

THE EFFECT OF HERBAL EXTRACT ON HAIR GROWTH IN FEMALE ANDROGENIC ALOPECIA

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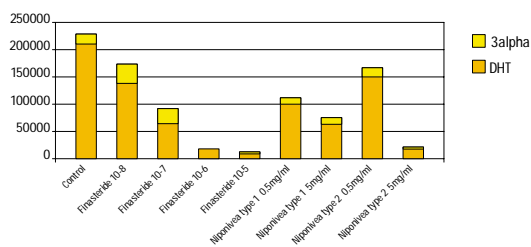
** Giuliani S.p.A. - Milan - Italy

An estimated 30 million women suffer from some form of hair loss, and the incidence of Androgenic Alopecia (AGA) in women is high, more frequently after the menopause (almost 50%), with important dermatological, aesthetic and psychological consequences.

It is well-known that one of the chief mechanisms is represented by the conversion of testosterone (T) into 5- α -dihydrotestosterone (5- α -DHT) by 5- α -reductase enzyme. 5- α -DHT then binds to androgen receptors and functions in the nucleus to regulate specific gene expression in hair follicle. Inhibition of 5- α -reductase can limit the availability of 5- α -DHT, therefore specific inhibitors are useful in selective treatment of AGA.

Of these finasteride, as steroid derivative, is a very effective therapy of AGA, but is not indicated for women. Fewer natural inhibitors have been reported for treatment of AGA, for example, unsaturated fatty acids, Saw Palmetto, epigallocatechin-3-gallate.

A specific extract from leaves of *Boehmeria nipoonivea* (a plant of nettle family from Japan and China, well known in traditional medicine) has a very effective 5- α -reductase inhibitory activity for the presence of several specific fatty acids. The receptor affinity and the most efficacy dose, compared with finasteride has been tested. In this evaluation *Boehmeria nipoonivea* shows a very significance inhibitory activity on 5- α -reductase receptor, anyway lower than finasteride (Giuliani S.p.A. Internal Report).



Furthermore, "In vivo" study has then been performed to evaluate rat LD50 for type 2 nipponivea. Acute toxicity is low and similar between sexes: - after 48 hours: male LD50 is 1412.53 mg/kg (891-2570)- female LD50 is 1380.38 mg/kg (757-2555) - after 72 hours: male LD50 is 1000 mg/Kg (426-1949) (Giuliani S.p.A. Internal Report)

The aim of our study was to verify the efficacy and tolerability of a product containing *Boehmeria nipoonivea* in the treatment of female AGA

MATERIALS AND METHODS

We undertook a randomised, double blind, parallel groups, controlled versus placebo, pilot study to evaluate the effectiveness of a new product in tablets formulation containing 200 mg of specific extract of *Boehmeria nipoonivea*.

Women suffered from AGA received either one active tablet, once a day, or placebo tablet for 4 months.

After the first examination (baseline, T0), three more examinations were performed after 2 (T1), 3 (T2) and 4 months (T3). Each examination included trichogram execution with anagen and telogen count, hair shaft, diameter evaluation and hair count in a defined scalp area (1cm²) identified by a tattoo. These efficacy parameters were evaluated with a photographic method, in accordance with literature*. The statistical analysis was performed on all randomised subjects (Intention to Treat analysis, ITT population). Missing data of withdrawn subjects were replaced by the worse value registered during the study, whilst missing data of completed subjects were replaced by using the "Last Observation Carried Forward" method.

As regards efficacy parameters, the analysis was performed on changes of T1, T2 and T3 values vs Baseline data. Baseline values of the two treatments were analysed by using a Student's t-test whereas efficacy data were analysed by means of an Analysis of CoVariance (baseline value as covariate).

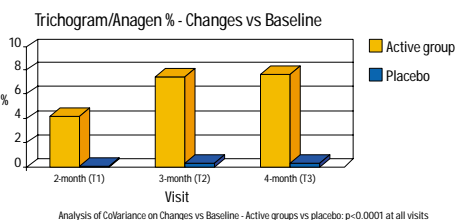
RESULTS: EFFECTIVENESS PARAMETERS STUDY

Sixty women suffered from AGA, thirty per group, aged from 44 to 69 years (mean age: 54 years) were enrolled

1. Trichogram: anagen count (%)

No increase in anagen count was observed in women treated with placebo, whereas, patients treated with active tablet showed an anagen percentage count progressive increase, from 6% at T1 to 10% at T3.

Variation statistical analysis showed a highly significant statistical difference (p<0,0001) between treatment and placebo at T1, T2 and T3 compared with T0.



2. Trichogram: telogen count (%)

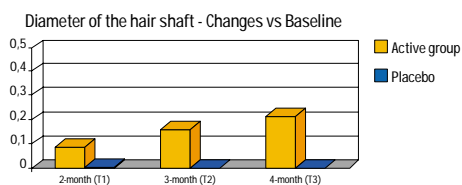
Anagen and telogen count pointed out similar results. Telogen count percentage reduction was nearly 35%

in the treatment group at the end of the study while the mean telogen count percentage in the placebo group didn't change during the study period. Except from T1 examination, telogen count difference between treatment group and placebo group resulted highly significant at T2 and T3 (p<0,0001).

3. Hair shaft diameter

Hair shaft diameter percentage variation showed a progressive increase at T1, T2 and T3 in the treatment group.

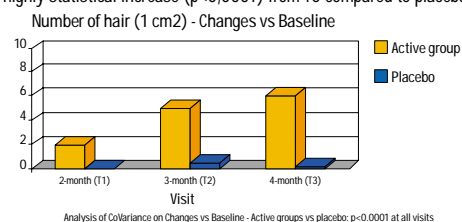
No variation has been observed in the placebo group. Difference between treatment and placebo group resulted to be highly significant (p<0,0001).



4. Hair count

Hair count percentage variation in the treatment group at T1, T2 and T3 showed a highly statistical increase (p<0,0001) from T0 compared to placebo group.

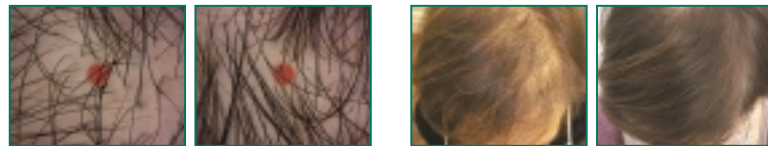
Statistical analysis was performed on all the sixty enlisted patients ("Intention To Treat" - ITT analysis) and on the fifty-five patients who concluded the study ("Per Protocol" - PP analysis). Similar results have been observed in both ways.



DISCUSSION

Androgenic Alopecia in women is a very important aesthetic and psychological problem that often decreases the quality of life in many women. The androgen dependent mechanism is one of the most important etiological factors of AGA, and the inhibition of 5- α -reductase is, at the moment, the most efficacious way to treat AGA. The efficacy of finasteride has been most extensively studied and showed. It has the possibility of a high affinity for androgen receptors, but as steroid derivative is expected to produce anti-androgen side effects and to be teratogenic in fertile women.

Some natural inhibitors of 5- α -reductase may be useful to treat AGA for their high affinity with the specific receptors. A specific extract from leaves of *Boehmeria nipoonivea* (a plant of nettle family from Japan and China, well known in traditional medicine) has a very effective 5- α -reductase inhibitory activity for the presence of several specific fatty acids. We evaluated the receptor affinity and the most efficacy dose, compared with finasteride. In this evaluation *Boehmeria nipoonivea* shows a very significant inhibitory activity on 5- α -reductase receptor, anyway lower than finasteride. In particular, all the analyses have identified the compounds in the active fraction as α -linolenic acid, linoleic acid, palmitic acid, oleic acid, elaidic acid and stearic acid. 5- α -reductase is a cellular membrane-bound enzyme that appears to require the unique environment of the lipid bilayer for activity, and perturbation of the lipid matrix of the membranes may affect reductase activity non specifically. Only certain unsaturated fatty acids with specific configurations are potent inhibitors of the enzyme. According to Liang and Liao, the inhibitory fatty acids have 14 - 22 carbon chains and one to six double bonds. Saturated fatty acids are totally inactive. In the dermal papilla cells of hair follicle with reductase activity, specific fatty acids enter cells and exert their inhibitory action on the nuclear or endoplasmic reticulum membrane bound 5- α -reductase. With this mechanism of inhibition, unsaturated fatty acids do not inhibit 5- α -reductase by competing with testosterone, and dramatically reduce the side effects incidence. We studied the efficacy of an extract with 200 mg of *Boehmeria nipoonivea* versus placebo (1 tablet per os once a day) in the treatment of AGA in women. As our results show, we obtained a significant reduction of hair miniaturization (P<0.0001), the improvement of anagen hair (P<0.0001) and of anagen/telogen ratio, and an interesting hair regrowth stimulation (P<0.0001) in the group treated with the active extract respect the placebo group.



It is interesting to point out a significant decrease of sebum production in the scalp of the treated women (P<0.005) evaluated by sebometry: this data confirm the inhibitory effect on the 5- α -reductase enzyme.

All the evaluations about toxicity and safety of *Boehmeria nipoonivea* have been studied, and no risks have been pointed out. No side effects have been noted during our clinical trial in both groups.

As general consideration, *Boehmeria nipoonivea* must not be administered to subjects suffered from asthma and allergy to nettle family plants. A *Boehmeria nipoonivea* specific extract can be considered as a potent inhibitor of 5- α -reductase, safe, and efficacy in the treatment of female androgenic alopecia.

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