Full proposal research

Title: Effectiveness and safety evaluation of hair growth promotor containing teak leaf extract

Project summary

The causative factors of androgenic alopecia (AGA), or male pattern baldness is the abnormal impact of the hormone dihydrotestosterone (DHT), derived from the conversion of testosterone through the action of the enzyme steroid 5 alpha-reductase (S5AR). Currently, there are treatments, including topical solutions and oral medications. In the case of topical solutions, minoxidil has demonstrated efficacy in treating hair loss. Its mechanism of action involves stimulating blood supply to the hair follicles. For oral medications, finasteride is a drug classified as a 5-alpha-reductase type-II enzyme inhibitor. This functionality is effective in the treatment of AGA. The prior study, we discovered S5AR inhibitory properties of the teak leaf extract. Subsequently, a hair tonic containing teak leaf extract (HT-teak) was developed with the objective of assessing effectiveness and safety in humans. Ninety male participants aged 20-60 with male pattern baldness were recruited for the study. The participants were randomly assigned to three groups. These groups received either HT-teak, 5% minoxidil, or placebo. The products were topically applied to the temporal and vertex regions of the scalp twice daily, over a period of 6 months. The results were assessed of various parameters, including the total area hair count (TAHC), hair shedding, anagen and telogen hair, and the observation of side effects after application of the tested products. The findings revealed that the application of HT-teak led to increasing TAHC and anagen-to-telogen ratio, concurrently with a reduction in hair shedding. Therefore, HT-teak emerges as a viable alternative for promoting hair growth and holds promise for continued exploration in commercial applications.

Ethical number:

This study was approved the protocol by Naresuan University, Institutional Review Board. The IRB number is P10123/64.

Sponsor/funder:

The study was funded by the National Research Council of Thailand (NRCT). The grant number was N21A640421.

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Rationale of the study

Steroid 5-alpha-reductase (S5AR) is an enzyme responsible for the conversion of testosterone to dihydrotestosterone (DHT), a more potent androgen hormone implicated in androgenic alopecia (AGA)(1). Currently, the accepted oral administration for AGA treatment involves the use of finasteride or S5AR inhibitor drug(2). However, finasteride has been associated with adverse effects on the male reproductive system, including a decrease in libido, ejaculatory dysfunction, sexual dysfunction, and impotence(3). Minoxidil, a vasodilator topical drug, is another approved medicine for AGA treatment(2), but it has been reported to cause skin irritation such as redness, rash, and itching(4).

The exploration of new S5AR inhibitors for promoting hair regrowth is imperative. Our study demonstrated that teak leaf extract exhibits promising S5AR inhibitory activity and other bioactivities relevant to applications in hair growth including anti-testosterone effects on Human Follicle Dermal Papilla Cells (HFDPCs) and the inhibition of IL-1β secretion(5). Furthermore, the two diterpenes were isolated from teak leaf extract and represented as S5AR inhibitor(6). Therefore, teak leaf extract emerges as a potential natural ingredient for inclusion in hair regrowth products. Subsequently, a phototype of hair tonic containing teak leaf extract (HT-teak) was successfully developed. The evaluation of effectiveness and safety of HT-teak in human participants is important to validate its performance. Thus, the objective of this study is to assess the effectiveness and safety of HT-teak through a randomized controlled trial.

Reference

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Objective

To evaluate the effectiveness and safety of hair tonic containing teak leaf extract

Keyword

Teak, *Tectona grandis* L., 5 alpha-reductase, Androgenic alopecia

Methodology

- Study design

The study was conducted as a double-blind study, with the participants and researchers all being blinded. The 90 participants who were classified as AGA (type II-V) patient by dermatologist were enrolled in the study, then the participants were randomized equally into three groups: (1) received a placebo, (2) received HT-teak, and (3) received 5% Minoxidil. A Unicode code was randomly assigned to each participant in accordance with the blinding protocol. The participants had to apply the received hair tonic twice a day at a vertex and temporal scalp. Time points of effectiveness and safety evaluation occurred at baseline (week 0) and every 4 weeks until the end of the process (week 24). The user satisfaction questionnaires and the systemic side effects on the male reproductive system and palpitation were asked after applying the received product for 24 weeks.

- Participants

The analysis of the sample size with the 80% power of test and a significance level of 0.05. The resultant calculation indicates that each group should consist of 25 participants, resulting in a total of 75 participants. Additionally, accounting for a 20% loss of follow-up, equivalent to 15 participants, the total number of required study participants is 90 individuals. The participants were identified by individual Unicode and randomized into 3 groups using Microsoft Excel. The researcher who was responsible for the coding and the randomization process was not involved in the investigation process.

Inclusion criteria

1. Men diagnosed with Androgenetic Alopecia (AGA), as described by Hamilton-Norwood types II-V.
2. Age between 20 and 60 years.
3. No history of hair growth promoters or Minoxidil allergies

Exclusion criteria

1. Men sensitive to topical treatment or with scalp lesions.
2. Men with a history of hair transplantation.
3. Men who used topical minoxidil within the 6 months before enrolled the study.
4. Men treated with anti-5-alpha-reductase (S5AR) products or isotretinoin within the 6 months before enrolled the study.
5. Men who received scalp radiation within the 1 year before enrolled the study.
6. Men who used botanicals for hair regrowth within the last 3 months before enrolled the study.
7. Men who used systemic steroids for more than 14 days within 2 months before enrolled the study.

8. Men with personal diseases, including chronic kidney disease and uncontrolled blood pressure.

Withdrawal criteria

1. Participants who were allergic to the received product.
2. Participants who used other hair regrowth products during the research project.
3. Participants expressing a desire to discontinue participation.
4. Participants using the research product less than 80% of assign uses dose.

- Informed consent forms

The protocol was clearly explained to participants. The potential risks associated with participating in the study were thoroughly communicated. Following the explanation, participants were afforded the opportunity to ask questions and read the information sheet that comprehensively delineated the research protocol. The participants who decided to participate in the research formally endorsed their participation by signing the consent form. Both the information sheet and the consent form were already approved by the NU-IRB (Naresuan University Institutional Review Board).

- The hair tonic formulations

There are 3 formulations of hair tonic including (1) Hair tonic containing teak leaf extract (HT-Teak) or the test product, (2) placebo was prepared as base of HT-teak, and (3) 5% Minoxidil was used as a positive control. All formulations of hair tonic were uniformly packaged and labeled the participant codes by the researcher who responsible for the code. The participants had to apply 3-5 drops twice daily, in the morning and at night, targeting the vertex and temporal scalp areas.

- Follow-up

Visit 1

All participants undergo a scalp examination by the dermatologist. Additionally, participants were provided with comprehensive information about participation in the research study and signed an informed consent form. Prior to the examination, participants were required to rest for 5 minutes and then measure their blood pressure. Subsequently, a single point was tattooed on the desired examination area. The mark will persist on the skin for a duration of 8-12 months and will naturally fade thereafter. Participants were then scheduled for a follow-up appointment three days later to assess the tattoo.

Visit 2 (Baseline evaluation)

The participants underwent blood pressure measurement, similar to the procedure in the first appointment. Subsequently, a tattoo assessment was processed by the dermatologist. Then, the participants were required to assess the baseline effectiveness through three evaluation processes, including:

(1) Shed Hair Counting by Combing Test: Participants combed their hair from the vertex down to the frontal region for 60 seconds. The investigator counted the number of shed hairs.
(2) Photographic Assessment: Participants had photographs taken of the frontal and vertex areas to evaluate the progression of hair growth and identify any side effects resulting from hair tonic usage. The photographic tools were designed to consistently control light and angle for each time point evaluation.

(3) Total Area Hair Count and Hair Type Assessment: The number of total area hairs and the assessment of hair types were evaluated by capturing images with the Leviacam® on the targeted area.

During this visit, participants were instructed to apply for the received products for one week before commencing the research for allergy test.

Visit 3 (Day 7: Allergy test)

Following one week of product application, any potential allergic reactions were assessed by the dermatologist. Participants who did not experience adverse effects continued using the received product, while those exhibiting allergic symptoms were excluded. Subsequently, the participants underwent blood pressure measurements. Then after, the effectiveness of the products was evaluated using the same procedures outlined in Visit 2.

Visit 4-8 (Every 4 weeks after baseline evaluation)

The participants were required to undergo an effectiveness evaluation after using the products every four weeks. The evaluation processes were using the same methods described in detail of visit 2.

Visit 9 (Week 24)

The same evaluation processes were conducted as in the previous time point evaluation (detail in visit 2). Additionally, dermatologists conducted interviews regarding participant satisfaction with the products and the presence of any systematic side effects.

- Venue of the Study

Cosmetics and Natural Products Research Center, faculty of Pharmaceutical Sciences, Naresuan University, Thailand

Safety considerations

The potential side effects that may arise for participants include irritation or an allergic reaction to the received products, which could result in redness, erythema, edema, papules, vesicles, and pruritus on the skin. These skin irritations were investigated by dermatologist every 4 weeks. The participant can contact the researcher directly by phone if they have any problems. In the event of side effects arising, participants will receive medical treatment until a complete recovery, without incurring any associated costs.

Data management and statistical analysis

The results was as mean ± standard errors (SEs). Significant differences were determined at a 95% confidence interval (p-value < 0.05) through the comparison between baseline and time-point evaluations and between group using repeated measures ANOVA, estimating mean effects.

Privacy and Confidentiality of participants

During the experiment, the documents were not identity of the participants, including facial photographs. The participant codes are used instead of their names. The collected data was kept confidential and will not be disclosed to the public. In the event of research results being published, the information of participants will always be anonymized and the images used will be manipulated to conceal facial features. Authorized access to the data is limited to the project leader, and all co-researchers. All

documents of this study were securely stored at the Faculty of Pharmacy, Naresuan University, in a private room with restricted access. The information will be stored for a period of 3 years, and then disposed of through a paper shredder.

Expected outcomes of the study

This research provided the phototype of a hair tonic containing teak leaf extract that nourishes and stimulates hair growth, incorporating the effective and safe. It serves as an alternative product with benefits for consumers, particularly those experiencing androgenic alopecia.

Dissemination of results and publication policy

The research findings will be disseminated through publication in a scientific journal, with a commitment to ensuring the anonymization of participant data. The role of corresponding authorship will be assumed by the principal investigator. Acknowledgments will be extended to recognize research funding and additional support provided.

Duration of the project

The project spanned a duration of 12 months (20 July 2021 until 20 July 2022)

- August 2021: Initiated the recruitment process for participants.
- September 2021: Initiated the enrollment of participants (Round 1).
- September 2021 – March 2022: Conducted effective and safety evaluations of the tested products every four weeks for participants in Round 1.
- February 2022: Ceased the enrollment of participants.
- February to July 2022: Continued the effective and safety evaluations of the tested products every four weeks for participants in Round 2.