**Usıng Transdermal Patches on Controlled Drug Release**

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|  **Abstract**The aim of the given study is the formation as well as the development of patches of Donepezil HCl, which is used in the treatment of Alzheimer's disease (AD). AD is a progressive brain disease and the leading cause of dementia in the elderly. Conventional treatments for the management of AD have all been given orally, thus Donepezil is commonly used as an oral tablet, although a transdermal patch may offer advantages as an alternate therapyTransdermal medication administration for Alzheimer's disease has been shown to enhance patient compliance through reduced dosage frequency, improve bioavailability, reduce undesirable side effects, and make it easier to attain optimal levels. Furthermore, it promotes patient compliance in older patients since the patient does not have to remember to take their prescription or bring tablets for further administration later in the day. The transdermal approach provides various advantages over the oral route, including the ability to maintain sustained therapeutic plasma. In the present work, matrix-type transdermal patches of Donepezil HCl were prepared using the solvent casting method. Formulations were synthesized using Hydroxyethyl-cellulose (HEC), Poly (acrylic acid sodium salt) and Poly (acrylic acid) as polymers -individually- with varying degrees of hydrophilicity with Gelatin as a jellify to provide flexibility and Glycerol as a plasticizer additive, and to improve drug release by increasing permeability.  |
| Keywords: Transdermal patch, donepezil HCl, solvent casting method, plasticizer. |

1. **Introduction** Every pharmaceutical researcher and company aspire to create a safe and effective medication delivery mechanism [1-2] Traditional oral medication administration methods have some drawbacks, including pass metabolism, plasma level fluctuations, drug disintegration in the gastrointestinal tract owing to enzymes, pH, and so on. The introduction of innovative (novel) drug delivery technologies solves these problems. Transdermal drug delivery techniques are one of them. Drug administration via the transdermal method can have both local and systemic therapeutic effects. Because medications are given through the skin at a predefined and regulated rate, this approach is meant to increase therapeutic efficacy and safety. Selfadministered transdermal medication administration allows the medicine to flow through undamaged skin for a specified amount of time, achieving a local or systemic impact. Many drugs have been developed that can be injected directly into the bloodstream through the skin. The transdermal drug delivery system (TDDS) allows for medication release to be sustained while also reducing the intensity of action, reducing the adverse effects associated with oral treatment [3]. Patches are the most widely used transdermal technology on the market. Drugs can be given in dissolved lipid-based form via transdermal patches, allowing them to achieve the desired effectiveness. A transdermal patch is a medical patch that adheres to the skin and used to deliver a certain amount of medicine into the bloodstream via the skin. It (the Skin patch) employs a unique membrane to regulate how quickly the liquid medicine stored in the patch's reservoir passes through the skin and into the circulatory system. The fundamental goal of a transdermal medication distribution system is to transfer pharmaceuticals into the systemic circulation via the skin at a predefined rate with little fluctuation between and within patients [1,4]. Transdermal drug delivery systems (TDDSs) are ways for applying preparations across the skin without causing discomfort. The drug initially enters the stratum corneum (SC), then moves into the inner epidermis and dermis, leaving no drug deposit at the dermal level. As soon as the medicine reaches the dermal layer, it seems to be ready for systemic absorption via skin microcirculation [5]. The essential components of any transdermal administration system are the drug(s) dispersed or distributed in a reservoir or inert polymer matrix; an exterior backing sheet of paper, foil or plastic; and a pressure-sensitive adhesive that adheres the patch to the skin. A release liner that covers the adhesive must be pulled off before placing the patch on the skin. Transdermal delivery provides for not only regulated and uniform medications delivery, but also continuous input of drugs with short biological half-lives and avoids pulsed entry into the blood circulation, which can lead to unwanted side effects (Jawale et al., 2017a). [6].
2. **Materials and Methods**

**2.1. Experimental materials**

All the chemicals used in this research were of standard pharmaceutical grade. The list of chemicals used in the experiments is given in the table below.

**Table 1** List of chemicals and their brands

|  |  |
| --- | --- |
| **Components** | **Brand** |
| Donepezil Hydrochloride | Abdi İbrahim İlaç |
| Hydroxyethyl-cellulose (HEC) | Sigma |
| Poly (acrylic acid sodium salt) | Sigma |
| Poly (acrylic acid) | Sigma |
| Glycerol | Sigma |
| Gelatin | Carlo Erba |

**2.2. Preparation and formulation of matrix transdermal patches**

In the present study, matrix-type transdermal patches of Donepezil Hydrochloride were produced by using the solvent casting method (molding technique). Formulation of transdermal patches using the solvent casting method are given in Table 2.

**Table 2** Formulations

|  |  |  |  |
| --- | --- | --- | --- |
| **Ingredients** | **Formulation 1 (F1)** | **Formulation 2 (F2)** | **Formulation 3 (F3)** |
| Donepezil Hydrochloride | 0.2 g | 0.2 g | 0.2 g |
| Hydroxyethyl-cellulose (HEC) | 1 g | - | - |
| Poly (acrylic acid sodium salt) | - | 1 g | - |
| Poly (acrylic acid) | - | - | 1 g |
| Glycerol | 0.3 g | 0.3 g | 0.3 g |
| Gelatin | 2 g | 2 g | 2 g |
| Distilled water | 6.5 g | 6.5 g | 6.5 g |

**3. Results and Discussion**

**3.1. Drug Release Evaluation**

In-vitro drug release studies were performed by using a Franz diffusion cell with a receptor chamber capacity of 30 ml. First of all, circular-shaped sections were cut from the HEC polymer-based patch with specific dimensions that fit the cover of the cell. The cellulose acetate membrane was used as a diffusion controlling membrane for the determination of drug release from the prepared transdermal matrix type patches. The cellulose acetate membrane having a pore size of 0.45μ was mounted between the donor and receptor chamber of the diffusion cell. The receptor chamber of the diffusion cell was filled with buffer pH 7.4 up to the lid part. Here the membrane will be acted as the skin while prepared pH 7.4 solution will act as the blood and the whole cell present the body. The prepared transdermal film was placed on the cellulose acetate membrane that is located in the part between the cover and the receptor chamber. The upper part of the cover, the end of the sampling tube, and the heater circulators of the diffusion cell are covered with parafilm so that no evaporation or foreign body escapes into the cell. The whole assembly was placed in a hot shaking ultrasonic bath, to remain the solution in the receptor chamber constantly and continuously in motion for uniform distribution and the temperature was maintained at 37 °C, as the normal body temperature of a human. Sampling was carried out by withdrawing samples of 5 ml (1 ml from the cell and completed with 4 ml of pH 7.4 solution) for each at different time intervals throughout 24 h (1, 2, 3, 4, 6, 8, 20 and 24 h). Each sample withdrawn from the cell, the receptor phase was replaced with an equal amount of fresh dissolution buffer solution (pH 7.4 solution). The absorbance of the solution of samples was measured and analyzed after suitable dilution using a UV-visible spectrophotometer at a wavelength of 270 nm for determining drug content. The cumulative percent drug permeated at various time intervals were calculated and plotted against time. The drug release was plotted on the graph as Time (min) on X-axis and Absorbance on Y-axis.

The study's goal was to create a Donepezil HCl transdermal treatment device employing a polymeric matrix film. The transdermal patch of Hydroxyethyl-cellulose (HEC) polymer was effectively formulated via the solvent casting method. As illustrated in Figure 1, the produced film was found to be uniform, flexible, smooth, and transparent. Physical inspection of the formulations revealed that the films were homogeneous and somewhat transparent, indicating that the medication was not totally solubilized but rather suspended/dispersed in the matrix. This allows one to manage the total release of the medicine by selecting the right polymers and polymer blends. The polymer-created diffusion pathways aid in achieving the ultimate goal of consistent and sustained pharmaceutical delivery from the patches.



**Figure 1** Formulation of various transdermal patches after drying

In-vitro release studies use UV-vis spectroscopy to investigate the presence and amount of donepezil hydrochloride medication released from the patch, as well as the release efficiency of drug active components. Furthermore, it is a useful technique for predicting how medicine would act in vivo. Drug release studies are also necessary to predict the repeatability and reproducibility of drug release rate and duration. Figure 2 illustrates the drug release profiles and percentages. It has been shown that the release rate rises with time, reaching a peak of 65.5% after 24 hours. However, as seen in Figure 2, the medication was released rapidly from the patch at first. This fast drug release (burst effect) from the manufactured transdermal patch might be attributed to the surface drug's quick breakdown. The burst release can be effective in a variety of situations.

**Figure 2** Drug release study of Donepezil HCl transdermal patch

Because studies have demonstrated that the medication active component of Donepezil HCl is effective for transdermal delivery, transdermal patches of Donepezil HCl were created and produced in this study. Transdermal patches improve patient compliance over traditional dose forms. Transdermal medication provides a continuous infusion of medicine over an extended length of time. Transdermal drug input can have an equal curative effect with a lower daily prescription dosage than is necessary, e.g. the drug is delivered orally. Hence, it is reasonable to conclude that Donepezil HCl can be formulated into transdermal matrix type patches to maintain its release characteristics, and the polymeric composition of (HEC) was found to be the best choice for manufacturing Donepezil HCl transdermal patches among the formulations studied because it was similar to standard transdermal patch properties. According to an in-vitro release study, a transdermal patch of HEC can release 65.5 % of the medication in the first 24 hours. To be employed in transdermal patches, films with positive findings needed to be validated by in vivo research.

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