ISSN No:-2456-2165

Design Formulation and Evaluation of Transdermal Patch of Aspirin Using Polymer Variation

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Abstract:- Oral aspirin treatment in the secondary prevention of heart and cerebral vascular disease is well known. However, oral administration can cause damage to the gastrointestinal mucosa until bleeding occurs. These problems can be overcome by development of transdermal drug delivery system. The objective of this study was to develop and evaluate the transdermal patches of aspirin.Giving aspirin by transdermal patch with matrix type to increase the antithrombotic efficiency of aspirin. The principle of making transdermal patches by solvent evaporation with aspirin and polymer such as Eudragit RS 100, Eudragit RL 100, Ethyl Cellulose, Polyvinyl pyrrolidone, and Polyvinylacetate. The prepared formulations were uniform in their physical characteristics. The formulation F1-F4, combination of polymer (Eudragit RL 100 :EudragitRS 100) showed better performance. The results specify that aspirin transdermal patch can be designed for obtaining better therapeutic benefits.

Keywords *:- Aspirin; Polymers; Eudragit; Ethyl Cellulose; Polyvinyl pyrrolidone; Polyvinylacetate.*

I. INTRODUCTION

In 2013, cardiovascular disease accounted for 800,937 of 2,596,993 deaths and is the number five death in the United States [1]. Cardiovascular disease is one of the main causes of morbidity and mortality worldwide, so the development of effective drugs for the prevention and treatment of these diseases has increasingly attracted worldwide attention [2].

Platelet anti-agregration and anti-inflammatory have played an important role in the prevention and treatment of myocardial infarction and thrombosis since the 1970s [2]. Evidence-based has shown that anti-platelet therapy such as aspirin is a common management in the management of vaso-occlusive events such as stroke, myocardial infarction, and coronary artery disease; can reduce the incidence rate of 25% in heart, brain and peripheral thromboembolic disease; and is a major contributor to primary and secondary prevention of cardiovascular disease [3].

Aspirin given orally requires high doses and is frequent because aspirin undergoes extensive pre-systemic hydrolysis in the intestine and liver to salicylic acid and thus has no antiplatelet activity [4]. Aspirin is rapidly absorbed in the acidic environment of the stomach and alkaline in the small intestine, resulting in less than 50% of oral bioavailability [5]. Giving aspirin orally can cause gastrointestinal mucosal damage to bleeding, due to inhibition of cyclooxygenase which limits clinical use as a primary and secondary prevention of cardiovascular disease and can lead to treatment discontinuation [6].

Transdermal delivery offers an alternative route for administration of aspirin that is more convenient and safer for long-term use of low-dose aspirin as a primary and secondary prevention of cardiovascular disease; and inhibits platelet function by maintaining the inhibitory effect of COX-2 and minimizing the vascular effect of COX-1, so that aspirin therapy can be used without risk to the gastrointestinal tract.Aspirin is polar at physiological pH and rapidly hydrolyzes to salicylic acid in the skin, making it not a good candidate for transdermal delivery. However, a low dose of aspirin is needed per day to suppress platelet COX [6].

Therefore, efforts are needed to improve the bioavailability of drugs administered transdermally by formulating aspirin into transdermal patch preparations with the aim of increasing the therapeutic effect, safety and stability, and to deliver controlled doses of drugs through the skin within a certain period of time. Transdermal patch is a drug delivery system that can distribute drugs to systemic circulation with controlled release rates using polymers [7].

In general, the patch formulation method is divided into 2 types of systems, namely the matrix system and the membrane system [8]. This research will use a matrix system type that can regulate the release of active medicinal ingredients from patch preparations by considering the type of polymer to be used [9]. In addition, the formed patch is thin and elegant so it is comfortable to use. [10].

II. MATERIALS AND METHODS

2.1 Materials

Aspirin, Ethyl Cellulose, Polyvinyl pyrrolidone, and Polyvinylacetate were purchasedfrom ASEAN Indonesia. Eudragit RL 100 and RS 100 were kindly gifted by IMCD Indonesia. All other chemical were of analytical or higher grade.

2.2 Formulation of Transdermal Patch

To determine the optimum combination of polymers, plasticizer and solvents, placebo films were formulated. Matrix type transdermal patch of Aspirin were prepared by

ISSN No:-2456-2165

solvent evaporation technique using different proportions of polymers like Eudragit RS 100, RL 100, Ethyl Cellulose, Polyvinyl pyrrolidone, and Polyvinylacetate in beaker glass, then add diethyl phthalate as plasticizer, while stirring using a magnetic stirrer for 2 hours. The mixture was prepared in a homogeneous dispersion, under slow stirring under magnetic stirrer for 2 hours. After that, it was poured in aluminum foil and dried at room temperature for 24 hours.

Table 1. Composition of Transdermal Patch

Formulation Code	Drug (w/w)	Polymer	Ratio	Plasticizer (w/w)	Solvent
F1	30	ERL 100 : ERS 100	3 : 1	Propylene glycol	Ethanol
F2	30	ERL 100 : ERS 100	3 : 1	Diethyl Phthalate	Ethanol
F3	30	ERL 100 : ERS 100	1: 0	Propylene glycol	Ethanol
F4	30	ERL 100 : ERS 100	1 : 0	Diethyl Phthalate	Ethanol
F5	30	EC : PVP	3 : 1	Propylene glycol	Ethanol
F6	30	EC : PVP	3 : 1	Diethyl Phthalate	Ethanol
F7	30	PVA : PVP	1 : 0	Propylene glycol	Ethanol
F8	30	PVA : PVP	1 : 0	Diethyl Phthalate	Ethanol

2.3 Evaluation of Transdermal Patch

All the prepared transdermal patches were evaluated by the following parameters:

a. Physical appearance

All the prepared patches were visually inspected for color, clarity, entrapment of any air bubble, flexibility andsmoothness.

b.Thickness

Thickness of the patch was measured by using screw micrometer at five different points and average thickness was determined.

c. Weight variation

5 patches from each formulation were weighed individually and the average weight was calculated. The individualweight should not deviate significantly from the average weight.

d.Folding endurance

Folding endurance was determined by repeatedly folding a small strip of patches at the same place till it broke. The number of times patches could be folded at the same place, without breaking gave the value of folding endurance and it was recorded.

e. Moisture content

The patches were accurately weighed and kept in a desiccator containing calcium chloride 24 hrs. Then theconcluding weight was noted. It can be calculated by following formula

$$\% \text{ Moisture content} = \frac{\text{Initial Weight} - \text{Final Weight}}{Final\ Weight}\ x\ 100\%$$

f. Drug content

A specified area 2x2 of patch was dissolved in mixtureof ethanol. It was closed and magnetic stirrer for 24 hours in a shaker. The resulting solutionwas filtered and the amount of drug present in the filtered was determined by using UV-VIS spectrophotometer at 528 nm.

Organoleptic properties of the drug were found within limits as shown in Table 2.

Table 2: Organoleptic Properties of Transdermal Patch

Formulation Code	Color	State	Odor
F1	Transparent	Less Crystalline	Odorless
F2	Transparent	Less Crystalline	Odorless
F3	Transparent	Less Crystalline	Odorless
F4	Transparent	Less Crystalline	Odorless
F5	White to off white	More Crystalline	Odorless
F6	White to off white	More Crystalline	Odorless
F7	White to off white	More Crystalline	Odorless
F8	White to off white	More Crystalline	Odorless

The formulated patch at F1 until F4 were found to be transparent, smooth, uniform, less crystalline and odorless, while F5 until F8 were found to be white, uniform, more crystalline and odorless. All formulated patches were found free from entrapment of air bubble.

The thickness of the transdermal patches for 8 different polymer ratio varied from 0.154±0.005 to 0.182±0.002 mm. Low standard deviation values indicates that all the prepared patches were are nearly uniform thickness. The results are given in table 3.

The weight of the transdermal patches for 8 different polymer ratio varied from 67.133±0.208 mg to 68.633±0.208 mg. The variation in weight uniformity of the

ISSN No:-2456-2165

prepared patches was within acceptable range. The results are given in table 3.

The folding endurance of the transdermal patches for 8 different polymer ratio is up 700. The result was found satisfactory indicating that the patches would not break and would maintain their integrity when used. The results are given in table 3.

The percentage moisture content is found to be high for the patches formulated with EC:PVP when compared to the patches formulated with ERL100:ERS100 and PVA. The reason behind this might be the higher proportions of hydrophilic polymer, PVP along with EC; whereas patches with ERL100:ERS100 combination shows lesser moisture content because of the highly hydrophobic polymer, ERS100. The results are given in table 3.

The drug content of the transdermal patches for 8 different polymer ratio varied from 95.367±4.87 to 99.652±2.489 mg. The results are given in table 3.

Table 3. Evaluation of Transdermal Patch

Formulation Code	Thickness (mm) ± SD	Weight Variation (mg) ± SD	Folding Endurance ± SD	Moisture Content (%) ± SD	Drug Content (%) ± SD
F1	0.154± 0.005	67.133 ±0.208	≥700	1.142± 0.231	95.367 ±4.87
F2	0.155± 0.003	67.567 ±0.208	≥700	1.038± 0.150	96.355 ±3.088
F3	0.156± 0.004	67.5±0. 265	≥700	1.134± 0.150	97.509 ±2.897
F4	0.157± 0.002	67.4±0. 2	≥700	0.791± 0.308	96.85± 1.978
F5	0.178± 0.002	68.633 ±0.208	≥700	2.566± 0.215	98.663 ±1.736
F6	0.182± 0.002	68.3±0. 2	≥700	1.952± 0.365	96.85± 6.313
F7	0.172± 0.004	67.667 ±0.153	≥700	1.527± 0.168	99.652 ±2.489
F8	0.172± 0.005	67.333 ±0.153	≥700	1.386± 0.226	97.344 ±4.047

III. CONCLUSION

Preparation transdermal patches of aspirin have been successfully by solvent evaporation technique. Evaluation of the prepared patches in terms oforganoleptic, weight, thickness, moisture content and drug content uniformity recommend that the method employed for formulation of the transdermal patches was reproducible and assured outstanding quality and uniformity in patch characteristics with least variability.

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