Follicular delivery study design for hairDAO

(Note on patents: I am not sure how this would work, if a particular vehicle from a research paper is used, if this can be patented or if the authors have any say or rights in this, to develop an entire novel solution is probably difficult because we do not have this kind of expertise)

Overview

Due to the localized upregulation of 5AR isoenzymes in the root sheath and dermal papilla, it is reasonable to assume that androgenic alopecia can be treated entirely by locally modulating the activity of those enzymes, preventing the undesirable systemic side effects of hair loss's most effective drugs today. Many topical finasteride products have entered the market. However, the extent to which they go systemic is significant and evident.

The proposal is an investigation of a delivery system that is good at delivery 5AR into the hair follicle to the target cells being able to reach high drug concentrations there while maintaining low concentrations in the serum. This can be achieved investigating and using nano delivery systems which have been a major focus of research in recent years. The most suitable drug for such a delivery system appears to be dutasteride since it has a short systemic half life when administered in small doses (non linear half life). Dutasteride also has a poor ability to penetrate the skin on its own due to high molecular weight, making it a strong candidate for not going systemic. Furthermore, it shows very high response rate at over 92%, and it targets all isotypes of 5AR.

Design

In a phase of screening, multiple vehicle candidates are selected in a literature review and feedback from the respective authors. The chosen carriers will further be screened for tolerability based on excipients cost and then synthesized. After that, an in vitro/ex vivo study will be conducted on human scalp skin. As a control, a commercially available solution for topical dutasteride with ethanol/pg or conventional liposomal will be used. Drug will be applied repeatedly for a few days on the scalp skin mounted on a franz diffusion cell model. The one with the best ex vivo penetration properties will be selected for a further investigation, which could be evaluated in a subsequent in vivo study that could investigate

- tolerability by measuring the change in serum sex hormones and the amount of drug in the blood after application in certain time intervals
- hair growth parameters like density, hair weight and terminal hair count after a 6 month application

Evaluation of performance an efficacy

The performance of a given delivery system can be evaluated with the following proposed end points:

- assessment of amount of drug that permeated into the receptor compartement of the franz diffusion cell for each vehicle, not only after 1 application and a few hours of soaking in but multiple applications and a longer observation period

- follicular targeting factor of each system which is defined as:
    - amount of drug in the hair follicle(at the site of target cells) vs the amount of overall applied drug
    - this can then be compared to conventional delivery systems
    - since the efficacy of dutasteride has been proven many times and the mechanism is clear, an increased concentration and bioavailability at the target site is likely to produce a more desirable efficacy outcome
    - still optionally, follicular DHT and 5AR activity and expression can be measured

Market Opportunity

5ARi are a well studied, very effective and proven method for treat AGA. Dutasteride has been shown to be even more effective than Finasteride with very high response rates. There is a large group of people who are either non responders to oral therapy or who cannot tolerate those drugs due to sexual side effects and in recent years, many countries have now black listed 5ARi among them the US with FDA with a black letter warning, France(red box warning) and Germany(red letter) and doctors in various countries are increasingly hesitant to even recommend this line of therapy.

Furthermore it is very plausible that many would drop the oral use even if they are side effect free due to long term safety concerns and the desire to not alter androgen levels at all. Currently there is no available formulation for dutasteride, let alone an evidence baked targeted therapy based on nano formulations.

Additionally, reformulating already established and approved drugs has a significantly shorter road to commercialisation than designing an entirely new drug with a different MAO.

Past Research

https://docs.google.com/document/d/1iqs5k7pI09mjKvymdK4AoyI7ofgyCYUSrGm7u5jnE24/edit