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Research Article

FORMULATION AND EVALUATION OF KETOPROFEN TRANSDERMAL MATRIX PATCH CONTAINING DIFFERENT POLYMER COMPONENTS

ALI AFFAN SILALAHI*, KASMIRUL RAMLAN SINAGA, SUMAIYAH SUMAIYAH

Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Sumatera Utara, Medan, Indonesia.
Email: aliaffansilalahi@gmail.com

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ABSTRACT

Objective: The present study is to formulate and evaluate the ketoprofen transdermal matrix patch which containing different polymer components.

Methods: The transdermal matrix patch of ketoprofen was formulated using four formulas using polyethylene glycol 400, polyvinylpyrrolidone K-30, and ethyl cellulose as the polymer. The transdermal matrix patch was evaluated for various physicochemical characteristics and drug contain. The interaction between the polymers and ketoprofen was characterized using Fourier-transform infrared.

Results: Surfactants, cosurfactants, and oils used for the nanoemulsion formula are tween 80, ethanol, and isopropyl myristate (IPM). Formulation of ketoconazole nanoemulsion with comparison of tween 80 concentration with ethanol (smix) 4:1 and smix with oil 9:1 was found that the formulae F1, F2, F3, F4, F5, F6, and F7 are unstable and formulae F8, F9, F10, F11, and F12 are stable at the period of manufacture. The best physical stability tests from F8, F9, F10, F11, and F12 are F10.

Conclusions: Optimization of ketoconazole nanoemulsion formula was obtained at tween 80 36% concentration, 9% ethanol, and IPM 5%

Keywords: Ketoprofen, Transdermal, Patch, Polymer.

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INTRODUCTION

Topical drug delivery methods have advantages over other delivery methods, one of which is to avoid the metabolism of the first pass effect on the liver [1]. Physical-chemical characteristic of drugs and excipients are taken into consideration in designing formulas to produce a product that is stable, efficacious, attractive, easy to formulate, and safe. These characteristics affect several factors: Particle size distribution, drug dissolution rate, bioavailability, uniformity of content, taste, texture, color, and stability. The particle size and solubility of the drug have an effect on the formulation because the drugs entering the blood circulation must be in solution form to produce the desired effect (Fig. 1).

Ketoconazole is included in Class II of Biopharmaceutical Classification System means, including a class of low solubility and high permeability, the increased solubility of this drug is of concern to pharmaceutical researchers [2]. The absorption of ketoconazole orally is not maximal due to the solubility and the side effects it causes; to overcome the deficiencies of this conventional system a new drug delivery system is required. Topical ketoconazole available on the market today, such as cream has side effects such as rash, itching, irritation, pain, and redness; therefore, to overcome this problem requires a new drug delivery system such as nanoemulsion. Nanoemulsion has been widely used as a vehicle in topical medicine and is an alternative to insoluble, topical, or oral drugs.

Nanoemulsions are thermodynamically stable dispersions of two immiscible liquids (oil and water) which is stabilized using a surfactant and cosurfactant molecule. They may be either transparent or translucent and have a droplet size of 5–200 nm [3]. They are well-tolerated orally, on the skin and mucous membrane when used to deliver topically active drugs. Nowadays, increasing drug loading, enhancing drug solubility, and bioavailability are the most important advantages of encouraging the usage of nanoemulsion as drug delivery carriers. A topical nanoemulsion is a form of delivery for a drug that is difficult to dissolve and has side effects when administered orally by increasing the penetration of the drug through the skin [4]. Nanoemulsions comprise safe surfactants with or without other emulsifiers to improve stability, oil (natural/synthetic/semi-synthetic), and cosurfactant [4].

The method of nanoemulsion formulation is divided into two methods that use high energy and low energy. High energy formulations require tools such as high-pressure homogenizers, Microfluidizers, and sonicators, and low energy formulation methods dependent on the solubility of the active substance so that it is more efficient to make a small droplet nanoemulsion. Nanoemulsions produced with low energy methods depend on the spontaneous formation of emulsions based on the phase behavior of certain surfactant, oil, and water systems. There is interest in using lower energy techniques in the emulsion formation process due to the economic benefits, and increasing amounts of research have been conducted to investigate the utility of different low-energy approaches. Self-emulsifying systems offer a strategy for dealing with the low bioavailability of compounds (drugs and oils) that are not easily dissolved in water [5].

A low energy emulsification or spontaneous emulsification method used by the laboratory scale to achieve small droplet size using simple instruments [6]. The advantage of the low energy method is that it can use simple equipment such as a magnetic stirrer, which includes low energy manufacturing methods are phase inversion temperature and phase inverse composition. The nanoemulsion method of PIC which is often performed for laboratory scale is by spontaneous emulsification [7-10].

MATERIALS AND METHODS

Materials

Ketoprofen was purchased from PT. Dexa Medica (Indonesia). Polyethylene glycol (PEG) 400 (Merck), polyvinylpyrrolidone (PVP) K-30 (Merck), ethyl cellulose (EC) (Merck), Chloroform (Merck), Methanol (Merck), and Menthol (Merck) were used. All the ingredients were of analytical grade.

Formulation of ketoprofen matrix transdermal patch

Matrix transdermal patch of ketoprofen was prepared using the solvent evaporation method. The polymeric solvent was prepared by dissolving all the polymer (PEG, PVP, and EC), menthol and active chemical compound (ketoprofen) in the blend of chloroform and methanol (1:1). The polymeric mixtures then poured into a mold and kept at room temperature until dry. The formulas design of ketoprofen matrix transdermal patch is shown in Table 1.

Physicochemical compatibility of drug and polymers

The compatibility of the drug and polymers was studied using a Shimazu Fourier-transform infrared (FTIR) spectrophotometer in range 4000–400/cm. The FTIR spectra of drug and polymers in the mixture are compared for the presence or absence of incompatibility [11].

Evaluation of ketoprofen matrix transdermal patch

Visual

The visual of matrix transdermal patch parameters is color, odor, texture, and film flexibility [12].

Weight variation

The weight variation five patches were weighed on an electronic balance, and the average of weight was taken with SD [12].

Film thickness

The thickness of films was measured by micrometer screw at five different sites, and average of five readings was taken with SD [12].

Moisture uptake

The percentage of moisture uptake was calculated as the difference between final and initial weight with respect to initial weight [12].

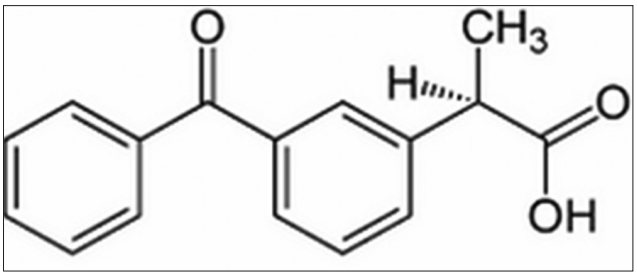

Fig. 1. The structure of ketoprofen

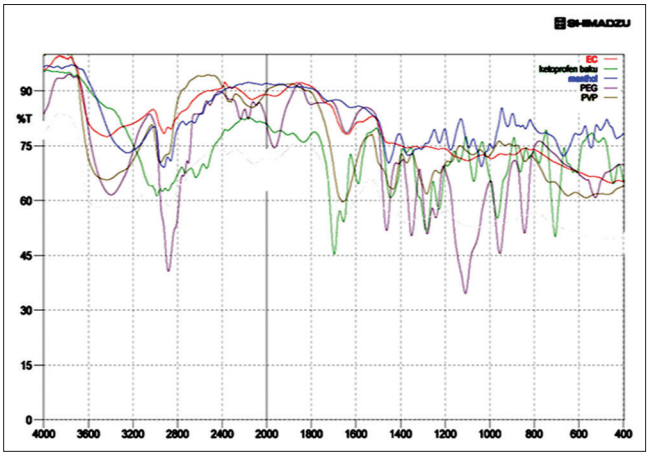

Fig. 2. The Fourier-transform infrared spectra of drug and polymers

$$\%\,\text{of Moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Intial weight}} \times 100\%$$

Folding endurance

The folding endurance was measured manually for prepared films. A strip of film was folded at the same place till it broke. The number of time the film can be folded at the same place without breaking was the folding endurance value [13].

Drug content

A 0.1 mm thickness of the film was cut and put it into a 100 ml phosphate buffer (pH 7.4) and ultrasonicated for 15 min with a stirrer. After filtration, the drug was estimated spectrometrically at wavelength of 260 nm and determined the drug content compared using the calibration curve of ketoprofen [12].

RESULTS AND DISCUSSION

Physicochemical compatibility study

All the characteristic peaks of the pure drug ketoprofen were retained in drug and polymers physical mixtures, which indicate that the drug and polymers are compatible. The result of the FTIR studies was shown in Figs. 2 and 3.

Evaluation of ketoprofen matrix transdermal patch

The results of evaluation of various visual and physicochemical parameters of the ketoprofen matrix transdermal patch were presented

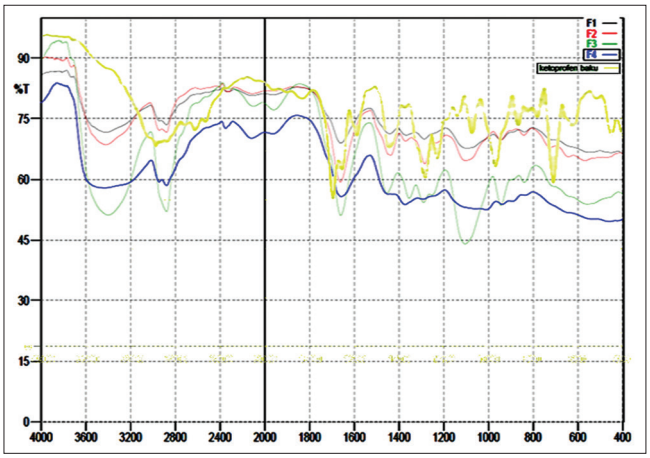

Fig. 3. The Fourier-transform infrared spectra of drug and polymers in a physical mixture of four formula

Table 1: Formula design of ketoprofen matrix transdermal patch

Composition (in mg)	Formula			
	F1	F2	F3	F4
PEG	85	170	42.5	42.5
PVP	85	42.5	170	42.5
EC	85	42.5	42.5	170
Menthol	25	25	25	25
Ketoprofen	20	20	20	20

PEG: Polyethylene glycol, PVP: Polyvinylpyrrolidone, EC: Ethylcellulose

Table 2: Visual evaluation of ketoprofen matrix transdermal patch

Formula	Color	Odor	Texture	Flexibility
F1	White	Odorless	Flat surface	Not flexible
F2	Transparent	Odorless	Flat surface	Flexible
F3	Transparent	Odorless	Flat surface	Flexible
F4	White	Odorless	Flat surface	Not flexible

Table 3: Physicochemical evaluation and drug content

Formula	Physicochemical parameter				
	Weight (mg)	Thickness (mm)	Moisture uptake (%)	Folding endurance	Drug content (%)
F1	272±5.89	0.977±0.00057	1.1±0.015	<200	97.68
F2	2.82±1.52	0.968±0.00057	2.57±0.214	<200	95.26
F3	283±2.51	0.961±0.00057	2.83±0.050	<200	97.98
F4	265±3	0.989±0.0066	1.68±0.158	<200	97.50

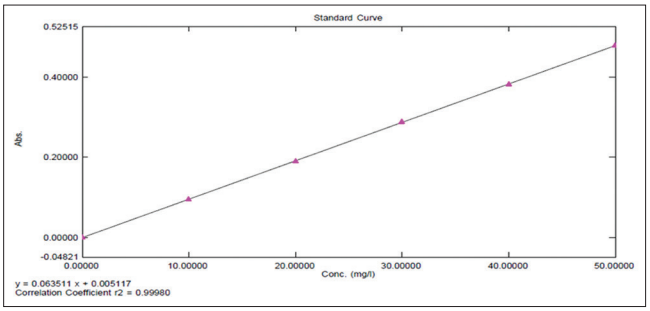

Fig. 4. The calibration curve of ketoprofen

in Tables 2 and 3. The calibration curve of ketoprofen was presented in Fig. 4. All the physicochemical parameters meet the applicable requirements. The drug content was also studied for all formulations indicating that the method used to formulated this ketoprofen matrix transdermal patch was suited or not.

F3 showed the heaviest weight compared to other formulas. In F3, it showed that the PVP is the main factor that affects the weight because PVP is a hygroscopic agent. F4 showed the thickest thickness layer compared to other formulas. It can happen due to the ES content. This is because the ES polymer if excessively given will form a thick and uneven fiber that affects the weight of the patch [14-16]. The calibration curve of ketoprofen in 260 nm wavelength showed a good coefficient correlation (0.9998). The coefficient correlation can be accepted which the value of the coefficient correlation should not smaller than 0.995 [17,18]. Moisture uptake and drug content result, all the formula showed a good percentage in the range that can be accepted. Folding endurance result showed that all formula can be accepted [19,20].

CONCLUSIONS

In the present study, various formulations of the ketoprofen matrix transdermal patch were prepared. On the evaluations and FTIR study, all the formulas showed good uniformity and acceptable. Hence, it can be concluded that these three type of polymers (PEG, PVP, and ES) can be used as a polymer base for formulating ketoprofen transdermal drug delivery system.

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AUTHOR'S CONTRIBUTION

All the author have contributed equally.

CONFLICTS OF INTEREST

Declared none.

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