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Formulation And Evaluation Of Transdermal Patches Of Ketoprofen Drug

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Abstract: Considering that most inflammatory diseases occur locally and near the body surface, transdermal drug delivery of non-steroidal anti-inflammatory drugs (NSAIDs) may be an interesting strategy for delivering these drugs directly to the diseased site. Ketoprofen (KP), a potent non-steroidal anti-inflammatory drug (NSAID) inhibits arachidonic acid metabolism by cyclo-oxigenase and lipoxygenase. The compound has been widely used in the treatment of rheumatoid arthritis, osteoarthritis, as well as a mild to moderate painkiller. In these study ketoprofen transdermal patches was prepared by solvent evaporation method using polymer PVP and Ethyl cellulose. Dibutyl phthalate used as a plasticizer. The prepared patches will evaluated for thickness, folding endurance, tensile strength, flatness, drug contain uniformity, *in-vitro* permeation study. *In vitro* release study was performed by using Franz-diffusion cell.
Keywords: Ketoprofen, PVP, ethyl cellulose, dibutyl phthalate.

Introduction

Transdermal drug delivery systems have increased in popularity since their introduction to the market in 1981, as witnessed by the increasing number of drugs available in this formulation. There are more than 20 patches currently marketed in the United States with several drugs under investigation for transdermal use including albuterol, enalapril, alprazolam, cytarabine, and prazosin.[1,2]

Transdermal patch or adhesive patch or skin patch used to deliver a controlled dose of a drug through the skin over a period of time. [3,4] Transdermal patch (Skin patch) uses a special membrane to control the rate at which the liquid drug contained in the reservoir within the patch can pass through the skin and into the bloodstream.[5] Ketoprofen is a non-steroid anti-inflammatory drug with analgesic and antipyretic action. It inhibits cyclo-oxigenase activity with a reduction in the tissue production of prostaglandins such as PGE 2. The aim of present study is to formulate and evaluate transdermal drug delivery of ketoprofen.[6]

Preparation of Transdermal patch:

Transdermal patches containing ketoprofen were prepared by solvent evaporation technique, using Ethyl cellulose, PVP and dibutyl pthalate (Table1). The polymer(ethyl cellulose) were weighed in requisite ratios and mix with chloroform(10ml) Then the PVP was added to the polymeric solution. In this solution dibuyl phthalate and drug was added with continous stirring,

Finally the resulting solution was poured within a glass bangle of 5cm diameter placed on mercury surface in a petridish. The rate of evaporation of the solvent was controlled by inverting cut funnel over the petridish. After 24 hr the dried patches were taken out and stored in a desiccator.

Evaluation Of Transdermal Patch

Physical characterization

The physicochemical parameters such as thickness, weight variation, tensile strength, flatness and folding endurance of various films were determined.

Thickness

The thickness of the films was determined by measuring the thickness at random sites on the formulated films using micrometer screw gauge and the average thickness was determined.[7]

Tensile strength

The tensile strength of the patches was determined by using a tensile strength instrument . Average reading of three patches was taken as the tensile strength. The transdermal patch was fixed to the assembly, the weights required to break the patch was noted, and simultaneously elongation was measured with the help of a pointer mounted on the assembly and calculated the tensile strength of the patch using the following formula

T. S. = break force/ a.b (1+ΔL/L)
Where a, b and L are width, thickness and length of the patch
respectively.
ΔL is the elongation of patch at break point.
Break force = Weight required to break the patch (Kg) [8]

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.[9]

Flatness

Longitudinal strips were cut out from the prepared transdermal patches. The flatness was determined at various points by using vernier calipers . The percentage elongation brake was determined by noting the length just before the break point and substituted in the eq.1.

Elongation (%) = L1 – L2 X 100/ L2 (1)

Where
L1 = final length of each strip
L2 = initial length of each strip. [10]

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/ chloroform. 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 ketoprofen content at 258 nm by using UV spectrophotometer.[11]

In-vitro permeation study

The *in-vitro* permeation study of fabricated transdermal patches of ketoprofen 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 2.2 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.

Table 1: Composition of batches of transdermal patches of ketoprofen

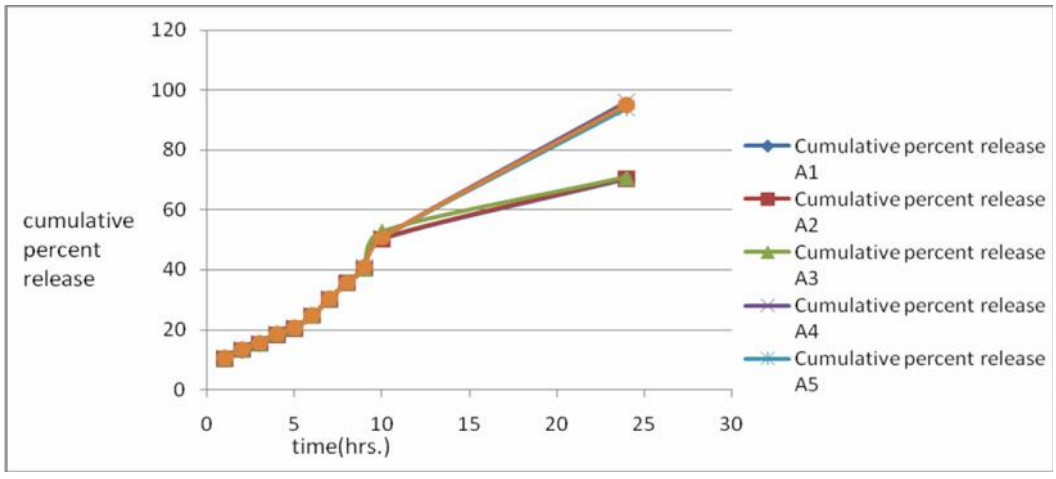
Batch	Drug(ketoprofen) (mg/ml)	Polymer (Ethyl cellulose:PVP)	Dibutyl phthalate (%w/v)	Casting solvent
A1	300	1:1	0.078ml	Chloroform
A2	300	2:1	0.1173ml	Chloroform
A3	300	3:1	0.156ml	Chloroform
A4	300	4:1	0.195ml	Chloroform
A5	300	5:1	0.234ml	Chloroform
A6	300	6:1	0.273ml	Chloroform

Table2: Thickness, tensile strength, folding endurance drug content and flatness of batches of ketoprofen transdermal patch

Batch	**Thickness** (S.D. (mm)	**Tensile strength** (S.D.)(kg/mm^2)	**Folding endurance** Mean (S.D.)	**Drug Content** (%)	**Flatness (%)**
A1	0.164± 0.0034	1.165±0.05	275±2.64	98.52	100
A2	0.158±1.0038	1.164±0.04	213±0.23	97.45	100
A3	0.164±0.0045	1.163±0.07	245±1.13	98.50	100
A4	0.164±0.0164	1.165±0.05	389±1.03	98.54	100
A5	0.158±0.0019	1.167±0.08	245±3.45	96.52	100
A6	0.165±0.0064	1.164±0.09	278±4.45	97.51	100

Table 3: Results of in-vitro permeation study of batch of ketoprofen transdermal patch (batch A1-A6)

Time (hr)	**Cumulative percent release**					
	A1	**A2**	**A3**	**A4**	**A5**	**A6**
1	10.213	10.223	10.364	10.435	10.534	10.657
2	13.002	13.212	13.387	13.478	13.568	13.664
3	15.245	15.345	15.467	15.554	15.675	15.778
4	18.223	18.334	18.498	18.585	18.678	18.756
5	20.354	20.434	20.567	20.645	20.765	20.878
6	24.768	24.765	24.554	24.698	24.734	24.876
7	30.356	30.112	30.234	30.354	30.454	30.547
8	35.878	35.665	35.776	35.665	35.767	35.875
9	40.223	40.365	40.496	40.845	40.965	40.989
10	50.243	50.365	52.76	50.576	50.645	50.743
24	70.345	70.557	70.876	95.998	93.994	94.992



Conclusion:

Ketoprofen transdermal delivery patches can be successfully formulated by using various ratios of ethyl cellulose and PVP. The appearances of the patches were transparent without any air bubbles and their surface was smooth. Patches prepared with ratio 4:1 shows best drug release i.e (97.87%) in 24 hrs.

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