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Formulation and Evaluation of Transdermal Patches Containing Paracetamol

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Abstract

It is the most important part of Pharmaceutical dosage forms; Transdermal Drug Delivery System (TDDS) established itself as an integral part of Novel Drug Delivery Systems. On the application of Transdermal patches, the delivery of the drug across dermis gives the systemic effect. Paracetamol is widely used as Antipyretics as well as mildly Analgesics. In this study Transdermal patches were prepared by Mercury Substrate Method using ethyl cellulose polymer and Poly Vinyl Pyrrolidone (PVP) was used as a plasticizer. The prepared patches was evaluated for Thickness, Folding endurance, Drug contain uniformity, Drug content, Percent Moisture Absorption and Percent Moisture loss. Average thickness was found to be 0.282mm, Folding endurance was 190, Tensile strength (2.399kg/mm2) and Drug content uniformity was found to be 9.46. In vitro permeation study was performed by using Franz diffusion cell.

Keywords: TDDS, Transdermal film, Paracetamol, Ethyl cellulose, Drug polymer, etc.

Contents

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1. Introduction

Transdermal drug delivery is the non-invasive delivery of medications from the surface of skin-the largest and most accessible organ of human body- through its layers, to the circulatory system. TDDS offers many advantages over conventional injection and oral methods. It reduces the load that the oral route commonly places on the digestive tract and liver. It enhances patient compliance and minimizes harmful side effects of a drug caused from temporary overdose. Another advantage is convenience, especially notable in patches that require only once weekly application. Such a simple dosing regimen can aid in patient adherence to drug therapy. Designing and development of transdermal patches can be described as state of the art. The development of TDDS is multidisciplinary activity that encompasses fundamental feasibility A studies starting from the selection of drug molecule to the demonstration of sufficient drug flux in an ex vivo and in vivo model followed by fabrication of a drug delivery system that meets all the stringent needs that are specific to the drug molecule (physicochemical and stability factors), the patient (comfort and cosmetic appeal), the manufacturer (scale up and manufacturability) and most important the economy [1]. Earlier skin was considered as an impermeable protective barrier, but later investigations were carried out which

proved the utility of skin as a route for systemic administration [2].Skin is the most intensive and readily accessible organ of the body as only a fraction of millimeter of tissue separates its surface from the underlying capillary network. The various steps involved in transport of drug from patch to systemic circulation are as follows [3,4]:

1. Diffusion of drug from drug reservoir to the rate controlling membrane.
2. Diffusion of drug from rate limiting membrane to stratum corneum.
3. Sorption by stratum corneum and penetration through viable epidermis.
4. Uptake of drug by capillary network in the dermal papillary layer.
5. Effect on target organ.

2. Materials and Methods

2.1 Material

Ethyl cellulose, Poly Vinyl Pyrrolidone (PVP), Mercury, Ethyl alcohol, Chloroform, Methanol and Paracetamol was obtained from well reputed research laboratory and U.V. Spectrophotometer.

2.2 Method

Transdermal film of Ethyl cellulose and PVP was prepared by Mercury Substrate Method. Ethyl cellulose was dissolved in Ethyl alcohol, Chloroform and Methanol (1:2:3) mixture at concentration proportion of Ethyl cellulose was used (10% solution). PVP is used as plasticizer into both polymeric solution, after that Paracetamol was slowly dissolved at 50 to 100 rpm by mechanical stirrer into polymeric solution which was closed by Aluminium foil to prevent solvent evaporation. Finally plasticizer was added and mixed well and then polymeric solution containing drug was pored within a glass Bengal, placed on a mercury film in the petridice. Thin film was separated, and then it was completely dried.

3. Evaluation

3.1 Physical characterization

Physicochemical parameters like thickness, weight variation, tensile strength and, folding endurance of the patches was determined.

3.2 Thickness

The average thickness of the patches was determined by measuring the thickness by using micrometer screw gauge

3.3 Tensile strength

Initially we have taken a small film strip of paracetamol and fixed one end between adhesive tapes to give support to the film when placed in film holder, and the other end of the film was fixed between adhesive tapes with a small pin sandwitched between them to keep the strip straight while stretching. A hook was inserted near the pin in adhesive tape with a small hole. A thread was tied to this hook, passed over the pulley and a small pin attached to the other end to hold the weights. A small pointer was attached to the thread, which travels over the graph paper affixed on the base plate for the determination of tensile strength the film was pulled by pulley system. Weight was gradually added to the pan to increase the pulling force till the film was broken. The weight required to break was noted as break force [5].

3.4 Folding endurance

Folding endurance of the film was determined by repeatedly folding a small strip of film at the same place till it broke. The number of times, the film could be folded at the same place without breaking, gave the value of folding endurance [5].

3.5 Drug content uniformity

The uniformity of drug content of the transdermal film was determined, based on dry weight of drug and polymer used by means of a UV spectrophotometer method. The formulated patch was cut into pieces and dissolved in 10 ml of methanol. The resulting solution was quantitatively transferred to volumetric flasks, and appropriate dilutions were made with phosphate buffer pH 7.4 and filtered through 0.22 μ filter and analyzed for Paracetamol content at 258 nm by using UV spectrophotometer [6].

3.6 Percent Moisture Absorption

The percent moisture absorption test was carried out to check the physical stability and integrity of the films at high humid conditions. In the present study the moisture absorption capacities of the films were determined in the following manner. The films were placed in dessicator containing saturated solution of aluminum chloride, keeping the humidity inside the dessicator at 79.5% RH. After 3 days the films were taken and weighed the percentage moisture absorption of two films was found [7].

$$\% \text{ moisture content} = \frac{\text{final wt-initial wt}}{\text{Initial wt}} \times 100$$

3.7 Percent Moisture Loss

This test was also carried to check the integrity of films at dry condition. Three films of 5 square centimeter area was cut out and weighed accurately and kept in a dessicator containing fused anhydrous calcium chloride. After 72 hours the films were removed and weighed. Average percentage moisture losses of three films were found out [8].

$$\% \text{ moisture loss} = \frac{\text{initial wt-final wt}}{\text{Initial wt}} \times 100$$

3.8 In-vitro permeation study

The *In vitro* permeation study of fabricated transdermal patches of Paracetamol was carried out by using excised rat abdominal skin and Franz diffusion cell. The skin was sandwiched between donor and receptor compartments of the diffusion cell. A 1.80 cm diameter patch was placed in intimate contact with the stratum corneum side of the skin; the top side was covered with aluminum foil as a backing membrane. Teflon bead was placed in the receptor compartment filled with 12ml of normal saline. The cell contents were stirred with a magnetic stirrer and a temperature of 37 ± 5°0C was maintained throughout the experiment. Samples of 1ml were withdrawn through the sampling port at different time intervals for a period of 24 h, simultaneously replacing equal volume by phosphate buffer pH 7.4 after each withdrawal. The samples were analyzed spectrophotometrically at 258 nm [8].

4. Results and Discussion

The formulated transdermal patches of Paracetamol were evaluated for thickness, tensile strength, folding endurance and content uniformity. The Thickness of transdermal patches was measured by micrometer screw gauge. The average thickness of the films was found to be 0.282 mm. The tensile strength of the films was found 2.399 kg/mm2. The Tensile strength of transdermal patches prepared from cellulose acetate and ethyl cellulose alone also showed lower values which suggest that addition of polyvinyl pyrrolidone in to cellulose acetate and ethyl cellulose matrix increases tensile strength of patches. Folding endurance of the transdermal patches was measured and it was found to be 190.The drug content uniformity was determined by spectrophotometric method. The drug content for prepared transdermal patches of Paracetamol was found to be 9.46. It was considered that the drug is dispersed uniformly throughout the film. *In-vitro* permeation, this study was carried out for 24 hours and cumulative percent permeated was calculated based on the amount of drug originally present in the patches.

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