Preparation Characteristic and Wound Healing Activity of Papaya Leaves Extract on Spray Gel

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Preparation, Characterization, and Wound Healing Activity of Papaya Leaves Extract on Spray Gel

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ABSTRACT

Papaya leaves have been using for wound healing that contains flavonoids, saponins, phenolics, chymopapain, and papain enzymes. The aim of this research was preparation, characterization, and wound healing activity of papaya leaves extract on spray gel. Spray gel was formulated with the variation of a gelling agent such as carbopol 940, HPMC, gellan gum, and hydroxyethylcellulose. The spray gel was characterized by organoleptic, pH, stickiness test, viscosity, homogeneity, weight, and wound healing activity in rats. The results showed were all of the formula spray gel have brown and homogeneous, pH between 5,947-6,347 within pH range of skin, stickiness test between 1,92-8,12 s, viscosity between 880-1740 cPs. Papaya leaves extract on spray gel has wound healing activity in rats faster than extract and positive control that is 16 days. The wound healing of papaya leaves extract on spray gel exhibited significantly different ($p<0,05$) than the negative control.

Keywords: Spray gel; papaya leaves; carbopol 940; HPMC; hydroxyethylcellulose

INTRODUCTION

Wound is damage or loss of body tissue due to factors such as trauma, temperature changes, chemicals, explosion, electric shock, or animal bites (Pusponegoro, 2005). Based on the cause, the wound is divided into two namely open wounds and close wounds. The wound healing process is influenced by fibroblast components. This component is a cell that exists in connective tissue that produces collagen precursor substances, elastic fibers, and reticular fibers (Marcovitch, 2005).

The medicinal plants that can be used as wound healing and antibacterial activities are the papaya (*Carica papaya* L.) especially the leaves. Papaya leaves contain are flavonoids, phenolics, saponins, papain enzymes, and chymopapain that have the activity of wound healing. Flavonoids have antioxidant and inflammatory activity possible in the wound healing process. The ability of flavonoids in the wound healing process is to inhibit uncontrolled inflammation. Inflammation can inhibit skin regeneration and exacerbating the wound into chronic (Hatahet *et al.,* 2016). Saponins can trigger collagen synthesis which is directly related to the formation of fibroblasts that play a role in the wound healing process (Femilian *et al.,* 2019). Papain enzymes and chymopapain reported have antibacterial and anti-inflammation activities. Papain enzymes have potent anti-inflammatory activity that works with vitamin A, C, and E to inhibit inflammation. Papain enzyme has antibacterial activity by break protein bonds into arginine that phagocytic activity of macrophages increases by producing NO which is toxic to kill bacteria (Mahmood *et al.,* 2005).

The development of topical pharmaceutical dosage forms in increasingly rapid, including gels, creams, and ointments. The gel is the ideal dosage form as a wound cover because it feels cold on the surface of the skin that is injured and easily penetrates the skin (Boateng *et al.,* 2008). The development of topical preparations is spray gel which has a fairly low viscosity. Besides being easy and practical in its use, these spray gel preparations have advantages such as being cool, moisturizing, and can penetrate the skin (Ansel, 1989). Spray delivery can increase polymer penetration into the wound area, making the potential for the delivery of active substances more efficient. According to Suyudi (2014) the spray gel formulations required additional ingredients such as humectants, preservatives, and gelling agents.

In the spray gel formulation, the gelling agent is the main component of this preparation. Many types of gelling agents can be used to make spray gel preparations including carbopol 940, gellan gum, HPMC 60SH, and hydroxyethylcellulose. The addition of a gelling agent can affect the physical properties of the preparation such as viscosity and dispersion (Dahlizar *et al.*, 2018). Harahap (2018) study showed that the concentration of carbopol 940 had significantly improving the response of study and washability.

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The purpose of this study are the preparation, characterization, and wound healing activity of papaya leaves extract on spray gel with a variation of gelling agents to show an effect on physical characteristics and wound healing activity.

METHODOLOGY

Materials

The materials used in this study were papaya leaves extract (Farmasi FMIPA UNSRI), ethanol 70% (Bratachem), methanol (Bratachem), quercetin (Sigma Aldrich), carbopol 940(Sigma Aldrich), gellan gum (Sigma Aldrich), HPMC 60SH (Sigma Aldrich), hydroxyethylcellulose (Sigma Aldrich), propylene glycol (Bratachem), triethanolamine, lidocaine, ethyl acetate (Sigma Aldrich), Tekasol® (*Centella asiatica* extract 1%).

Test Animal Preparation

The animals used in this study (according to procedures and ethics) were male *Sprague dawley* rats with a weight of 100-150 g and aged 2-3 months obtained from Palembang Tikus Centre.

Methods

Extract Preparation

Samples of papaya leaves were taken in Desa Lubuk Kelik of Provinsi Kepulauan Bangka Belitung. Papaya leaves determined by Herbarium ANDA Jurusan Biologi FMIPA Universitas ANDALAS. Papaya leaves washed with tap water, sorted, dried under the sun,

The 6 kg of papaya leaves macerated in 20 L ethanol 70% then filtered. The filtrate re-macerated with ethanol 70% until was clear. The filtrate was then concentrated with a rotary evaporator at 50°C. The calculated value of rendemen papaya leaves extract (Melia azedarach Linn.)

Spray Gel Preparation

The spray gel of papaya leaves formulations were prepared by heating-cooling method; carbopol 940 and HPMC 60SH were dispersed and dissolved in water at 90°C; Gellan gum was dispersed and dissolved in water at 70°C; hydroxyethylcellulose was dispersed and dissolved in warm water. Then, Methylparaben and propylparaben dissolved in propylene glycol and stir into the basis until homogeneous. Extract of papaya leaves added to the mixture and stirred until homogeneous. After stirring, spray gel was remained at room temperature. The spray gel without papaya leaves extract was also prepared. Table I shows the compositions of the spray gel of papaya leaves formulation.

Characterization of Papaya Leaves on Spray Gel Formulations

Characterization of the papaya leaves on spray gels such as organoleptic, pH, stickiness test, viscosity, and homogeneity. Organoleptic were performed to show the physical appearance of the preparation. The pH of spray gel formulations were measured by pH meter (Lutron®). The stickiness was measured by place filter paper which has been immersed in NaCl in a 40° slope. Spray gel was sprayed with distance of 3 cm on the filter paper. The time until drop was calculated. The viscosity of spray gel was measured by viscometer (RION®). The homogeneity of papaya leaves on spray gel was observed aggregate on spray gel. The weight of a single spray of formulation was measured by weighing the samples.

Wound Healing Activity Test

Rats with open wound made using puch biopsy with a diameter ± 1 cm and a dept of ± 2 mm in the dorsal part of the rats (Figure 1). The divisin of animal group test as in Table II of each animal group was given treatment in each formula of spray gel one spray every 24 hours for 20 days.

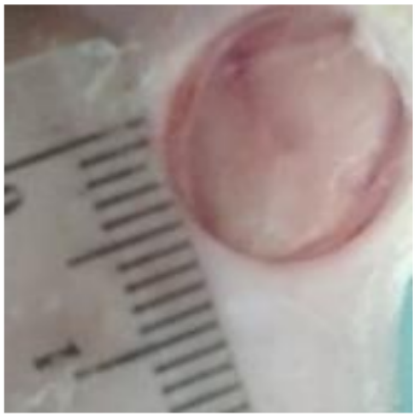

Figure 1. Excision skin wound before application of spray gel

Wound Healing Observation

Observation made on this wound healing test are the area of wound healing (%recovery). The area of wound observed was measured by the average diameter of the wound in the vertical direction (d1), horizontal (d2), and second diagonally (d3 and d4). Observation of wound

Table I. Conposition of The Papaya Leaves on Spray Gel Formulation

Ingridient (%)	P1	P2	P3	F1	F2	F3
ExPl	-	-	-	5	5	5
Cb_{940}	0,92	1,2	-	0,92	1,2	-
HPMC	1,2	-	0,56	1,2	-	0,56
GG	-	0,21	-	-	0,21	-
HEC	-	-	0,61	-	-	0,61
PG	15	15	15	15	15	15
MP	0,18	0,18	0,18	0,18	0,18	0,18
PP	0,02	0,02	0,02	0,02	0,02	0,02

Abbreviations: ExPl, papaya leaves extract; Cb_{940}, carbopol 940; HPMC, hidroxypropylmethylcellulose 60SH; GG, gellan gum; HEC, hydroxyethylcellulose; PG, propylene glycol; MP, methyl paraben; PP, propyl paraben.

Table II. Physical Characterization of Papaya Leaves on Spray Gel Formulations

Sample code	pH	Stickiness (s)	Viscosity (cPs)	Homogeneity	Weight (g)
P1	7,377±0,021	17,407±0,021	10500±0	√	-
P2	7,327±0,015	82,177±0,238	9500±0	√	-
P3	7,330±0,010	1,277±0,050	2900±0	√	24,982±0,013
F1	5,947±0,015	10,562±0,435	1740±0	√	24,981±0,012
F2	5,597±0,015	1,740±0,036	880±0	√	24,958±0,015
F3	6,347±0,015	1,543±0,050	1440±0	√	24,962±0,021

healing was carried out on the 4^{th}, 8^{th}, 12^{th}, 16^{th}, and 20^{th} days. The wound healing activity was marked by a decrease in the diameter of the wound area.

$$\text{Average diameter (d)} = \frac{d1+d2+d3+d4}{4}$$

The percentage of wound healing is calculated by the formula:

$$\% \text{ Recovery} = \frac{d0-dx}{d0} \times 100$$

Information: d = average diameter; d0 = diameter of wound after making wound; dx = diameter of wound on day-x observation

Statistical Analysis of Data

Statistical analysis for wound healing was performed using one way ANOVA method to find out the difference between significant formulas if the p-value <0,05.

RESULTS AND DISCUSSION

Physical Characterization of Spray Gel Formulations

This study has developed a gel to spray formulation using gelling agents as an approach to increase papaya leaves extract on the wound skin and increase wound healing process. The spray gel application has many advantages such as easy to the administration on the skin, decrease side effects compared injection and oral administration, and to prevent infection by direct skin contact.

Table II is summarized of physical characterizations (pH, stickiness test, viscosity, homogeneity, and weight) of papaya leaves on spray gel formulations with the variation of gelling agent and with and without papaya leaves extract. The pH of spray gel formulations was showed in the range 5.9-6,3 which about normal pH skin of human (4,5 to 6,5). In addition, the viscosity of papaya leaves on spray gel ranging between 880-1740 cPs which suitable viscosity was easy to sprayed on the skin and also suitable for topical application. The addition of extract can affect the viscosity of spray gel formulations. Also, the highest viscosity that was have increased stickiness which is spray gel formulation without papaya leaves extract (P1 & P2), and also it can't sprayed using a spraying pump. All of the spray gel formulations showed good homogeneity and also alike weight was spray from the spraying pump.

Wound Healing Activity

The study showed that papaya leaves on spray gel accelerated of the wound healing process (Table III; Figure 2). Wound treated with spray gel with and without papaya leaves extract. The wound healing process was treated with papaya leaves on spray gel showed major signs of wound

Table III. The Time Required for Wound Healing by Papaya Leaves on Spray Gel Formulations in Rats

Animal Group	No of Animals	Healing Tine (days)
Group 1 (negative)	3	26
Group 2 (positive)	3	20
Group 3 (extract)	3	20
Group 4 (P1)	3	23
Group 5 (P2)	3	24
Group 6 (P3)	3	22
Group 7 (F1)	3	16
Group 8 (F2)	3	22
Group 9 (F3)	3	16

Figure 2. Wound healing in spray gel treatment

healing and significantly ($p<0,05$) considerable wound healing if than negative control. Table III also showed that placebo significant differences exist among positive control. This show that placebo of spray gel does not accelerate to wound healing process. Then, extract, F1, F2, and F3 no significant differences than positive control.

Papaya leaves extract has wound healing and antibacterial activities. Papaya leaves contains secondary metabolites such as flavonoids, phenolics, saponins, papain enzymes, and chymopapain. Antiinflamatory and antioxidant activities obtained accelerate wound healing process by catch free radicals that damage tissue and trigger collagen formation. Papaya leaves extract was formulated into spray gel in order increased effectiveness so it can accelerate wound healing process. Papaya leaves extract on spray gel were formulated with variation of gelling agents so obtained maximum effectiveness. The delivery using spray gel can increase penetration into wound area and decrease contamination because nondirect contact. In the present study, we tried to develop a spray gel formulation using variations of the gelling agent such as carbopol 940, HPMC 60SH, gellan gum, and HEC to get ideal spray gel formulation. The ideal characteristics (pH, viscosity, stickiness, weight) of spray gel obtained affect the activity of the active substance used.

CONCLUSION

Variations of the gelling agent between carbopol 940 and HPMC 60SH and the combination of HPMC 60SH and hydroxyethylcellulose provide the pastest wound healing process. The data showed that the application of papaya leaves on spray gel formulation as an alternative to wound healing. The spray gel may contribute to increase the concentration of the papaya leaves extract into the skin from topical formulations. Further research should be performed histopathology of rats' skin.

REFERENCES

Ansel, H. C, 1989, *Pengantar bentuk sediaan farmasi*, Edisi ke-4, UI Press, Jakarta, Indonesia.

Boateng, Joshua, C., Kerr, H. Matthews, Howard, N. E. Stevens, Gillian, M. Eccleston, 2008, Wound healing dressing and drug delivery system, *Journal of Pharmaceutical Sciences*, 97(8): 11.

Dahlizar, S., Futaki, M., Okada, M., Kadhum, W.R., Todo, H., Sugibayashi, K., 2018, Design of a topically applied gel spray formulation with ivermectin using novel low molecular weight gelling agent, palmitoyl-glycine-histidine, to traet scabies, *Chem. Pharm. Bull*, 327-333.

Femilian, A., Dewi, A., Goeno, S., 2019, The effect of papaya leaf (*Carica papaya* L) on healing process of buccal traumatic ulcer in wistar rats, *Majalah Kedokteran Gigi Indonesia,* 15-22

Gurtner, G.C. 2007. 'Wound healing: normal and

abnormal'. Edisi ke-6, Lippincott Williams & Wilkins, Philadelphia, USA.

Harahap, R., 2018, 'Formulasi dan optimasi *spray gel* ekstrak etanol daun pepaya (*Carica papaya* Linn.) dengan basis kombinasi carbopol®940 dan gellan gum menggunakan desain faktorial', *Skripsi*, S. Farm., Jurusan Farmasi, Fakultas MIPA, Universitas Sriwijaya, Indralaya, Indonesia.

Hatahet, T., Morille, M., Hammos, A., Devoissele, J.M., Muller, R.H., Begu, S., 2016, Quercetin topical application, from conventional dosage forms to nanodosage forms. *European Journal of Pharmaceutics and Biopharmaceutics*, 41-53

Lawrence, W.T, 2002, Wound healing biology and its application to wound management, Dalam: O'Leary P. *ThePhysiologic Basis of Surgery*, Edisi ke-3, Lippincott Williams & Wilkins, Philadelphia, USA.

Mahmood, A.A., K. Sidik, I. Salmah, 2005, Wound healing activity of *Carica papaya* L. aqueous leaf extract in rats, *International Journal of Molucules Medicine and Advance Sciences,* 398-401.

Marcovitch, H, 2005, 'Black's medical dictionary'. 41st edition, A&C Black, London, Inggris.

Rajab, Nawal A., 2013, Preparation and evaluation of ketoprofen as dermal spray film. *Kerbala Journal of Pharmaceutical Sciences*, 6.

Suyudi, S.D. 2014, 'Formulasi gel semprot menggunakan kombinasi karbopol 940 dan hidroksipropil metilselulosa (HPMC) sebagai pembentuk gel', *Skripsi*, S.Farm., Program Studi Farmasi, Fakultas Kedokteran dan Ilmu Kesehatan, UIN Syarif Hidayatullah Jakarta, Jakarta, Indonesia.

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