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Randomized Double-Blind Control Trial to Study the Efficacy of Topical Herbal Product-*Curcuma xanthorrhiza* (Temulawak) in the Treatment of Hyperpigmented Scar

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Abstract: *Curcuma xanthorrhiza* (Temulawak) has been tested to have a certain properties that can be used in treatment of hyperpigmentation which is tyrosinase inhibitor, anti-oxidant, broad spectrum anti-bacterial, antiseptic and anti-inflammatory. In this study, we want to explore the potential of Temulawak as an alternative solution for skin hyperpigmentation treatment. A randomized double blind placebo control trial involving 58 patients with hyperpigmented scar were randomly divided into two groups. Patients were required to apply the topical cream evenly to their scar twice a day; One in the morning and the other during bed time. The patients were screened after at least 6 weeks after wound has healed. The evaluations of scar were done by medical practitioner, patient himself and also by independent photographic assessor. Patients, investigator and independent photographic assessor were blinded to the topical application. The mean age of patients was 39 years old (between 24-53 years old), 32 were female and 6 participants lost to follow up and excluded from study. Analyzed hyperpigmented scars were distributed at head and neck area (53.8%), limbs (40.4%) and trunk (5.8%). Hyperpigmentation, pain, itchiness and overall scar rating showed higher score decrement (better scar outcome) in the intervention group compared to control group. There was no adverse skin reaction recorded in both intervention and control groups. The result of our study were not statistically significant. This is due to the limitation of the Vancouver Scar Scale and small sample size. However, we still believe that Temulawak has the potential role as an alternative treatment for scar hyperpigmentation.

Key words: Curcuma, anti-inflammatory agent, antioxidant, hyperpigmentation, rating, role

INTRODUCTION

Treating hyperpigmentation which result from melanin formation should start at the biochemical level. Tyrosinase is an essential enzyme in the biosynthesis pathway for melamin formation. One of the treatment of hyperpigmentation is by inhibition of tyrosinase enzyme agents (Nieuweboer-Krobotova, 2013; Rendon and Horwitz, 2012; Couteau and Coiffard, 2016). There are two types of tyrosinase inhibitors which are suitable for treatment of Post Inflammatory Hyperpigmentation (PIH): chemical (hydroquinone) and natural tyrosinase inhibitors. Although, Hydroquinone remains the gold standard when treating PIH as the cosmeceutical industry grows and continues to make new discoveries, the variety of treatments for PIH will inevitably expand, offering natural alternatives to those who prefer to avoid dermatologist prescribed skin lighteners.

Natural tyrosinase inhibitor as an alternative PIH treatment is widely available. Commonly recognized natural tyrosinase inhibitors are arbutin, kojic acid, vitamin C and vitamin C derivatives. Due to their low toxicity to melanocytes, these agents are used in cosmetics. Their mechanism of action has been investigated in vitro and in vivo while their toxicology has been documented (Petit and Pie, 2003). Kojic acid is a potent tyrosinase inhibitor by chelating copper at the active site of tyrosinase enzyme. The common side effect

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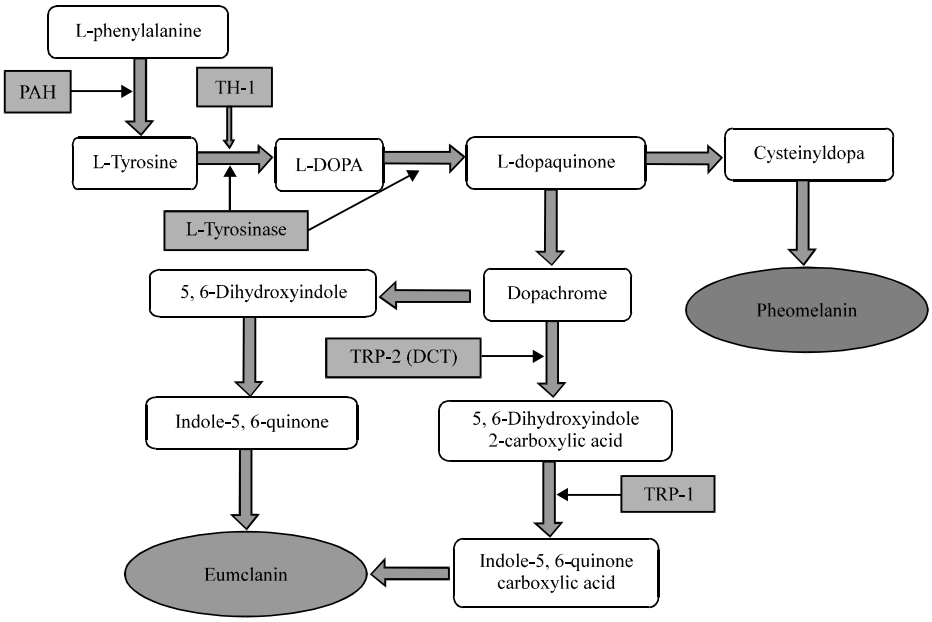

Fig. 1: Melanin biosynthetic pathway

of kojic acid includes contact dermatitis (Davis and Callender, 2010). Arbutin reacts by inhibit melanosomal tyrosinase activity and by competing for active binding site in tyrosinase enzyme. The side effect of it is paradoxical hyperpigmentation in higher concentration (Parvez *et al*., 2006). Vitamin C interacts with copper ions at the site of tyrosinase activity to decrease pigmentation (Rendon and Horwitz, 2012). These natural tyrosinase inhibitors provide a safer alternative to the chemical compound hydroquinone.

Previously reported by Barbutara *et al*. (2010) the *Curcuma xanthorrhiza* (locally known as Temulawak) plant has the potential for treatment of hyperpigmentation. Temulawak is a perennial rhizomatous herb belonging to the plant family Zingiberaceae (Fig. 1 and 2). Temulawak has been tested to have certain property that can be used in treatment of hyperpigmentation which is tyrosinase inhibitor (Kartika, 2015), anti-oxidant (Masuda *et al*., 1992), broad spectrum anti-bacterial (Hwang *et al*., 2000) and antiseptic (Diastuti *et al*., 2014). Claeson *et al*. (1993) proved that there is active ingredients in Temulawak called non-phenolic linear 1,7-dirylheptanoids have a potency of anti-inflammatory agents. While Batubara *et al*. (2015) reported that Temulawak flower bract had a potency as an antibacterial and lipase inhibitor.

There were studies show that extract of Temulawak has whitening agent action (Diastuti *et al*., 1996; Batubara *et al*., 2015). This whitening potential is related to tyrosinase inhibition on monophenolase and

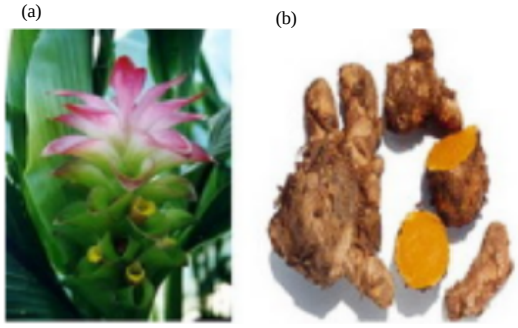

Fig. 2: a) Temulawak bark flower and b) Rhizome

diphenolase reaction. Tyrosinase is responsible in conversion of L-tyrosine to Dihydroxyphenylalanine (DOPA) and conversion of DOPA to DOPA quinone. When tyrosinase activity is inhibit, so, melanin formation also will be inhibit and no skin colour formation (Batubara *et al*., 2015). In Temulawak, it is also consisted of an alkaloid and a flavonoid. Flavonols also were reported to have some whitening properties (Batubara *et al*., 2010). Due to the beneficial effect of Temulawak, we would like to discover the effectiveness of Temulawak in treating hyperpigmented scar.

Treatment for skin hyperpigmentation remains challenging as the treatment is limited and expensive. Therefore, it is sensible to research on other cheaper and readily available material. The Temulawak has been extensively researched in vitro for its anti-hyperpigmentation effect (Couteau and Coiffard,

2016; Kartika, 2015; Diastuti *et al*., 2014). However, clinical data on human subjects on its potential treatment for hyperpigmentation has not been studied. Due to the beneficial effect of Temulawak, therefore, we have studied the effectiveness of Temulawak in treating hyperpigmented scars in human subjects as a safer alternative for skin depigmentation therapy. By conducting this study, we hope that Temulawak can be used as an alternative treatment for skin hyperpigmentation and for treatment to control scar symptoms.

MATERIALS AND METHODS

Study design: This was a double blinded Randomized Controlled Trial (RCT) study that was conducted in the Hospital Universiti Sains Malaysia (HUSM). Ethical approval obtained from Research Ethics Committee (Human), Universiti Sains Malaysia: USMKK/PPP/JEPeM [206.3.5] Subjects were recruited from Reconstructive Sciences Clinic and randomized using web-based software at www.randomization.com according to the treatment group and the controlled group with block randomization. The Primary Investigator (PI) recruited and screened for subject's eligibility with an assessment form. Subjects who fulfilled the inclusion criteria were given a briefing regarding the treatment protocol and cream application.

Subjects: Eligible and consented subjects were recruited. Subjects applied topical cream according to the treatment protocol. Evaluation of the scars by their appearance were conducted at 0, 2, 6 weeks and again after 16-24 weeks by clinical and photographic assessments.

Material: Both Temulawak and placebo creams were supplied by SIRIM, Malaysia. Temulawak cream has 33% Temulawak water extract. Temulawak cream preparation process is as described in Fig. 3.

Treatment protocol: Patients were required to apply the preparation evenly to their scar twice a day; one in the morning and the other one during bedtime. The treatment should last for 16-24 weeks. If there were local irritation or reactions, treatment was ceased temporarily for 2 days before recommencement. If patient continued to develop local skin reactions, he or she would be discontinued from the study. Patients should not receive other concomitant scar treatment. Non-compliant patients were discontinued from the study (Fig. 4).

During each visit, scars were photographed using identical frontal and side views under standard lighting

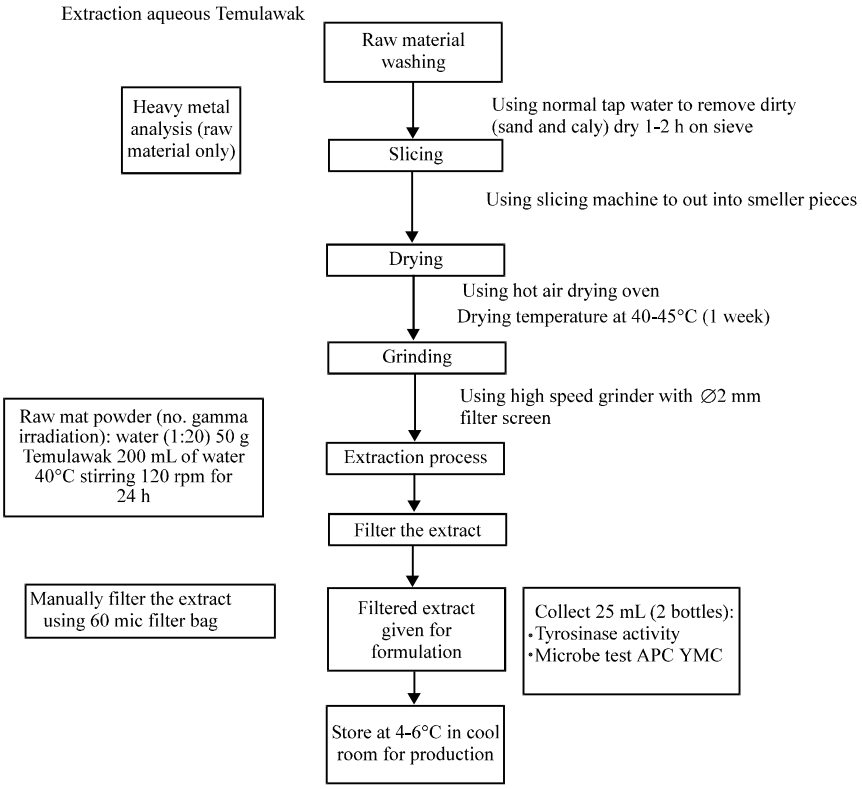

Fig. 3: The work flow shows the upstream processing of Temulawak (C. *xanthorrhiza*) aquaeous extract

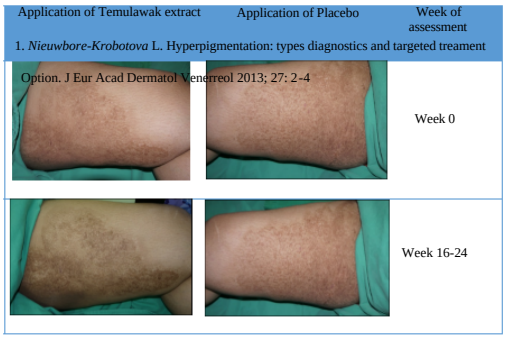

Fig. 4: Appearance of scar on week 0 and week 16-24 for application for Temulawak extract and placebo

conditions by the same investigator. The standard lighting conditions will be using axial lighting with green color background using camera CASIO Exilim Exz400. The lens aperture, exposure time, subject distance and room lightning were kept constant for each patient. The images were then be subsequently assessed by an image panel. The scars were rated as hyperpigmented, if they were darker than surrounding normal skin. They were rated normal if they were of the same colour compared to the surrounding skin and hypo-pigmented if lighter.

Image panel: The image assessment panel consisted of 2 medical practitioners from the same department, who agreed to take part in the study and not directly involved in wound healing research. Each panel member were sent batches of photos taken during every assessment. They were scoring the images using a scale. The scores from the panels were then calculated for each wound for each parameters assessed.

Assessment

Patient's subjective symptoms and clinical assessment: A beneficial effect is seen if reduction recorded in scar score both in patient's subjective scar assessment and modified Vancouver Scar Scale.

Patient's symptoms of pain and pruritus were also be recorded during each follow-up. Clinical assessment were carried out by the investigator using the Clinical Assessment Sheet which includes scar colour/pigmentation, vascularity, pliability and height as per Modified Vancouver Scar Scale. Special emphasis were given to the colour of the scar compared with the surrounding skin. Each of these parameters were given a score of between 0-5, increasing values indicating increasing scar severity based on Modified Vancouver Scar Scale.

This score, expressed in cm to one decimal place was then added to the sum of the individual parameter scores to give an overall score for each scar. This ranged from 0-15, low scores representing scars of good cosmetic appearance and high scores representing clinically poor scars. The results at week 0, 2, 6 and 16-24 were analyzed using one way repeated measure ANOVA.

Statistical analysis: Data entry, cleaning and analysis were done by using SPSS Version 22. Descriptive analysis were done using mean and standard deviation for numerical variables and frequency and proportion for categorical variables. The results for each group were analyzed with repeated measures ANOVA. Comparison was made between the treatment groups for the assessment of pigmentation, pain, pruritus and total scar score. Statistical significance were evaluated using a statistical software package (SPSS 22.0). A $p<0.05$ were considered to be significant.

RESULTS AND DISCUSSION

The 58 subjects were recruited. Six participants were lost to follow-up (because of logistic reason) and excluded from the study. The remaining fifty two were analyzed. Mean age of the subjects was 39 years old (between 24-53 year old) with SD = 14.43. Predominantly, female 61.5% (n = 32) participated in the study. The majority of them had hyperpigmented scar distributed at head and neck 28 (53.8%), followed with limbs 21 (40.4%) and trunk 3 (5.8%).

Effects on scar pigmentation: Vancouver Scar Scale (pigmentation) Table 1 showed that there was no significant difference of mean total score between control and treatment groups using repeated measure ANOVA ($F = 0.658$, $p = 0.522$). Multiple comparisons performed with adjusted á based on Bonferroni correction because the test within subject effect is significant to identify either the pairwise comparison was significant or not as illustrated in Table 2. The results showed that there were no significant differences between times (week 0, 2, 6 and 16-24) in both placebo and Temulawak group. The mean difference of each comparison group showed that there was decrement in mean score in the Temulawak group.

For patient subjective assessment, as presented in Table 1, there was significant difference of mean total score within control and treatment groups in repeated measure ANOVA ($F = 15.46$, $p<0.001$). Multiple comparisons is performed with adjusted a based on

Table 1: Hyperpigmented scar score using various subjective and objective assessments for week 0, 2, 6 and 16-24

Variables	Groups	W0 mean (SD)	W2 mean (SD)	W6 mean (SD)	W1 6-24 mean (SD)	p-values
Vancouver Scar Scale (pigmentation)	Placebo (n = 26)	1.96(0.20)	2.0(0.0)	2.0(0.0)	2.0(0.0)	0.327
	Temulawak (n = 26)	1.96(0.20)	1.96(0.19)	1.96(0.04)	1.88(0.43)	0.625
Patient subjective assessment colour	Placebo (n = 26)	2.88(0.83)	2.76(0.97)	2.40(0.96)	2.32(1.07)	0.005
	Temulawak (n = 26)	3.15(0.83)	2.62(0.80)	2.15(0.78)	1.77(0.91)	<0.001
Independent photographic assessor (colour)	Placebo (n = 26)	2.28(0.68)	2.16(0.80)	2.04(0.68)	1.84(0.69)	0.004
	Temulawak (n = 26)	2.10(0.70)	2.31(0.79)	2.08(0.69)	1.92(0.69)	0.015

p-value is significant if <0.05, p-value represent overall comparison between each group from F-test in repeated measure ANOVA

Table 2: Comparison of mean total score of each groups based on time (time effect) (n = 52) for Vancouver Scar Scale (pigmentation)

	Placebo		Temulawak	
Comparison	MD (95%CI)	p-values[b]	MD (95%CI)	p-values[b]
W0-W2	-0.04(-0.15,0.07)	>0.95	0.00(0.16,0.16)	>0.95
W0-W6	-0.04(-0.15,0.07)	>0.95	0.00(0.16,0.16)	>0.95
W0-W16-24	-0.04(-0.15,0.07)	>0.95	0.08(-0.20,0.35)	>0.95
W2-W6	-0.04(-0.15,0.07)	>0.95	0.00(0.00,0.00)	>0.95
W2-W16-24	-0.04(-0.15,0.07)	>0.95	0.08(-0.14,0.30)	>0.95
W6-W16-24	-0.04(-0.15,0.07)	>0.95	0.08(-0.14,0.30)	

Table 3: Comparison of mean total score of each groups based on time (time effect) (n = 52) for patient subjective assessment colour

	Placebo		Temulawak	
Comparison	MD (95%CI)	p-values[b]	MD (95%CI)	p-values[b]
W0-W2	0.15(-0.11,0.42)	0.620	0.54(0.25,0.82)	<0.001
W0-W6	0.54(0.18,0.90)	0.002	1.00(0.39,1.62)	0.001
W0-W16-24	0.62(0.16,1.07)	0.004	1.39(0.71,2.06)	<0.001
W2-W6	0.39(0.06,0.71)	0.012	0.46(-0.05,0.97)	0.092
W2-W16-24	0.46(0.07,0.86)	0.016	0.85(-0.20,0.05)	0.006
W6-W16-24	0.08(-0.14,0.30)	>0.950	0.39(-0.04,0.81)	0.091

Table 4: Comparison of mean total score of each groups based on time (time effect) (n = 52) for independent photographic assessor (colour)

	Placebo		Temulawak	
Comparison	MD (95% CI)	p-values[b]	MD (95% CI)	p-values[b]
W0-W2	0.12(-0.07,0.30)	0.498	0.08(-0.14,0.30)	>0.950
W0-W6	0.23(-0.01,0.47)	0.067	0.31(-0.001,0.62)	0.051
W0-W16-24	0.42(0.14,0.71)	0.001	0.46(0.10,0.83)	0.007
W2-W6	0.12(-0.13,0.36)	>0.950	0.23(-0.01,0.47)	0.067
W2-W16-24	0.31(-0.001,0.62)	0.051	0.39(0.06,0.71)	0.012
W6-W16-24	0.19(-0.42,0.03)	0.133	0.15(-0.05,0.36)	0.258

Repeated measures ANOVA within group analyses were applied followed by multiple comparisons; MD = Mean Difference; [b]Bonferroni correction applied by correcting level of significance (a/number of pairs = 0.05/3 = 0.017)

Bonferroni correction because the test within subject effect is significant to identify either the pairwise comparison was significant or not. The results in Table 3 showed that there were significant differences between majority times (week 0, 2, 6 and 16-24) in both placebo and Temulawak group except for week 6 to week 16-24. For pair 1 (week 0-2) and pair 2 (week 0-6) and there were significant mean difference for Temulawak participants only (mean difference = 0.54, 95% CI: 0.25, 0.82, p<0.001) and (mean difference = 1.00, 95% CI: 0.39, 1.62, p = 0.001) and placebo (mean difference = 0.54, 95% CI: 0.18, 0.90, p = 0.002) group.

The trend continues in pair 3 (week 0 with 16-24) and pair 5 (week 2 with week 16-24) where there both were significant difference of mean score for both group, Temulawak (mean difference = 0.62, 95% CI: 0.16, 1.07, p = 0.004) and placebo (mean difference = 1.39 , 95% CI: 0.71,2.06, p<0.001) group and (mean difference = 0.46, 95% CI: 0.07, 0.86, p = 0.016) and placebo (mean difference = 0.85 , 95% CI:-0.20, 0.05, p = 0.006) . For pair 4 (week 2-6), only placebo have significant difference. The mean difference of each comparison group showed that there was higher decrement in mean score in Temulawak group (Table 4).

For independent photographic assessor (colour), Table 1 shows that there was significant difference of the mean total score within control and treatment groups in repeated measure ANOVA (F = 9.912, p<0.001). Multiple comparisons is performed with adjusted α based on Bonferroni correction because the test within subject effect is significant to identify either the pairwise comparison was significant or not as illustrated in Table 5. The results showed that there were no significant differences between majority times (week 0, 2, 6 and 16-24)

Table 5 : Itchiness and pain scores for week 0, 2, 6 and 16-24

Variables/Groups	W0 mean (SD)	W2 mean (SD)	W6 mean (SD)	W16-24 mean (SD)	p-values
Itchiness					
Placebo (n = 26)	1.32(2.21)	1.16(2.10)	0.92(1.99)	0.72(1.75)	0.062
Temulawak (n = 26)	1.42(2.32)	0.58(1.17)	0.50(1.03)	0.54(1.14)	0.212
Pain					
Placebo (n = 26)	0.44(1.53)	0.28(1.40)	0.28(1.40)	0.24(0.88)	0.383
Temulawak (n = 26)	0.27(0.83)	0.0(0.0)	0.0(0.0)	0.0(0.0)	0.110

p-value is significant if <0.05; Repeated measure ANOVA

Table 6: Comparison of mean total score of each groups based on time (time effect) (n = 52) for Itchiness

	Placebo		Temulawak	
Comparison	MD (95%CI)	p-value[b]	MD (95%CI)	p-values[b]
W0-W2	0.15(-0.34,0.65)	>0.950	0.85(-0.25,1.94)	0.219
W0-W6	0.39(-0.12,0.89)	0.231	0.92(-0.23,2.08)	0.185
W0-W16-24	0.58(-0.04,1.20)	0.079	0.89(-0.28,2.05)	0.231
W2-W6	0.23(-0.14,0.60)	0.498	0.08(-0.20,0.35)	>0.950
W2-W16-24	0.42(-0.03, 0.88)	0.079	0.04(-0.30,0.38)	>0.950
W6-W16-24	0.19(-0.16,0.55)	0.806	-0.04(-0.29,0.21)	>0.950

Table 7: Comparison of mean total score of each groups based on time (time effect) (n = 52) for pain

	Placebo		Temulawak	
Comparison	MD (95% CI)	p-values[b]	MD (95% CI)	p-values[b]
W0-W2	0.15(-0.41,0.72)	>0.95	0.27(-0.20,0.72)	0.657
W0-W6	0.15(-0.41,0.72)	>0.95	0.27(-0.20,0.73)	0.657
W0-W16-24	0.20(-0.26,0.64)	>0.95	0.27(-0.20,0.73)	0.657
W2-W6	0.00(0.00,0.00)	>0.95	0.00(0.00,0.00)	>0.950
W2-W16-24	0.04(-0.68,0.76)	>0.95	0.00(0.00,0.00)	>0.950
W6-W16-24	0.04(-0.68,0.76)	>0.95	0.00(0.00,0.00)	>0.950

Repeated measures ANOVA within group analyses were applied followed by multiple comparisons; MD = Mean Difference; [b]Bonferroni correction applied by correcting level of significance (a/number of pairs = 0.05/3 = 0.017)

Table 8: Overall score effects for week 0, 2, 6 and 16-24

Variables/Groups	W0 mean (SD)	W2 mean (SD)	W6 mean (SD)	W16-24 mean (SD)	p-values
Vancouver Scar Scale					
Placebo (n = 26)	4.16(3.22)	3.64(2.86)	3.60(2.58)	3.68(3.02)	0.164
Temulawak (n = 26)	3.50(1.98)	3.57(2.39)	3.46(2.34)	2.96(1.66)	0.147

p-value is significant if <0.05; Repeated measure ANOVA

in both placebo and Temulawak group except for week 0 to week 16-24. For pair 3 (week 0 with week 16-24) where there were significant difference of mean score for both group, Temulawak (mean difference = 0.46, 95% CI: 0.10, 0.83, p = 0.007) and placebo (mean difference = 0.42 , 95% CI: 0.14,0.71, p = 0.001) group. For pair 5 (week 2 with week 16-24), mean different is significant only for participants in Temulawak group (mean difference = 0.39, 95% CI: 0.06, 0.71, p = 0.012). The mean difference of each comparison group showed that there was higher decrement in mean score in Temulawak group.

Effects on itchiness and pain: Table 5-7 provides the summary of analysis on itchiness and pain score for week 0, 2, 6 and 16-24. Both for itchiness and pain, result shows that there was statistically no significant difference of mean total score within control and treatment groups.

Total effect on scar: Table 8 provides the summary of analysis of overall score for week 0, 2, 6 and 16-24. There was no significant difference of mean total score within control and treatment groups in repeated measure ANOVA (F = 1.934, p = 0.134). The results showed that there were no significant differences between times (week 0, 2, 6 and 16-24) in both placebo and Temulawak group. The mean difference of each comparison group showed that there was decrement in mean score in Temulawak group (Table 9).

Adverse effect on human skin: There was no adverse reaction on both Temulawak cream and placebo cream group.

Hyperpigmentation can be a common, yet challenging, sequelae of cutaneous inflammation, especially in those with darker skin. Post inflammatory hyperpigmentation and melasma are difficult conditions for many patients generating a negative impact on their quality of life. The goal of treatment is to reduce the hyperpigmentation without causing undesirable hypopigmentation or irritation in the surrounding area (Woolery-Lloyd and Kammer, 2011).

Despite being extensively studied on multipurpose beneficial effect of Temulawak for anti-oxidant, anti-inflammatory, antiseptic, anti-tumour, anti-bacterial,

Table 9: Comparison of mean total score of each groups based on time (time effect) (n = 52) for Vancouver Scar Scale

	Placebo		Temulawak	
Comparison	MD (95% CI)	p-values[b]	MD (95% CI)	p-values[b]
W0-W2	0.50(-0.16,1.16)	0.238	-0.077(-0.71, 0.56)	>0.950
W0-W6	0.54(-0.32,1.40)	0.508	0.04(-0.78,0.86)	>0.950
W0-W16-24	0.46(-0.44,1.36)	0.931	0.54(-0.26,1.34)	0.390
W2-W6	0.04(-0.48,0.55)	>0.950	0.12(-0.42,0.65)	>0.950
W2-W16-24	-0.04(-0.47,0.40)	>0.950	0.62(-0.13,1.36)	0.158
W6-W16-24	-0.08(-0.60,0.45)	>0.950	0.50(-0.16,1.16)	0.238

Repeated measures ANOVA within group analyses were applied followed by multiple comparisons; MD = Mean Difference; [b]Bonferroni correction applied by correcting level of significance (a/number of pairs = 0.05/3 = 0.017)

anti-fungal, whitening agent and lipase inhibitor (Batubara *et al*., 2010, (2015); Kartika, 2015; Hwang *et al*., 2000; Diastuti *et al*., 2014; Claeson *et al*., 1996; Dietrich, 2013), only few study focus on treatment for hyperpigmentation scar (Batubara *et al*., 2010, 2015; Kartika, 2015; Diastuti *et al*., 2014). Furthermore, there is no specific study looking at the treatment of scar hyperpigmentation in vivo. Therefore, this study was aimed to explore positive outcome of Temulawak for treatment of hyperpigmentation.

Our clinical study has shown positive effect of Temulawak for the treatment of hyperpigmented scar. The result showed that both groups have hyperpigmentation reduction.

However, Temulawak group had higher hyperpigmentation score reduction compared to placebo in patient subjective assessment.

On the other hand in Vancouver Scar Scale assesment neither group has significant result (p>0.05), this can be explained by small assesment range of pigmentation in Vancouver Scar Scale (0-normal, 1-hypopigmentation, 2-hyperpigmentation).

Other factor which might cause Temulawak to be less effective is the efficacy of temulawak cream skin penetration which might fail to reach target cells-melanocyte at the basement membrane.

Never the less, hyperpigmentation score reduction in mean difference is higher in the Temulawak group compared to placebo group. This positive outcome was similar with previous study showing Temulawak potential as whitening skin agent (Batubara *et al*., 2015). Batubara preliminary research proved that Temulawak acts as anti-hyperpigmentation in two ways: as tyrosinase inhibitor and anti-oxidant (Batubara *et al*., 2010).

Our findings showed progressive pain and itchiness score reduction in both Temulawak and placebo group. However, this reduction was not statistically significant (p>0.05). In Temulawak group, the mean different for pain and itchiness score reduction between week 0 and 16-24 is higher than in control group. This might be explained by the formulation of both Temulawak and placebo cream using water based preparation which help to moisturize the scar. Apart from it, Temulawak has the anti-inflamatory property as proved in previous study (Diastuti *et al*., 2014; Claeson *et al*., 1996) that helped in reducing pain.

Scar assessment using modified Vancouver Scar Scale showed higher mean difference between week 0 and week 16-24 in the intervention group (MD = 0.54,-0.26,1.34 95% CI) compared to control group (MD = 0.46,-0.44,1.36 95% CI). This showed that better overall scar rating in Temulawak group compared to placebo albeit the result is not significant (p>0.05). With these findings, Temulawak has a potential to be marketed as one of solution in treating hyperpigmented scar.

CONCLUSION

The usage of Temulawak on hyperpigmented scar were not statistically significant. We attribute this to the limitation of the Vancouver Scar Scale in describing the degree of pigmentation and small sample size. In spite of this, Temulawak had positive effect on perceived degree of pigmented scar, pain score, reduce itchiness and overall scar appearance. Therefore, we feel Temulawak has the potential in the treatment of hyperpigmented scar.

LIMITATIONS

The limitations of this study are in term of unsupervised topical cream application which might affect the result. The different location of treated hyperpigmented scar which might be more exposed to sunlight and render the treatment efficacy.

RECOMMENDATIONS

For further study, we recommend skin penetration test of Temulawak cream to determine the percentage of active ingredient able to reach target cells.

In order to realize full potential of Temulawak in treatment of hyperpigmented scar, further clinical trial with a larger sample size is needed. It is also recommended to study in vivo effect of Temulawak for it's special property such as: anti-oxidant, anti-inflammatory, antiseptic, anti-tumour, anti-bacterial, anti-fungal,

whitening agent and lipase inhibitor. Most of the previous studies were limited to laboratory analysis only.

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