Protocol

Title: Safety and efficacy of a topical scalp treatment for dry scalp conditions in children and adults

Principal Investigator

Lucy Bilaver, PhD
Northwestern University
750 N Lake Shore Drive, Suite 680
Chicago, Illinois 60611

Email: l-bilaver@northwestern.edu

Co-Investigators

Peter Lio, MD
Northwestern University
Medical Dermatology Associates of Chicago
363 W Erie Street, Suite 350
Chicago, IL 60654

p-lio@northwestern.edu

Statistician

Christopher Warren, PhD

Version Date: March 10th, 2023

Table of Contents

STUDY TITLE

Safety and efficacy of a topical scalp treatment for dry scalp conditions in children and adults

1. BACKGROUND AND RATIONALE:

Dry scalp conditions (dandruff, seborrheic dermatitis, atopic dermatitis) impacts half of the human population and is characterized by dry scalp and fine, loosely adherent, white flakes (Borda 2015). Patients report pruritus, irritation, and a tight-feeling scalp. Dry scalp may be caused by an imbalance of bacteria, colonization of fungi, or abnormal sebum production. Current treatment is limited in efficacy and involves moisturizing or prescription creams or shampoos, along with avoiding triggers or behaviors that exacerbate the condition. A study in 2003 reported the prevalence of seborrheic dermatitis in children and found that seborrheic dermatitis is very prevalent in children younger than 5 months. Of the children in the study, nearly 72% of children younger than 3 months old had seborrheic dermatitis and 50% of children ages 3-5 months had seborrheic dermatitis (Foley 2003).

Recent studies have highlighted the potential role of changes in the skin bacterial and fungal community—the skin microbiome—in exacerbating inflammation of atopic skin. The changes show differing dominating bacterial and fungal strains in healthy and diseased skin (Park 2017). Lesional skin has been shown to be dominated by *Staphylococcus* bacteria and contain a lower microbial diversity than adjacent non-lesional skin (Kong 2012, Seite 2014). It is hypothesized that *Staphylococcus aureus* plays a critical role in the pathogenesis of eczema: the density of *S. aureus* in eczema patients can be staggering at 10^7 colonies per square centimeter of atopic skin, representing a far greater burden than those observed in other forms of skin inflammation (Lin 2007, Cho 2001). Staphylococcus is also a major bacteria found on atopic scalps (Park 2017). Though the precise link between dysbiosis, eczema, and dry scalp in humans remains unclear, these results warrant further investigation into the role of antimicrobial therapy in reversing dysbiosis and its' potential exacerbation of disease severity.

The use of hydrating emollients is effective on atopic skin, in which dry cracks allow irritants to pass and exacerbate the condition (Hanifin et al 2004). Emollients have been found to change skin communities from a disease to healthy state (Seite 2014). Of especial relevance, a 2014 study showed that topically allied emollients containing *Lactobacillus sakei* were effective in a split body trial at reducing common symptoms of eczema (Park 2014). As topical therapy, honey has been shown to work synergistically with antibiotics to treat methicillin-resistant *S. aureus* (Liban 2013). Honey possesses the antibacterial potency needed to stop the growth of *S. aureus.* and histologic studies show early decreases in inflammation, better infection control, and faster healing times (Lusby 2002). In addition, curcumin, the

active ingredient in turmeric, has also shown to be beneficial in skin disease. Although research on curcumin is not extensive, it has demonstrated antioxidant and anti-inflammatory properties in preclinical trials. Its lack of toxicity, even at high doses, makes it an attractive, natural treatment option (Thangapazham et al 2007).

We aim to characterize the safety and efficacy of a topical preparation of *Lactobacillus sp.*, honey, and turmeric in an emollient base in restoring the scalps of those with dry scalp to more closely resemble the healthy scalps.

2. STUDY DESIGN AND SYNOPSIS:

This pilot study consists of participants diagnosed with dry scalp. Participants will receive the required topical vehicle with the treatment condition (containing dead bacteria) on their scalp. This study will consist of 15-40 participants' ages 1 years old to 17 years old and 20-40 participants 18 and older with a clinical diagnosis of dry scalp. Participants will be recruited either while visiting a dermatologist for a standard office visit, while visiting a pediatrician for a standard office visit, or by coming into Children's Healthcare Associates, Medical Dermatology, or our Northwestern research office to be assessed by a physician. Each study visit will take approximately 15-20 minutes.

No randomization will occur, as all participants will receive the active treatment. Each adult participant will apply the active treatment once daily for a study period of 14 days and discontinue using all other scalp management therapies. Each child participant (with the help of a caregiver, if needed) will apply the active treatment once every 2 to 3 days for a study period of 14 days and discontinue using all other scalp management therapies.

The primary goal of this study is to determine the safety and effectiveness of *Lactobacillus sp.,* honey, and turmeric in reducing dry scalp symptomology.

There are three goals in the comparison of these conditions:

- The first is to find the effectiveness of the active treatment in improving clinical disease severity. To accomplish this, an investigator will assess the severity of dry scalp before and after the treatment period using the 11-point flaking scale (Neumann 1996), respectively.
- The second goal is to determine whether the active treatment is safe. This will be accomplished by contacting the patient via over the phone and through daily emails designed to document adverse events and Overall Safety Score. The Overall Safety Score is a 4-point assessment ranging from "no signs of irritation" (0) to "patient discontinued due to irritation" (3). Participants will be asked about the Overall Safety score at the halfway point and the end point of the study.
- The third exploratory goal is to determine whether the microbiome can be changed. This will be

accomplished by obtaining swab samples from the participants' scalps, before and after the treatment period. The samples will be analyzed using 16s RNA sequencing and internal transcribed spacer (ITS) sequencing. Additionally, the change in colony count of bacterial and fungal colonies on the scalp before and after the treatment will be assessed using the Replicate Organism Detection and Counting (RODAC) method. We aim to characterize the effects of *Lactobacillus sp.,* honey, and turmeric on dry scalps.

- Finally, this study will determine the quality of life of participants before and after the treatment period. Quality of life will be calculated using the ScalpDex tool, a validated 23-item instrument that explains the way that patients with scalp dermatitis are affected by symptoms, functioning, and emotions.

3. STUDY OBJECTIVES:

The first goal of this study is to determine the effectiveness of introducing *Lactobacillus sp.*, honey, and turmeric, in reducing dry scalp symptomology.

Hypothesis 1a: Participants' scalps treated with vehicle plus *Lactobacillus sp.*, honey, and turmeric preparation will exhibit decreased dry scalp severity on assessment by an investigator when compared to the scalps before treatment, as measured by an 11-point flaking scale.

The next objective is to determine the safety of introducing *Lactobacillus sp.*, honey, and turmeric, in reducing dry scalp symptomology

Hypothesis 2a: The product containing *Lactobacillus sp.,* honey, and turmeric will be safe for participant's scalps as measured by the Overall Safety Score and patient logs.

The final objective of this study is to compare the determine if an active *Lactobacillus*, honey, and turmeric topical preparation changes the microbiome after use for a dry scalp condition to more closely resemble healthy scalp

Hypothesis 3a: Participants' scalps treated with the active *Lactobacillus*, honey, and turmeric preparation will have a microbiome similar to those with healthy scalps.

4. STUDY POPULATION:

We aim to recruit participants with diagnosed dry scalp and with clinical signs on the scalp. Recruitment will consist of male and female participants. This will include 15-40 children between the ages of 1 year to 17 years old, and 20-40 adults over the age of 18.

4.1.1. Inclusion criteria

a. Age 1 year (or corrected age of 1 year, for those born prematurely) to 17 years for children, and adults 18 and older

b. Patients with dry scalp and dandruff symptoms as determined by a board-certified Dermatologist, Allergist, or Pediatrician

c. Good general health

d. Participant and/or their parents are able to read, write, and understand study materials in English

4.1.2. Exclusion criteria

e. Infants younger than 1 year old

f. Patients diagnosed with other scalp diseases such as psoriasis, tinea capitis, and pediculosis capitis

g. Systemic steroid or oral antibiotic use during the past two months

h. Allergy to any of the preparation components

5. STUDY PROCEDURES:

For this study, 20-40 subjects over the age of 18 and 15-40 subjects aged 1 year to 17 years, all with a clinical diagnosis of dry scalp, will be enrolled. 5-10 adults participants will be enrolled and complete the study prior to enrolling children. All participants who fit the inclusion criteria and are currently being seen at either a Lurie Children's location, Children's Health Associates, the Medical Dermatology Associates of Chicago, or other outside locations, will be verbally invited to participate in the study, immediately following their regularly scheduled appointment, by a study coordinator will be administered informed consent. Additionally, those not able to attend a standard office visit, will come into our Northwestern office to be assessed by a board-certified physician. Study staff will identify potentially eligible study patients from clinic databases or those who have previously shown interest and mail or email these patients a letter with information on the study protocol, eligibility criteria and participant compensation, as well as instructions to contact study staff if interested in participation. We will also wait a week after mailing the potentially eligible study patients and call and/or e-mail them to see if they are interested in participation.

A research coordinator will obtain bilateral culture swabs of the scalp, in order to assess the composition of the local bacterial community. A research coordinator will also obtain bilateral cultures of each participant's scalp via the RODAC plate method in order to assess the burden of *S. aureus* on the skin. Swab and culture samples will be sent to the lab of Dr. Patrick Seed at Lurie Children's or to Dr. Mahboobeh Mahdavinia's lab at Rush University to be processed via 16s rRNA sequencing and colony count, respectively. Lastly, a board-certified physician will assess the clinical severity of the participant's dry scalp via the 11-point flaking scale. Photographs will be taken as record for both adult and child studies.

Each participant will then fill out a baseline survey including demographics in REDCap.

Participants will be supplied with the scalp treatment and relevant instructions. Participants will be instructed to apply the preparation to their scalp. Adults will apply the scalp treatment on the site of active dry scalp once per day at home at a consistent time, every day for 14 days. Children will apply the hair care regiment at home at a consistent time two to three times a week over a 14-day period. -. Participants will be instructed to discontinue their regular scalp-care therapies. Adult participants will be contacted daily via email or telephone regarding scalp care regimen, usage of treatment, and any adverse events. Child participants will be contacted weekly via email or text regarding scalp care regiment, usage of treatment, and any adverse events. One week from the baseline visit (7 days), the participant will be contacted via phone, text or email to complete surveys regarding treatment experience and to confirm correct usage of treatment. Fourteen days following the baseline visit, adult participants will be seen, where repeat scalp cultures will be obtained via the swab and RODAC methods, and a repeat scalp flaking survey (IGA) (with photographs) will be assessed by a physician. Final experience surveys will be administered via REDCap. Fourteen days following the baseline visit, child participants will attend a secondary visit, where a physician will assess the participants' scalp and re-evaluate the IGA placement.

Study Schema

VISIT 1: (baseline)

- Recruitment and electronic informed consent of participants via REDCap.
- Obtain baseline scalp culture skin swabs from participant for microbiome diversity analysis.
- Obtain baseline scalp cultures from participant via RODAC method to obtain initial bacterial burden level. The RODAC (Replicate Organism Detection and Counting) method is used to measure the number of colony forming units (CFU) per skin surface area. The primary purpose of the RODAC method is to monitor presence and number of microorganisms as determined by the appearance of colonies on the surface of an agar medium.
- Local scalp flaking survey performed to the participant by investigator. Photographs will be taken. - Administer baseline demographics survey via REDCap.
- Demonstrate/teach patients the treatment regimen. The treatment for adults will be applied daily for 14 days for 5 minutes. The treatment for children will be applied 2 to 3 times a week over the course of 14 days for 5 minutes.
- Instruct adult participants to respond to the daily scalp care emails or phone calls. Instruct child participants to weekly scalp care emails, text messages, or phone calls.- Provide participants with all study materials, including instruction handout.
-Instructions for adults will be given stating: Wash your hands and make sure scalp/hair is dry, and then apply the treatment to your entire scalp. Massage the treatment in, wait around seven minutes, and then rinse it from your scalp. Please be sure to apply the treatment daily. Instructions for children will be given stating: Wash your hands and make sure scalp/hair is dry, and then apply the treatment to your entire scalp. Massage the treatment in, wait approximately five minutes, and then rinse it from your scalp. Please be sure to apply the treatment 2 to 3 times a week.

FOLLOW-UP:

- Study coordinator will contact participant or caregiver via phone or email daily to ensure safety of treatment regimen. Dr. Bilaver will follow-up with patients if adverse events are reported.
-Quality of life and overall safety score surveys will be sent to participants at the 7 day mark.

VISIT 2 at Lurie Children's, Northwestern University, or Medical Dermatology Associates of Chicago: (14 days after baseline)

- Obtain scalp culture skin swabs from patient for microbiome diversity analysis.
- Obtain scalp cultures from patient via RODAC method to obtain final bacterial burden level.

- Local scalp flaking survey performed to patient by investigator. Additional photographs will be taken.
- Ask participants to fill out the follow-up questionnaire via REDCap during the visit on a study iPad.

Events performed outside of patient visits:
-Skin swabs and RODAC plates will be transported from the collection site to the laboratory of Dr. Patrick Seed or to Dr. Mahboobeh Mahdavinia's lab at Rush University. The team will use an insulated carrier to transport the samples directly following each visit.

For visit 1 and 2, the study visit will take place at either Lurie Children's, Northwestern University, Children's Healthcare Associates, or Medical Dermatology Associates of Chicago. A board certified Dermatologist, Allergist, or Physician/pediatrician will conduct a scalp assessment to determine whether the participant is eligible for the study. Dr. Lucy Bilaver, the PI, will be the primary contact in the event of an adverse event, but will not be involved directly with any items in visit 1, the follow up, or visit 2. A research coordinator will consent the participant, explain the procedures of the study, swab the scalp, and administer the surveys. Either a research coordinator or physician will take pictures of the patient's scalp. The same responsibilities for the physician and research coordinator will take place at visit 2. For the adult follow ups, a research coordinator will either email or call the participant daily (based off their preference) regarding treatment use and adverse effects. Storage will occur at Dr. Patrick Seed's Lab (Lurie Children's) and Dr. Mahboobeh Mahdavinia's lab at Rush University, and analysis will be done by Dr. Seed's lab and Dr. Mahdavinia's lab at Rush University.

Parents will be asked to perform the treatment on children ages 1-11, but children ages 12 years-17 years will be asked to perform the treatment themselves. Parents will complete surveys for all children regardless of age.

-

6. DATA COLLECTION AND REPORTING:

At baseline, culture swabs will be obtained from all patients' scalp via both the swab and RODAC method. Patients will fill out an intake survey including demographics via REDCap. The physician will complete a scalp flaking survey to evaluate initial disease severity.

At the 7-day mark, adult patients will be emailed or texted surveys to ensure the treatment regimen and daily instructions are being completed correctly as well as to assess the safety and efficacy of the treatment. At the 7-day mark, child patients will be emailed or texted surveys to ensure the treatment regimen and weekly instructions are being completed correctly as well as to assess the safety and

efficacy of the treatment. All questions will be answered and noted on a secure Northwestern server.

At the 14-day follow-up visit, cultures will again be obtained from the patients' scalp via the swab and RODAC methods. The investigator will complete the scalp flaking survey to evaluate endpoint disease severity. Patients will then fill out a follow-up questionnaire via REDCap.

At the 14-day follow-up visit for child participants, the investigator will complete the scalp flaking survey to evaluate endpoint disease severity. Patients will then fill out a follow-up questionnaire via REDCap.

Participants will only be identified via their coded numeric subject ID. The document linking the code to the participant will be stored on a secure Northwestern server and all study team members will have access to the server.

Informed consent and all surveys will be programmed into REDCap NUBIC by a member of the study team. All other data will be stored in an electronic database and stored on a secure Northwestern server. Only those outlined in the IRB will have access to the information.

6.1. Primary Outcome Measures

The primary objective is to determine the safety and efficacy of YoBee in improving dry scalp conditions. Efficacy will be determined using the Investigator's Global Assessment (IGA) scale (Table 1), a 5-point assessment ranging from clear (0) to severe disease (4) and the Total Severity Scale (TSS) (Table 2), an assessment that averages erythema, scaling, and pruritus severity scores of scalp lesions. The TSS uses a 4-point scale ranging from none (0) to severe (3). Lastly, photographs of the scalp will be collected before and after treatment. Safety will be determined by contacting the patient via over the phone or through email to document adverse events and Overall Safety Score. The Overall Safety Score (Table 4) and the reporting of adverse events throughout the study will measure the safety of YoBee. The Overall Safety Score is a 4-point assessment ranging from "no signs of irritation" (0) to "patient discontinued due to irritation" (3). Participants will include the Overall Safety Score assessment in their daily journal.

An exploratory aim of this study is to find whether YoBee changes the microbiome after use for a dry scalp condition to more closely resemble healthy scalps. This will be accomplished by obtaining swab samples from the participants' scalps, before and after the treatment period. The samples will be analyzed using 16s RNA sequencing and internal transcribed spacer (ITS) sequencing. Additionally, the change in colony count of bacterial and fungal colonies on the scalp before and after the treatment will be assessed using the Replicate Organism Detection and Counting (RODAC) method. Finally, ScalpDex, a validated instrument, will assess the change in quality of life of participants. ScalpDex is a 23 question survey that will be administered electronically via RedCap to participants.

7. DATA DISCLOSURE AND SUBJECT CONFIDENTIALITY:

Subject medical information obtained as a result of this study is considered confidential, and disclosure to third parties other than the principal investigator and the co-investigators is prohibited. Data may only be disclosed in relation to compliance with mandatory state and federal disclosure laws, and will not be disclosed in any other circumstance. All reports and communications relating to subjects in this study will identify each subject only by their initials and study identification number. Medical information resulting from the subject's participation in this study may be given to the subject's personal physician or the appropriate medical personnel responsible for the subject's welfare. Data gathered as a result of this study are available to inspection on request by the Lurie Children's Hospital Institutional Review Board (LCHIRB).

8. EFFICACY ASSESSMENT

The efficacy of our trial will be measured by an 11-point scalp flaking scale (IGA). Second, we will employ 16S rRNA gene sequencing to analyze the composition of the scalp microbiome before and after treatment. Finally, efficacy toward reducing Staph colonization will be quantified via colony count of *S. aureus* scalp

cultures from patients plated on RODAC plates, and compared against each patient's baseline measurements.

9. SAFETY ASSESSMENT

All of the ingredients contained in our topical formulation are either foods or commonly used in cosmetics and skin care products. As such, we have minimal reason to believe that participants will experience major adverse events from treatment. There may be a risk of mild irritation, given the nature of already inflamed skin, but this should be minimal as compared to current accepted topical treatments for dry scalp. This study utilizes dead *Lactobacillus* species to eliminate the risk of growth and thus, the risk of new disease or symptomatology. Furthermore, dead bacteria are easier to store and offer a longer shelf life, eliminating the risk of application of an unknown size or species of bacteria.

10. STATISTICAL ANALYSIS

Responses for the scalp flaking survey are measured on an 11-point scale. The identification and relative quantities of scalp bacteria will be measured via 16S-tag count and expressed as a percentage of the total number of 16S-tags per sample, while the total quantity of bacteria in the sample will be measured by real-time quantitative PCR and expressed in picograms of bacterial DNA. Colony count measurements will be recorded in colony-forming units (CFU) per skin surface area, to the nearest whole number.

10. 1 Power analysis

The study is powered. An important goal of this study is to determine the changes in severity score pre/post treatment based on a 5 point severity scale. As we expect a decrease in severity score based off IgA scale post-treatment, we powered the study based on the ability to detect at least a one point difference in change of severity score with 80% power and an alpha level of 0.05.

11. POTENTIAL PITFALLS

Potential pitfalls include participant bias and lack of diversity, as this pilot study is recruiting from one dermatology clinic.

12. STUDY SITE

Medical Dermatology Associates of Chicago
363 W Erie Street, Suite 350
Chicago, IL 60654

Lincoln Park Outpatient Center
2515 N. Clark Street 8th Floor, Suite 801
Chicago, IL 60614-3393

Lurie Children's Hospital
225 E. Chicago
Chicago, IL, 60611

Northwestern University
750 N. Lake Shore Dr, Suite 680
Chicago, IL 60611

Children's Healthcare Associates
2900 N Ashland Ave.
Chicago, IL 60657

13. ETHICAL CONSIDERATIONS

13.1. Human Subjects Protection

A periodic review must be submitted to the IRB at least once a year. The IRB must be noticed of completion of the study. After study completion or termination, a final report must be provided to close the study. The investigator must maintain an accurate and complete record of all submissions made to the IRB, including a list of all reports and documents submitted. Adverse events will be submitted promptly to the IRB per IRB guidelines.

At least once per year, the IRB must review and give written approval in order to continue the study. This trial will be conducted in accordance with Good Clinical Practices and the Declaration of Helsinki.

13.2. Consent Forms

Prior to study entry, a written informed consent and/or assent must be obtained from the subject or the subject's guardian. A copy of the subject's signed consent or assent form must be retained in the study file.

13.3. Protocol Amendments

All changes must be submitted to the IRB. Protocol modifications that impact subject safety or the validity of the study must be approved by the IRB before initiation.

13.4. Retention of Records

We will retain subject identification codes, subject files, and source data for the maximum period of time permitted by the hospital, institution, or private practice, but not less than 2 years after the completion or discontinuation of the trial.

13.5. Use of Information and Publication

The Principal Investigator and sub-investigators may publish the results of this study in conjunction will appropriate scientific and medical personnel.

14. APPENDIX

All the ingredients used in this study were ordered from manufacturers who have current good manufacturing practices. Additionally, all of the ingredients used in the treatment have been approved by the FDA. The bacteria is heat-killed in Dr. Seed's lab and Dr. Mahdavinia's lab at 121°C (249 °F) for 15 minutes and be stored at room temperature away from other organisms to ensure sterility. Afterwards, the heat-killed bacteria will be added to the base, honey and turmeric

mixture in a sterile biosafety cabinet, separate from contaminants. To ensure batch safety, the mixture will be plated and observed to verify that nothing grows and all of the bacteria are dead.

REFERENCES

1. Borda, L. J., & Wikramanayake, T. C. (2015). Seborrheic dermatitis and dandruff: a comprehensive review. *Journal of clinical and investigative dermatology*, *3*(2).
2. Foley P, Zuo Y, Plunkett A, Merlin K, Marks R. The Frequency of Common Skin Conditions in Preschool-aged Children in Australia Seborrheic Dermatitis and Pityriasis Capitis (Cradle Cap). Arch Dermatol.2003;139(3):318–322.
3. Cho, S. H., Strickland, I., Tomkinson, A., Fehringer, A. P., Gelfand, E. W., & Leung, D. Y. (2001). Preferential binding of Staphylococcus aureus to skin sites of Th2-mediated inflammation in a murine model. *J Invest Dermatol, 116*(5), 658-663. doi: 10.1046/j.0022-202x.2001.01331.x
4. Hanifin, J. M., Thurston, M., Omoto, M., Cherill, R., Tofte, S. J., & Graeber, M. (2001). The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. EASI Evaluator Group. *Exp Dermatol, 10*(1), 11-18.
5. Hanifin JM, Cooper KD, Ho VC, Kang S, Krafchik BR, Margolis DJ, et al. Guidelines of care for atopic dermatitis, developed in accordance with the American Academy of Dermatology (AAD)/American Academy of Dermatology Association "Administrative Regulations for Evidence-Based Clinical Practice Guidelines". J Am Acad Dermatol 2004;50: 391-404.
6. Kong, H. H., Oh, J., Deming, C., Conlan, S., Grice, E. A., Beatson, M. A., Nomicos E., Polley E.C., Komarow H.D., NISC Comparative Sequence Program, Murray P.R., Turner, M. L., Segre J.A. (2012). Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. *Genome Res, 22*(5), 850-859. doi: 10.1101/gr.131029.111
7. Liban, Kyle. "The Efficacy of Topical Manuka Honey and Combination Antibiotic Therapy in the Treatment of MRSA Skin Infections." (2013).
8. Lin, Y. T., Wang, C. T., & Chiang, B. L. (2007). Role of bacterial pathogens in atopic dermatitis. *Clin Rev Allergy Immunol, 33*(3), 167-177. doi: 10.1007/s12016-007-0044-5
9. Lusby PE, Coombes AL, Wilkinson JM. Honey: A Potent Agent for Wound Healing.? J Wound Ostomy Continence Nurs. 2002;29:295–300.
10. Marks, R., A. D. Pearse, and A. P. Walker. "The effects of a shampoo containing zinc pyrithione on the control of dandruff." *British Journal of Dermatology* 112, no. 4 (1985): 415-422.
11. Neumann, P. B., T. W. Coffindaffer, P. E. Cothran, J. F. Jones, J. A. McCoy, G. Y. Rains, and B. R. Reed. "Clinical investigation comparing 1% selenium sulfide and 2% ketoconazole shampoos for dandruff control." *COSMETIC DERMATOLOGY-CEDAR KNOLLS*- 9, no. 12 (1996): 20-26.
12. Park, S., Lee, J., Park, Y. H., & Seo, Y. (2014). Effect of emollients containing vegetable-derivedlactobacillusin the treatment of atopic dermatitis symptoms: split-body clinical trial. *British Journal of Dermatology*, *170*(6), e38.
13. Park, T., Kim, H. J., Myeong, N. R., Lee, H. G., Kwack, I., Lee, J., Kim B.J., Sul W.J., An, S. (2017). Collapse of human scalp microbiome network in dandruff and seborrhoeic dermatitis. *Experimental dermatology*.
14. Seite S., Flores G.E., Henley J.B., Martin R.M., Zelenkova H., Aguilar L., Fierer N. (2014). Microbiome of affected and unaffected skin of patients with atopic dermatitis before and after emollient treatment. *Journal of Drugs in Dermatology*, *13*(11).
15. Seité, S., Zelenkova, H., & Martin, R. (2017). Clinical efficacy of emollients in atopic dermatitis patients–relationship with the skin microbiota modification. *Clinical, cosmetic and investigational dermatology*, *10*, 25.
16. Thangapazham, Rajesh L., Anuj Sharma, and Radha K. Maheshwari. "Beneficial role of curcumin in skin diseases." *The Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease*. Springer US, 2007. 343-357.