5-α Avocuta®: an innovative tool for the management of hyper-seborrhoea

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Introduction

Hyper-seborrhoea, acne and alopecia are among the most common diseases encountered by dermatologists in daily practice. These pathologies are in part related to the hyper-activity of the 5-alpha reductase (5-αR), the enzyme that metabolises (Figure 1) testosterone into 5α-dihydrotestosterone (5α-DHT) a major potent androgen in human skin[1].

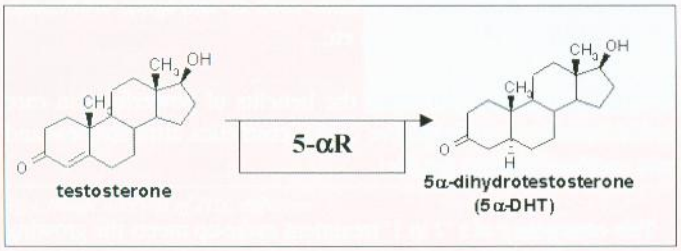

Figure 1

Two different isotypes have been characterized (5α-R1 and 5α-R2) and differ especially by their tissue expression patterns[2]. 5α-R2 is mainly found in the prostate and in genital skin, but also in hair follicle[2,3]. 5α-R1 is principally localized in the skin and in the hair follicle[4]. Within the skin, 5α-R1 activity predominates in sebaceous glands where it may be involved in sebum production.

The development of new and original 5-αR, especially type 1, inhibitors is thus of outmost importance for the management of hyper-seborrhoea.

The purpose of this work was first to select among different free fatty esters the most potent inhibitor of 5α-R1. The selected inhibitor, 5-α Avocuta® (or butyl avocadate), was then tested for its ability to reduce scalp and face hyper-seborrhoea.

Protocol

In vitro evaluation

- *Cells*
  Human skin fibroblasts were obtained from excess plastic surgery.
- *Treatment*
  Tested products were dissolved in DMSO and pre-incubated with the cells during 2h before the addition of radio-labelled testosterone. The tested products were chosen among free fatty esters varying in the length and functionality of the fatty chain and the nature of the alkoxy group.
- *Evaluation of 5-alpha reductase activity*
  The formation of DHT from testosterone is directly correlated to 5-αR activity. The different androgens were separated by thin layer chromatography and DHT was quantitated using a radioactivity analyser.

In vivo evaluations

The clinical trials described in this work were both designed to mimic the normal conditions of use of the products (shampoo & skin care).

1. Scalp hyper-seborrhoea and greasy hair

Firstly, we sought to determine whether a shampoo containing 1% of the selected 5 α-R1 inhibitor, was able to improve scalp hyper-seborrhoea and greasy hair.

- *Subjects*
  27 volunteers (16 females and 11 male, mean age 33.4) having hyper-seborrhoea and greasy hair conditions were enrolled by 6 dermatologists. The main exclusion criteria were scalp seborrheic dermatitis, folliculitis, or psoriasis.
- *Treatment*
  Subjects were placed on 1% 5-α Avocuta® containing shampoo for 3 weeks (1 application each 2 days).
- *Methods of evaluation*
  A clinical evaluation was performed by the dermatologists before (V0) and at the end of the treatment (V2) using a 10 points scale according to the following criteria: scalp and hair seborrhoea, stinging, pruritus, scalp erythema, dandruff.
  Scalp sebum secretion (Sebufix® F16, a white foil which gets black spots when coming in contact with sebum) was analysed by visual scoring (Figure 2) and by image analysis on 13 subjects (Skin Visiometer®, SV600, CK, Germany) before (V0) and at the end of the treatment (V2).
  The efficiency of the shampoo was also evaluated by the volunteers themselves at the end of the study.

Figure 2: Qualitative scale (five levels) for sebum evaluation

2. Face hyper-seborrhoea

The goal of this second trial was to determine the efficiency of 5-α Avocuta® in the management of face hyper-seborrhoea.

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- *Subjects*

  23 volunteers (female, mean age 30.8) having face hyper-seborrhoea were enrolled by 6 dermatologists. 87% of the volunteers have reported acne antecedents. The main exclusion criteria were active acne, acne treatment stopped less than 15 days before the beginning of the study, use of cosmetics containing vitamin C, retinol or AHA in the past 15 days.

- *Treatment*

  Subjects have to apply the day cream containing 2% 5-α Avocuta®, twice a day during 3 weeks.

- *Methods of evaluation*

  A clinical evaluation was performed by the dermatologists before (V0) and at the end of the treatment (V2) weeks using a 10 points scale.

  Fronthead sebum secretion (Sebufix® F16) was analysed by visual scoring (Figure 2) before (V0) and at the end of the treatment (V2).

  The efficiency of the product was also evaluated by the volunteers themselves at the end of the study.

Results

In vitro selection of 5α-R1 most potent inhibitor

In our experimental conditions, all the tested fatty ester acids were able to significantly inhibit the formation of DHT. Moreover® 5-α Avocuta, was significantly more potent than the other tested product, with a dose-dependent effect (Figure 3).

These results demonstrate that there is a relation between the structure and the ability of the different free fatty esters to inhibit 5-αR activity. The length of the alcohol chain seems to play a key role.

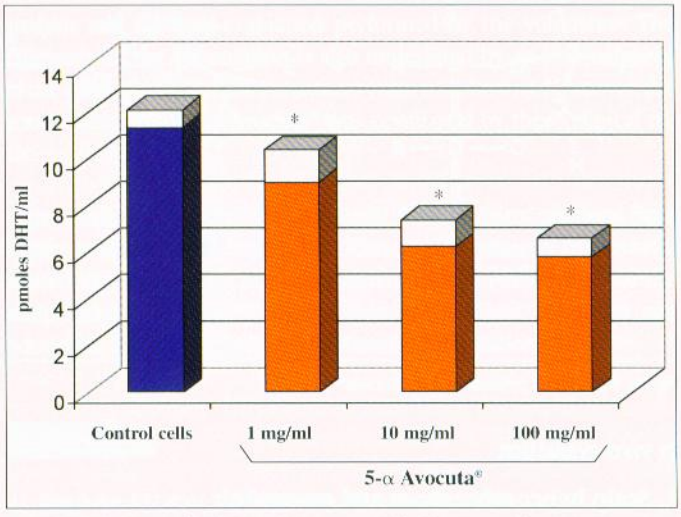

Figure 3: Inhibition of 5-alpha reductase type 1 by 5-α Avocuta®.
** difference statistically significant.*

5-α Avocuta® is composed of a complex blend of fatty acid butyl esters, obtained from a cold-pressed avocado oil, according to a patented process[5]. This process includes a first purification step of virgin avocado oil by short path distillation and a trans-esterification reaction in presence of butanol and enzyme as catalyst (biotechnological process, Figure 4). In a final step, butyl esters are purified by molecular distillation to give 5-α Avocuta®.

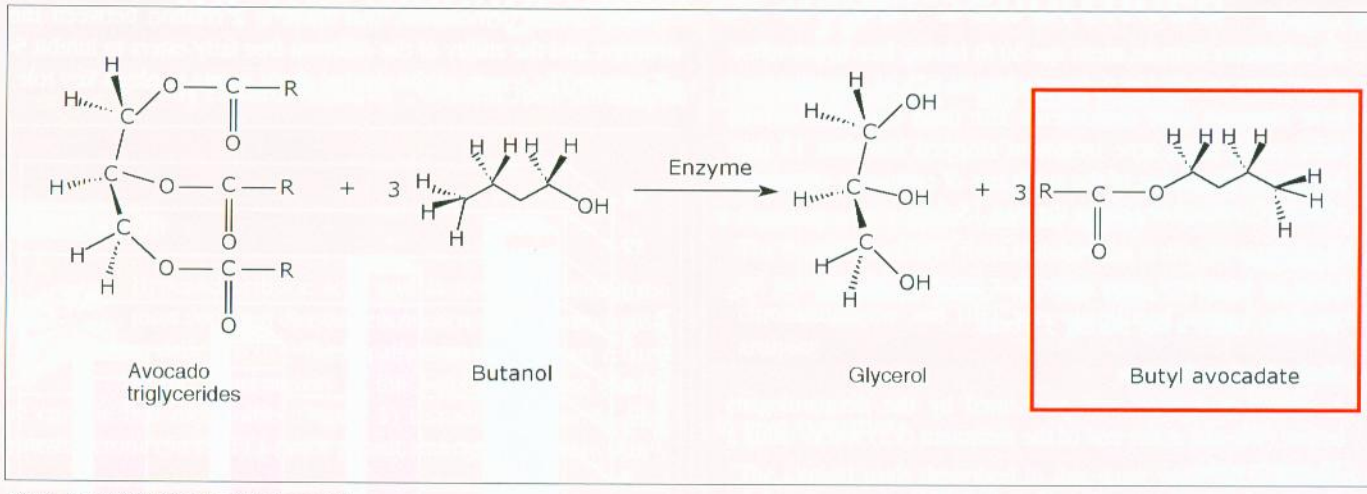

Figure 4: Synthesis process of 5-α Avocuta®

In vivo evaluation

1. Scalp hyper-seborrhoea and greasy hair

Clinical investigations performed by the dermatologists have shown that the shampoo clearly improved greasy hair aspect and was able to reduce itching and pruritus as well as dandruffs (Figure 5).

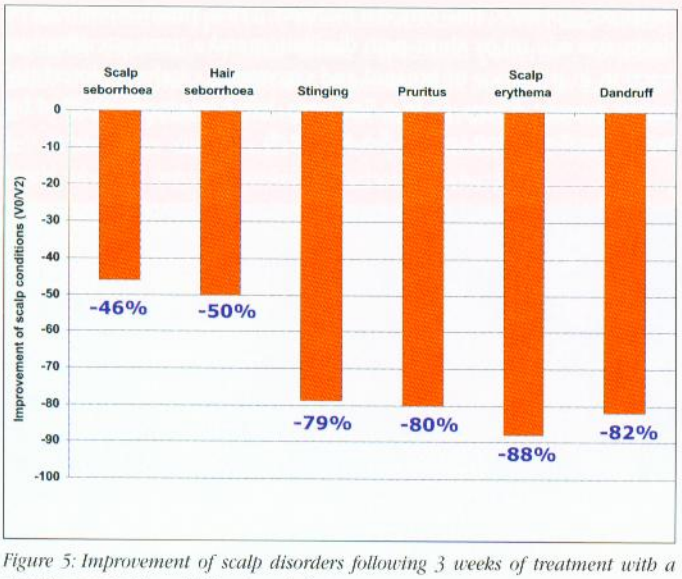

Figure 5: Improvement of scalp disorders following 3 weeks of treatment with a shampoo containing 1% 5-α Avocuta®

Comparison of the visual scoring (V0/V2), of SEBUFIX® F16, showed a decrease of 34% of the sebum secretion, decrease which was confirmed by image analysis (Table I and Figure 6).

	Mean for 13 subjects (V0/V2)
Lipidic area/total area (%)	-7.8 pts
Cumulative total lipidic area (mm²)	-69%
Number of lipidic spots	-137

Table I: Results of sebum secretion as recorded by image analysis

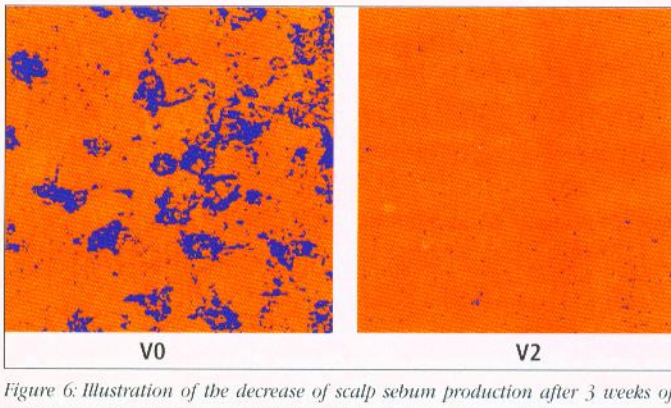

Figure 6: Illustration of the decrease of scalp sebum production after 3 weeks of treatment with a shampoo containing 1% 5-α Avocuta® (case n°12)

The auto-evaluation by the volunteers have confirmed these data (Table II).

	% of good opinions
Decrease of greasy hair	78
Decrease of scalp seborrhoea	74
Improvement of hair tightness	81
Decrease of dandruff	67
Decrease of scalp itching	59
Decrease of scalp irritation	63

Table II : Results of the auto-evaluation by the volunteers (% of good opinions)

2. Face hyper-seborrhoea

As shown in Figure 7, the regular application (twice a day, during 3 weeks) of 5-α Avocuta, led to a clear decrease of sebum secretion on the face.

Sebum secretion was also evaluated using SEBUFIX® F16. The analyse of the patch by comparison with a qualitative scale confirmed the clinical scores with a decrease of 30% of sebum production.

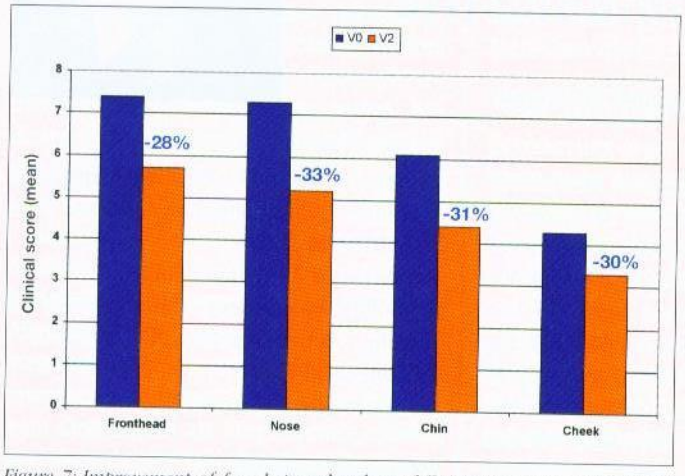

Figure 7: Improvement of face hyper-seborrhoea following 3 weeks of treatment with a cream containing 2% of 5-α Avocuta®

The efficiency of the formulation was also approved by the volunteers (Figure 8). The anti-seborreheic effect of the formulation reported by the panellists is in correlation with the clinical evaluation performed by the dermatologists and with the lipidic score measured with the SEBUFIX® F16. Moreover, 61% of the volunteers pointed out that the product was active as early as the first applications.

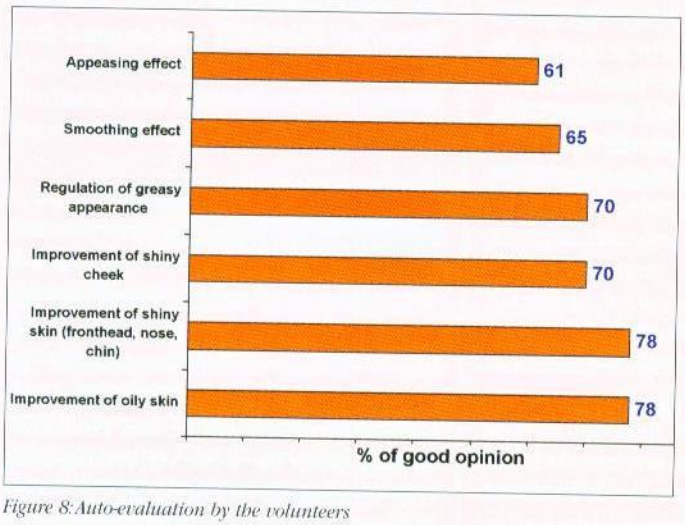

Figure 8: Auto-evaluation by the volunteers

Conclusion

Using an *in vitro* model, which was accurate to screen the relation between structure and activity of potential 5-αR inhibitors, we have selected 5-α Avocuta® (butyl avocadate) as the most potent inhibitor of 5-αR1.

This inhibitor was then tested for its ability to treat scalp hyper-seborrhoea and greasy hair conditions. After 3 weeks, clinical evaluation by the dermatologists, auto-evaluation made by the volunteers as well as the objective evaluation of sebum production were in accordance and allow us to conclude that 5-α Avocuta® is effective in the management of scalp disorders.

The second clinical trial has demonstrated that 5-α Avocuta® was also adapted to face hyper-seborrhoea, with an unambiguous decline of sebum production as attested by clinical evaluation, SEBUFIX® F16 analysis and the auto-evaluation performed by the volunteers. The efficiency of the formulation is also underlined by an improvement of the quality of life of the volunteers (data not shown). Moreover, the good tolerance of 5-α Avocuta® was confirmed by these clinical trials.

In conclusion, 5-α Avocuta®, a specific 5-αR inhibitor obtained from virgin avocado oil through a biotechnological process, has demonstrated its usefulness in the management of hyper-seborrhoea of the scalp and of the face. Finally, 5-α Avocuta® is liquid, colourless and odourless. Its is thus ideal for all cosmetic formulations.

References

1) *Bingham KD et al, J Endocrinol, 57: 111-121, 1973.*
2) *Eicheler et al, J Invest Dermatol, 103: 403, 1994.*
3) *Thigpen AE et al, J Clin Invest, 92: 903-910, 1993.*
4) *Luu-The V et al, J Invest Dermatol, 102: 221-226, 1993.*
5) *Patent WO0152837.*