venkateshwar Rao J, Kottai Muthu A. Development and *in Vitro*Characterisation ofTransdermal therapeutic system of ketorolac tromethamine. Issue. Vol. 02(January 11); 2021.
12. Trivedi D, Goyal A. Formulation and evaluation of transdermal patches containing dexketoprofentrometamol. Int J Pharm Chem Anal. 2020;7(2):87-97. doi: 10.18231/j.ijpca.2020.014.
13. Shikha Baghel Chauhan, Tanveer navedb, nayyarparvez. Formulation Dev Transdermal Drug Deliv Syst Ethinylestradiol Testosterone Vitro Eval. 2019;11(1).
14. Kriplani P, Abhishek Sharma A, Pun P, Chopra B, Dhingra A, Deswal G. Formulation and evaluation of transdermal patch of diclofenac sodium. GJPPS. February 19, 2018;4(5). doi: 10.19080/GJPPS.2018.04.555647.
15. Jagtap S, Badhe P, Dr.NayanGujarathi , Amit Jadhav , Sayali Daware, Deepali Shewale. Formulation and evaluation of transdermal patch of diclofenac sodium as ladies bindi for treatment of rheumatoid arthritis. Int J Pharm Sci Rev Res. March-April 2018;49(1):65-70:Article No. 11.
16. Cherukuri S, Batchu UR, Mandava K, Cherukuri V, Ganapuram KR. Formulation and evaluation of transdermal drug delivery of topiramate. Int J Pharm Investig. 2017;7(1) | Issue 1| January-March:10-7. doi: 10.4103/jphi.JPHI_35_16, PMID 28405574.
17. Mounika Pokala KP, Tammira RK, Mamidi P, Racha U, Samudrala L. Formulation and evaluation of transdermal patches of salbutamol. Vol. 5(6); 2016.
18. Kanabar Vishvesh B, Patel Vipul P, Doshi SM. Formulation and evaluation of transdermal patch of cefdinir with various polymers. The Pharm Innov J. 2015;4(6):74-7.
19. Soujanya C, Satya BL, Reddy ML, Manogna K, Prakash PR, Ramesh A. Formulation and in vitro & in vivo evaluation of transdermal patches of lornoxicam using natural permeation enhancers.
20. Madhulatha A, Naga Ravikiran T. Formulation and evaluation of Ibuporfen transdermal patches. Int J Res Pharm Biomed Sci. 2013;4(1):351-62.

21. john L, Kumar A, Samuel S. Formulation and evaluation of amlodipine transdermal patches using ethyl cellulose. Int Res J Pharm. 2013;4(10):84-8. doi: 10.7897/2230-8407.041019.
22. Koteswararao P, Duraivel S, Sampath Kumar KP, Bhowmik D. Formulation and evaluation of transdermal patches of Antihypertensive Drug metaprolol succinate. Indian J Res Pharm Biotechnol. 2013;1(5):629-34.
23. Radha GV, Swetha N, Bharathi P, Gowri PSSRKA, Neeraja K. Formulation and evaluation of transdermal films of enalapril maleate. J Pharm Sci Innov. 2013;2(1):57-60.
24. Rajabalaya R, Tor L-Q, David S. Formulation and in vitro evaluation of ondansetron hydrochloride matrix transdermal systems using ethyl cellulose/polyvinyl pyrrolidone polymer blends. World Acad Sci Eng Technol. 2012;6:12-28.
25. Gudapareddyrajareddy. vallururajashekar, jayanthi, saleemshaik, k.a Sridhar. Formulation and in-vitro evaluation of transdermal films ofan anti-hypertensive drug. Int Res J Pharm. 2013;4(6):66-71.
26. Kumar SahuR, Ashish J, Satish N. Development and evaluation of transdermal patches of colchicine. Scholars Research Library; 2012, 4 (1). p. 330-43.
27. Rathore P, Bhatia R, Nayak S. Preparation and characterization of ciprofloxacin loaded transdermal patches. Int J Pharm Sci Res. 2012;3(4):1184-7.
28. Ijrap. Gottipati dinesh babu, kantipotuchaitanyasagar, miteshr.bhoot. Des Eval Valsartan Transdermal Patches. 2012;3(3):461-4.
29. Pachisia N, Agrawal SS. Formulation, development and evaluation of transdermal drug delivery system of glimepiride. Int J Pharm Pharm Sci Research. 2012;2(1):1-8.
30. Darwhekar G, Jain DK, Patidar VK. Formulation and evaluation of transdermal drug delivery system of clopidogrel bisulfate. Asian J Pharm Life Sci. 2011;1(3):269-78.
31. K. Kavitha and more mangeshrajendra. Design and evaluation of transdermal films of lornoxicam. Int J Pharm Biol Sci. 2011;2(2):54-62.
32. Sharma S, Aggarwal G, Dhawan Sanju. Design and evaluation of olanzapine transdermal patches containing vegetable oils as permeation enhancers. Scholars Research Library; 2010: 2(6). p. 84-98.
33. Krishnan SR.P.N. Dilip.C. Shabir Ali T.K.formulation and evaluation of transdermal patches of curcumin. Scholars Research Library.2010; 2(5): 117-26.
34. Dwarakanadhareddy P, Swarnalatha a, Dinakar p. Naresh babu, c. Raghunath guptha, c. H. Venkureddy, b. Sravani, s. Shankar rao and b. Sudheer chowdary.Formulation and evaluation of ramipril transdermal patch.Int. J. Chem. Sci. 2010; 8(1): 681-686.
35. Nishida N, Taniyama K, Sawabe T, Manome Y. Development and evaluation of a monolithic drug-in-adhesive patch for valsartan. Int J Pharm. 2010;402(1-2):103-9. doi: 10.1016/j.ijpharm.2010.09.031, PMID 20933069.
36. Gupta JRD, Irchiayya RN.Garud. Formulation and evaluation of matrix type transdermal patches of glibenclamide. Int J Pharm Sci Dev Res. 2009;1(1):46-50.
37. Patel Hj, Patel js, Patel kd. transdermal patch for ketotifen fumarate (ktf) as asthmatic drug. Int J PharmTech Res;1(4):1297-304.
38. Patel RP, Patel G, Baria A. Formulation and evaluation of transdermal patch of aceclofenac. Int J Drug Deliv. 2009;1(1):41-51. doi: 10.5138/ijdd.2009.0975.0215.01005.
39. Raynaud J-P, Aumonier C, Gualano V, Betea D, Beckers A. Pharmacokinetic study of a new testosterone-in-adhesive matrix patch applied every 2 days to hypogonadal men. J Steroid Biochem Mol Biol. 2008;109(1-2):177-84. doi: 10.1016/j.jsbmb.2008.02.004, PMID 18325758.
40. Melero A, Garrigues TM, Almudever P, Villodre AM, Lehr CM, Schäfer U. Nortriptyline hydrochloride skin absorption: development of a transdermal patch. Eur J Pharm Biopharm. 2008;69(2):588-96. doi: 10.1016/j.ejpb.2007.11.012, PMID 18191555.
41. Hai NT, Kim J, Park E-S, Chi SC. Formulation and biopharmaceutical evaluation of transdermal patch containing benztropine. Int J Pharm. 2008;357(1-2):55-60. doi: 10.1016/j.ijpharm.2008.01.024, PMID 18417307.
42. Li T, Ren C, Wang M, Zhao L, Wang X, Fang L. Optimized preparation and evaluation of indomethacin transdermal patch. Asian J Pharm Sci. 2007;2(6):249-59.
43. Liu Y, Fang L, Zheng H, Zhao L, Ge X, He Z. Development and in vitro evaluation of a topical use patch containing diclofenac diethanolamine salt, Topical use patch containing diclofenac diethanolamine salt. Asian J Pharm Sci. 2007;2(3):106-13.
44. Rathore RPS, Chauhan CS, Naruka PS, Tanwar YS, Chauhan LS. transdermal formulation of terbutaline sulphate pharmacy online.
45. Davaran S, Rashidi MR, Khandaghi R, Hashemi M. Development of a novel prolonged-release nicotine transdermal patch. Pharmacol Res. 2005;51(3):233-7. doi: 10.1016/j.phrs.2004.08.006, PMID 15661573.
46. Sugibayashi K, YasunooriMorimoto. Polymers for transdermal drug delivery systems. J Control Release. 1994;29:17-23.
47. Man M, Chang C, Lee PH, Broman CT, Cleary GW. New improved paddle method for determining the in vitro drug release profiles of transdermal delivery systems. J Control Release. 1993;21:59-68.