Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20170457

Original Research Article

Efficcacy of *Lantana camara* Linn. leaf extracts ointment on dermal wound healing were infected with *Staphylococcus epidermidis*

Mauritius Lambertus Edy Parwanto*

Department of Biology, Faculty of Medicine, University of Trisakti, Jakarta, Indonesia

Received: 03 January 2017
Accepted: 23 January 2017

***Correspondence to:**
Dr. Mauritius Lambertus Edy Parwanto,
Email:
edyparwanto@trisakti.ac.id

ABSTRACT

Background: Dermal infections by *Staphylococcus epidermidis* can cause problems for patients. Antibiotic resistance have been reported to treat the bacteria, therefore need to develop new drugs, among others sourced from herbs. For this purpose, study is needed to find an efficacy of *Lantana camara* Linn. leaf extract ointment on dermal wound healing were infected with *S. epidermidis*.
Methods: Wistar rats divided into 4 groups randomly. Group I=dermal wounded, infected with *S. epidermidis*, untreated. Group II=dermal wounded, infected with *S. epidermidis*, treated with *L. camara* Linn. leaf extract ointment 5%. Group III=dermal wounded, infected with *S. epidermidis*, treated with *L. camara* Linn. leaf extract ointment 10%. Group IV=dermal wounded, infected with *S. epidermidis*, treated with sodium fusidate 2%. Bacterial colonies number observed on 6 days, while the quality of wound healing, measurement of DNA and protein levels on 6, 14 and 18 days. Mean ± SD between groups were analyzed by ANOVA.
Results: Wound healing in group II qualitatively better than group I, III and IV. Bacterial colonies number in group II was lower than groups I, III and IV ($p<0.05$), whereas DNA and protein levels was higher in group II compare to groups I, III and IV ($p<0.05$). On 6, 14 and 18 days observations there are trend similarly ie DNA levels decreased, conversely protein levels increased.
Conclusions: *L. camara* Linn. leaf extract ointment 5% more effective than 10% on dermal wound healing.

Keywords: DNA, *Lantana camara* Linn., Protein, *Staphylococcus epidermidis*, Wound healing

INTRODUCTION

Naturally, dermal wound will be infected by *Staphylococcus epidermidis*. The bacteria infection can cause problems serious dermal wound healing to patients. The use of antibiotics against these bacteria have also been reported to cause resistance. Injuries to the dermal naturally experience healing. Wound healing of the dermal after the damage occurred is a complex process involving multiple cells in the dermal, primarily keratinocytes, fibroblasts, endothelial cells of vessels and recruited immune cells, and their associated extracellular matrix.[1] Wound healing begins immediately after an injury, platelets come to the place of injury and contact with collagen. As a result of the aggregation of platelets, clotting factors are released, resulting in the deposition of fibrin clot at the site of injury. Fibrin clot serves as a temporary matrix and the subsequent healing process.[2] Wound healing also involves a variety of cytokines and growth factors.[3] Generally wound healing can be divided into four distinct phases as hemostasis, inflammation, proliferation, and remodeling.[4]

Factors affecting wound healing among other bacterial infections. Activities bacteria that infect disabling wound healing.[5] One of the bacteria that commonly infects the wounds are *S. epidermidis*. The bacteria live on the human skin as normal flora.[6,7] We know that *S. epidermidis* is a Gram-positive bacteria which are aerobic or facultative anaerobic and spherical irregular groups.

S. epidermidis that infect on dermal wound can be quickly causes problems, because the ability to reproduce and spread widely into the tissues.[8] The bacterial infection be able cause a human diseases.[9] Transcutaneous infection from these bacteria has potential as beginning bacterial entry into the body, and the subsequent induce local or systemic infection.[10] The survey showed that >40% of *S. epidermidis* infections occur in the circulatory system, whereas *S. aureus* infection <20%.[11] *S. epidermidis* treated with antibiotics be able develop resistance, partly because these bacteria form a biofilm. Biofilms are formed by *S. epidermidis* are difficult degraded.[12] Therefore necessary to find a new pharmaceutical preparations, such as *Lantana camara* Linn.

In the last decade, scientists have studied the chemical composition and pharmacological activities of all parts of *L. camara* Linn.[13] Phytochemical composition of *L. camara* Linn. include essential oils, phenols, flavonoids, carbohydrates, proteins, alkaloids, glycosides, iridoid glycosides, etanoid phenyl, oligosaccharides, quinine, saponins, steroids, triterpin, sesquiterpenoid and tannin as a main component.[14-16] *L. camara* Linn. extract is known to cure several diseases and is used in various medicinal preparations. *L. camara* Linn. extract has an antibacterial effect against *Escherichia coli*, *Bacillus subtilis* and *Pseudomonas aeruginosa*. *L. camara* Linn. extract has been reported has low activity against *Staphylococcus aureus*, *Proteus vulgaris*, *Bacillus cereus* and *Salmonella typhi*.[17-19] In addition *L. camara* Linn. extracts as antibacterial, also reported as antifungal and antiulcerogenik.[20,21] It has been proven that *L. camara* Linn. extracts has activity for wound healing. *L. camara* Linn. extract topically at a dose of 100 mg/kg/day increased wound contraction, collagen synthesis and reduces wound healing time.[22]

Results of previous studies have shown that extracts of *L. camara* Linn. formulated in the soap, has antibacterial effect of *S. epidermidis*. Extracts of *L. camara* Linn. 4, 6, 8 and 10% showed inhibition against *S. epidermidis*.[23] It has been tested an ointment formulation that contain of *L. camara* Linn. extracts include organoleptic, homogeneity and pH.[24] Therefore require further research on the effecacy of *L. camara* Linn. extracts ointment.

There have been studies on the antibacterial effects of *L. camara* Linn. extracts. The effect of *L. camara* Linn. extracts on dermal wound healing has also been studied, but there are no studies on effecacy of *L. camara* Linn. leaf extracts ointment on dermal wound healing were infected with *S. epidermidis*. The purpose of this study to know the effecacy of *L. camara* Linn. leaf extracts 5% and 10% in the ointment preparation on dermal wound healing were infected with *S. epidermidis*.

METHODS

Ointment formulation of L. camara Linn. leaf extract

L. camara Linn. identified beforehand to determine the species of plants. Leaves of *L. camara* Linn. obtained locally, covered with a black cloth and then dried in the sun to dry. The dried leaves are then weighed and made powder. Next phase, powder extraction using 70% ethanol and then filtered to yield a viscous supernatant as crude extracts. Aliquot of the extract lyophilized and the results are weighed. *L. camara* Linn. leaf extract used as an active ingredient of ointments. Extracts standardization was done before use in this study (data not showen). *L. camara* Linn. leaf extract ointment 5% and 10% were used in this study. Ointment containing *L. camara* Linn. leaf extract 5% was made by incorporating 5 grams leaf extract to 95 grams of ointment base (British Pharmacopoeia=BP), whereas ointment containing leaf extract 10% were made by incorporating 10 grams leaf extract to 90 grams of ointment base (BP).

Experimental treatment on Wistar rat

Wistar Rats used in this study were selected based on body weight between 150-200 grams, declared healthy after being examined by a Veterinarian. Rats were placed in individual cages. Rats given food and drink at libitum according to the standard. Treatment room be equipped fully air conditioned with a temperature of 22±3°C, humidity 55±5%, and artificial fluorescent lamps (12:12 hour light and dark cycle). Acclimatization on rats carried out for 2 weeks, then continued treatment suitable group. This study has ethical clearance by the Commission on Research Ethics, Faculty of Medicine, University of Trisakti, Jakarta, Indonesia.

The number of Wistar rats per group was calculated using formula $(n-1)(t-1)\geq 15$. Each treatment group requires a minimum of 6 Wistar rats. Twenty four male Wistar rats were used in this study. Wistar rats divided into 4 groups were randomized. Group I, ie group of Wistar rats were wounded, infected with *S. epidermidis* and untreated (as negative control). Group II, ie group of Wistar rats were wounded, infected with *S. epidermidis* and treated with *L. camara* Linn. leaf extract ointment 5%. Group III, ie group of Wistar rats were wounded, infected with *S. epidermidis* and treated with *L. camara* Linn. leaf extraxt ointment 10%. Group IV, ie group of Wistar rats were wounded, infected with *S. epidermidis* and treated with Fucilex ointment containing sodium fusidate 2% (as positive control).

Dermal back of each Wistar rats were wounded 2 cm, under ether local anasthesia. After wounded, each rats inoculated with 100 micro liter (uL) isolates of *S. epidermidis* 5×10^5 colony-forming units/milli-liter (CFU/mL) in a homogeneous liquid medium. Treatment of ointment containing *L. camara* Linn. leaf extract either sodium fusidate 2% performed once a day for 18 days after wounded.

Calculation of bacteria colonies number

Bacteria number in the granulation tissue was calculated by Hirsch et al.[25] One hundred mL of granulation tissue homogenates were taken for counting bacterial colonies. These solutions were inoculated on selective media in petridish, and incubated aerobically at 37°C for 24 hours. Bacteria colonies number expressed as log 10 CFU per gram of tissue. Number of bacteria $>1\times10^5$ declared infected.[26] Calculation of bacteria colonies number carried on 6 days after inoculation.

Measurement of DNA and protein levels

Measurement of DNA and proteins levels in the granulation tissue on 6, 14 and 18 days. Rats are anesthetized using a combination of xylazine (10 mg/kg) and ketamine (100 mg/kg), then do dermal tissue sampling is 0.8×0.5 cm. The tissue is collected into a solution of 10% formalin, then used as a sample for DNA and proteins levels measurement.

DNA extraction

DNA extracted using QIAamp DNA Blood and Tissue Mini Kit (Qiagen). Samples derived from dermal rat tissues (100 mg) finely chopped, then added 180 uL ATL buffer. Next phase, added 20 mL proteinase-K, 200 mL phosphate buffered saline (PBS) and 200 mL AL buffer (lysis buffer). Incubation was performed in water bath for 10 minutes on 56ºC. Lysat then added 200 mL absolute ethanol and do vortex. All the solution was transferred into columns, then added 500 mL AW1 buffer, then centrifuged in 6000 rotations per minute (rpm) for 1 minute. Supernatant was discarded and then added 500 mL AW2 buffer into column, centrifuged in 20000 rpm for 3 minutes. Collection tube is removed, while column laid at new micro tube then added 100 mL AE buffer (elution buffer), room incubated for 5 minutes and then centrifuged on 6000 rpm for 1 minute. The next phase, DNA levels in the micro tube measured using UV spectrophotometer at wavelength (λ) 260/280 nm (NanoDrop, Biorad).

Protein isolation

Samples derived from dermal rat tissues (100 mg) finely chopped, then added 500 uL of phosphate buffered saline (PBS), and then homogenized using a mortar. The next phase was added buffer solution A containing 6M guanidine HCl, 0.1M NaH_2PO_4 and 0.01 M Tris-HCl at pH 8, centrifugation was done at 10000 rpm for 10 minutes. Supernatant was collected in a vial 1.5 mL and then protein levels measured by bichinchocinic acid (BCA) assay. Sample used as many as 10 mL, standard solution of bovine serum albumin (BSA) was used with concentration 25-1250 ug/mL. Mixture of reagent A and B (BCA) were used as many as 200 mL with ratio of 50:1, incubation time for 30 minutes at 37^{o}C. Measurement of protein levels using microplate reader at λ 595 nm.

Statistical analysis

Data for all groups are expressed as mean±SD. Comparisons of mean±SD between groups were statistically evaluated using one way ANOVA, followed by least significant different test (LSD). Considered were statistically significant at $p<0.05$.

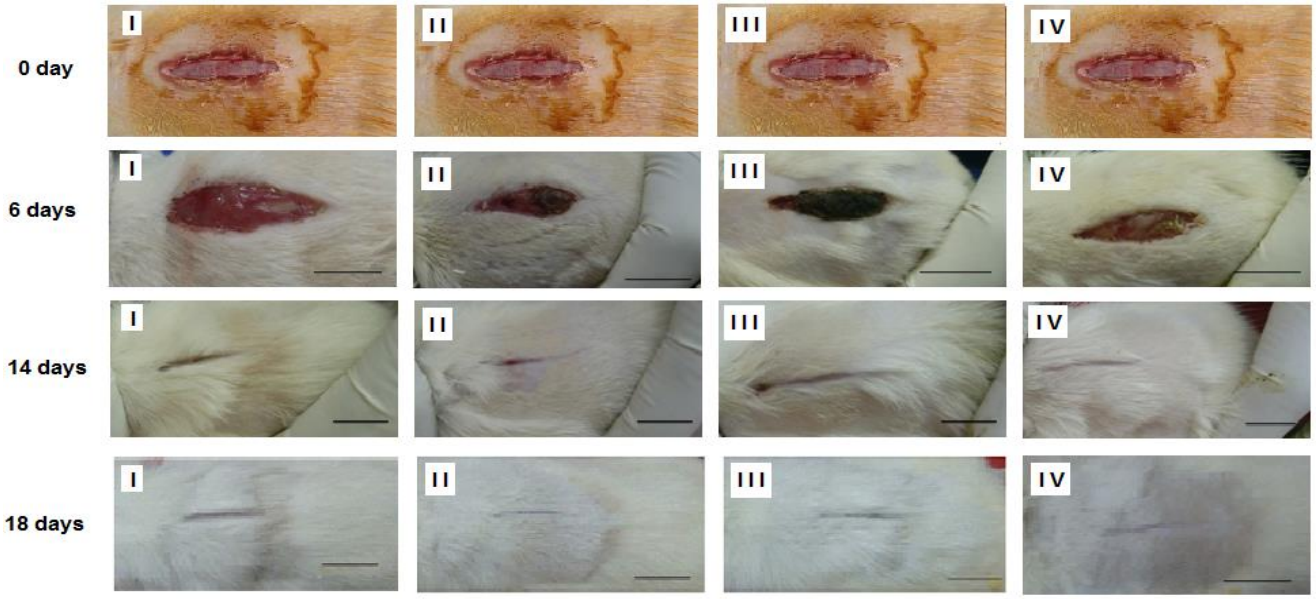
RESULTS

Taxonomy of *L. camara* Linn. as well as; Kingdom: Plante; Division: Magnoliophyta; Class: Magnoliopsida; Order: Lamiales; Family: Verbenaceae; Genus: Lantana; Species: *Lantana camara* Linn. Identification result of *L. camara* Linn. presented in Figure 1.

Figure 1: Plant of *L. camara* Linn.

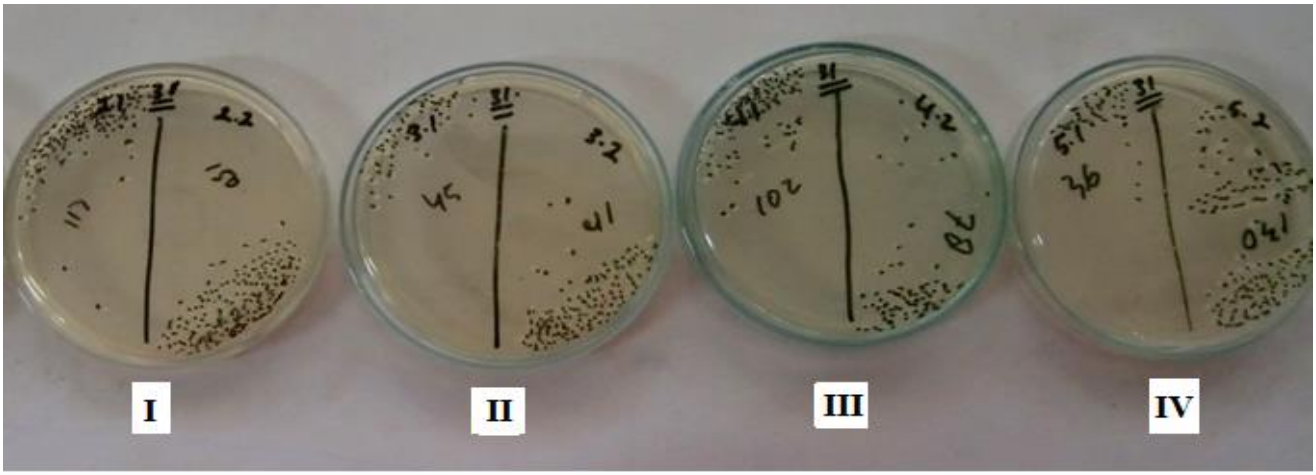
Photographical result of *L. camara* Linn. leaf extract oitnment effects on dermal wound healing presented in Figure 2. On 0 day, dermal wound in Wistar rats uniform. On 6, 14 and 18 days, groups II and III shows the results that wound healing better than in group I (negative

control) and Group IV (positive control). Group II showed better wound healing than in group III and IV, while group I worst. The fact show that *L. camara* Linn. leaf extract ointment 5% and 10% accelerating dermal wound healing. Qualitatively, the effect of *L. camara* Linn. leaf extract ointment 5% was better than 10% on dermal wound healing.



I, II, III and IV=treatment groups.

Figure 2: Photographical result of *L. camara* Linn. leaf extracts ointment effects on dermal wound healing.



I, II, III and IV=treatment groups.

Figure 3: *S. epidermidis* culture at 6 days.

Culture result of *S. epidermidis* culture at 6 days, presented in Figure 3. Effect of *L.camara* Linn. leaf extract ointment on colonies number of *S.epidermidis* at 6 days, presented in Figure 4. On 6 days, colonies number of *S. epidermidis* in group I was higher compare to group II, III and IV ($p<0.05$). Colonies number of *S. epidermidis* in group II was lower than in group I, III and IV ($p<0.05$). Colonies number of *S.epidermidis* in group III did not differ than group IV ($p>0.05$). These data showed that *L. camara* Linn. leaf extract ointment 5% most excellent effect to suppress the growth of *S.epidermidis* on 6 days.

Effect of *L. camara* Linn. leaf extract ointment on DNA levels in dermal wound healing, presented in Table 1. DNA levels on 6 and 14 days showed that between groups was different ($p<0.05$). DNA levels in group II was highest compare to other groups, while group I was lowest ($p<0.05$). DNA levels in group II was higher

compare to group III, as well as group III was higher compare to group IV ($p<0.05$). On 18 days showed that DNA levels between groups was different ($p<0.05$). DNA levels in group III did not different compare to group IV ($p>0.05$), while both groups was higher compare to group I and II ($p<0.05$).

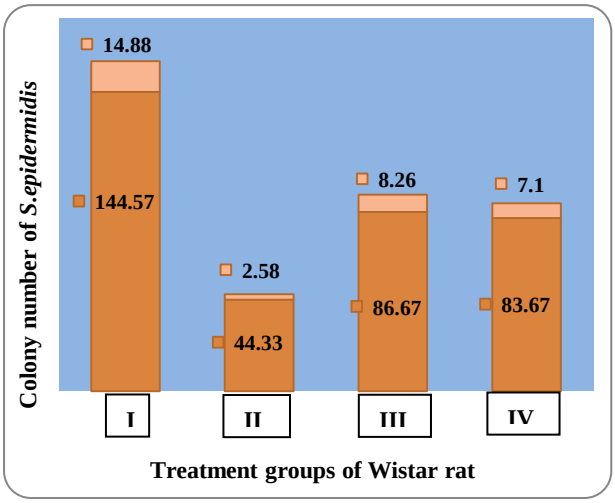


Figure 4: Effect of *L.camara* Linn. leaf extracts ointment on colonies number of *S.epidermidis* at 6 days.

Table 1: Effect of *L. camara* Linn. leaf extracts ointment on DNA levels in dermal wound healing.

DNA (ng/uL)				
Groups	**6 days**	**14 days**	**18 days**	
I	16.49± 0.47 [a]	13.72± 0.55 [b]	10.27± 0.5 [c]	a>b>c (p<0.05)
II	52.66± 0.42 [d]	45.42± 0.4 [e]	17.54± 0.78 [f]	d>e>f (p<0.05)
III	37.93± 0.70 [g]	34.27± 0.39 [h]	18,41± 0.48 [i]	g>h>i (p<0.05)
IV	36.48± 0.37 [j]	33.41± 0.49 [k]	18.27± 0.44 [l]	j>k>l (p<0.05)
	d>g>j>a (p<0.05)	e>h>k>b (p<0.05)	i=l (p>0.05), i,l>f>c (p<0.05)	

DNA=deoxyribo nucleic acid; ng/uL=nano gram per micro litter; I, II, III and IV=treatment groups; p=significancy

Similar trends of DNA levels for all groups in the time of observation was decreases. DNA levels for all groups was highest on 6 days and decreases on 14 and 18 days. Compared to 6 days of observation, DNA levels on 14 days decreases 16.79%, while on 18 days decreases 37.75%. Compared to 6 days, DNA levels in group II on 14 days decreases 13.74%, while on18 days decreases 66.69%. DNA levels in group III on 14 days decreases 9.6% compare to 6 days, while on 18 days decreases 51.46%. DNA levels in group IV decreases 8.41% on 14 days compare to 6 days, while on 18 days decreases 49.91%.

Effect of *L. camara* Linn. leaf extract ointment on protein levels in dermal wound healing presented in Table 2. Protein levels on 6 and 14 days showed that was different between groups ($p<0.05$). Protein levels in group II was highest, while group I was lowest ($p<0.05$). Protein levels in group II was higher compare to group III, as well as group III was higher compare to group IV ($p<0.05$). On 18 days showed that protein levels between groups was different ($p<0.05$). Protein levels in group III did not differ compare to group IV ($p>0.05$), while both groups was higher compare to group I, and lower compare to group II ($p<0.05$).

Table 2: Effect of *L. camara* Linn. leaf extracts ointment on protein levels in dermal wound healing.

Protein (mg/mL)				
Groups	**6 days**	**14 days**	**18 days**	
I	8.83 ± 0.79 [a]	13.67 ± 0.46 [b]	11.92 ± 0.36 [c]	b>c>a (p<0.05)
II	16.79 ± 0.53 [d]	25.9 ± 0.68 [e]	18.62 ± 0.72 [f]	e>f>d (p<0.05)
III	15.54 ± 0.59 [g]	22.79 ± 0.73 [h]	17.6 ± 0.58 [i]	h>i>g (p<0.05)
IV	13.72 ± 0.74 [j]	20.44 ± 0.85 [k]	17.48 ± 0.52 [l]	k>l>j (p<0.05)
	d>g>j>a (p<0.05)	e>h,k>b (p<0.05)	i=l(p>0.05) f>i,l>c (p<0.05)	

mg/mL=milli gram per milli liter; I, II, III and IV=treatment groups; p=significancy

Protein levels in all groups at 6 days observation was lowest and 14 days was highest, while the protein levels on 18 days was lower than 14 days. Compared to 6 days, protein levels on 14 days in group I increased 54.81%, and on 18 days increased 34.99%. Compared to 6 days, protein levels in group II at 14 days increased 54.25%, and on 18 days increased 10.89 %. Compared to 6 days, protein levels in group III on 14 days increased 46.65%, and on 18 days increased 13.25%. Compared to 6 days, protein levels in group IV at 14 days increased 48.98%, and on 18 days increased 27.40%.

DISCUSSION

Several studies gives expectations for new drugs development from herbs on dermal wound healing. Result of study showed that wound healing effects of *Centella asiatica* extracts for both incision and burn wounds.[27] *Elaeis guineensis* accelerated wound healing in rats and topical herbal of *C.asiatica*, *Echinacea purpurea* and *Sambucus nigra* patch improved gingival healing.[28,29] The other research showed that the ointments containing oil of *Cordia verbenacea* seem to accelerate wound healing, probably due to their involvement with the increase of angiogenesis and dermal remodeling.[30]

In this study, inoculation of *S.epidermidis* in untreated group (negative control) showed that bacterial colonies number most widely. Effect of *L. camara* Linn. leaf extracts ointment and sodium fusidate 2% showed decreases of bacterial colonies number on dermal wound healing. The greatest emphasis on bacteria colonies number in this study showed by *L. Camara* Linn. leaf extract ointment 5%. *S. epidermidis* infections on dermal wound healing in untreated group showed obstacle wound healing process, conversely in other groups (Figure 2). We argued that rat dermal wound on 6 days had chronic. In these circumstances, number and activity of *S. epidermidis* increases and then inhibit on dermal wound healing process. *S. epidermidis* has been largely opportunistic and likely have formed biofilms. This opinion is consistent with the statement that *S. epidermidis* as an opportunistic pathogen is closely linked to the biofilm forming capability of the species.[31]

Further explained that in the process of biofilm formation, there is increased activity of bacteria to break down the extracellular matrix host.[32] The event is important that in chronic wounds has been the prolongation of the inflammatory phase of repair.[33] It has also been demonstrated that chronic wounds are an ideal environment for biofilm formation. Futher more, the necrotic tissue and debris allow bacterial attachment, and wounds are susceptible to infection due to impaired host immune response.[34] Biofilms are important as environmental reservoirs for pathogens. Biofilm growth may provide organisms to survival advantages in natural environments and increase their virulence.[35]

Other study showed that delayed reepithelialization caused by bacterial biofilm. Biofilm administration on dermal wound inhibit the use of peptides to biofilms formation. Therefore, biofilm formed by bacteria inhibit on dermal wound healing.[36] Based on the study result, it turn out that local infection inhibits on dermal wound healing. This happens can caused by host immune response and synergistic interactions among bacteria species that infect.[37] Result of the other research showed that bacteria form biofilms, so bacteria are protected and increasingly resistant to antibiotic treatment. To overcome antibiotic resistance, the researchers developed herbal medicine. It has been demonstrated that administration of herbal medicine in Thailand turned out to inhibit biofilm formation by *S. epidermidis*.[38] Also been observed that herbs have antibacterial activity and antibiofilm that can be an alternative to combat pathogenic microorganisms, particularly *S. epidermidis*.[39] In addition of antibacterial activity and antibiofilm, has been studied about medicinal plants againts on *S. epidermidis* biofilms.[40]

Based on bacterial colonies number on 6 days, turned out that *L. camara* Linn. leaf extract ointment 5% have better than 10% to protect dermal wound from *S. epidermidis* infections. These results can be used as the basis development of *L. camara* Linn. leaf extract ointment 5% in order to protect dermal wound from *S. epidermidis* infections. Protection capabilities of *L. camara* Linn. leaf extract ointment it can be used for dermal wounds healing in human.[41]

In this study, DNA levels on 6 days highest and decreases until 18 days observation. These data showed that *L. camara* Linn. leaf extract ointment 5% bettter than 10% for dermal wound healing. Other research showed that DNA levels increases on 12 days treatment of *Butea monosperma* extract for dermal wound healing.[42] In the process of dermal wound healing certainly occur cell division. During cell division occured DNA replication so that increases DNA levels. Increased levels of DNA in group II highest among other groups, this suggests the stimulation of cell division is most active. We argue that occurs the possible effects of *L. camara* Linn. leaf extract ointment 5%. Previous study showed that genes expressed during wound healing process. Futhermore, nearly 100 genes are expressed with an immediate early gene profile at the wound site. More over, study in mouse wound transcriptome have revealed numerous genes upregulated after damage, and many of these gene inductions occur in the wound edge epithelium.[43]

Result in this study showed that *L. camara* Linn. leaf extract ointment 5% more better for dermal wound healing. In this treatment, DNA and protein levels was higher compare to control. We argue that provision of *L. camara* Linn. leaf extracts ointment 5% most effective increases gen expression. Normally, after dermal wound occurs formation of fibrous tissue and known as fibroplasia. These process involves fibroblast proliferation and formation of type III collagen and other matrix proteins.[44]

Collagen is protein extracelluler in the granulation tissue of wound healing. Increasing collagen amount in the wound area determines strength and integrity of matrix in the tissue. Because *L. camara* Linn. leaf extract ointment 5% more better in dermal wound healing, we have opinion that collagen levels in the granulation tissue highest among other groups. These opinion was also consistent with the statement that fibroblasts can differentiate into myofibroblasts, the which are responsible for collagen deposition and wound contraction.[45] Previous study showed that the faster collagen synthesis, then the sooner of wound healing. Beside that locally collagen synthesis in need of oxygen and other nutrients. Supplying of oxygen and nutrients for collagen synthesis completed in the process of angiogenesis.[46]

L. camara Linn. leaf extract ointment 5% more better than 10% for wound healing. *L. camara* Linn. leaf extract ointment 5% and 10% also more better than the ointment containing sodium fusidate 2% (fucilex). These result showed that *L. camara* Linn. leaf extract ointment 5% and 10% can be developed as dermal wound healing ointment. Similar results were obtained that *L.camara*

Linn. leaf extract 100mg/kg body weight/day has been reported has contraction rate 98% and decrease wound healing time.[47]

In this study, there are limitations such as not done observations of bacterial colonies number from the time of inoculation until dermal wound becomes dry. Beside that not done to showed associations of collagen type III gen expression with the levels of collagen type III. Also not done to measurement of total collagen levels and wound strenght contraction.

CONCLUSION

Base on the fact in this study apparently that *L. camara* Linn. leaf extract ointment 5% more effective than 10%. Both these ointment has effect on decrease of bacterial colonies number, DNA levels and increase protein levels as well as the quality of wound healing. Because that we concluded that *L. camara* Linn. leaf extract ointment 5% and 10% can be developed as dermal wound healing ointment. Development of *L. camara* Linn. leaf extract ointment for dermal wound healing more focused on the dose of 5%.

ACKNOWLEDGEMENTS

This work was supported by the Faculty of Medicine, University of Trisakti, Jakarta, Indonesia. This research was funded in the budget year 2013. We thanks to Dr. Hardy Senjaya Msi; Dr. Jihan Samira and Hosea JE, SFarm, Apt. M Si who wish to help this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Martin P, Nunan R. Cellular and molecular mechanisms of repair in acute and chronic wound healing. Br J Dermatol. 2015;173(2):370-8.
2. Clark RA. Fibrin and wound healing. Annals of the New York Acad of Sci. 2001;936:355-67.
3. Bhat RS, Shankrappa J, Shivkumar HG. Formulation and evaluation of polyherbal wound treatments. Asia J Pharma Sci. 2007;2(1):11-7.
4. Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. Nature. 2008;453:314-21.
5. Wall SJ, Sampson MJ, Levell N, Murphy G. Elevated Matrix metallo proteinase 2 and 3- production from human diabetic dermal fibroblast. Brit J Dermatol. 2003;149(1):13-6.
6. von Eiff C, Peters G, Heilmann C. Pathogenesis of infections due to coagulase-negative *staphylococci*. Lancet Infect Dis. 2002;2:677-85.
7. Gandelman G, Frishman WH, Wiese C, Green-Gastwirth V, Hong S, Aronow WS, et al. Intravascular device infections: Epidemiology, diagnosis, and management. Cardiol Rev. 2007;15(1):13-23.
8. Joo SS, Jang SK, Kim SG. Anti-acne activity of Selagineela involvens extract and its non antibiotic anti-microbial potential on Propionibacterium acnes. Phytother Res. 2008;22:335-9.
9. McCann MT, Gilmore BF, Gorman SP. *Staphylococcus* epidermidis device-related infections: pathogenesis and clinical management. J of Pharm and Pharmacol. 2008;60(12):1551-71.
10. Arrecubieta C, Toba FA, von Bayern M, Akashi H, Deng MC, Naka Y, et al. A *Staphylococcus* epidermidis Surface Protein, Contributes to the Initiation of Ventricular Assist Device Driveline-Related Infections. PLoS Pathog. 2009;5(5):1-13.
11. Suetens C, Morales I, Savey A. European surveillance of ICU-acquired infections (HELICS-ICU): methods and main results. J of Hospital Infect. 2007;65(2):171-3.
12. Schoenfelder SMK, Lange C, Eckart M, Hennig S, Kozytska S, Ziebuhr W. Success through diversity-how *Staphylococcus* epidermidis establishes as a nosocomial pathogen. Int J of Med Microbiol. 2010;300(6):380-6.
13. Kalita S, Kumar G, Karthik L, Rao KVB. A Review on Medicinal Properties of Lantana camara Linn. Research J Pharm and Tech. 2012;5(6):711-5.
14. Bhakta D, Ganjewala D. Effect of leaf positions on total phenolics, flavonoids and proantho-cyanidins content and antioxidant activities in Lantana camara (L). J of Scient Res. 2009;1(2):363-9.
15. Venkatachalam T, Kumar VK, Selvi PK, Maske AO, Kumar NS. Physicochemical and preliminary phytochemical studies on the Lantana Camara (L.) fruits. Int J of Pharm and Pharmaceut Scienc. 2011;3(1):52-4.
16. Kensa VM. Studies on phytochemical screening and antibacterial activities of Lantana camara Linn. Plant Sciences Feed. 2011;1(5):74-9.
17. Ganjewala D, Sam S, Khan KH. Biochemical compositions and antibacterial activities of Lantana camara plants with yellow, lavender, red and white flowers. EurAsian J of BioSci. 2009;3:69-77.
18. Barreto FS, Sousa EO, Campos AR, Costa JGM, Rodrigues FFG. Antibacterial activity of Lantana camara Linn and Lantana montevidensis brig extracts from Cariri-Ceará, Brazil. J of Young Pharm. 2010;2(1):42-4.
19. Badakhshan MP, Sasidharan S, Rameshwar NJ, Ramanathan S. A comparative study: antimicrobial activity of methanol extracts of Lantana camara various parts. Pharmacog Res. 2009;1(6):348-51.
20. Srivastava D, Singh P. Antifungal potential of two common weeds against plant pathogenic fungi-Alternaria sps. Asian J of Experiment Biol Scienc. 2011;2(3):525-8.
21. Thamotharan G, Sekar G, Ganesh T, Sen S, Chakraborty R, Kumar S. Antiulcerogenic effects of Lantana camara Linn. leaves On in vivo test models

in rats. Asian J of Pharm and Clin Res. 2010;3(3):57-60.
22. Nayak BS, Raju SS, Eversley M, Ramsubha A. Evaluation of wound healing activity of Lantana camara L. - a preclinical study. Phytother Res. 2009;23(2):241-5.
23. Hosea JE. Antibacterial opaque soap formula of Lantana camara L. leaf extract on Staphylococcus epidermidis (in Indonesia language). Progdi Farmasi-FMIPA, Universitas Sam Ratulangi, Manado, Sulawesi Utara, Indonesia; 2012.
24. Parwanto E, Senjaya H, Jaya Edy H. Antibacterial ointment formulation of Lantana camara L. leaf ethanol extract (in Indonesia language). Pharmacon. 2013;2(03):104-8.
25. Hirsch T, Spielmann M, Zuhaili B, Koehler T, Fossum M, Steinau HU, et al. Enhanced susceptibility to infections in a diabetic wound healing model. BMC Surg. 2008;8(5):1-8.
26. O'Meara S, Nelson EA, Golder S, Dalton JE, Craig D, Iglesias C. Systematic review of methods to diagnose infection in foot ulcers in diabetes. Diabetic Med. 2006;23:341-7.
27. Somboonwong J, Kankaisre M, Tantisira B,Tantisira MH. Wound healing activities of different extracts of Centella asiatica in incision and burn wound models: an experimental animal study. BMC Compl Altern Med. 2012;12(103):1-7.
28. Sasidharan S, Logeswaran S, Latha LY. Wound healing activity of Elaeis guineensis leaf extract ointment. Int J Mol Sci. 2012;13(1):336-47.
29. Chaushu L, Weinreb M, Beitlitum I, Moses O, Nemcovsky CE. Evaluation of a topical herbal patch for soft tissue wound healing: an animal study. J of Clin Periodontol. 2015;42:288-93.
30. Perini JA, Angeli-Gamba T, Alessandra-Perini J, Ferreira LC, Nasciutti LE, Machado DE. Topical application of Acheflan on rat skin injury accelerates wound healing: a histopathological, immunohistochemical and biochemical study. BMC Compl and Altern Med. 2015;15(203):1-8.
31. Büttner H, Mack D, Rohde H. Structural basis of Staphylococcus epidermidis biofilm formation: mechanisms and molecular interactions. Frontiers in Cell and Infect Microbiol. 2015;5(14):1-15.
32. Otto M. Staphylococcal biofilms. Curr Top Microbiol Immunol. 2008;322:207-28.
33. Zhao G, Usui ML, Lippman SI, James GA, Stewart PS, Fleckman P, et al. Biofilms and Inflammation in Chronic Wounds. Adv in wound care, 2013;2(7):389-99.
34. Siddiqui AR, Bernstein JM. Chronic wound infection: facts and controversies. Clin Dermatol. 2010;28:519-26.
35. Parsek MR, Singh PK. Bacterial biofilms: an emerging link to disease pathogenesis. Annu Rev Microbiol. 2003;57:677-701.
36. Schierle CF, De la Garza M, Mustoe TA, Galiano RD. Staphylococcal biofilms impair wound healing by delaying reepithelialization in a murine cutaneous wound model. Wound Repair Regen. 2009;17(3):354-9.
37. Grice EA, Segre JA. Interaction of the microbiome with the innate immune response in chronic wounds. Adv Exp Med Biol. 2012;946:55-68.
38. Lin MH, Chang FR, Hua MY, Wu YC, Liu ST. Inhibitory effects of 1, 2, 3, 4, 6-penta-O-galloyl- β-D-glucopyranose on biofilm formation by Staphylococcus aureus. Antimicrob Agents and Chemother. 2011;55(3):1021-7.
39. Escaich S. Antivirulence as a new antibacterial approach for chemotherapy. Current Op in Chem Biol. 2008;12(4):400-8.
40. Chusri S, Sompetch K, Mukdee S, Jansrisewangwong S, Srichai T, Maneenoon K, et al. Inhibition of Staphylococcus epidermidis Biofilm Formation by Traditional Thai Herbal Recipes Used for Wound Treatment. Evidence-Based Compl and Altern Med. 2012:1-8.
41. Fujii T, Wakaizumi M, Ikami T, Saito M. Amla (Emblica officinalis Gaertn.) extract promotes procollagen production and inhibits matrix metalloproteinase-1 in human skin fibroblast. J Ethnopharmacol. 2008;119(1):53-7.
42. Sumitra M, Manikandana P, Suguna L. Efficacy of Butea monosperma on dermal wound healing in rats. www.aseanbiodiversity.info/.../51003935.pdf. 2004; asseced on January 12; 2013;11.42.
43. Cooper L, Johnson C, Burslem F, Martin P. Wound healing and inflammation genes revealed by array analysis of 'macrophageless' PU.1 null mice. Genome Biol. 2004;6(1)R5:1-17.
44. Lewis CJ, Mardaryev AN, Sharov AA, Fessing MY, Botchkarev VA. The Epigenetic Regulation of Wound Healing. Adv in wound care. 2014;3(7):468-75.
45. Rosique RG, Rosique MJ, Jayme AFJ. Curbing Inflammation in Skin Wound Healing: A Review. Int J Inflam. 2015;316235:1-9.
46. Buemi M, Galeano M, Sturiale A. Recombinant human erythropoietin stimulates angiogenesis and healing of ischemic skin wounds, Shock. 2004;22(2):169-73.
47. Abdulla MA, Hassandarvish P, Ali HM, Noor SM, Mahmoud FH, Bashah NSA, et al. Acceleration of Wound Healing Potential by Lantana camara Leaf Extract in Experimental Rats. Res J of Med Scienc. 2009;3(2):75-9.

Cite this article as: Parwanto MLE. Efficcacy of *Lantana camara* Linn. leaf extracts ointment on dermal wound healing were infected with *Staphylococcus epidermidis*. Int J Basic Clin Pharmacol 2017;6:503-10.