Study protocol for Investigator Initiated Research
(Version 2 – September 15, 2020)

Title

Is 100% pure Stabilized Whole Rice Bran (SWRB) effective when used as a cleanser and an emollient in patients with mild to moderate atopic dermatitis?

Principal Investigator (PI)

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Aim

To study whether the natural product, SWRB, is effective to control the symptoms and signs of mild to moderate Atopic Dermatitis (AD)

Literature review & study proposal

This clinical trial serves to look at the effectiveness of SWRB for the treatment of mild to moderate Atopic Dermatitis in patients below the age of 18.

1. Atopic Dermatitis is a common condition seen in dermatology, paediatric and primary care clinics in Malaysia. The overall prevalence of Atopic Dermatitis in the paediatric population in Malaysia was shown to be around 13.4% in 2018 (Goh et al., 2018)
2. AD poses a significant biopsychosocial burden among sufferers and their families. (Carroll et al., 2005). Current management patterns of AD sufferers in South-east Asia mainly involve use of topical moisturizers and topical corticosteroids (Chan et al., 2006).
3. There are many concerns among parents of sufferers of AD regarding the side effects of these therapies, causing them to seek alternative therapies (Lee and Bielory, 2010).
4. Many emollients are available in the market which are either occlusives, hemectants or both. There are also bath emollients and directly applied ones. Very little has been studied regarding their effectiveness. Emollients

available may also contain preservatives and fragrances that can prove to be irritants when applied topically (Rubel et al., 2013).

5. Rice bran and products derived from it have been studied regarding their anti-oxidant, nutritional, cholesterol lowering and health promoting properties (Nagendra Prasad et al., 2011).

However, there are very few studies that have focused on the benefits of SWRB when used topically.

6. One study had used rice bran broth bath therapy in patients with Atopic Dermatitis, with positive results (Fujiwaki and Furusho, 1992).

SWRB is cost-effective and easily available, while being an under-utilised product. We wanted to study its effectiveness in controlling the signs and symptoms of Atopic Dermatitis when used as a cleanser and topical paste (emollient) as very little is known on this subject.

Methodology / Protocol

This is a clinical trial involving topical therapy with pure SWRB which is in powder form, on patients below 18 years of age, who suffer from mild to moderate atopic dermatitis.

The SWRB is from locally grown rice and locally milled rice bran. This has been recently stabilised, for the first time in Malaysia, and made suitable for human use by Rice Bran Nutraceuticlas Sdn. Bhd.

The SWRB is provided Free of Charge for this Study by RBN

Sample size: The proposed sample size is 50-100 patients of the abovementioned age group.

The severity of disease in the selected sample will be assessed using the widely used SCORAD index.

Patients will be selected from out-patient clinics of

- Dato' Dr S Sellappan's clinic at Loh Guan Lye Specialist Centre.
- Klinik Derma Sivasantha at 11, Jalan Sungai. 10150 Pulau Pinang.
- Any other Doctor or Clinic who is interested in participating in this study.

Written consent to participate in this study will be obtained from the parent/guardian via a consent form, which includes Information Leaflet for the Parent/Guardian and Participant as well as Instructions to Patients for Use of SWRB as cleanser or as moisturiser

Assent from the subjects from the ages from 8 to below 18 will be obtained using the assent form attached. Both, the consent and the assent forms will be attached to the child's medical records.

Confidentiality of patient information and anonymity will be maintained at all times.

Inclusion criteria:
Patients below 18 years of age with mild and moderate Atopic Dermatitis

Exclusion criteria:
1. Those over 18 years of age
2. Patients with other forms of dermatitis
3. Severe disease
4. Those already on other forms of topical therapies, which are likely to interfere with outcomes

Proposed intervention:
Patients with mild AD will be given SWRB in powder form, to be used as a cleanser after adding water to it according to set proportions given as instructions, one time per day.
Patients with moderate disease will be instructed to use SWRB as a cleanser as above. In addition, they will also use SWRB as an emollient after constituting it into a paste as in instructions, apply at night and leave it overnight.
This study does not involve any enteral or parenteral administration of SWRB. Neither does it involve any invasive procedures.

Management of adverse effects of SWRB
Adverse reaction is very unlikely as this is a 100% rice- based product with no bacterial growth or heavy metals. The only rare adverse effect that might occur is allergy to the protein in SWRB causing an increase in the rash. Should this occur, the investigator will undertake the following measures:

1. Withdraw the SWRB.
2. Withdraw the patient from the study.
3. Initiate symptomatic treatment.
4. Administer oral anti-histamine if indicated.
5. Treat with topical corticosteroid if indicted.
6. Follow-up the child every 2 days till adverse effect is controlled.

Data collection
The patients will be followed up for four to six (4 - 6) weeks and the clinical features tabulated . Where appropriate, photographs of the lesion/s will be taken for evaluation of progression / regression at the end of the study, while protecting the identity of the patient.
A questionnaire using the Likert scale, will be prepared for the patient's parent/s to complete. This will be to assess:

- Parents' opinion of the product
- Ease of application
- Convenience (cleaning the bed of the powder, etc.)
- Parents' perception regarding improvement seen/not seen

Duration of study

The study will commence on 21st September 2020.

The duration of this study will be 4 to 6 weeks i.e. each patient will be followed up for 4 - 6 weeks for the purpose of obtaining results for this study. However, follow up beyond the duration of this study may continue as per patients' wishes, for the purpose of continued therapy of the long -term condition, which may or may not involve SWRB.

Each patient will be followed up every two (2) weeks and the progression or regression of the skin lesions recorded.

Resources required

No fee will be paid to any of the investigators.

Any incidental expenses, i.e. stationary, printing, telephone charges, etc. will be borne by the PI.

Strengths of this study

1. Sample size of 50-100 may be achieved within a short duration.
2. Short duration of study enables the research question to be addressed within a short span of time.
3. The low cost of the SWRB and its abundant availability
4. SWRB is a waste product converted to human use. Therefore, it has a beneficial effect on the environment.
5. There are few or no studies to show adverse effects of topical use of SWRB in humans.
6. Patients can be obtained from just a few centres.
7. As studies of this nature using SWRB are rare, this study may encourage further research into SWRB and comparative studies.
8. The SWRB is edible and hence should not cause side effects if small amounts are ingested orally.
9. **Study limitations**

1. Lack of sufficient literature or preliminary studies on topical use of SWRB for Atopic Dermatitis.
2. Possibility of patients deciding to withdraw from the study before completion.
3. The application of SWRB as an emollient may be inconvenient in paste form.

Ethical approval

This study requires ethical review and approval. Application for the same will be submitted to JPEC (Joint Penang Independent Ethics Committee).

Data collection, management and analysis

Data collection will be done via clinical assessments. Data collection and storage will be in accordance with the data protection laws and regulations of Malaysia. All data will be stored in a password protected electronic form accessible to and managed by the Principal Investigator. Data collected will be analysed using sequential analysis.

Project management and administration

The study will be managed by the Principal Investigator, Dato' Dr Sellappan.

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The SCORAD Index

Area

Head and neck	(9% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%
Upper limbs (left)	(9% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%
Upper limbs (right)	(9% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%
Lower limbs (left)	(18% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%
Lower limbs (right)	(18% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%
Anterior trunk	(18% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%
Back	(18% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%
Genitals	(1% BSA)	○ 0%	○ 25%	○ 50%	○ 75%	○ 100%

Intensity

A representative area of eczema is selected. In this area, the intensity of each of the following signs is assessed as none (0), mild (1), moderate (2) or severe (3).

Redness	○ 0	○ 1	○ 2	○ 3
Swelling	○ 0	○ 1	○ 2	○ 3
Oozing / Crusting	○ 0	○ 1	○ 2	○ 3
Scratch marks	○ 0	○ 1	○ 2	○ 3
Skin thickening (lichenification)	○ 0	○ 1	○ 2	○ 3
Dryness	○ 0	○ 1	○ 2	○ 3

Subjective symptoms

Using a visual analogue scale where 0 is no itch (or no sleeplessness) and 10 is the worst imaginable itch (or sleeplessness).

Itch	○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10
Sleeplessness	○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10

Source: http://scorad.corti.li/

Clinical assessment and tabulation of findings

Area		0%	25%	50%	75%	100%
Head and neck	(9% BSA)					
Upper limbs (left)	(9% BSA)					
Upper limbs (right)	(9% BSA)					
Lower limbs (left)	(18% BSA)					
Lower limbs (right)	(18% BSA)					
Anterior trunk	(18% BSA)					
Back	(18% BSA)					
Genitals	(1% BSA)					

Intensity	0 (none)	1 (mild)	2 (moderate)	3 (severe)
Redness				
Swelling				
Oozing / Crusting				
Scratch marks				
Skin thickening (lichenification)				
Dryness				

Subjective symptoms

0 is no itch (or no sleeplessness) and 10 is the worst imaginable itch (or sleeplessness).

Symptom/Score	0	1	2	3	4	5	6	7	8	9	10
Itch											
Sleeplessness											