in vitro models to test
5α-Reductase Inhibition

Biochemistry

5a reductase (3-oxo-5a-steroid-D4-dehydrogenase; 5aR), a NADPH-dependent membrane protein, irreversibly catalyses the reduction of 4-en-3-oxosteroids, resulting in the corresponding 5a-3-oxosteroids. The most important reaction is the conversion of testosterone (T) to the most potent androgen 5a-dihydrotestosterone (DHT), which displays the highest affinity towards the androgen receptor. The irreversible reduction of T to DHT represents the final step in androgen biosynthesis. In humans, two 5a reductase isoenzyme are expressed: 5a reductase type I and 5a reductase type II. The isoenzymes have a different distribution pattern, which is still under discussion. In principle, type I is predominantly expressed in skin, scalp and follicles, whereas type II is mainly found in prostate tissue. However, more recent reports describe that 5a reductase I is the predominant form in oil and sweat glands. In stroma and basal cells of the prostate, 5a reductase type II is expressed, but Shirakawa et al. (2004) demonstrated that in epithelial cells of the prostate, also 5a reductase I is expressed. 5a-reductase type I and type II display distinct biochemical and pharmacological properties, such as pH-optimum, Km etc.

Pathophysiology

Male pattern hair loss (MPHL, androgenic alopecia) is caused by an overproduction of 5a reductase and DHT in the hair follicles. The hair loss associated with increased levels of DHT in hair follicles is due to the effect of DHT on the cycle by which scalp hair grows; in the presence of increased levels of DHT in hair follicles, the natural hair cycle is interrupted and newly produced hairs are miniaturized rather than achieving full growth. Thus, the 5a reductase isoenzymes are associated with MPHL, which has been successfully treated with drugs that lower the level of DHT available to hair follicles, so-called 5a reductase inhibitors, blocking the action of the enzyme 5a reductase that converts T into DHT.

At VivaCell, we offer to test compounds or extracts for in vitro 5α-Reductase Inhibition (Type I and Type II)

Literature:
**in vitro models to test oral care products**

*Tissue models:*

Besides the various cellular models, VivaCell offers highly specialised tissue models to approach closer to the *in vivo* situation.

The tissue models can be used for testing pure compounds as much as galenic formulations.

- Gingival epithelial and buccal epithelial tissues

**Parameters to be determined:**

- Inflammatory parameters (PGE2, cytokines etc.)
- Cytotoxicity: MTT, LDH, Neutral Red, etc...

**Determination of inflammatory parameters in gingival samples from clinical studies**

We offer the determination of inflammatory parameters in various biological materials or samples from clinical studies.

- PGE2, LTB4, IL-1, IL-8 and other cytokines, isoprostone (free radicals etc.)

**Models to develop oral care products for the treatment of chemotherapy-induced Stomatitis/Mucositis (please ask for detailed study design)**

Radiation therapy to the head, neck or mouth and systemic chemotherapy cause severe side effects including oral lesions (stomatitis/mucositis) and pain. Because the complicated nature of this lesion, no effective treatment is available for the patients so far and most of the treatments are symptomatic for pain and infections. We suggest to perform various “in vitro” models specifically directed to analyse key cellular and molecular targets involved in the progression of stomatitis/mucositis.

- Effects of an anti-stomatitis formulation in the apoptotic pathway induced by chemotherapeutic drugs in primary human fibroblast or epithelial cell lines.
- Effects of an anti-stomatitis formulation in the metabolism of NO either in primary human dermal microvascular endothelial cells or macrophages
- Effects of an anti-stomatitis formulation on NF-κB and AP-1 activation
- Effects of an anti-stomatitis formulation on phagocytosis
- Effects of an anti-stomatitis formulation on inflammatory events in primary human fibroblasts and fibroblast proliferation