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Original Article
บทวิทยาการ

Preliminary study of effects of a standardized extract of *Centella asiatica* ECa 233 on minor aphthous ulcers

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Abstract

Objective The present pilot study aimed to investigate the effects of a standardized extract of *Centella asiatica* ECa 233 on an oral paste form on minor recurrent aphthous ulceration (MiRAU).

Materials and methods A randomized, single-blind, placebo controlled trial was conducted on 24 eligible subjects with MiRAU and randomly divided into four groups: 0.05, 0.10 and 0.20% ECa 233 paste and placebo oral paste. On entry to the trial at day 0, subjects were instructed to apply the oral paste three times per day (after breakfast and lunch and at bedtime) for 10 days or until the ulcer was completely healed. In addition, numbers of ulcer, size and pain score were daily evaluated and recorded in a log diary booklet by subjects themselves. Follow-up visit was made on day 3 and 10 in which subjects were interviewed for the occurrence of unwanted effects. Analysis of data reported was made by one-way ANOVA followed by Least Significant Different.

Results Twenty four subjects enrolled and completed the study. Healing of ulcer over time was observed in all subjects, however, with differences in time courses. In comparison to the ulcer size in day 0, significant reduction in ulcer size was initially noted at day 9 in a placebo group whereas they were at day 2, 6 and 4 in 0.05, 0.10 and 0.20% ECa 233 treated groups, respectively. Reduction of mean pain score was observed in the same manner. Significant reduction of pain score was initially

observed at day 2, 4 and 3 in 0.05, 0.10 and 0.20% ECa 233 treated groups, respectively whereas their respective value in placebo group was found at day 6. Erythema which was gradually resolved and completely disappeared at day 10 in all ECa 233 treated groups, remained slightly visible at day 10 in placebo group. In parallel with its efficacy, no unwanted effect of ECa 233 was reported or noted.

Conclusion Our preliminary study demonstrated for the first time that oral paste containing ECa 233 was safe and effective in reducing pain, ulcer size and erythema of MiRAU suggesting the potential of the test compound to be further developed for the management of oral minor aphthous ulcers.

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Key words: *Centella asiatica; ECa 233; MiRAU; ulcer size*

Introduction

Recurrent aphthous ulceration (RAU), typically manifested as an erosion of epidermal layer of non-keratinized oral mucosa, is a common oral mucosal disease with the frequency of 5-20% in general population worldwide.[1-3] RAU is classified into 3 specific classes: minor (MiRAU), major (MaRAU), and herpetiform (HuRAU) according to the size, number and duration of the ulcers. Among them, MiRAU is the most common form, consisting of 70-87% of the population with RAU. MiRAU is clinically manifested as 1-5 small round to ovoid lesions with less than 1 cm in diameter surrounded by a distinct erythematous halo.[4,5] As the specific cause of MiRAU remains unknown and the treatment is usually supportive or symptomatic, a variety of topical and systemic therapies including antibiotics, enzymatic preparations, and corticosteroids have been used to relieve pain, reduce the duration of the ulcers and to prevent recurrence.[6-9] Varying degree of success has been reported and in some cases significant side effects were noted.[10-12]

Centella asiatica (Umbelliferae) is a medicinal plant containing mainly asiaticoside, asiatic acid, madecassoside and madecassic acid. Traditionally, *Centella asiatica* has been used for the treatment of eczema, psoriasis, and leprosy.[13] It is extensively evaluated for a wide spectrum of pharmacological activity including wound and ulcer healing.[14-19] Furthermore, lesion size in MiRAU was significantly reduced by an oral gel containing a crude extract of *Centella asiatica.*[20] In order to overcome a fluctuation of biologically active constituents normally exists in the crude extract of medicinal plants, activity-guided isolation was used to establish a standardized extract of *Centella asiatica* ECa 233 which is a white to off-white titrated extract of *Centella asiatica* containing triterpenoids at least 80% and the ratio of madecassoside and asiaticoside would always be kept at 1.5 ± 0.5.[21] Recently, wound healing effects on burn wound of ECa 233 in which 0.05% was identified as an optimal concentration has been demonstrated in animals.[22]

In an acute toxicity testing with the observation period of 14 days, neither toxic sign nor lethality was observed in mice receiving a single oral administration of ECa 233 in the dose up to 10 mg/kg indicating a very high safety profile of the extract. In accordance with a favorable safety profile observed in acute toxicity testing, a daily oral administration of ECa 233 in the doses of 10, 100 and 1000 mg/kg/day into rats of both sexes for 90 days did not produce any significant toxic effects in terms of growth, haematology, blood

chemistry and histopathology of the vital organs.[21] Based on its advantages with regards to consistency of constituents, beneficial effect on wound healing and striking safety profile, it is of our interest to conduct a preliminary study to evaluate clinical efficacy of ECa 233 in an oral paste form on MiRAU.

Materials and methods

Preparation of oral paste

ECa 233 was kindly supplied by Assistant Professor Chamnan Patarpanich and Associate Professor Suwanna Laungchonlatan, Department of Food and Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Chulalongkorn University. As 0.10% of triamcinolone oral paste is widely used in the treatment of MiRAU and 0.05% ECa 233 has been previously demonstrated a wound healing effect, concentrations of 0.05, 0.10 and 0.20% were then selected. Oral paste containing 0.00, 0.05, 0.10 and 0.20% of ECa 233 in hydrocarbon base was prepared by Medica Innova Pharma Co. Ltd., Bangkok, Thailand. Study drugs were dispensed in similar coded collapsible tubes.

Subjects and study design

The protocol of a randomized, single-blind, placebo-controlled trial was approved by the Ethics Committee of the Faculty of Pharmaceutical Sciences, Chulalongkorn University (08-33). Subjects were recruited by advertising in the general population and detailed informed consent form was obtained from each individual subject prior to enrollment. The inclusion criteria required subjects of either male or female at the age between 18 to 65 years with a history of recurrent minor aphthous ulcers; presentation of 1-2 minor aphthous ulcers of less than 48 hours of onset in an area of the mouth accessible for an evaluation; normal liver and kidney function tests; and normal complete blood count. Exclusion criteria included treatment of antibiotics, steroid or other oral topical preparations during and within 7 days prior to study entry; presence of illness or diseases which might affect the study, including diabetes, active infectious disease, behcet's disease and coeliac disease; using chewing tobacco products, smoking pipe or cigar and consumption of alcohol within six months prior to study entry; pregnancy or breast feeding; and abnormal hematological values.

Eligible subjects were assigned randomly to one of four treatment groups: placebo oral paste and oral paste containing 0.05, 0.10 and 0.20% ECa 233. On day 0, the baseline values of number of ulcer, ulcer size, pain score and erythema levels (inflammatory halo surrounded the ulcer) were evaluated by the dentist or a trained nurse under the supervision of the dentist.[3] Diameter of ulcer size was measured from edge to edge by a sterile calibrated ruler with millimeter markings.[3] Two measurements crossed at 90 degrees were made for an estimation of an average radius of the ulcer (r) in mm. Cross-sectional area of the ulcer in mm was then calculated by a formula of πr^2. A numerical visual analog scale (VAS 0-10) was used to record the level of pain induced by a touch of a dry cotton bud.

Subjects were instructed to do self-assessment of the ulcer size, pain score and self-application procedure. They were asked to apply 0.05 cm of an oral paste three times daily, after breakfast and lunch and at bedtime for another 10 days or until the ulcer was completely healed, if it occurred before 10 days. Daily recording (day 0-10) of the application time of the tested oral paste, size and number of ulcers as well as pain score in response to a touch of a cotton bud were recorded in a log diary booklet by the subjects themselves. In addition to self-assessment, the patients were interviewed for the occurrence of unwanted effect and being re-evaluated by the same investigator on the second and third visits at day 3 and 10, respectively.

The diary booklet and the remaining of the test drugs were returned to the investigator at the end of the trial (day 10).

Data and statistical analyses

Demographics data were summarized with descriptive statistics. The values were reported as mean ± SE. One-way ANOVA followed by least significant different (LSD) post test was used to test differences within group and between groups. The level of significance was established at a p value < 0.05. All data were analyzed using SPSS software (version 17.0).

Results

Demographics

Twenty four subjects, 8 males and 16 females, enrolled in the study. Most of them presented with single ulcer located mainly on non-keratinized labial and buccal mucosa. As a result of the blinded randomization procedure, all treatment groups were well-matched with regards to age (mainly middle age), baseline values of number and size of ulcers and pain score (Table 1).

Reduction of ulcer size

As shown in Fig. 1, mean ulcer size in the treatment groups of 0.00, 0.05, 0.10 and 0.20% ECa 233 oral paste were gradually reduced over the course of the study of 11 days. The mean time to complete healing (ulcer size = 0) was 8.25 ± 0.85 days in placebo group whereas they were 6.00 ± 0.97, 7.60 ± 1.03 and 6.67 ± 0.67 days in 0.05, 0.10 and 0.20% ECa 233 treated groups, respectively. Apparently, ulcer in all ECa 233 treated groups healed better than those in placebo group. In comparison to their respective baseline values in day 0, the mean ulcer size in 0.05, 0.10 and 0.20% ECa 233 treated groups were initially found to be significantly reduced at day 2, day 6, and day 4, respectively whereas significant reduction of mean ulcer size in placebo group was initially noted at day 9.

Table 1 Subject demographics

Description	Percentage of ECa 233 (W/V)			
	0.00 (n= 6)	0.05 (n= 6)	0.10 (n= 6)	0.20 (n= 6)
Age (year)	34.17 ± 2.91	30.00 ± 3.92	27.00 ± 9.26	36.67 ± 6.30
Male/Female	4/2	6/0	1/5	5/1
Number of ulcer	1.17 ± 0.16	1.00 ± 0.00	1.17 ± 0.16	1.33 ± 0.21
Initial ulcer size (mm^2)	8.47 ± 1.09	8.14 ± 2.42	9.32 ± 1.10	9.39 ± 1.23
Initial pain score (VAS)	6.83 ± 0.75	7.17 ± 0.54	7.00 ± 0.63	6.83 ± 0.40

VAS= Visual analog scale

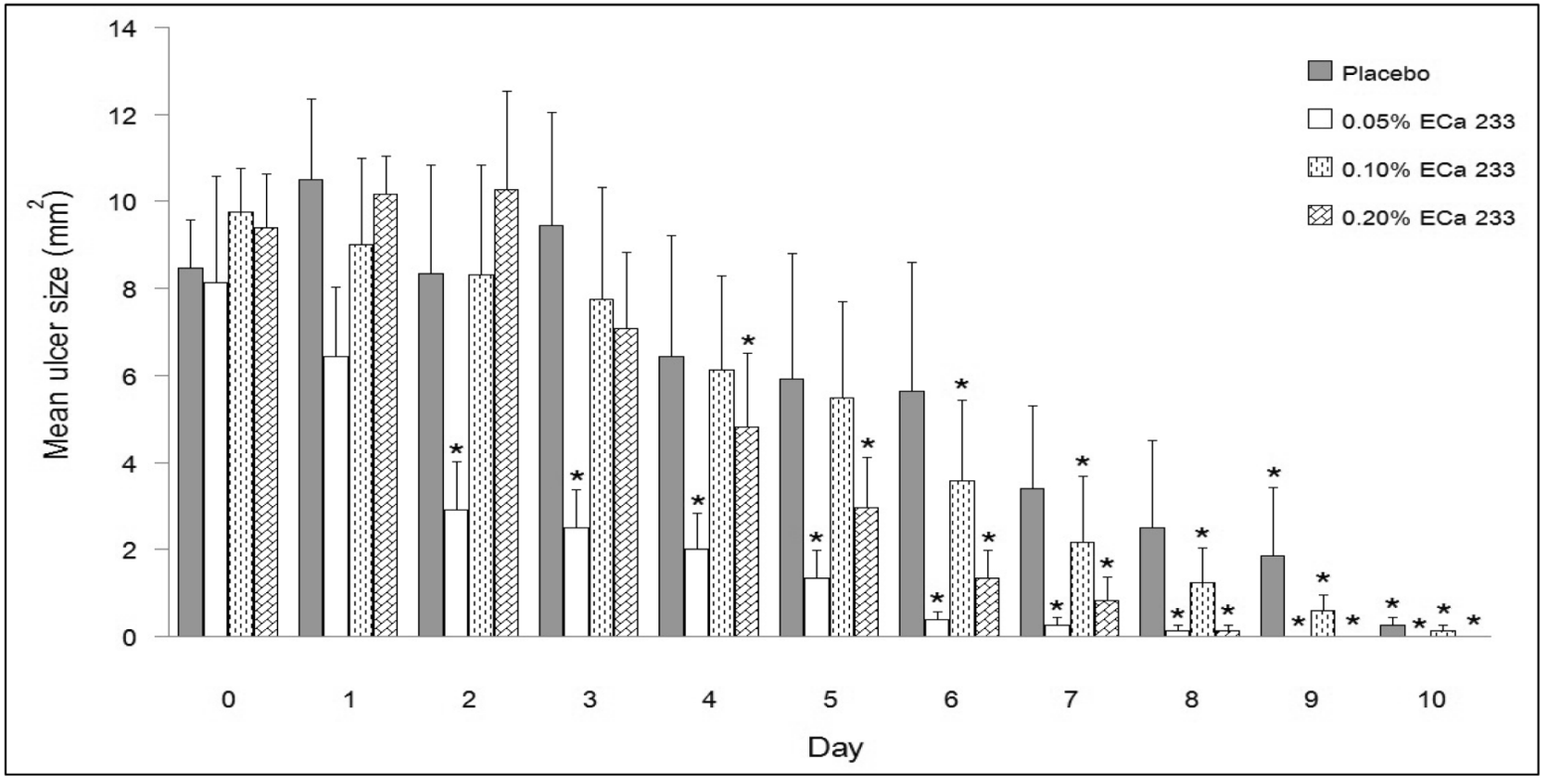

Fig. 1 Mean ulcer size (mm^2) in different time course of placebo oral paste, 0.05% ECa 233, 0.10% ECa 233 and 0.20% ECa 233. Values represent the mean ± SE for each group (n=6).

* Significant difference as compared to initial value at day 0 ($p < 0.05$)

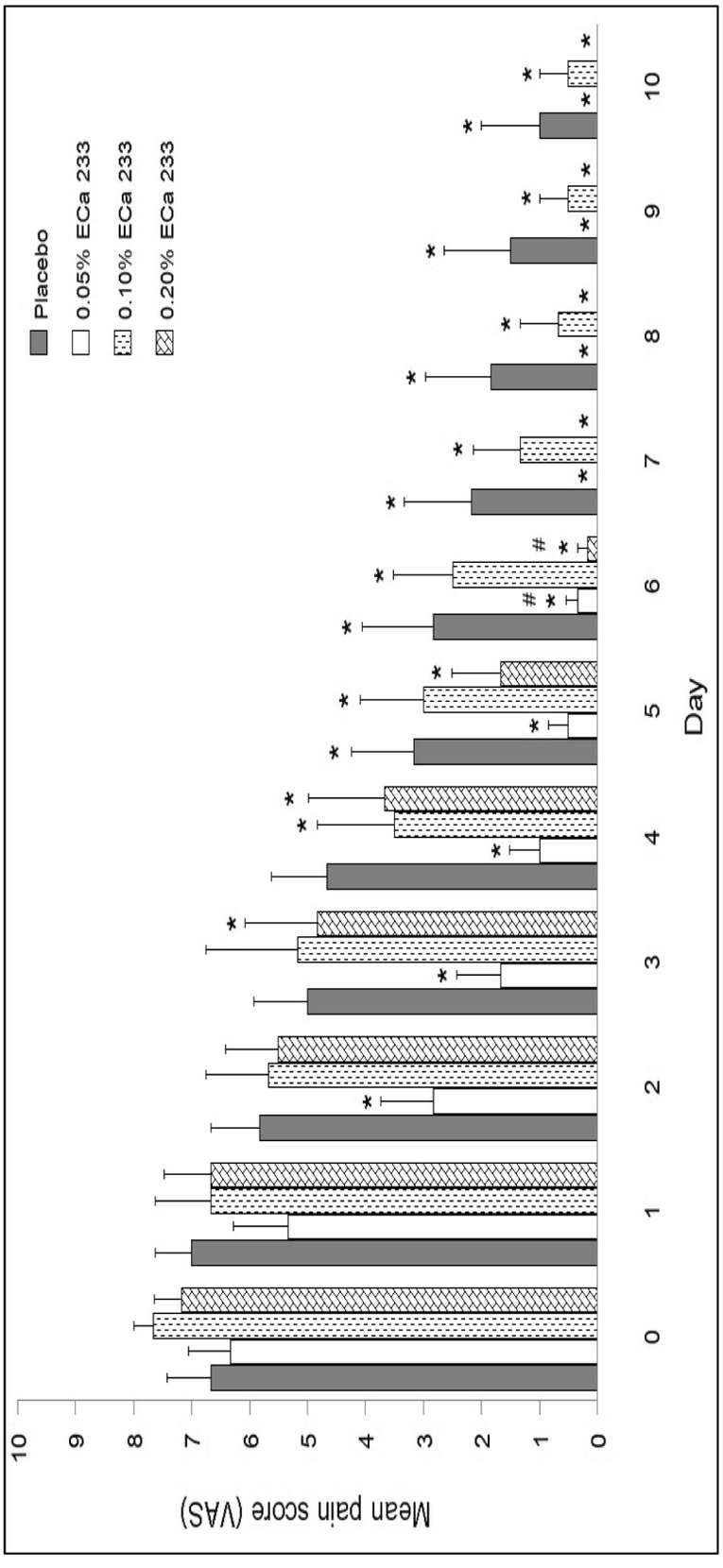

Fig. 2 Mean pain scores in different time course of placebo oral paste, 0.05% ECa 233, 0.10% ECa 233 and 0.20% ECa 233. Values represent the mean ± SE for each group (n=6).
* Significant difference as compared to initial value at day 0 ($p < 0.05$)
\# Significant difference as compared to placebo oral paste group on the same day ($p < 0.05$)

Reduction of pain score

According to the self-reported daily pain score, the mean pain score in all groups were decreasing during the course of treatment. The mean time to reach a complete pain relief (a VAS of 0) in the placebo group was 7.60 ± 0.81 days whereas they were 4.83 ± 0.75, 6.00 ± 1.05 and 5.00 ± 0.58 days in 0.05, 0.10 and 0.20% ECa 233 treated groups, respectively. In agreement with a reduction of ulcer size, ECa 233 seemed to relieve ulcer pain better than did the placebo oral paste. Furthermore, significant reduction of pain score, in comparison to the pain score obtained on day 0 was initially reported at day 2, day 4 and day 3 in 0.05, 0.10 and 0.20% ECa 233 treated groups whereas significant reduction of pain in placebo group was demonstrated at day 6 (Fig. 2). For comparison between groups, it was found that significant reduction of pain score in comparison to their corresponding value in placebo group was exclusively noted on day 6 of both 0.05 and 0.20% ECa 233.

Reduction of erythema

Erythema level was estimated by the same investigator at day 0, day 3 and day 10. Initially almost all of the ulcers were surrounded by an inflammatory halo. As shown in Table 2, there was no difference on erythema levels across the four groups of treatment at day 0. No improvement was observed in the placebo group at day 3 and a minor degree of the erythema still existed at day 10. In contrast, all ECa 233 treated groups demonstrated a reduction of erythema at day 3 and furthermore no sign of erythema could be visualized at day 10.

Safety evaluation

All subjects completed the trial without any absence or withdrawal. No subject experienced any allergic reaction due to the treatment received. Throughout the course of treatment, no sensation of pain, burning taste or some other discomfort was reported to the investigators.

Discussion

The goal for the treatment of RAU which is a common oral disease of uncertain etiopathogenesis is largely directed toward symptomatic treatment. Treatment usually aims to decrease the symptom, reduce ulcer size and number as well as prolong the

Table 2 Erythema level of ulcers

Treatment	Erythema level* (mean ± SE)		
(% ECa 233)	Day 0	Day 3	Day 10
0.00	2.17 ± 0.17	2.17 ± 0.31	0.33 ± 0.21
0.05	2.17 ± 0.17	1.00 ± 0.26	0.00 ± 0.00
0.10	2.17 ± 0.17	1.83 ± 0.31	0.00 ± 0.00
0.20	2.17 ± 0.17	1.83 ± 0.31	0.00 ± 0.00

* Erythema level: 0 = no erythema, 1 = light red/pink, 2 = red but not dark in color, 3 = very red, dark in color

ulcer free period.[23] Topical corticosteroids which has been approved for any inflammation in the mouth, remain the mainstay for the treatment of RAU to relieve pain.[2] In agreement with previous reports on healing effects on RAU of *Centella asiatica*.[20] preliminary result obtained in the present study has demonstrated an ameliorating effects on MiRAU of the ECa 233, a colorless standardized extract of *Centella asiatica* with known amount of triterpenoids and favorable safety profile. Severity of aphthous ulcer in terms of ulcer size, pain score and erythema were significantly reduced by the application of oral paste containing 0.05, 0.10 and 0.20% ECa 233 better than those observed in placebo group.

Taken into consideration that ECa 233 is not a single substance but a standardized extract with 2 known markers as well as limited number of subjects in this pilot study, it is not surprising that responses to different concentrations of ECa 233 did not show a dose-dependency. Among the three concentrations used, 0.05% ECa 233 which has been identified as an optimal concentration in healing of burn wound,[22] seemed to relief pain and stimulated ulcer healing better than the other two concentrations, however, similar effects were observed on erythema. Discrepancy of the findings possibly dues to the fact that ulcer size and pain score were more accurately evaluated on a daily basis whereas erythema was intermittently evaluated by the investigator on day 0, day 3 and day 10. Ameliorating effects of ECa 233 on MiRAU observed in the present study could possibly be, at least in part, accounted by inhibitory effect of *Centella asiatica* on inflammation seen in the present experiment as a decrease in erythema. It is thus suggesting that ECa 233 might reduce pain score via its anti-inflammatory activity, in the same manner as did the topical corticosteroids.[2] Additionally, *Centella asiatica* has been reported to promote ulcer healing process by increasing angiogenesis, stimulation of extracellular matrix accumulation, collagen synthesis and granulation tissue accumulation.[24,25] Whether ECa 233 could exert its wound healing effects by some other mechanisms e.g. stimulation of the expression of growth factors such as the basic fibroblast growth factor (bFGF) which involved in ulcer healing process, suppression of myeloperoxidase (MPO) activity which in turn may decrease the production of reactive oxygen species and reduce tissue damage remains to be further investigated.[26] Considering that ECa 233 is a well-defined standardized herbal extract with a proof of efficacy and safety profile as shown in the present study, in addition to study of underlying mechanisms of wound healing, a comparative study of the efficacy of ECa 233 in relation to some other clinically approved medication for the treatment of MiRAU such as 0.1% triamcinolone should be further carried out.

Conclusion

In conclusion, treatment of MiRAU by oral paste containing 0.05, 0.10 and 0.20% ECa 233 resulting in a significant relieving of pain, reduction of ulcer size and erythema associated with MiRAU better than those exhibited by placebo whereas no discomfort or unwanted effect of ECa 233 was reported during the course of treatment. The results suggest the potential use of ECa 233 for the treatment of MiRAU. Studies on the mechanism involved and comparative clinical study should be further conducted.

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References

1. Natah SS, Konttinen YT, Enattah NS, Ashammakhi N, Sharkey KA, Hayrinen-Immonen R. Recurrent aphthous ulcers today: review of the growing knowledge. Int J Oral Maxillofac Surg. 2004;33:221-34.
2. Scully C. Clinical practice. Aphthous ulceration. N Engl J Med. 2006;355:165-72.
3. Khandwala A, Van Inwegen RG, Alfano MC. 5% amlexanox oral paste, a new treatment for recurrent minor aphthous ulcers: I. clinical demonstration of acceleration of healing and resolution of pain. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997;83:222-30.
4. Woo SB, Sonis ST. Recurrent aphthous ulcers: a review of diagnosis and treatment. J Am Dent Assoc. 1996;127:1202-13.
5. Shashy RG, Ridley MB. Aphthous ulcers: a difficult clinical entity. Am J Otolaryngol. 2000;21:389-93.
6. Murray B, McGuinness N, Biagioni P, Hyland P, Lamey PJ. A comparative study of the efficacy of aphtheal in the management of recurrent minor aphthous ulceration. J Oral Pathol Med. 2005; 34:413-9.
7. Ylikontiola L, Sorsa T, Hayrinen-Immonen R, Salo T. Doxymycine-cyanoacrylate treatment of recurrent aphthous ulcers. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997;83:329-33.
8. Chandrasekhar J, Liem AA, Cox NH, Paterson AW. Oxypentifylline in the management of recurrent aphthous oral ulcers: an open clinical trial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;87:564-7.
9. Saxen MA, Ambrosius WT, Rehemtula al-KF, Russell AL, Eckert GJ. Sustained relief of oral aphthous ulcer pain from topical diclofenac in hyaluronan: a randomized, double-blind clinical trial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997;84:356-61.
10. Herlofson BB, Barkvoll P. Sodium lauryl sulfate and recurrent aphthous ulcers. a preliminary study. Acta Odontol Scand. 1994;52:257-9.
11. Delavarian Z, Delavarian Z, Molashahi L, Pakfetrat A. The effect of topical sucralfate suspension on oral aphthae. J Dent. 2007;4:72-7.
12. Kerr AR, Drexel CA, Spielman AI. The efficacy and safety of 50 mg penicillin G potassium troches for recurrent aphthous ulcers. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003;96:685-94.
13. Sampson JH, Raman A, Karlsen G, Navsaria H, Leigh IM. *In vitro* keratinocyte antiproliferant effect of *Centella asiatica* extract and triterpenoid saponins. Phytomedicine. 2001;8:230-5.
14. Maquart FX, Chastang F, Simeon A, Birembaut P, Gillery P, Wegrowski Y. Triterpenes from *Centella asiatica* stimulate extracellular matrix accumulation in rat experimental wounds. Eur J Dermatol. 1999; 9:289-96.
15. Cho MK, Sung MA, Kim DS, Park HG, Jew SS, Kim SG. 2-Oxo-3,23-isopropylidene-asiatate (AS2006A), a wound-healing asiatate derivative, exerts anti-inflammatory effect by apoptosis of macrophages. Int Immunopharmacol. 2003;3:1429-37.
16. Lu L, Ying K, Wei S, Fang Y, Liu Y, Lin H, et al. Asiaticoside induction for cell-cycle progression, proliferation and collagen synthesis in human dermal fibroblasts. Int J Dermatol. 2004;43:801-7.
17. Cheng CL, Guo JS, Luk J, Koo MWL. The healing effects of *Centella* extract and asiaticoside on acetic acid induced gastric ulcers in rats. Life Sci. 2004;74:2237-49.
18. Kimura Y, Sumiyoshi M, Samukawa K, Satake N, Sakanaka M. Facilitating action of asiaticoside

at low doses on burn wound repair and its mechanism. Eur J Pharmacol. 2008;584:415-23.

19. Yun KJ, Kim JY, Kim JB, Lee KW, Jeong SY, Park HJ, et al. Inhibition of LPS-induced NO and PGE_2 production by asiatic acid via NF-κB inactivation in RAW 264.7 macrophages: possible involvement of the IKK and MAPK pathways. Int Immunopharmacol. 2008;8:431-41.
20. Wangrangsimakul K. Treatment of recurrent oral aphthous ulcerations. Ann Dent. 1999;6:58-9.
21. Tantisira MH. Bioactive standardized extract of *Centella asiatica* (ECa 233). Proceeding of the 8th NRCT-JSPS Joint Seminar; 2009 Feb 2-3; Bangkok, Thailand.
22. Wannarat K, Tantisira MH, Tantisira B. Wound healing effects of a standardized extract of *Centella asiatica* ECa 233 on burn wound in rats. Thai J Phamacol. 2009;31:120-3.
23. Scully C, Gorsky M, Lozada-Nur F. The diagnosis and management of recurrent aphthous stomatitis: a consensus approach. J Am Dent Assoc. 2003; 134:200-7.
24. Shetty BS, Udupa SL, Udupa AL, Somayaji SN. Effect of *Centella asiatica* L (umbelliferae) on normal and dexamethasone-suppressed wound healing in wistar albino rats. Int J Low Extrem Wounds. 2006;5:137-43.
25. Shetty BS, Udupa SL, Udupa AL. Biochemical analysis of granulation tissue in steroid and *Centella asiatica* (Linn) treated rats. Pharmacology online. 2008;2:624-32.
26. Shukla A, Rasik AM, Jain GK, Shankar R, Kulshrestha DK, Dhawan BN. *In vitro* and *in vivo* wound healing activity of asiaticoside isolated from *Centella asiatica*. J Ethnopharmacol. 1999; 65:1-11.

การศึกษาเบื้องต้นของผลของสารสกัดมาตรฐานบัวบก อีซีเอ 233 ต่อโรคแผลร้อนในชนิดไม่รุนแรง

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บทคัดย่อ

วัตถุประสงค์ การศึกษานำร่องเพื่อดูผลของสารสกัดมาตรฐานบัวบก อีซีเอ 233 ในรูปของยาป้ายปากต่อแผลร้อนในชนิดไม่รุนแรง

วัสดุและวิธีการ ทดลองโดยวิธีการสุ่มคัดเลือกและมียาหลอกเป็นกลุ่มควบคุม กลุ่มตัวอย่างที่เป็นแผลร้อนในชนิดไม่รุนแรงจำนวน 24 ราย ได้รับการสุ่มคัดเลือกแบ่งออกเป็น 4 กลุ่มการทดลอง คือ กลุ่มที่ได้รับยาป้ายอีซีเอ 233 ความเข้มข้นร้อยละ 0.05 0.10 และ 0.20 และกลุ่มที่ได้รับยาหลอก โดยในวันที่เริ่มเข้าร่วมโครงการอาสาสมัครจะได้รับยาป้ายปากซึ่งมีอีซีเอ 233 ในความเข้มข้นร้อยละ 0.00 (ยาหลอก) 0.05 0.10 และ 0.20 โดยให้ป้ายยาวันละ 3 ครั้ง (หลังอาหารเช้า กลางวัน และก่อนนอน) เป็นระยะเวลา 10 วัน หรือจนกว่าแผลจะหาย อาสาสมัครจะเป็นผู้บันทึกข้อมูลประจำวัน อันได้แก่ ระดับความปวดและขนาดของแผล โดยผู้วิจัยจะนัดตรวจติดตามผลเพื่อประเมินการหายของแผลและอาการไม่พึงประสงค์อันอาจเกิดจากการใช้ยาในวันที่ 3 และ 10 จากนั้นวิเคราะห์ผลโดยใช้สถิติการวิเคราะห์ความแปรปรวนทางเดียว และทดสอบความแตกต่างระหว่างค่าเฉลี่ยในแต่ละกลุ่มด้วยการเปรียบเทียบเชิงซ้อนชนิดเลส ซิกนิฟิแคนท์ ดิฟเฟอเรนซ์

ผลการศึกษา อาสาสมัครจำนวน 24 ราย ซึ่งผ่านเกณฑ์การคัดเลือกได้เข้าร่วมโครงการวิจัยจนเสร็จสิ้น เมื่อเปรียบเทียบกับขนาดแผลในวันที่เริ่มเข้าร่วมโครงการพบว่าในกลุ่มที่ได้รับยาหลอกขนาดแผลจะลดลงอย่างมีนัยสำคัญในวันที่ 9 ในขณะที่กลุ่มซึ่งได้รับยาป้ายปากที่มีอีซีเอ 233 ในความเข้มข้นร้อยละ 0.05 0.10 และ 0.20 สามารถลดขนาดแผลได้อย่างมีนัยสำคัญทางสถิติ ตั้งแต่วันที่ 2 6 และ 4 ตามลำดับ ซึ่งเป็นไปในทิศทางเดียวกันกับการลดลงของค่าเฉลี่ยของระดับความปวด ที่พบว่าเมื่อเปรียบเทียบกับวันที่เริ่มเข้าร่วมโครงการ กลุ่มซึ่งได้รับ

ยาป้ายปากที่มีอีซีเอ 233 ในความเข้มข้นร้อยละ 0.05 0.10 และ 0.20 สามารถลดระดับความปวดได้อย่างมีนัยสำคัญทางสถิติตั้งแต่วันที่ 2 4 และ 3 ตามลำดับ ในขณะที่กลุ่มซึ่งได้รับยาหลอกระดับความปวดจะลดลงอย่างมีนัยสำคัญทางสถิติตั้งแต่วันที่ 6 จากการศึกษานี้ยังพบว่ายาป้ายปากที่มีอีซีเอ 233 สามารถลดระดับขอบแดงของแผลได้ โดยในวันที่ 10 กลุ่มที่ได้รับยาป้ายปากที่มีอีซีเอ 233 ทุกกลุ่มจะไม่พบการอักเสบของแผล ขณะที่กลุ่มที่ได้รับยาหลอกนั้นยังคงพบระดับการอักเสบของแผลอยู่เล็กน้อย และไม่พบอาการไม่พึงประสงค์จากการใช้ป้ายปากที่มีอีซีเอ 233 แต่อย่างใด

สรุป การศึกษาฤทธิ์เบื้องต้นของอีซีเอ 233 ในรูปของยาป้ายปากในครั้งนี้เป็นการศึกษาครั้งแรกที่แสดงให้เห็นถึงความปลอดภัยและประสิทธิภาพของอีซีเอ 233 ในการลดระดับความปวด ระดับการอักเสบ และขนาดของแผลร้อนในชนิดไม่รุนแรง ควรจะมีการศึกษาต่อไปเพื่อพัฒนาสารทดสอบดังกล่าวมาใช้ในการรักษาแผลร้อนในชนิดไม่รุนแรง

(ว ทันต จุฬาฯ 2553;33:131-42)

คำสำคัญ: *ขนาดแผล; บัวบก; แผลร้อนในชนิดไม่รุนแรง; อีซีเอ 233*