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Research Article

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# FORMULATION AND EVALUATION OF METHYLPREDNISOLONE TRANSDERMAL MATRIX PATCHES USING VARYING CONCENTRATIONS OF POVIDONE - CARBOPOL AND POVIDONE - HPMC POLYMERS

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## ABSTRACT

The present study was designed to develop a suitable matrix type transdermal drug delivery system (TDDS) of methylprednisolone using blends of two different polymeric combinations, povidone (PVP) with carbopol & PVP with hydroxypropylethylcellulose (HPMC). Physical studies including moisture content, flatness were done to study the stability of the formulations and *in-vitro* skin permeation and drug content of the experimental formulations were performed. *In-vitro* skin permeation study was conducted in a modified Franz's diffusion cell. All the formulations were found to be suitable for formulating in terms of physicochemical characteristics. *In-vitro* dissolution studies showed that the drug distribution in the matrix was homogeneous. The formulations of PVP:Carbopol provided slower and more sustained release of drug than the PVP:HPMC formulations during skin permeation studies and the formulation PVP:Carbopol (1:5) was found to provide the slowest release of drug. Based on the above observations, it can be reasonably concluded that PVP-Carbopol polymers are better suited than PVP–HPMC polymers for the development of TDDS of methylprednisolone.

**Keywords:** Methylprednisolone; Transdermal patches; PVP; HPMC; Carbopol; *In-vitro* skin permeation studies.

## INTRODUCTION

Transdermal drug delivery is the delivery of drugs across epidermis to achieve systemic effects. The success of transdermal patches lies in their commercialization. Transdermal patches control the delivery of drugs at controlled rates by employing an appropriate combination of hydrophilic and lipophilic polymers.[1,2,3,4]

Methylprednisolone is a synthetic glucocorticoid or corticosteroid drug. Like most adrenocortical steroids, methylprednisolone is typically used for its anti-inflammatory effects. Methylprednisolone is also prescribed for non penetrating spinal cord injuries. It has been shown that a dose of 30 mg/kg intravenously (IV) followed by IV drip at 5.4 mg/kg/h for 23 hours improves sensory and motor recovery if given within eight hours of the injury.[5] It is also used for vestibular neuritis.[6] After egg retrieval for a cycle of *in-vitro* fertilization, methylprednisolone may be prescribed to prevent the body from rejecting the embryos being transferred, up to the time of implantation.[7,8] Methylprednisolone may also be beneficial in the treatment of patients in cardiac arrest.[9] Unbound glucocorticoids cross cell membranes and bind with high affinity to specific cytoplasmic receptors, modifying transcription and protein synthesis. By this mechanism, glucocorticoids can inhibit leukocyte infiltration at the site of inflammation, interfere with mediators of inflammatory response, and suppress humoral immune responses. The anti-inflammatory actions of corticosteroids are thought to involve phospholipase A2 inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes. Early methyl prednisolone therapy, both oral and pulse steroid, is equally effective in achieving remission in drug-induced Acute Interstitial Nephritis.[10] Methylprednisolond has also shown improvement in children with CSWS.[11] The drug has a potein binding to the extent of 78%, gets metabolized in the liver and excreted by kidneys.

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## MATERIALS & METHODS

### Material

Carbopol, HPMC, polyvinylpyrrolidone, Dibutylphthalate, chloroform, polyvinyl alcohol, polyethyleneglycol, sodium chloride & methylprednisolone were obtained commercially.

### Preparation of films

TDDS composed of different ratios of Carbopol and PVP as well as HPMC and PVP containing methylprednisolone. (1.5 mg/square centimeter patch) were prepared using the glass mould solvent evaporation technique. Dibutylphthalate was incorporated as a plasticizer at a concentration of 20% w/w of dry weight of polymers. Backing membrane was cast by pouring and then evaporating 4% aqueous solution of polyvinyl alcohol in glass moulds covered on one side with aluminium foil, at 60°C for 6 h. The matrix was prepared by pouring the homogeneous dispersion of drug with different blends of either type of lipophilic polymer (Carbopol or HPMC) with

PVP in chloroform on the backing membrane in glass moulds. The above dispersion was evaporated slowly at 40°C for 2 h to achieve a drug-polymer matrix patch. The dry patches were kept in desiccators until use.

### Physical characteristics of the prepared films

***Moisture content:*** The film was weighed and kept in a desiccator containing calcium chloride at 40° C in a drier for at least 24 h or more until it showed a constant weight. The moisture content was the difference between the constant weight taken and the initial weight and was reported in terms of percentage (by weight) moisture content. (Table **1**; Figure **1**)

***Flatness:*** Longitudinal strips were cut out from the pre-medicated patches and the lengths of each strip were measured and then the variation in the lengths due to the non-uniformity in flatness was measured. Flatness was calculated by measuring constriction of strips and a zero percent constriction was considered to be equal to a hundred percent flatness. (Table **2**)

$$Constriction\ (\%) = \frac{l_1 - l_2}{l_2} \times 100$$

Where, $l_1$= initial length of each strip; $l_2$=final length of each strip.

**Table 1. Average percentage of moisture content (by weight) of different formulations.**

| Formulation | % Moisture content |
|---|---|
| PC1 | 2.5±0.005 |
| PH1 | 2.7±0.002 |
| PC2 | 3.5±0.0019 |
| PH2 | 2.9±0.001 |

*Values are expressed as Mean±SD*

**Figure 1. Average Percentage of Moisture Content (by weight) of Different Formulations**

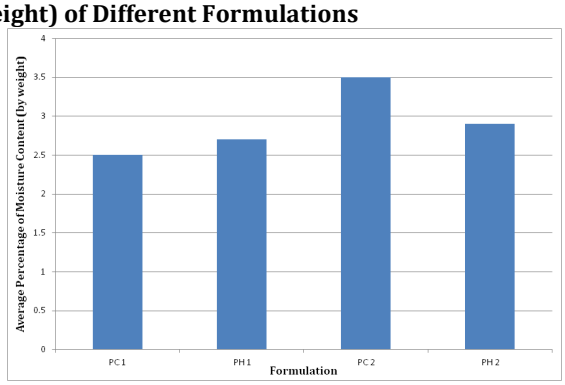



**Table 2. Average thickness and flatness of different formulations**

| Polymeric blend | Formulation code | Ratio (w/w) | Strip length (cm) | Constriction of strip | Mean thickness (µm) | Mean flatness (%) |
|---|---|---|---|---|---|---|
| PVP-Carbopol | PC1 | 3:4 | 3±0.005 | 0 | 46±0.02 | 100±0.02 |
| PVP-HPMC | PH1 | 3:4 | 3±0.006 | 0 | 59±0.05 | 100±0.04 |
| PVP-Carbopol | PC2 | 4:3 | 3±0.004 | 0 | 52±0.01 | 100±0.03 |
| PVP-HPMC | PH2 | 4:3 | 3±0.004 | 0 | 54±0.02 | 100±0.10 |

*Values are expressed as Mean±SD*

### Determination of drug content in the patches

The amount of API (methylprednisolone) was determined in the formulated patches using dissolution apparatus and 20% PEG-400 solution in normal saline and performing UV spectroscopic studies of the samples withdrawn at 244 nm. (Table **3**)

**Table 3. Drug concentration in the patches by *in-vitro* drug dissolution study**

| Formulation | Cumulative drug permeated (mg/cm²) |
|---|---|
| PC 1 | 0.778±0.0004 |
| PC 2 | 0.746±0.0009 |
| PH 1 | 0.797±0.0007 |
| PH 2 | 0.815±0.0005 |

*Values are expressed as Mean±SD*

### *In-vitro* skin permeation studies

The *In-vitro* skin permeation of methylprednisolone from the selected TDDS through depilated goat skin was conducted using a modified Franz diffusion cell. Normal saline containing 20% v/v of polyethylene glycol 400 was used as bathing solution in the receptor compartment of a modified Franz diffusion cell.

The selection of the receptor fluid is an important criterion in the *in-vitro* skin permeation studies. Biphasic characteristics of the receptor fluid are desirable as the diffusion of drug molecules is through both aqueous and non-aqueous heterogeneous media. PEG 400 and normal saline are commonly chosen to provide the biphasic characteristics to the receptor fluid.[12] Moreover, PEG 400 is a non-interacting fluid for the receptor media.

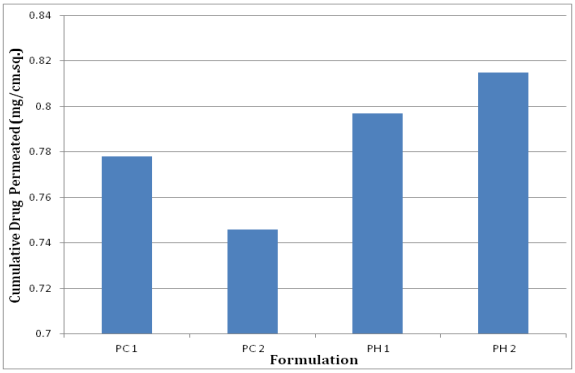
Samples (1 ml in each case) were withdrawn at regular intervals and fresh receptor fluid was added to maintain a constant volume of receptor fluid. The samples were analyzed spectrophotometrically at 244 nm and the drug content was determined from the calibration curve**.** (Table **4**; Figure **2**).

**Table 4. Mean Cumulative Amount of Drug Premeated after 15 h**

| Formulation code | Average drug concentration (mg/cm²) |
|---|---|
| PC1 | 1.5±0.03 |
| PH1 | 1.5±0.04 |
| PC2 | 1.5±0.02 |
| PH2 | 1.5±0.06 |

*Values are expressed as Mean±SD*

**Figure 2. Mean Cumulative Amount of Drug Permeated after 15 h**




## RESULTS AND DISCUSSION

The physicochemical studies like moisture content, flatness etc. provide information regarding the stability of the formulations. The moisture content varied to a small extent in all the formulations studied. The moisture content was found to be greater with the increase of carbopol as compared to HPMC. All the patches showed 100% flatness (Table **1**), which indicates no amount of constriction of the formulated patches.

*In-vitro* dissolution studies were carried out for the different formulations using USP dissolution apparatus using 20% PEG-400 solution in normal saline as the dissolution fluid at 35°C to determine the drug content in

the patches. The average methylprednisolone contents in the PVP-carbopol transdermal drug delivery systems PC1 & PC2 were 1.5±0.03[a]& 1.5±0.02[a](mg/cm$^2$) respectively and in PVP-HPMC transdermal drug delivery systems PH1 & PH2 were1.5±0.04[a]& 1.5±0.06[a](mg/cm$^2$). An *in-vitro* study was carried out in a modified Franz's diffusion cell to determine the drug release profiles of the prepared formulations through the depilated goat skin. Mean cumulative amounts of drug permeated from the patch after 15 h are shown in Table **4** and Figure **2**.

## CONCLUSION

A suitable matrix type transdermal drug delivery system (TDDS) of methylprednisolone was developed using blends of two different polymeric combinations, povidone (PVP) with carbopol & PVP with HPMC. *In-vitro* skin permeation study was conducted in a modified Franz's diffusion cell. All the formulations were found to be suitable for formulating in terms of physicochemical characteristics and there was no significant interaction noticed between the drug and polymers used. *In-vitro* dissolution studies showed that the drug distribution in the matrix was homogeneous. The formulations of PVP: Carbopol provided slower and more sustained release of drug than the PVP:HPMC formulations during skin permeation studies and the formulation PVP:Carbopol (1:5) was found to provide the slowest release of drug.

## REFERENCES


1. Keith A D; Polymeric matrix consideration for transdermal devices. *Drug Dev Ind Pharm*. 1983; 9:605-621.
2. Chien Y W; Development of transdermal drug delivery system. *Drug Dev Ind Pharm*. 1987; 13:589-651.
3. Misra A N; Transdermal drug delivery in: Jain N K (Ed.), Controlled and Novel Drug Delivery, Varghese Publication, NewDelhi, 1988, pp. 100–129.
4. Walters K A; Transdermal drug delivery: system design andcomposition in: Swarbrick K, Boylan J C (Eds.), Encyclopedia of Pharmaceutial Technology, Marcel Dekker, New York, NY, 1999; pp. 306–320.
5. McDonald John (September 1999). "Repairing the Damaged Spinal Cord". *Scientific American*: 65.
6. Strupp M, Zingler V C, Arbusow V, Niklas D, Maag K P, Dieterich M, Bense S, Theil D, Jahn K, Brandt T; Methylprednisolone, valacyclovir, or the combination for vestibular neuritis. *N Engl J Med.* 2004; 351(4):354-61.
7. Medications Commonly Used During the IVF Cycle. *Continuum Reproductive Center*. Retrieved 14 June 2013.
8. *In-vitro* Fertilization (IVF). *Reproductive Medicine Associates of Michigan*. Retrieved 14 June 2013.
9. Arora P, Mukherjee B; Design, development, physicochemical and *in-vitro* and *in-vivo* evaluation of transdermal patches containing diclofenac diethylammonium salt. *J Pharm Sci*. 2002; 91:2076-2089.
10. Ramachandran R, Kumar K, Nada R, Jha V, Gupta K L, Kohli H S; Drug-induced acute interstitial nephritis: A clinicopathological study and comparative trial of steroid regimens. *Indian J Nephrol*. 2015; 25(5):281-6.
11. Fatema K, Rahman M M, Begum S; Characteristics and Management of Children with Continuous Spikes and Waves during Slow Sleep. *Mymensingh Med J*. 2015; 24(4):806-12.
12. Sarpottdar P P, Gaskill J, Giannini R P; Effect of polyethyleneglycol 400 on the penetration of drugs through human cadaver skin *in-vitro*. *J Pharm Sci*. 1986; 75:26-28.