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Research Article

Formulation and physicochemical evaluation of Indomethacin transdermal patches

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ABSTRACT

Indomethacin is a NSAID available for several decades, highly effective against any condition of pain. In this study drug dispersion with different polymers like hydroxyl propyl methyl cellulose (HPMC), polyvinyl pyrolidine (PVP), ethyl cellulose(EC), either in individual or combination were used, with or without rate controlling membrane of 1%W/V of ethyl cellulose to formulate matrix type of transdrmal patches. All the patches were prepared by added 20%W/V of di butyl phthalate (DBP) as plasticizer to make the film flexible and free from brittleness and the solvent used for dispersion was ethanol as common solvent. The prepared patches were evaluated for various physico-chemical parameters like film thickness, film weight variation, folding endurance, water absorption capacity, percentage moisture loss, percentage moisture absorption, weight vapor transmission rate, tensile strength & percentage elongation and drug content uniformity.

Keywords: Transdermal therapeutic system (TTS); hydroxy propyl methyl cellulose (HPMC); Ethyl cellulose (EC).

INTRODUCTION

Indomethacin is non Cox selective NSAID available in the market. Inflammatory are difficult task for public health concern in so many countries. Indomethacin is used in the treatment and management of arthritis with the recommended dose of 25 mg thrice a day. But management of pain and control of inflammation needs the blood concentration of drug in a steady manner for better results, so alternate route of administration is adopted by prepared in transdermal therapeutic system of Indomethacin.

MATERIALS AND METHODS

Indomethacin, HPMC K-10, PVP K-30, EC 14cps, ethanol, DBP and other chemicals used were of analytical grade.

Preparation of matrix patches

Polymers of ethyl cellulose, hydroxyl propyl methyl cellulose and polyvinyl pyrolidine were accurately weighed and dissolved individually or combinations in 5 ml of ethanol. The drug was then dispersed in the polymeric solution and then plasticizer of dibutyl phthalate was added. The solution was stirred to attain semisolid like consistency and casted on a glass substrate containing 'o' ring, the rate of evaporation of solvent from polymeric solution was controlled by placed a inverted funnel at room temperature for a day (Samanta et al 2002; Kulkarni et al 2002; Singh et al 1993; Kanikannan1 et al 1993). The formed films were separated. Formulation of Indomethacin patches was given in table. no: 1.

Preparation of rate controlling membrane

Ethyl cellulose 1% W/V was dissolved in ethanol of 5 ml, to this plasticizer of dibutyl phthalate was added, the solution was mixed to get the semisolid like consistency and casted on a glass substrate containing 'o' ring, the rate of evaporation of solvent from polymeric solution was controlled by placed a inverted funnel at room temperature for a day. The drug contained patch was fixed with rate controlling membrane by ethanol, then wrapped in aluminium foil and stored in a dessicator (Sankar et al 2003).

Physicochemical evaluation of transdermal patches

Thickness: Film thickness was measured by a screw guage at three different points on the film. Then an average reading was taken (Chowdary et al 2007).

Weight variation: Each film was weighed individually, then the average weight of six films taken as the weight of the film (Koteshwar et al 2004).

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Table 1: Formulation of Indomethacin Transdermal patches

CODE	HPMC (%)	EC (%)	PVP (%)	RCM (%)
F 1	1	-	-	-
F 2	2	-	-	-
F 3	3	-	-	-
F 4	-	1	-	-
F 5	-	2	-	-
F 6	-	0.75	0.25	-
F 7	-	0.50	0.50	-
F 8	0.33	0.33	0.33	-
F 9	2	-	1	-
F10	3	-	1	-
F11	3	-	1	1

30 mg of Indomethacin in all the patches; 20 % w/v of Di-butyl phthalate is used as plasticizer in all the patches; 5 ml of ethanol is used as solvent in all the patch.

Table 2a: Physicochemical evaluations of indomethacin transdermal patches

Formulation code	Film thickness (mm)	Film weight Variation (mg) ± SD	Folding Endurance (no) ± SD	Water absorption Capacity (mg) ± SD	Percentage moisture loss % ± SD
F1	0.12	80.12 ± 0.30	168.33 ± 0.94	2.503 ± 0.009	3.23 ± 0.008
F2	0.17	130.80 ± 0.20	155.00 ± 2.16	5.023 ± 0.016	3.47 ± 0.029
F3	0.22	180.22 ± 0.15	153.66 ± 0.81	7.496 ± 0.009	3.72 ± 0.007
F4	0.10	79.97 ± 0.17	141.66 ± 0.47	0.753 ± 0.004	0.92 ± 0.006
F5	0.15	130.20 ± 0.40	144.00 ± 0.81	1.010 ± 0.008	1.14 ± 0.006
F6	0.11	80.09 ± 0.34	145.33 ± 1.24	1.253 ± 0.004	1.25 ± 0.180
F7	0.12	80.77 ± 0.17	151.66 ± 2.05	1.543 ± 0.004	1.59 ± 0.009
F8	0.12	80.17 ± 0.23	158.33 ± 1.24	1.996 ± 0.008	2.17 ± 0.003
F9	0.23	180.44 ± 0.40	140.32 ± 0.21	6.496 ± 0.004	3.68 ± 0.002
F10	0.25	230.55 ± 0.48	138.66 ± 0.47	8.503 ± 0.04	3.87 ± 0.03
F11	0.28	281.00 ± 0.23	134.00 ± 0.81	9.513 ± 0.004	4.15 ± 0.004

The average of 6 readings was mentioned for each parameter.

Folding endurance: Folding endurance of the film was determined by repeatedly folding a small strip measuring 2 x 2 cm size at same place till it breaks (Manvi et al 2003).

Water absorption capacity: Three film units of each formulation were kept in an atmosphere of relative humidity RH = 82%. For one week and the difference in weight of the film was taken as the water absorption capacity for that film (Koteshwar et al 2004).

Percentage moisture loss: The films were weighed accurately and kept in a desiccator containing anhydrous calcium chloride. After 3 days, the films were taken out and weighed (Kusumdevi et al 2003).

$$Percentage\ moisture\ loss = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

Percentage moisture absorption: The percentage moisture absorption was studied by placing preweighed six films in a desiccator containing 100ml of saturated solution of aluminium chloride, which maintained 79.5% RH. After 3 days, the films were taken out and weighed (Lewis shaila et al 2006).

$$Percentage\ moisture\ absorption = \frac{Final\ weight - Initial\ weight}{Initial\ weight} \times 100$$

Water vapor transmission rate: The vials of equal diameter were used as transmission cells. These cells were washed and dried. About one gm of fused calcium chloride was taken in the cells and the films were fixed over the brim with the help of solvent. Then the cells were weighed accurately and kept in a closed desiccator containing saturated solution of potassium chloride [200ml]. The cells taken out and weighed after 1,2,3,4,5,6 and 7th day of storage. From increased in the weights, the rate of water vapor transmitted were calculated (Kulkarni raghavendra et al 2000).

$$WVT\ Rate = \frac{WL}{S}$$

where

W – gm of water transmitted

L – Thickness of film

S – Exposed surface area of film.

Table 2b: Physicochemical evaluations of indomethacin transdermal patches

Formulation code	Percentage moisture absorption % ± SD	Water vapor transmission gm.mm/cm^2. 24hrs % ±SD	Tensile strength and percentage elongation Kgf/cm^2	Drug content uniformity (mg)
F1	3.51 ±0.020	8.035 x 10^{-8} ± 0.437	240.73 & 0.290	29.73±0.02
F2	3.63 ±0.067	2.098 x 10^{-7} ± 0.035	237.53 & 0.284	29.53±0.21
F3	3.73 ±0.035	4.025 x 10^{-7} ± 0.080	222.41 & 0.279	29.81±0.19
F4	0.99 ±0.011	4.908 x 10^{-8} ± 0.361	200.32 & 0.279	29.44±0.35
F5	1.22 ±0.001	1.450 x 10^{-7} ± 0.031	189.51 & 0.273	29.68±0.48
F6	1.32 ±0.007	8.035 x 10^{-8} ± 0.437	222.01 & 0.282	29.88±0.35
F7	1.67 ±0.012	5.891 x 10^{-7} ± 0.400	231.52 & 0.286	29.71±0.09
F8	2.23 ±0.004	6.785 x 10^{-7} ± 0.252	213.54 & 0.279	29.71±0.29
F9	3.69 ±0.020	4.420 x 10^{-7} ± 0.049	217.72 & 0.262	29.66±0.32
F10	3.87±0.055	5.098 x 10^{-7} ± 0.048	223.49 & 0.273	29.87±0.19
F11	4.39 ±0.012	7.791 x 10^{-7} ± 0.561	221.01 & 0.271	29.61±0.22

The average of 6 readings was mentioned for each parameter.

Tensile strength & percentage elongation: The tensile strength and percentage elongation of film was measured by using tensile strength instrument. A film strips with the dimension [15 cm x 7.5 cm] and free from air bubbles (or) physical imperfection were prepared. This test was carried out with 50% humidity at 20^{o}C. The cross head speed employed were 100 mm / min, with full scale load range of 500 Kgf. The force and percentage elongation were measured, when the films were broken (Panigrah et al 2002).

Drug content uniformity: The film units of each formulation were cut in to smaller pieces, placed in media and then dissolved and made up to 100 ml in volumetric flask. From this sample was taken and analyzed for drug content by U.V. Spectrophotometer at 319 nm after dilution (Table.no:2).

RESULTS AND DISCUSSION

The prepared films of Indomethacin with polymers of hydroxyl propyl methyl cellulose, ethyl cellulose, poly vinyl pyrolidine either in combination or individual were found to be thin, flexible, smooth and transparent. The method adopted for casting the patch on the 'o' ring of glass substrate was found to be satisfactory.

From the results obtained from some of the physico – chemical evaluation such as water absorption capacity, percentage moisture loss, percentage moisture absorption, the formulation F11 (HPMC -3%, PVP -1%, WITH EC -1% as rate controlling membrane), shown higher values due to its hydrophilic nature and the formulation F4(EC-1 shown lower values due to its hydrophobic nature. Other formulations were between these values F2 (HPMC -2%), F3 (HPMC-3%), F9(HPMC-2%, PVP-1%) F10 (HPMC-3%, PVP-1%), values were high due to its higher concentration of hydrophilic polymers. Formulation F4(EC-1%), F5(EC-2%), F6(EC-0.75%, PVP-0.25%), F7(EC-0.5%, PVP-0.5%), F8 (HPMC-0.33%, EC-0.33%, PVP-0.33%), values were low due to its high concentration hydrophobic concentration (or) low concentration of hydrophilic polymers.

The thickness of the patches varied from 0.10mm for formulation F4 (EC-1%) to 0.28mm for formulation F11 (HPMC -3%, PVP -1%, EC -1% as rate controlling membrane). Other formulations were between these values like F1(HPMC-1%), F2(HPMC-2%), F3(HPMC-3%), F5 (EC-2%), F6(EC-0.75%, PVP-0.25%), F7(EC-0.5%, PVP-0.5%), F8(HPMC-0.33%, EC-0.33%, PVP-0.33%), F9(HPMC-2%, PVP-1%), F10 (HPMC -3%, PVP-1%), because propionate increase in concentration of polymer increases thickness of films. The folding endurance of the formulation F1 (HPMC-1%) was high and formulation F11(HPMC-3%, PVP-1% with EC-1% as rate controlling membrane) was low, others were between these values F2(HPMC-2%), F6(EC-0.75%, PVP-0.25%), F7(EC-0.5%, PVP-0.5%), F8(HPMC-0.33%, EC-0.33%, PVP-0.33%), F9 (HPMC -2%, PVP -1%), F10 (HPMC-3%, PVP-1%), the folding endurance values were high for hydrophilic polymers with less concentration. The film weight uniformity of the prepared formulation have shown that the process used to prepare the films in this study was capable of giving films with minimum intra batch variability. The water vapor transmission shown higher value for formulation F11 (HPMC -3%, PVP -1%, with EC -1% as rate controlling membrane) due to its hydrophilic nature and low values for formulation F4 (EC-1%) due its hydrophobic nature. Other formulation values were between these values, F1(HPMC-1%), F2(HPMC-2%), F3(HPMC-3%), F5 (EC-2%), F6(EC-0.75%, PVP-0.25%), F7(EC-0.5%, PVP-0.5%), F8(HPMC-0.33%, EC-0.33%, PVP-0.33%), F9(HPMC-2%, PVP-1%), F10 (HPMC -3%, PVP-1%) that indicates hydrophilic polymers of high concentration transmits more water. Drug content uniformity of 30mg confirms that prepared formulation have shown that the process used to prepare the films in this study was capable of giving films with uniformity in weight of intra batch variability. The Tensile strength and the percen-

tage elongation were also favorable to HPMC based matrix patches.

CONCLUSION

The selection of polymers to formulation of matrix type of transdermal patches and rate controlling membrane of transdermal therapeutic system are difficult. In the present research it proves that the drug Indomethacin along with the polymers of HPMC, EC , PVP & plasticizer of DBP produces smooth flexible patches with good tensile strength & percentage elongation. Drug content uniformity also confirms that the method selection for casting of the film was found to be reproducible.

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