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THE INFLUENCE OF PROPYLENE GLYCOL AND PEG 400 AS PLASTICIZER AGAINST PHYSICAL PROPERTIES PATCH OF ARECA CATECHU L. SEEDS EXTRACT

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ABSTRACT
Extract of *Areca catechu* L. seeds was formulated in patch preparation. Components that affect the physical properties of the patch are polymers and plasticizers. The polymer that used was a combination of HPMC-PVA. While Propylene Glycol and Poly Ethylene Glycol (PEG) 400 as a plasticizer. The research aim is to determine the influence of Propylene Glycol and PEG 400 as a plasticizer on physical properties of the patch. The evaluation includes weight uniformity, the percentage of water content, thickness, tensile strength and the percentage of elongation patch. The results showed that Propylene Glycol plasticizer can produce the patch with average weight 0,4546 g, the percentage of water content 8,6731%, thickness 0,1898 mm, tensile strength 0,15 Kgf/mm^2 and the percentage of elongation 65,2222%. While plasticizer PEG 400 produces patch with average weight 0,5032 g, the percentage of water content 7,4234%, thickness 0,2123 mm, tensile strength 0,5370 Kgf/mm^2 and the percentage of elongation 58,95%. The conclusion is that Propylene Glycol and PEG 400 as plasticizers affect the physical properties of the patch including uniformity of weight, thickness, and tensile strength, which PEG 400 is the best plasticizer in patch formulation of *A. catechu* L extract.

KEYWORDS: Patch, plasticizer, propylene glycol, PEG 400.

INTRODUCTION

A. catechu L. seeds is one of the plants in Indonesia that can be used to treat wounds.[1] Tannin compound from *A. catechu* L. seeds have an astringent effect. Astringent works to shrink open skin tissues and to stop infections.[2] Previous research showed that *A. catechu* L. seeds extract could accelerate wound healing in male white rats on Wistar strain with an effective concentration of 2%.[3]

Extract used as a wound healer which has limitations in its application, then the alternative preparation is needed that can deliver the effects of *A. catechu* L. seeds extract. One alternative that can be used is to formulate it into a patch.[4] The polymers are used to deliver active substances to specific locations and to optimize drug delivery due to longer contact.[5] The polymers that can be used are Hydroxy Propyl Methyl Cellulose (HPMC) and Polyvinyl Alcohol (PVA). HPMC as a polymer has the advantage of being able to produce the patch with maximum bioadhesion properties.[6] The advantages of using PVA as a polymer that can cause elastic and flexible patch.[7] The plasticizer can increase tensile strength, elongation, and flexibility of patch.[5] Plasticizers commonly are used propylene glycol (PG) and PEG 400. PG as a plasticizer can produce transparent films with highest folding endurance, tensile strength, and elongation percent.[8] Meanwhile, PEG 400 as a plasticizer that is able to produce a patch matrix with the highest tensile strength.[9]

Research on the formulation of *A. catechu* L. seeds is still limited, then making the patch of *A. catechu* L. seeds extract is relatively new and has never been done. This study aims to determine the influence of using PG and PEG 400 as plasticizers that can produce *A. catechu* L. seeds patch with a uniformity of weight, the minimum the percentage of water content, the highest thickness, tensile strength and the percentage of elongation.

MATERIALS AND METHOD

Extract of *A. catechu* L. seeds, HPMC type M60SH50, PVA, PEG 400, PG (Dow Chemical Co.), methylparaben, ethanol 96% (E Merck), distilled water (local), anhydrous sodium sulfate (technical).

Extraction of *A. catechu* L.

The simplicia powder from of *A. catechu* L. seeds was used 500 g. The powder was added ethanol 70% with occasional stirring, then let stand for 2x24 hours. The obtained macerate is separated by filtration by Buchner funnel. This process is repeated 3 more times with the same type of solvent. Maceration was carried out for 13 days. All the macerates are collected, then evaporated with Rotary Evaporator.[3] Then it was oven at 40^0C until a viscous extract was obtained.

Standardization of extracts
Standardization of extracts was carried out includes organoleptic, water-soluble compound and loss on drying.

Preparation of patch
The composition of the formula was described as shown in Table (1).

Table 1: Patch formulations of *A. catechu* L. Extract.

No.	Materials	F1 (%)	F2 (%)
1.	*A. catechu* L. Seeds extract	2	2
2.	HPMC	6	6
3.	PVA	4	4
4.	PG	10	-
5.	PEG 400	-	10
6.	Methylparaben	0,3	0,3
7.	Ethanol	40	40
8.	Distilled water	Add 100	Add 100

The patch was prepared by dissolving extract in distilled water and ethanol. HPMC was dissolved in distilled water and PVA was dissolved in hot water. Then both solution were mixed together until homogeneous. Methylparaben was dissolved in a plasticizer (PG/PEG 400) and it was added to the solution. Finally, distilled water was added up to 10 g of the total mixture. Then the mixture allowed to stand for ± 24 hours at room temperature to remove the bubbles. After 24 hours, ±3 g of the mixture was poured in the petri dish. Then the mixture was dried in an oven at 50ºC and stored in the desiccator for ±20 hours. The dried patch was removed from the petri dish and kept in sealed plastic pouches until further use. Patch was made up of 3 batches for each formula.[10,4,11]

Weight uniformity
Each patch was weighed individually and the average weight of the patch was calculated. This test was done in 3 replication.[10]

The percentage of water content
The patch was weighed and placed inside a desiccator containing anhydrous sodium sulfate for 24 hours. After 24 hours, the patch was taken out and weighed. The percentage of water content was calculated using the formula:[10]

$$\text{Water Content} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \text{ x } 100\%$$

Thickness
The thickness of each patch was measured using a digital micrometer at 5 different locations (center and four corners). The mean thickness and standard deviation values were calculated.[10]

Tensile strength
The tensile strength of the film was determined with Universal strength testing machine (Shimadzu type AGS-500D). The sensitivity of the machine was 1 g. The test film of size (4 × 2 cm^2) was fixed between these cell grips and force was gradually applied till the film broke. The tensile strength of the film was taken directly from the dial reading in kg. Tensile strength was calculated using the formula:[11]

$$\text{Tensile Strength} = \frac{\text{Force At Break (Kgf)}}{\text{Cross} - \text{sectional Area Of The Film } (mm^2)}$$

The percentage of elongation
The percentage of elongation is a measurement of the maximum deformation the film can stretch before tearing apart. The percentage of elongation was calculated using the formula.[10]

$$\%\ \text{Elongation}\ \frac{b-a}{a} \text{ x } 100\%$$

**Where, a = initial length*
b = length after breaking up

Data analysis
The data were analyzed to compare between PG and PEG 400 as plasticizer. The evaluation includes weight uniformity, the percentage of water content, thickness, tensile strength and the percentage of elongation of the patch. Data analysis was done using the SPSS program (PASW Statistics 22) by the Independent Sample T-Test method.

RESULTS

Table 2: Results of standardization of extracts.

No	Parameters	Result
1.	Organoleptic	Consistency: Thick Color: Reddish-brown Smell: Typical Taste: Chelate
2.	Water-soluble compound (%)	30,217±0,745
3.	Loss on drying (%)	19,138±2,013

Table 3: Result of weight uniformity.

Formula	Weight uniformity (g) ± SD
F1 (PG)	0,4546 ± 0,0115
F2 (PEG 400)	0,5032 ± 0,0138

Table 4: Result of the percentage of water content.

Formula	The percentage of water content (%) ± SD
F1 (PG)	8,6731 ± 3,2123
F2 (PEG 400)	7,4234 ± 2,2486

Table 5: Result of thickness.

Formula	Thickness (mm) ± SD
F1 (PG)	0,1898 ± 0,0103
F2 (PEG 400)	0,2123 ± 0,0244

Table 6: Result of tensile strength.

Formula	Tensile strength (Kgf/mm^2) ± SD
F1 (PG)	0,1500 ± 0,0433
F2 (PEG 400)	0,5370 ± 0,0320

Table 7: Result of the percentage of elongation.

Formula	The percentage of elongation (%) ± SD
F1 (PG)	65,2222 ± 12,5765
F2 (PEG 400)	58,9500 ± 8,8193

DISCUSSION

Extraction and standardization of extracts

Extraction of *A. catechu* L. was using maceration method with ethanol solvent. *A. catechu* L seeds extract was obtained 26.037% maceration result. Standardization of *A. catechu* extract is summarized in Table (2).

Preparation and evaluation of patch

Combination of HPMC-PVA was used as patch base. In this formulation, formula F1 used PG as plasticizer (Fig. 1) and F2 used PEG 400 as plasticizers (Fig. 2). Methylparaben is used as a preservative, ethanol as co-solvent and distilled water as solvent. At the preparation, F2 using PEG 400 as plasticizers produce more foam compared to F1 using PG as plasticizers. But the foam on F2 disappeared faster than F1, this is because the PEG 400 can also function as an antifoaming agent. The patch was dried for 210 minutes. Then the patch on F2 looked rigid than F1.[12]

Fig. 1: Patch using PG.

Fig. 2: Patch using PEG 400.

Evaluation of weight uniformity was done to determine the variation of patch weights between formula.[13] From the results are shown in Table (3), it was observed that all the patch was uniform in weight and there was no significant difference in the weight of the formulations. The mass of the patches heavier with PEG 400 (F2) as plasticizer than patch using PG as plasticizer (F1). Previous studies on Aceclofenac patches showed that using PEG 400 as a plasticizer can increase patch weight rather than using PG, this is due to the high molecular weight of PEG 400 while comparing to PG, where the molecular weight of PG is 76.09 g/mol, while PEG 400 is 380-420 g/mol.[14,15]

Evaluation of the percentage of water content as shown in Table (4). The high of the percentage of water content can reduce patch acceptance and the effectiveness of the patch. Formula F1 uses PG as a plasticizer, had more water content than the F2 patch using PEG 400. SPSS analysis showed no significant differences in the percentage of water content between the formula ($p > 0.05$). The percentage of moisture content F1 and F2 were low (<10%), it can help them to remain stable and protect the material from microbial contamination.[16,17]

Evaluation of thickness as shown in Table (5). From the results, F1 was thinner compared to F2 and the SPSS analysis showed that there was a significant difference in thickness between the formula ($p > 0.05$). This was related to the results evaluation of weight uniformity, which is patch thickness increases with increasing patch weight.[18]

Tensile strength evaluation was done to determine the strength of the film and explains the risk of film cracking.[19] From the result are shown in Table (6), F2 using PEG 400 produce greater tensile strength than F1 using PG. SPSS analysis showed a significant difference between the formula ($p > 0.05$). Tensile strength is affected by a decrease the disruption in continuity of polymer chain molecules.[20] The molecular weight of the plasticizer also affects the tensile strength. PG has a smaller molecular weight than PEG 400. The low molecular weight plasticizers can increase the space between the polymeric chains, then reducing the tensile strength.[21] The higher value of tensile strength, the resistance of the patch to damage due to stretching and pressure also increases.[22] Optimum tensile strength can keep the patch on the skin and withstand the movements of daily life.

The percentage of elongation is defined as the ability of film to deform before finally breaking. Evaluation of elongation percentage was done to determine the flexibility and stretchability of films.[23] Formula F2 using PEG 400 as a plasticizer was produced the greater percentage of elongation than F1 using PG as shown in Table (7). However, the SPSS analysis showed no significant differences between F1 and F2 ($p > 0.05$). The high percent of elongation patch was caused by the plasticizers which can reduce intermolecular attraction by forming hydrogen bonds between the polymer chain or by blocking the chains, allowing more flexibility and reduce rigidity.[24] The patch is expected to have the relative high tensile strength and elongation percentages.[25,26]

CONCLUSION

PG as plasticizer produces the patch with lighter, thinner, and lower tensile strength values. While PEG 400 as plasticizers produce the patch with heavier, thicker weight and higher tensile strength values. Then the best formula based on evaluation is F2 using PEG 400 plasticizer.

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