INTRODUCTION

Atopic dermatitis (AD) is an inflammatory skin condition characterized by intense pruritus in a waxing and waning course [1]. It affects 10-20% children and 1-3% adults worldwide, with a female to male ratio of 1.3:1.1 [1]. In 2013, the prevalence of AD according to Pediatric Dermatology Clinic data from five tertiary referral hospitals in Indonesia was 11.8% [2].

A complex interaction between genetic, immune system dysregulation and environmental factors have been documented as the pathogenesis of AD [2]. Filagrin mutation decreased ceramide, and increased endogenous proteolytic enzymes, often result in increased transepidermal water loss (TEWL) and scoring of atopic dermatitis (SCORAD) index value in mild atopic dermatitis (AD) pediatric patients in Bandung, Indonesia [12-14].

Various studies on SSO in both AD and non-AD child population have given evidence of its effectiveness in lowering the TEWL scores [14, 15]. However, to the best of the authors’ knowledge, there has been no study comparing SSO with common moisturizers.

### Materials and Methods

#### Material and preparation of drugs

The 20% SSO cream used in this study was made by pharmacists in Bandung Institute of Technology, Indonesia and had undergone
product animal testing prior to the experiment. The formula is presented in table 1. Meanwhile, the control product cream was common moisturizing lotions, which were repackaged in uniform opaque plastic pots.

Study design
This randomized, double-blind trial, in children with mild AD, was conducted in two locations: in the outpatient clinic of Dermatology Department in Dr. Hasan Sadikin Hospital Bandung and Sejahtera Elementary School Bandung. This study had been approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin Hospital Bandung, West Java, Indonesia with ethical clearance number: LB.04.01/A05/EC/296/IX/2016. Informed consent from one parent or caregiver and the assent of children were likewise secured prior to treatment.

Subject
The enrolled participants were those patients in the age range of 7-12 y of age with mild AD, who met the Hanifin and Rajka criteria and had SCORAD index of <25, were enrolled. The exclusion criteria were: (1) those with known hypersensitivity reactions to SSO cream and control product cream, (2) those who have used moisturizer other than the given treatment or any medication on both arms, legs, and lesions within one week prior to the study, (3) those who have taken anti-inflammatory and antihistamine drugs 2 w before and during the study, (4) those with other co-existing skin diseases in the area that were going to be treated, (5) those with co-existing recurrent atopic disease, (6) those who had AD with secondary bacterial infection.

Procedures
Twenty children with AD who met the criteria were randomly assigned into two groups: group I (9 participants) who were treated with 20% SSO cream and group II (11 participants) who were treated with a common commercial moisturizer. Both creams passed the animal testing and were repackaged in an opaque container. They were marked with random labels and only research assistant knew the contents of each label. Both researchers and subjects of the study were blinded to the content of the creams. TEWL was measured on the mid-volar of the lower arm, both popliteal fossa, and skin lesions. The cream was then applied on both arms, both limbs, and in AD lesions. Patient-applied the cream twice daily at home in the same instructed locations. No other creams or lotions may be used on the observation area. Clinical assessments were performed at baseline (day 0), and on follow up on week 1 (day 7), week 2 (day 14), and week 4 (day 28).

Outcome measures
The TEWL score was measured at baseline, week 1, week 2, and week 4 using the Tewameter TM 300 at four regions (head/neck, trunk, upper and lower limbs). On each visit, patients were observed for any adverse effect, which, if found, would be recorded. The SCORAD index was measured at every visit.

Statistical methods
Paired t-test was used to compare the TEWL scores. Meanwhile, the Mann-Whitney test was used to compare the mean of the TEWL scores and SCORAD index between the two groups. Results were considered to be significant if the p-value was less than 0.05.

RESULTS
Demographic profile
In both groups, the age ranges from 7 to 12 y old. The mean age for SSO cream group and control cream group were 8.56 ±1.51 y and 9.45±2.70 y respectively. Sixty-five percents (13 out of 20) of the patients were female.

Table 2: Demographic data in both groups

| Variables          | SSO 20% (n = 9) | Control cream (n = 11) | p-value |
|--------------------|----------------|------------------------|---------|
| Age (years)        | 7-11           | 7-12                   | 0.38    |
| Mean age (years)   | 8.56           | 9.45                   |         |
| Sex                | 5              | 2                      | 0.16**  |
| Male               | 4              | 9                      |         |
| Female             |                |                        |         |

*p-value<0.05 compared with the control group using paired t-test, **p-value>0.05 compared with the control group using fisher's exact test.

TEWL scores
The TEWL scores in both treatment groups were measured on the right arm, left arm, right leg, and left leg. There was a reduction of TEWL scores in both treatment groups. The average TEWL score was 17.26 in SSO cream group and 16.31 in the control cream group at baseline; 12.26 in the SSO cream group and 10.32 in control cream group on week 1; 8.93 in the SSO cream group and 8.69 in the control cream group on week 2; 6.67 in the SSO cream group and 7.74 in the control cream group on week 4, as presented in table 3. The paired t-test showed that TEWL scores did not differ significantly between both groups at baseline (p=0.927), week 1 (p=0.481), week 2 (p=0.899), and week 4 (p=0.472).

Table 3: Average of TEWL Scores after the application of SSO cream and control product cream

| Group   | Location | Time     | Baseline | Week 1 | Week 2 | Week 4 |
|---------|----------|----------|----------|--------|--------|--------|
| SSO cream | Right arm | 18.05 | 13.27 | 9.01 | 6.96 |
|         | Left arm  | 17.68 | 13.88 | 9.95 | 7.36 |
|         | Right leg | 16.42 | 10.84 | 7.87 | 6.06 |
|         | Left leg  | 16.87 | 11.06 | 8.89 | 6.27 |
|         | Mean      | 17.26 | 12.26 | 8.93 | 6.67 |
| Control | Right arm | 17.23 | 11.17 | 9.17 | 8.39 |
|         | Left arm  | 18.02 | 10.39 | 9.21 | 8.63 |
|         | Right leg | 15.74 | 10.18 | 8.23 | 7.07 |
|         | Left leg  | 14.23 | 9.56 | 8.15 | 6.88 |
|         | Mean      | 16.31 | 10.32 | 8.69 | 7.74 |

*p-value>0.05 compared with the control group using paired t-test
TEWL scores decrement

The TEWL score decrement (Δ) was measured from four different locations. The average TEWL scores decrement (Δ) was 4.98 in the SSO cream group and 5.97 in the control cream group after 1 w; 8.45 in the SSO cream group and 7.61 in the control cream group after 2 w; 9.83 in the SSO cream group and 8.56 in the control cream group after 4 w as presented in table 4. The Mann Whitney test showed that the average TEWL score decrement was not significantly different between both groups after 1 w (p=0.882), after 2 w (p=0.882), and after 4 w (p=0.2052).

| Group   | Time     | Δ Baseline-week 1 | Δ Baseline-week 2 | Δ Baseline-week 4 |
|---------|----------|------------------|------------------|------------------|
| SSO 20%| Week 1   | 4.98             | 8.45             | 9.83             |
| Control | Week 1   | 5.97             | 7.61             | 8.56             |
| P-value |          | 0.882***         | 0.882**          | 0.941**          |

**p-value>0.05 compared with the control group using Mann-Whitney test.

**Scorad**

A trend of decreasing SCORAD index was observed in both groups throughout the treatment session. Reductions of the SCORAD index were 100% in both groups. The SCORAD indices in the SSO cream group were 7.23, 2.45, 0.61, and 0, whereas in the control cream group were 9.33, 4.36, 1.87, and 0 on the baseline, week 1, week 2, and week 4, respectively. This considerable improvement in SCORAD index was observed in both groups, as presented in table 5.

| Group | Time     | Baseline | Week 1 | Week 2 | Week 4 |
|-------|----------|----------|--------|--------|--------|
| 20% SSO | Week 1   | 7.23     | 2.45   | 0.61   | 0      |
| Control | Week 1   | 9.33     | 4.36   | 1.87   | 0      |
| p-value |          | 0.456    | 0.412**| 0.131**| 1.000  |

**p-value>0.05 compared with the control group using Mann-Whitney test

Adverse effects

There were no adverse reactions reported by either both groups in this study.

DISCUSSION

The clinical manifestation of AD appeared at the age of 6 mo in forty-five percent of cases, and about eighty-five percent of AD cases were found before the age of 5 y [9]. In this study, the age of the participants with mild AD ranged from 2-12 y old, and the mean age was 8.5±1.51 y in the SSO cream group, and 9.45±2.70 y in the control cream group. Research showed that AD is slightly more common in women than in men with a 1.3:1.0 ratio [13]. In this study, there were 13 girls (65%) and 7 boys (35%) with a ratio of 1.85:1.0. This ratio is consistent with worldwide prevalence [1].

Sunflower seed oil is an occlusive moisturizer and has emollient properties [15]. It has a high content of essential fatty acids (EFA), especially linoleic acid which can increase the skin barrier [16-18]. Linoleic acid content in SSO can be converted into arachidonic acid, a precursor of prostaglandin E2 (PGE2), which is a known modulator of cutaneous inflammation [12]. In human keratinocytes, PPAR-α activators, including linoleic acid, have a regulatory effect by increasing involucrin and transglutaminase protein [15, 16].

The effect of SSO cream in decreasing TEWL was demonstrated in previous randomized controlled trials, and it was postulated to have anti-inflammatory activity, making it an effective treatment to AD [13]. Study done by Danby et al. (2012) revealed that SSO can maintain the integrity of the stratum corneum, repair the skin barrier, and decrease the TEWL value [14]. This was confirmed by Husna’s study (2012), which revealed that SSO application on the adult forearm could reduce the TEWL value [19].

In this present study, the efficacy of 20% SSO cream as a moisturizer to treat mild AD was compared with the control product as indicated by the decrement of TEWL and SCORAD score decrement. Both groups demonstrated a decreasing trend in both TEWL and SCORAD indices (table 4 and 5). Twenty percent of SSO cream decreased TEWL score by 29.89%, 48.99%, and 56.94% in week 1, 2, and 4 respectively. On the other hand, control product cream decreased TEWL score by 36.62% on week 1, 46.68% in week 2 and 52.54% at the end of the study period. Statistical analysis showed that the average TEWL score decrement was not significantly different between both groups. In the SSO 20% cream group, the SCORAD indices plummeted from 7.23 (baseline) to 0 (week 4), whereas in the control group, from 9.33 (baseline) to 0 (week 4). These results showed that the ability of 20% SSO cream to decrease TEWL and improve SCORAD indices is comparable with the control product cream in treating mild cases of AD. The limitation of this study was the relatively short follow-up time (4 w), which may not be able to observe late adverse effects of 20% SSO cream as a moisturizer.

CONCLUSION

Twenty percent SSO cream has a comparable efficacy compared with the control product in decreasing the TEWL and SCORAD index among children with mild AD. Further studies with larger samples are required, but this study demonstrated that 20% SSO cream can be considered as an alternative moisturizer in the treatment of mild AD due to its low cost, beneficial effect, and minimal side-effect.

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AUTHORS CONTRIBUTIONS

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CONFLICTS OF INTERESTS
The author of this study declared no conflict of interest

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