e-ISSN: 0976-822X, p-ISSN:2861-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(2); 60-65

Original Research Article

Optimizing Transdermal Patches of HMG-CoA Reductase Inhibitors: Evaluating Parameters with Bioadhesive Polymers as Excipients

Prasad Tandale, Vijay Naresh

Department of Pharmacy, Sunrise University, Alwar, Rajasthan, India

Received: 20-12-2022 / Revised: 25-01-2023 / Accepted: 20-02-2023
Corresponding author: Mr. Prasad Tandale
Conflict of interest: Nil

Abstract

Drug variations, gastrointestinal discomfort, hydrolysis and degradation in acidic environments, and first-pass hepatic metabolism are only some of the problems that may be avoided with transdermal drug administration as opposed to oral drug delivery. In the present research work different type of transdermal drug delivery system (TDDS) are mentioned here. There are many evaluation parameters discussed below which are utilized in the evaluation of TDDS like thickness of film, average weight and weight variation, tensile strength, hardness, percentage moisture content, moisture uptake percentage, determination of drug contents, invitro release test of medicaments, skin irritation test and stability studies. After successfully performing all the evaluation parameters the results obtained were satisfactory and were in limit.

Keywords: Gastrointestinal Discomfort, Invitro Release, Tensile Strength.

Introduction

Most medications are administered orally. First-pass metabolism, medication breakdown in the GI tract because of enzymes, pH, etc., are all drawbacks. An innovative method of medication distribution was created to circumvent these issues. Medicated adhesive patches are manufactured for this transdermal administration technique, and when applied to the skin, they release a therapeutically effective quantity of medicine across the skin. Transdermal or adhesive patches that deliver medication vary in size and include a variety of active ingredients. When applied to intact skin, the active components are able to enter the bloodstream. A patch that, when applied to the skin, releases a concentrated dosage of medication into the bloodstream over a lengthy period of time. Hair follicles, sebaceous glands, and the sweat duct all provide routes for the drug to enter the body. As well as treating skin conditions, angina, pain, quitting smoking, and neurological diseases like Parkinson's also benefit from transdermal medication delivery systems. [1,2]

Types of Transdermal Patches [3]

- Single layer drug-in-adhesive patches
- Multilayer drug-in-adhesive patches
- Vapor transdermal patches

- Membrane-moderated transdermal reservoir patches.
- Microreservoir transdermal patches
- Matrix system: drug-in-adhesive
- Matrix systems: Matrix-dispersion
- Miscellaneous transdermal patches

Evaluation of Transdermal Patches

Thickness of Film

The thickness has been measured using an Electronic Digital Micrometer (AEROSPACE- CHINA) in six distinct locations with the mean Value being determined. [4]

Estimation of Average Weight and Weight Variation [5]

Six patches were weighed using an electronic scale. The following methods were used to determine the mean and standard variation of a patch's weight.

Individual patches average mass = total mass of 5 patches/5

Standard deviations SD = 〖xX/nl〗^2

Considering

x represents the Molecular mass. for a particular patch

X represents the average weight.

n represents the number of patches

Tensile Strength Determination [6]

Tensile strength was evaluated with a device developed in our facility. The fastened end of the strip was then used to connect it to the railing's rotating rod. To raise the pull power, the pan's weights were progressively added until the film was split. The length was calculated in real time by tracking the path taken by the pointer just before the film snapped. The break force was recorded as the amount of weight needed to rupture the film. Allen's method was used to determine the tensile strength.

$$\text{Tensile Strength} = \frac{\text{Break Force} \times (1 + \Delta L)}{a \times b \quad L}$$

Hardness Determination [7]

Our lab's equipment for testing the strips' hardness consists of a 16centimeter x 16 cm square of wood that stands 11 cm tall. One end of a 2-millimeter-thick iron shaft has a tiny pan horizontally affixed to it, while the other end has been sharpened into a tip. The tip of the hardwood stand that holds the pan pole has a hole drilled into it with a width of 0.2 centimeters. A 3-volt battery was connected to an electric circuit that would only allow the lamp to light up upon impact between the metal plate along with the pointed the rod's terminus. The film has been inserted into the void created between the metallic sheet and the leading edge of the rod. Until the bulb was glowing, weights have been put on to the pan every ten seconds to maintain a constant tension. The finished mass was used as a quality indicator of rigidity.

Percentage Moisture Content Estimation [8]

In this study, the moisture content in the produced patches had been assessed by maintaining them in desiccator operated under vacuum till consistent mass values has been established, as proportions of moisture can affect a tensile strength as well as drug release behavior of transdermal therapeutic properties. systems. Using this method, we were able to determine the amount of moisture present in the area.

% moisture contents: (Preliminary weight-Final weight)/(Preliminary weight)

Determination of Moisture Uptake Percentage [9,10]

After 24 hours in a room temperature desiccator, the films were removed and exposed to seventy-five percent (a saturated solution containing sodium chloride) in the desiccator as long as the constant wt. for film had been calculated as the differential among the final & preliminary weight with a reference to the preliminary weight.

Percentage moisture uptake: (Closing weight-Preliminary weight)/ (Closing weight)

Determination of Drug Contents [11]

Pieces of a produced patches with an range of SA of 15.21cm2 were sliced off and placed into a 100 milliliter graduated glass stoppered beaker containing a combination comprising methanol and chloroform at a proportions (1:1). and a temperature of 45-50 C. It was sealed in a blender and agitated for a full day. After filtering the solution, the concentration of the substance in the resulting filtrate the spectrophotometer set at 241 nm on a SHIMADZU UV-1700 was employed to analyze the filtrate. A dummy patch was also used to create a blank answer. The process was repeated twice to ensure accuracy in assessing the drug's concentration. The following method was used to double-check the drug's potency.

Invitro Release Test of Medicaments [12,13]

Throughout the purposes of in vitro permeability testing, the Franz Diffusion device has been employed. It has two parts: the source area and the receiver area. Between the diffusion cell's donor and receiver chambers, a cellulose membrane was installed84. The membrane was patched with the prepared patches. Phosphate solution (pH 7.4) was used to saturate receptor segment of the diffusion cell. The whole thing fastened to magnetic stirrer utilizing magnetic bead agitated the solution that was in the receptor chamber at a steady 50 revolutions per minute while keeping the temperature at 37 degrees Celsius, plus or minus 10 degrees. The samples were taken at various times and then tested for the presence of drugs. Once each sample had been collected, a corresponding quantity of phosphate solution had been incorporated into the receptor phase. This was done at regular intervals. Cumulative drug permeation through patch area as a function of time was displayed.

Fundamental Investigations of Irritation of The Skin [14]

Albino rodents had patches affixed to their smooth-shaven backside and taped in place. A control patch and an experimental patch were each attached to one half of the back. For 24 hours, the animals were monitored for any signs of redness or oedema (swelling)

Stability Studies [15]

Innovative dosage types are required to be invented and evaluated with the long-term stabilization associated with the medicaments as a top priority. Chemical analysis may sometimes reveal subtle but significant modifications in chemical composition, but preparation variability(instability) can be identified through a modification in the drug's exterior look (color, odor, taste, or texture). Estimating the proposed product's shelf life and, if necessary, re-formulating the dosage form are both based on scientific data relating the durability of the formulation.

Therefore, the chosen films were stored in room temperature & at 40oC for 45 days to evaluate their durability. The patches' physicochemical characteristics and in vitro

diffusion experiments have been assessed on days 15, 30, and 45.

Result and Discussion

21-patches containing calcium Atorvastatin were molded using varying proportions of HPMC, EC, and ERS100. The generated patches were evaluated for their physico-chemical properties including their in-vitro release of medication behavior.

The calculated average patch weight for a surface area of 15.21cm2 revealed significant differences between patches prepared using various polymer ratios.

In the table given below, we can see that the typical patch weight from T1 to T21 is between 6 and 8 grams. The average patch weight was greatest for T1-T7 and the least for T15-T21 of the 21 total patches. T1-T7 patches are heavier than before because 10%w/w plastics are used instead of the standard 5%w/w.

Aerospace digital electronic micrometer measurements showed that there was no notable variation among patch width (T1-T21). This shows that the changes were consistent and easy to replicate.

Transdermal patches with different codes (T8-T14) had significantly different moisture levels, as shown by the results tabulated in tables below. The greater moisture content as well as moisture uptake observed in patches T8-T21 could be accredited to the greater concentration of the water loving polymer, HPMC. After combination of the two hydrophobic polymers reduced moisture quantity and uptake in areas T1 through T7.

The table 1-3 results show that T8-T15 patches have a greater tensile strength than the other patches.

The SHIMADZU UV-1700 spectrophotometer revealed that there was no distinction in the amount of medication present inside any of the patches.

T8 showed higher drug release as HPMC concentration was increased, while T1 exhibited reduced drug release since both EC along with ERS100 were hydrophilic polymers. The inclusion of the hydrophobic polymer ERS100 in Patch T15 resulted in a lower rate of release compared to Patch T8.

The skin irritation research shows, both the drug-loading as well as empty patche's did not produce anykind significant skin inflammation or oedema in albino rats, demonstrating the drug's and polymer matrix's skin compatibility.

Physicochemical and in vitro drug release tests show no variation in T1, T8, and T15 patches during the stable testing period.

Table 1: Atorvastatin calcium transdermal patch T1-T7 physicochemical characteristics

Formulation Code	Weight Variation (grams)	Thickness (mm)	Tensile Strength (kg/cm^2)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)
T1	0.592±0.028	0.175±0.009	0.946	3.31±0.18	5.43±0.01	0.5969
T2	0.566±0.017	0.184±0.013	0.927	2.77±0.16	4.97±0.004	0.547
T3	0.474±0.019	0.147±0.003	0.945	2.59±0.43	4.05±0.001	0.6449
T4	0.500±0.009	0.152±0.008	0.943	2.48±0.90	3.77±0.009	0.5437
T5	0.497±0.01	0.167±0.006	0.895	2.43±0.66	3.15±0.01	0.6219
T6	0.502±0.008	0.195±0.018	0.839	2.09±0.49	2.64±0.02	0.6002
T7	0.525±0.001	0.056±0.043	0.89	1.24±0.57	1.99±0.025	0.5739

Table 2: Atorvastatin calcium transdermal patch T8-T14 physicochemical characteristics

Formulation Code	Weight Variation (grams)	Thickness (mm)	Tensile Strength (kg/cm^2)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)
T8	0.322±0.006	0.157±0.015	1.755	8.75±0.015	10.12±0.006	0.5634
T9	0.322±0.006	0.120±0.07	1.645	7.55±0.007	9.88±0.009	0.5456
T10	0.327±0.008	0.119±0.001	1.599	7.09±0.017	8.98±0.013	0.5391
T11	0.304±0.005	0.102±0.008	1.555	6.63±0.002	8.17±0.016	0.5128
T12	0.284±0.008	0.084±0.016	1.6	5.88±0.01	7.76±0.035	0.5542
T13	0.293±0.005	0.134±0.005	1.504	5.14±0.03	6.85±0.048	0.6101
T14	0.286±0.008	0.135±0.006	1.551	4.36±0.009	5.67±0.009	0.6239

Table 3: T15–T21 Physicochemical Parameters of Atorvastatin Calcium Transdermal Patch Formulation

Formulation Code	Weight Variation (grams)	Thickness (mm)	Tensile Strength (kg/cm^2)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)
T15	0.283±0.01	0.152±0.009	1.36	6.09±0.24	7.51±0.017	0.6134
T16	0.318±0.001	0.150±0.008	1.247	5.77±0.009	6.93±0.083	0.5654
T17	0.310±0.001	0.112±0.017	1.389	4.98±0.017	6.22±0.037	0.5456
T18	0.304±0.004	0.167±0.006	1.338	4.08±0.038	5.95±0.009	0.6173
T19	0.337±0.009	0.188±0.016	1.287	3.56±0.061	5.28±0.044	0.5765
T20	0.289±0.01	0.150±0.008	1.241	2.83±0.17	4.53±0.006	0.5351
T21	0.361±0.02	0.144±0.003	1.124	2.14±0.19	3.45±0.002	0.6213

Conclusion

All the 21 formulations were evaluated with various parameters like weight variation, thickness, tensile strength, moisture content, moisture uptake, drug content, skin irritation and stability study. It was concluded that there was no significant variation in the thickness of the patches. The patches weight from T1 to T21 was between 6 and 8 grams. The average patch weight was greatest for T1-T7 and the least for T15-T21 of the 21 total patches. T1-T7 patches are heavier than before because 10%w/w plastics are used instead of the standard 5%w/w. The greater moisture content as well as moisture uptake observed in patches T8-T21. T8-T15 patches have a greater tensile strength than the other patches. T8 showed higher drug release as HPMC concentration was increased, while T1 exhibited reduced drug release since both EC along with ERS100 were hydrophilic polymers. The inclusion of the hydrophobic polymer ERS100 in Patch T15 resulted in a lower rate of release compared to Patch T8. Both the drug-loading as well as empty patches' did not produce any kind significant skin inflammation or oedema in albino rats. The in-vitro drug release tests show no variation in T1, T8, and T15 patches during the stable testing period.

References

1. Kesarwani A, Yadav AK, Singh S, Gautam H, Singh N, Shvarma A, Yadav C, A review Theoretical aspects of Transdermal Drug Delivery System. Bulletin of Pharmaceutical Research, 2013; 3(2): 78-89.
2. Kumar KP, Bhowmik D, Chiranjib B, Chandira RM, A review- Transdermal Drug Delivery System - A Novel Drug Delivery System and its market scope

and opportunities. International Journal of Pharma and Bio Sciences, 2010; 1(2):1-21.
3. Hanbali A, Khan Q, Shoaib H, Muhammad S, Mosab A, Transdermal patches: Design and current approaches to painless drug delivery. Acta Pharmaceutica, 2019; 69(2): 197–215.
4. Bharkatiya M, Nema R, Bhatnagar M, Designing and characterization of drug free patches for transdermal application, Int. J. Pharm. Sci. Drug Res. 2012; 2: 35–39.
5. Prosser JM, Jones BE, Nelson L, Complications of oral exposure to fentanyl transdermal delivery system patches, J. Med. Toxicol. 2010; 6: 443–447.
6. Banerjee S, Chattopadhyay P, Ghosh A, Datta P, Veer V, Aspect of adhesives in transdermal drug delivery systems, Int. J. Adhes. Adhes. 2014; 50: 70–84.
7. Mohapatra P K, Nagalakshmi C H, Tomer V, Gupta M K, Varma H C, Singh N, Sahoo S, Formulation and in Vitro Evaluation of Controlled Release Transdermal Drug Delivery System of Simvastatin A Model Hypocholesterolemia Drug, International Journal of Current Pharmaceutical Review and Research, 2018; 9(5): 71-76.
8. N. Maftoona, H. S. Ramaswamy and M. Marcotte, Evaluation of factors affecting barrier, mechanical and optical properties of pectin-based films using response surface methodology, J. Food. Process Eng. 2007; 30: 539–563.
9. Keleb E, Sharma RK, Mosa EB, Aljahwi A-AZ. Transdermal drug delivery system-design and evaluation. Int J Adv Pharm Sci. 2010; 1: 201–11.
10. Dey BK, Kar PK and Nath LK. Formulation design, preparation and in vitro-in vivo evaluation of propranolol hydrochloride transdermal patches using hydrophilic and hydrophobic polymer complex. Research J. Pharm. and Tech. 2009; 2(1): 155-60.
11. Garala KC, Shinde AJ, Shah PH. Formulation and in vitro characterization of monolithic matrix transdermal systems using HPMC/Eudragit S 100 polymer blends. Int J Pharm Pharm Sci 2009; 1:108–20.
12. Suksaeree J, Boonme P, Taweepreda W, Ritthidej GC, Pichayakorn W. Characterization, in vitro release and permeation studies of nicotine transdermal patches prepared from deproteinized natural rubber latex blends. Chem Eng Res Des. 2012; 90: 906–14.
13. Simon A, Amaro MI, Healy AM, Cabral LM, de Sousa VP. Comparative evaluation of rivastigmine permeation from a transdermal system in the Franz cell using synthetic membranes and pig ear skin with in vivo-in vitro correlation. Int J Pharm. 2016; 234–41.
14. Manosroi A, Chankhampan C, Manosroi W, Manosroi J, Transdermal absorption enhancement of papain loaded in elastic niosomes incorporated in gel for scar treatment, Eur. J. Pharm. Sci. 2013; 474–483.
15. Baichwal MR. Polymer films as drug delivery systems, Advances in drug delivery systems. Bombay, MSR Foundation,1985; 136-147.