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RESEARCH PAPER

Formulation and Evaluation of Oxyphenbutazone Transdermal Patches

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Abstract

Transdermal drug delivery system (TDDS) is a topical drug delivery system that designed to deliver drugs through intact skin for both local and systemic effects. It offers drug release following sustained release pattern when applied through skin. TDDS offers certain unique advantages like avoidance of fast pass metabolism, prolong therapeutic action, effective disease control etc. The purpose of this research work was to prepare transdermal patches using different polymers includes hydroxyl propyl methyl cellulose (HPMC), Polyvinyl alcohol (PVA) and Sodium Carboxy Methyl cellulose (SCMC) by means of solvent evaporation technique and to determine their suitability and effectiveness as polymer that may fulfilled the essential criteria's of a good transdermal patch. In this study Oxyphenbutazone was used as model drug. Different polymers were used in various ratios and combination. Glycerine was used as plasticizer. All the formulated transdermal patches were subjected for various evaluations like thickness, weight variation, surface pH patches, folding endurance, moisture content, swelling index and in-vitro drug release study and skin permeation study. The results of in-vitro screening parameters were found satisfactory. The performed in-vitro and ex-vivo drug release study results also shows significant results. It has been found that formulation prepared using high concentration of combination polymers shows poor folding endurance and moisture absorption capacity. It has been observed that the amount of drug release also get affected by changes in concentration of polymer.

Keywords: *Ex-Vivo Skin Permeation, Oxyphenbutazone, Topical Delivery, Transdermal Patches*

1 Introduction

Topical drug delivery systems are considered as one of the preferred drug delivery system for the treatment and management of certain health issues like pain, muscle cramps, skin infections, wound management, life style diseases like diabetes and Parkinsonism etc. The recent advancement in the field of topical drug delivery system open enormous scope for the future. Transdermal Drug Delivery System (TDDS) are defined as an unique topical dosage form which designed to deliver drug at required effective concentration across the patient's skin(1; 2). The main aim behind the development of TDDS is to deliver drugs into systemic circulation through skin at predetermined rate with minimal inter and intra patient variation(3; 4). The transdermal patches are mainly composed of different segments like drug, drug reservoir components, penetration enhancers, polymer matrix, adhesives and backing membrane(5; 6). Considering the above facts the present study has been designed. In this study Oxyphenbutazone, a well-known non-steroidal anti-inflammatory drug, that used for the treatment of Pain, Swelling, Arthritis Stiffness, Fever, Analgesic Antipyretic in lower dose was used as model drug(7). The oxyphenbutazone patches were prepared by solvent casting method(8). Polymers include hydroxyl propyl methyl cellulose (HPMC), Polyvinyl alcohol (PVA) and Sodium Carboxy Methyl cellulose (SCMC) were used at various concentration for the fabrication of patches. Glycerine was used as plasticizer. All the prepared formulations were subjected for different evaluation process to determine the quality and performance.

2 Materials and Methods

2.1 Chemical and Reagents

The drug Oxyphenbutazone was received a gift sample from Merck Specialities pvt. Ltd (Germany). Hydroxyl propyl methyl cellulose (HPMC) and acetone was procured from Merck Specialities pvt ltd, Sodium Carboxyl Methyl Cellulose (SCMC) and Polyvinyl Alcohol were purchased from Himedia Laboratories Pvt. ltd and lastly Glycerine received

Table 1: Working Formula of Different Batches of Transdermal Patches

Sl. No	Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	HPMC	0.5 gm	0.5 gm	-	1gm	1gm	-	1.5gm	1.5gm	-
2	PVA	-	0.5gm	0.5gm	-	1gm	1gm	-	1.5gm	1.5gm
3	SCMC	0.5gm	-	0.5gm	1gm	-	1gm	1.5gm	-	1.5 gm
4	GLYCERINE	1-2 ml	1-2 ml	1-2 ml	1-2 ml	1-2 ml	1-2 ml	1-2 ml	1-2 ml	1-2 ml
5	DRUG	100mg	100mg	100mg	100mg	100mg	100mg	100mg	100mg	100mg
6	ACETONE	10 ml	10 ml	10 ml	10 ml	10ml	10ml	10ml	10ml	10ml

from Glycerol Manufacturer.

2.2 Preparation of Transdermal Patch

Transdermal patches of Oxyphenbutazone were prepared by solvent casting method.

Accurate quantity of polymers like HPMC, SCMC, PVA and the drug was added inside a 50ml beaker (Table 1). After that 10 ml of acetone was added in beaker. The beakers were than seal properly with aluminium foil and kept aside for 12 hours. After that the whole content were mixed genteelly with the help of magnetic stirrer until a homogeneous mass formed(9). The mass was then transferred into pretridishes previously lubricated with glycerine. The solvent was allowed to dry uniformly at room temperature for duration of 24hours. After drying the patches was removed from Petri dish and stored inside desiccator until further use(10).

2.3 Evaluation of Transdermal Patch

2.3.1 Measurement of Weight and Thickness of the Prepared Patches

Three patches of uniform shape and size was randomly selected from the prepared formulation and weight of every formulation were measured individually using digital balance(9). The average weights were calculated. Similarly, three patches from each formulation were taken and the patch thickness was measured using screw gauge at three different places, and the mean value was to calculate(11). The process was repeated for all the prepared batches.

2.3.2 Determination of Surface pH of the Patches

The surface pH of all the batches was measured using three patches from each formulation batches. All the prepared patches were allowed to swell for 2 hours on the surface of freshly prepared agar plates. The surface pH was measured by using a digital pH meter by placing the electrode on the swollen patch surface. A mean of three reading was recorded and mean data was presented(11; 12).

2.3.3 Folding Endurance

Three patches from each formulation batches were cut into uniform size using sharp blade. Folding endurance was determined by repeatedly folding the patch at the same place, till it was broken. The number of time the patch could be folded at the same place without breaking was noted as value of folding endurance(13).

2.3.4 Moisture Content

The prepared patch was weighed individually and keeps in a desiccators containing calcium chloride at room temperature for 24hours. The patches were weighed again after a specified interval, until they show a constant weight. The percent moisture contain was calculated by using following formula(14).

$$\%Moisture\ Content = \frac{initial\ weight – final\ weight}{final\ weight} \text{x}100 \quad (1)$$

2.3.5 Swelling Index

The study was performed by taking the individual weight and diameter of three different patches of uniform size and shape from every prepared batches. Than the samples were allow to swell on the surface of freshly prepared agar plate. All the samples were keep in contact of agar plate for a duration of 5 hrs at room temperature. After that weight of the patches (n = 3) was measured at a time intervals (1 to 5) hours respectively. The percent swelling, % S was calculated using the following equation(15).

$$\%Swelling = \frac{[X_t - X_0]}{X_0} \text{x}100 \quad (2)$$

Where,

X_t =The weight of swollen patches after time t

X_0 =The initial patches weight at zero time

2.3.6 *In-vitro* drug release study

The study was performed to determine the amount of drug release from the prepared transdermal patches after a specific time interval.

Table 2: Results of in-vitro Parameters Study of Prepared Transdermal Patches

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Wt. Variation (gm)	0.52+0.013	0.53+0.08	0.50+ 0.09	0.60+0.08	0.55+0.07	0.57+ 0.04	0.58+0.11	0.61+.012	0.65+0.011
Thickness (mm)	0.13+0.015	0.14+0.12	0.16+0.18	0.23+0.11	0.25+0.21	0.28+0.23	0.16+0.14	0.15+0.17	0.19+0.18
Surface pH	7.12+0.02	7.18+0.06	7.11+0.06	7.20+0.09	7.16+0.11	7.15+0.08	7.17+0.07	7.14+0.08	7.15+0.05
Folding Endurance	236+09	255+11	254+08	266+12	274+11	268+14	288+03	274+06	280+08
Moisture Content (%)	8.22+0.33	7.84+0.28	8.75+0.47	7.89+0.38	8.15+0.36	9.34+0.37	8.69+0.33	8.44+0.24	7.56+0.41
Swelling Index	6.56+0.51	7.21+0.42	7.33+0.22	7.44+0.27	6.61+0.38	6.84+0.47	6.82+0.24	6.66+0.28	6.71+0.28

*Data presented in the format Mean +- Standard Deveiation

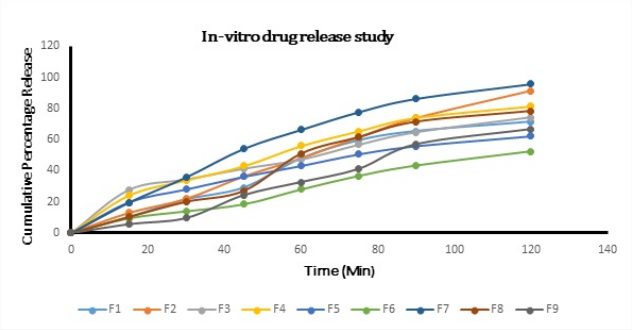

Figure 1: In-vitro Drug Release Study of Prepared Transdermal Patches

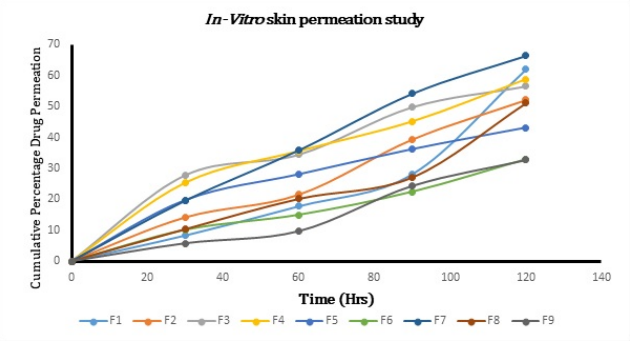

Figure 2: In-vitro Skin Permeation Study of Prepared Transdermal Patches

The study was performed using modified franz diffusion cell, where previously treated 0.45 Millipore cellophane membrane was placed in between the receptor and donor compartment. Now uniform size, circular shape patches from different batches was collected placed inside the receptor chamber. The study was carried out using phosphate buffer (pH 7.4) as dissolution medium. A temperature of 37°C ± 0.5°C, proper sink condition and uniform agitation was maintained throughout the study. Around 5ml of Sample was withdrawn after specific time intervals and analyzed after suitable dilution using UV- Visible spectrophotometer(16; 17).

2.3.7 *In-vitro* skin permeation study

In this study the uniformly sized prepared transdermal patches were subjected to an in vitro permeation study using a modified Keshary–Chien diffusion cell (cell capacity, 100 mL). After removing the epidermal hairs and subcutaneous fat layer of pig ear, the skin was treated with 0.32 M ammonia solution for 35 min. The procure skin was examined microscopically for any possible damage. The skin was kept in normal saline solution and stored at 4°C±1°C .The treated skin was placed overnight in side pH 7.4 phosphate buffer solution. Pig ear dorsal skin was clamped in between the donor and recipient compartments. Now the patches were placed in the donor compartment over the skin. The temperature of receptor as well as donor medium was maintained at 37°C±1°C throughout the experiment.

A uniform agitation was applied using magnetic stirrer and sink condition was maintain throughout the study. The amount of drug permeated through pig ear skin was determined using withdrawn samples of 1 mL at predetermined time intervals till the end of the study. The samples were then analyzed for using UV-visible spectro photometer at a wavelength max 281 nm(18; 19).

3 Result and Discussion

Total nine formulations were created using different ratios of polymers such as HPMC, PVA, and SCMC. In terms of texture, the prepared patches were found to be smooth, flexible, and uniform. Formulation prepared with HPMC was found to be comparatively better in terms of smoothness and flexibility. The thickness of all the prepared batches were found within the range from 0.13+0.015 to 0.19+0.18mm. It has been observed that the thickness of patches increases parallel with concentration of polymer. The folding endurance of patches was done which ranges between 236+09 and 280+08 times that reflects the effective flexibility of the prepared patches. Again in terms folding endurance patches prepared with HPMC and PVA shows comparatively better performance as compare to SCMC formulations. The presence of percentage moisture content availability of the prepared patches varies from 8.22+0.33 to 7.56+0.41 (Table 2). It was noticed that as the concentration rises, the amount of moisture retained increases.

The pH of the surface was measured using a digital pH meter, and patches were found to range from 7.12+0.02 to 7.15+0.05. In terms of drug absorption through the skin, the pH of the skin's surface can be a significant factor all the prepared batches fulfill the requisite criteria of good transdermal patches. The percentages swelling index different prepared formulations were found in the range from 6.56+0.51 to 6.71+0.28, where, the standard value for percentage of swelling index are reported to exist in the range of (0.5 to 13.9). The in-vitro release study suggests that all the prepared batches shows significant difference in the amount of drug release after suitable time interval. It has seen that formulations prepared with combination of polymers shows slow release as compared to those prepared using single polymer. Most of the formulation prepared with HPMC shows 65-89% of drug release after two hours followed by PVA and sodium CMC 49-75% 68-81% respectively (Figure 1). Further, the performed skin permeation study shows more than 55% of drug permeation taken place after two hour interval for SCMC and PVA patches, whereas patches prepared with HPMC shows around 67% of skin permeation, which may be considered as significant finding in terms of drug release through biological layer (Figure 2).

4 Conclusion

Based on the evaluated in-vitro parameters and results obtained there with it may be concluded that all the prepared formulations were found to be satisfactory in terms of the essential requirement of a good transdermal formulation. Formulation prepared with HPMC shows comparatively better result in context of parameters like in-vitro release study, ex-vivo skin permeation and folding endurance capacity. Aging the prepared patches of HPMC polymer were found to be uniform and smooth in texture. Further studies like stability study, tensile strength measurement, skin interaction, and other essential in-vivo parameters may be carried out in future to conclude the overall efficiency of the prepared formulations more accurately.

Conflict of Interest

The authors declare no conflict of Interest in this reported communication.

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