Subject: Flutamide- Wirkung und Vergleich
Posted by Homers on Wed, 16 Jan 2008 14:56:09 GMT
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da es soviele fragen um flutamide momentan gibt, unter anderem wie stark es ist gegenüber fin usw...

Compositions that Stimulate Hair Growth

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The pathogenesis of androgenetic alopecia (male-pattern baldness) involves increased scalp follicle susceptibility to androgens. Scalp follicles in this alopecia contain increased levels and activity of scalp 5a-reductase isoenzyme, which converts testosterone (T) to dihydrotestosterone (DHT). DHT shortens the hair cycle and progressively miniaturizes scalp follicles. The miniaturized follicles all remain present and thus the possibility of reversal by re-enlargement exists.

Finasteride is known to more effectively inhibit the prostate 5a-reductase isoenzyme than the scalp isoenzyme. Nevertheless, it decreased the level of DHT in bald scalps after a long-term oral administration. Finasteride was introduced by Merck in 1989 (MK-906, Proscarâ ). Another agent with a hair growth potential is a nonsteroidal anti-androgen named flutamide. This drug is produced by Schering-Plough and has been introduced as a new potent compound tested clinically for treatment of prostatic carcinoma. So far, flutamide has not been introduced to any clinical study for testing its efficacy in male-pattern baldness.

We have found that finasteride and flutamide (representing two anti-DHT categories) in a new pharmaceutically - accepted topical base, pre-designed to penetrate the agents deep into the skin, significantly increase hair growth in bald scalp skin. Figure 1 shows the skin permeation kinetics of the new formulation, demonstrating a relatively higher retention of the drug in the skin while providing a similar rate of transport through the skin as compared to a hydroalcoholic liquid vehicle. The rationale behind using these inhibitors topically is to reduce the systemic exposure of these drugs during their chronic use, and to increase the local efficacy on scalp follicles.

In addition to the penetration test, we have tested the effect of topical treatments on hair growth in human scalp punch biopsies grafted onto scid mice. We discovered that both model drugs, the 5a-reductase inhibitor and the androgenic blocker, were effective in re-enlarging hair follicles (i.e., in baldness remission). Flutamide, however, possessed a significant beneficial property over finasteride. The enclosed Figures 2-4 and Table I present the significant differences between gel formulations containing finasteride, flutamide, and placebo (gel vehicle only).

It is shown that finasteride and flutamide gels have a significantly higher effect than placebo in all tested parameters, however, flutamide (representing the anti-androgenic mechanism)

demonstrates significantly more hair per graft area and significantly longer hair shafts than finasteride (5a-reductase inhibition mechanism). Both compounds have a similar effect on the diameter of the hair shafts.

Table I

Distribution of the Histological Hair Structures in the treated Grafts

Anagen Catagen Telogen T+C
Before treatment 0% 35.7% 64.2% 100%
FINASTERIDE 30.4% 22.8% 46.8% 69.6%
FLUTAMIDE 47.0% 26.5% 26.5% 53.0%
VEHICLE (control) 10.5% 24.6% 64.9% 85.5%

Table II shows no difference in the systemic levels of testosterone or dihydrotestosterone following administrations of the drugs or their vehicle. This demonstrates the topical effect of this dermal drug application.

Table II
Serum T/DHT Levels (in nmole/L)

Group T DHT
Finasteride 7.2+6.9 0.91+0.57
Flutamide 5.8+3.1 1.06+1.62
Vehicle (control) 8.9+7.4 1.10+1.02

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