

# Comparative Study of Herbal Extracted Gel and 1% Hydrocortisone Gel in the Treatment of Mosquito Bite Reaction

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Received December 20<sup>th</sup>, 2013; revised January 14<sup>th</sup>, 2014; accepted January 21<sup>st</sup>, 2014

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## ABSTRACT

**Background:** Mosquito bite reaction is a common skin disease. Topical steroids and oral antihistamines are the conventional treatment. However, the side effects from prolonged use of topical steroids are the limitation of the treatment. Recently, herbal extracts are emerging interest for an alternative anti-inflammatory dermatoses therapy. **Objective:** To assess the effectiveness of herbal extracted gel containing, *Perilla frutescens*, *Portulaca oleracea*, *Ipomoea pescaprae*, *Aloe vera*, *Centella asiatica* and *Broussonetia papyrifera* in comparing with 1% hydrocortisone (HC) gel. **Material and Methods:** An experimental study was conducted on 50 mosquito bite hypersensitive volunteers (15 - 19 years old) with double-blinded split randomized control method. After the volunteers were exposed for one bite on their arms by a non-infectious mosquito, *Aedes albopictus*, the drugs were applied twice daily. The diameter of lesion, pruritus analog score, erythema and melanin index were measured at 2, 6, 24 hours and 2, 3, 4 weeks. The volunteers "self-satisfaction" and side effects were recorded. **Results:** The mean age was  $17.42 \pm 1.14$  years old. The diameter of lesion, pruritus analog score, erythema and melanin index were decreased on both sides at each visit with significant difference ( $p < 0.05$ ). There was no significant difference between two agents of all parameters and the satisfaction of the volunteers ( $p > 0.05$ ). The post-inflammatory hyperpigmentation rate of 1% HC and herbal gel was 64% and 54% respectively without significant difference ( $p = 0.267$ ). **Conclusion:** The herbal gel was as effective as 1% HC for the treatment of acute and late reaction of mosquito bite reaction in adolescent. It may be used as the alternative treatment for mosquito bite reaction.

## KEYWORDS

Herbal Extract; Mosquito Bite Reaction; Anti-Inflammatory; Hydrocortisone

## 1. Introduction

Mosquito bite reaction is very common in children especially who live in tropical countries [1,2]. The clinical manifestation is starting with an immediate type I hypersensitivity response which is presented as wheals and flares within 20 minutes. Then it is followed by the delayed type IV hypersensitivity reaction which is presented as itching, burning, erythematous, edematous papules, occurred approximately 24 hours later and may last for

several days. The common complications of mosquito bite reaction are secondary skin infection such as impetigo, ecthyma, post-inflammatory hyperpigmentation and scar.

Oral antihistamines or topical corticosteroids have been used for the standard treatment of this skin problem. Regarding the effectiveness of cetirizine, there was a study demonstrating that it was effective against both immediate and delayed mosquito bite reactions [3]. However, the side effects from prolonged use of topical corticosteroids limit their value. Moreover, some antihista-

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mines such as cetirizine, can cause drowsiness in the patients.

There are many herbal extract medicaments for various treatments of indications such as anti-inflammation, scar and pigmentation. Recently, there is an emerging interest in topical non-steroidal anti-inflammatory agents including herbal extracts [4], for example, the study which showed that moisturizer containing licochalcone A was as effective as 1% hydrocortisone (HC) in the treatment of childhood atopic dermatitis [5]. This present study, a combination of herbal extracted gel was assessed on the effectiveness in comparing with 1% HC gel. The herbal extracts included *Ipomoea pescaprae*, *Perilla frutescens*, *Portulaca oleracea*, *Centella asiatica*, *Aloe vera*, *Allium cepa* for the anti-inflammatory effect and *Broussonetia papyrifera* for the depigmentary effect. The hypothesis of this study is that the herbal extract is as effective as 1% HC in the treatment of mosquito bite reaction.

## 2. Patients and Methods

Fifty mosquito bite hypersensitive adolescences (aged 15 - 19 years old) who have history of popular urticaria (pruritic, edematous, erythematous papules with central punctum) with or without post-inflammatory hypo/hyperpigmentation, scars on extremities from mosquito bites in the field, were recruited in this study. They must have at least Fitzpatrick's photo-skintype III and normal skin on the tested areas. The volunteers who received topical corticosteroids, anti-inflammatory drugs, or oral antihistamines for 2 weeks and oral corticosteroids for 4 weeks before initiating the study were excluded. All eligible volunteers agree to participate by signing the informed consent form according to the Declaration of Helsinki (1964).

*Aedes albopictus* (aged 5 - 7 days) from Laboratory Mosquitoes supplied by Department of Entomology, Faculty of Topical Medicine, Mahidol University, Thailand were chosen for this study. The volunteers were then exposed to the mosquitoes which were in the cages with the size of  $5 \times 5 \text{ cm}^2$  on each forearm located 3 cm from the cubital fossa. After the volunteers were exposed for bites by the mosquitoes, a split randomized comparative study between herbal extracted gel (Cybele<sup>®</sup> Scagel Kids, Bangkok Botanica, Thailand) and 1% hydrocortisone gel was done with a twice daily topical application. Both agents were the same color, smelling and texture. They were packed into the same kind of tubes. The randomized technique was done by the third person. The secret code for each volunteer was disclosed after finishing the protocol. Clinical outcomes, which included diameter of lesion, the intensity of pruritus, erythema, and post inflammatory hyperpigmentation, were evaluated.

Vernier caliper series 530 (Mitutoyo, Kawasaki, Japan) was used to measure the diameter of the lesions. Measurement was done three times as rechecks. The Visual Analog Scale (VAS) was used to evaluate the itching parameter. Data were collected at a baseline (immediate after mosquito bite) with intervals of 2 hours, 6 hours, 24 hours, 1 week, 2 weeks, 3 weeks and 4 weeks of the study period. The erythema and post inflammatory hyperpigmentation outcomes were assessed by Mexameter<sup>®</sup> (Model MX16, Courage and Khazaka Electronic Co., Germany) with the average value of the triplicate measurements, which were collected at a baseline (immediate after mosquito bite) with intervals of 24 hours, 1 week, 2 weeks, 3 weeks and 4 weeks of the study duration.

The descriptive analysis was used on the demographic data. Comparison of the lesion size, the intensity of pruritus, erythema, hyperpigmentation between both arms was done by using paired t-test and the outcomes from each visit were analysed by using repeated ANOVA. The global satisfactory were evaluated by using McNemar Test. The significance of all values is attained when  $p < 0.05$ . This study was approved by the clinical ethic committee of Faculty of Medicine, Srinakharinwirot University.

## 3. Results

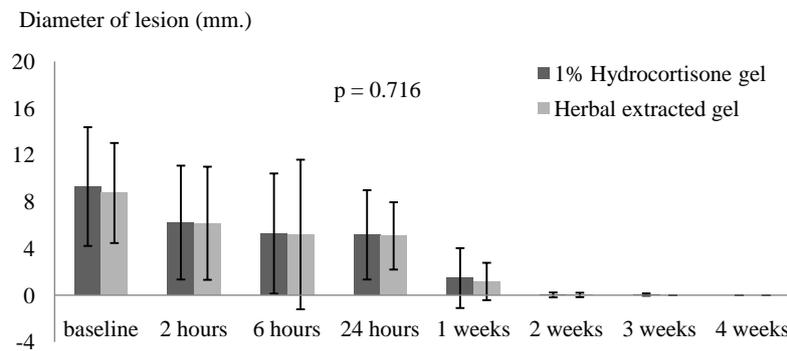
Fifty volunteers completed the study protocol. The mean age of the volunteers was  $17.42 \pm 1.14$  years old; 48 were female. Concerning the Fitzpatrick photo-skin type of the volunteers, 25/50(50%), 15/50(30%) and 10/50(20%) were types III, IV and V respectively.

The diameter of the papules and plaques were reduced after the treatments with 1% hydrocortisone gel and herbal extracted gel. The size of lesions were reduced significantly after 2 hours ( $p < 0.05$ ) and on each visit until the end of week 2 on the herbal extracted gel side and the end of week 3 on 1% HC side (Figure 1). There was no significance in size difference between the treatments with the two agents ( $p = 0.716$ ).

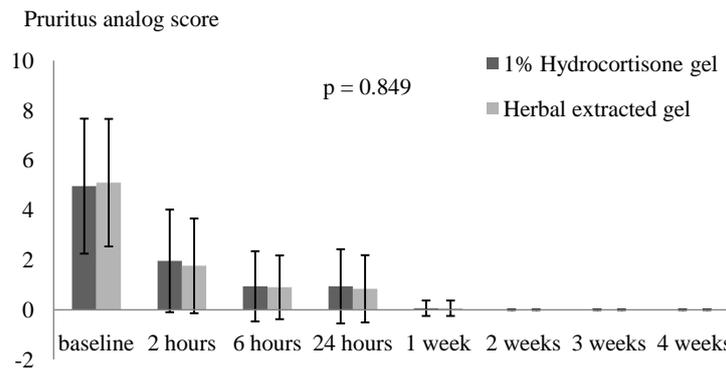
In both treatment groups, the pruritus score reduced significantly after 2 hours ( $p < 0.05$ ) and continued to decrease after 1 week. After 2 weeks, there was no pruritic symptom (Figure 2). There was no significance in size difference between the treatments with 1% hydrocortisone gel and herbal extracted gel ( $p = 0.849$ ).

Initially, on both sides, the erythema of the lesions increased within 24 hours and then decreased significantly at each visit ( $p < 0.05$ ) (Figure 3). There was no significant difference between the treatments with both agents ( $p = 0.860$ ).

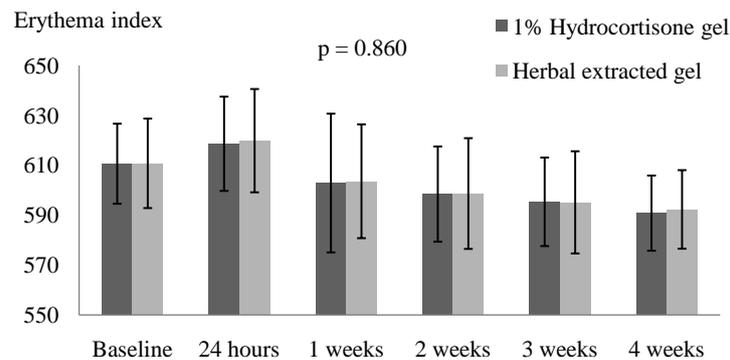
Less post-inflammatory hyperpigmentation was observed on the treatment group with herbal extracted gel



**Figure 1.** The comparison of diameter of the lesions between 1% hydrocortisone and herbal extracted gel.



**Figure 2.** The comparison of pruritus (VAS) between 1% hydrocortisone and herbal extracted gel.



**Figure 3.** The comparison of erythema index between 1% hydrocortisone and herbal extracted gel.

compared to 1% hydrocortisone gel (54% VS 64%). However, there was no significant group difference ( $p = 0.267$ ) (Table 1). By using Mexameter MX16, melanin index, both groups increased in pigment intensities by week 1 - 2 and then started to decrease in the week 3 and 4 (Figure 4). There was also no significant difference between the treatments with 1% hydrocortisone gel and herbal extracted gel ( $p = 0.562$ ).

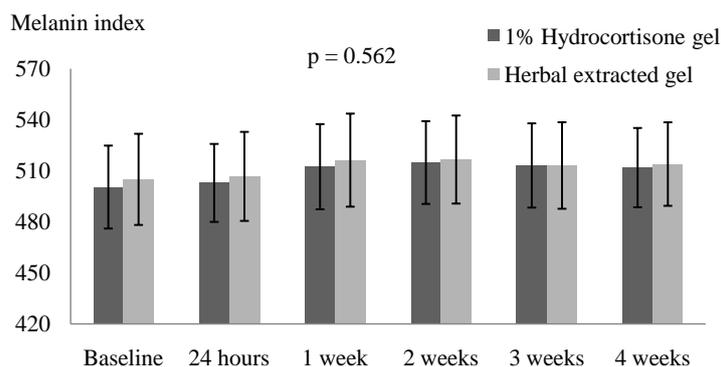
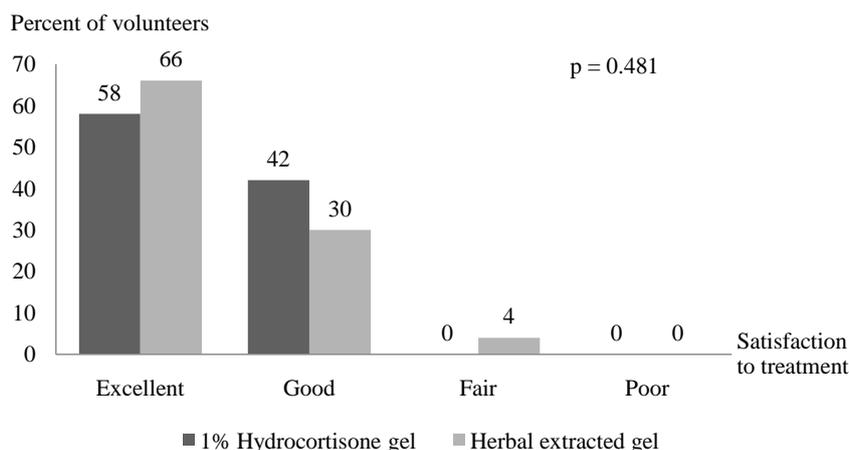
Regarding the volunteers' self satisfaction to the treatments, the volunteers evaluated the excellent outcomes in majority of the cases on both agents (58%—for 1% hydrocortisone gel; 66%—for herbal extracted gel) (Figure 5). There was no significant difference between the two agents ( $p = 0.481$ ).

#### 4. Discussion

The results of this experimental study showed that the combination of herbal extracts could improve the mosquito bite reaction both subjective measurements (diameter of lesions, pruritus score), objective assessments (erythema index, melanin index), and volunteer's self satisfactions evaluation with statistically significant difference from the base line. When the effectiveness was compared with 1% HC, it was demonstrated that there was no significant difference. Though the prevalence of post inflammation was lower in the herbal extracted gel treated group (54% for herbal extracted gel group VS 64% for 1% HC), there was no statistically signifi-

**Table 1. Post Inflammatory Hyperpigmentation (PIH) between two agents.**

	Total Value	PIH	% with PIH	p value
1% Hydrocortisone gel	50	32	64%	p = 0.267
Herbal extracted gel	50	27	54%	

**Figure 4. The comparison of melanin index between 1% hydrocortisone and herbal extracted gel.****Figure 5. The comparison of volunteer's satisfaction between 1% hydrocortisone and herbal extracted gel.**

cant group difference, as well as the melanin index reduction score.

The herbal extracted gel used in this study containing a combination of *Ipomoea pescaprae*, *Centella asiatica*, *Perilla frutescens*, *Portulaca oleracea*, and *Aloe vera* for the anti-inflammatory properties. There were studies demonstrated that these herbal extracts had anti-inflammatory actions. *In vitro* study, beta-damascenone, an active ingredient extracted from *Ipomoea pescaprae* [6,7], and asiaticoside from *Centella asiatica* [8] exhibit anti-inflammatory effect through prostaglandins formation inhibition. Oral intake of *Perilla frutescens* Britton leaves which contain high amount of rosmarinic acid, apolyphenolic phytochemical, demonstrated the inhibitory effect on mice ear passive cutaneous anaphylaxis reaction [9]. It can inhibit house dust mite induced asthma in mouse model by inhibiting the enhanced protein expression of Interleukin (IL)-4, IL-5, eotaxin and specific IgG

[10,11]. In addition, rosmarinic acid in *Perilla frutescens* also protects against UV-induced of murine skin [12].

Linolenic acid from *Portulaca oleracea* shows anti-inflammatory action via prostaglandins formation inhibition both *in vitro* and *in vivo* studies [13,14]. *In vitro* study of aloins and 1, 8 dihydroxyanthraquinone, the major active ingredients of *Aloe vera* demonstrated the inhibitory action on the prostaglandin E production [15], IL-8 [15-18], tumor necrotic factor-alpha, IL-6 [17], and leukocyte adhesion inhibition as well [17,19]. Concerning clinical trial, the systematic review of *Aloe vera* effectiveness shows that topical application of this agent might be effective for genital herpes [20] and psoriasis [16,20]. Moreover there was clinical trial demonstrated its effectiveness on a partial thickness burn wound [21].

Finally, regarding the treatment of post-inflammatory hyperpigmentation after the recovering from skin inflammation, Kazinol F extracted from *Broussonetia pa-*

*pyrifera* plays the major role. The mechanism of action is through the inhibition of tyrosinase [22], and L-dihydroxyphenylalanine (DOPA) auto-oxidation [23].

Some species of mosquito, for example, *Aedes albopictus* that was used in this study, can survive even in the cold weather. Although, mosquitoes bite reaction is the common problem of the people especially the children in tropical countries. Because of the global warming problem, this skin reaction might be the major problem of the people living in the temperate countries in the future. Taken together with the limitation of long term topical corticosteroid application as we described previously, this herbal extract medications which have anti-inflammatory properties may be an alternative treatment.

## 5. Conclusion

The herbal extracted gel with anti-inflammation and depigmentation properties used in this study is as effective as 1% hydrocortisone gel in treatment of both immediate and delayed mosquito bite reactions in adolescents. The herbal extracted gel might be used as the alternative treatment.

## Acknowledgements

We would like to acknowledge Department of Medical Entomology, Faculty of Topical Medicine, Mahidol University, Bangkok, Thailand for supplying the mosquitoes for this experimental study, Dr Suchada Boonit for the English grammars correction, Bangkok botanica Ltd., for herbal extracted gel.

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