Subject: vermutete wirkung von minox
Posted by pietrasch on Wed, 15 Oct 2008 08:51:53 GMT
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damit hier mal was reinkommt, ist allerdings nicht mehr taufrisch... die erste arbeit von 2004 is ne übersicht mit dem fazit: man weiß nich genau wie es funktioniert...

allerdings hat es mich eher positv überrascht, dass überhaupt noch aktuelle arbeiten erscheinen, die sich mit der wirkweise von minox beschäftigen, hätte nich gedacht, dass da noch forschungsgelder reinfließen...

Br J Dermatol. 2004 Feb;150(2):186-94.Click here to read Links
Minoxidil: mechanisms of action on hair growth.
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We have known for over 30 years that minoxidil stimulates hair growth, yet our understanding of its mechanism of action on the hair follicle is very limited. In animal studies, topical minoxidil shortens telogen, causing premature entry of resting hair follicles into anagen, and it probably has a similar action in humans. Minoxidil may also cause prolongation of anagen and increases hair follicle size. Orally administered minoxidil lowers blood pressure by relaxing vascular smooth muscle through the action of its sulphated metabolite, minoxidil sulphate, as an opener of sarcolemmal KATP channels. There is some evidence that the stimulatory effect of minoxidil on hair growth is also due to the opening of potassium channels by minoxidil sulphate, but this idea has been difficult to prove and to date there has been no clear demonstration that KATP channels are expressed in the hair follicle. A number of in vitro effects of minoxidil have been described in monocultures of various skin and hair follicle cell types including stimulation of cell proliferation, inhibition of collagen synthesis, and stimulation of vascular endothelial growth factor and prostaglandin synthesis. Some or all of these effects may be relevant to hair growth, but the application of results obtained in cell culture studies to the complex biology of the hair follicle is uncertain. In this article we review the current state of knowledge on the mode of action of minoxidil on hair growth and indicate lines of future research.

Effect of minoxidil on proliferation and apoptosis in dermal papilla cells of human hair follicle.
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BACKGROUND: Minoxidil has been widely used to treat androgenetic alopecia, but little is known about its pharmacological activity or about the identity of its target cells in hair follicles. We hypothesized that minoxidil has direct effects on the proliferation and apoptosis of dermal papilla cells (DPCs) of human hair follicle. OBJECTIVE: To elucidate the mechanism of topical minoxidil

action in terms of stimulating hair growth. METHODS: We evaluated cell proliferations in cultured DPCs by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) and measured the expressions of extracellular signal-regulated kinase (ERK), Akt, Bcl-2, and Bax by Western blot. We also measured elongation of hair follicles in organ culture. RESULTS: Minoxidil significantly increased the proliferation of DPCs. The levels of ERK phosphorylation and of phosphorylated Akt increased significantly 1 h post-treatment; percentage increase of ERK phosphorylation was 287% at 0.1 microM and 351% at 1.0 microM of minoxidil, and that of Akt phosphorylation was 168% at 0.1 microM and 257% at 1.0 microM of minoxidil. 1.0 microM of minoxidil increased Bcl-2 expression over 150%, while 1.0 microM of minoxidil decreased Bax expression by more than 50%. Moreover, a significant elongation of individual hair follicles in organ culture was observed after adding minoxidil. CONCLUSION: Minoxidil promotes the survival of human DPCs by activating both ERK and Akt and by preventing cell death by increasing the ratio of Bcl-2/Bax. We suggest that minoxidil stimulates the growth of human hairs by prolonging anagen through these proliferative and anti-apoptotic effects on DPCs.

Minoxidil upregulates the expression of vascular endothelial growth factor in human hair dermal papilla cells.
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The hair follicle dermal papilla which controls hair growth, is characterized in the anagen phase by a highly developed vascular network. We have demonstrated in a previous study that the expression of an angiogenic growth factor called vascular endothelial growth factor (VEGF) mRNA varied during the hair cycle. VEGF mRNA is strongly expressed in dermal papilla cells (DPC) in the anagen phase, but during the catagen and telogen phases. VEGF mRNA is less strongly expressed. This involvement of VEGF during the hair cycle allowed us to determine whether VEGF mRNA expression by DPC was regulated by minoxidil. In addition, the effect of minoxidil on VEGF protein synthesis in both cell extracts and DPC-conditioned medium, was investigated immunoenzymatically. Both VEGF mRNA and protein were significantly elevated in treated DPC compared with controls. DPC incubated with increasing minoxidil concentrations (0.2, 2, 6, 12 and 24 mumol/L) induced a dose-dependent expression of VEGF mRNA. Quantification of transcripts showed that DPC stimulated with 24 mumol/L minoxidil express six times more VEGF mRNA than controls. Similarly, VEGF protein production increases in cell extracts and conditioned media following minoxidil stimulation. These studies strongly support the likely involvement of minoxidil in the development of dermal papilla vascularization via a stimulation of VEGF expression, and support the hypothesis that minoxidil has a physiological role in maintaining a good vascularization of hair follicles in androgenetic alopecia.

Hair growth effect of minoxidil]
[Article in Japanese]

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The length and size of hair are depend on the anagen term in its hair cycle. It has been reported that the some cell growth factors, such as VEGF, FGF-5S, IGF-1 and KGF, induce the proliferation of cells in the matrix, dermal papilla and dermal papillary vascular system and increase the amount of extra cellular matrix in dermal papilla and then maintain follicles in the anagen phase. On the other hand, negative factors, like FGF-5, thrombospondin, or still unknown ones, terminate the anagen phase. If the negative factors become dominant against cell proliferation factors according to fulfilling some time set by the biological clock for hair follicles, TGF beta induced in the matrix tissues evokes apoptosis of matrix cells and shifts the follicles from anagen to catagen. Androgenetic alopecia is caused by miniaturizing of hair follicles located in the frontal or crown part of scalp and are hereditarily more sensitive to androgen. In their hair cycles, the androgen shortens the anagen phase of follicles and shifts them to the catagen phase earlier than usual. The mode of action of hair growth effect of minoxidil is not completely elucidated, but the most plausible explanation proposed here is that minoxidil works as a sulfonylurea receptor (SUR) activator and prolongs the anagen phase of hair follicles in the following manner: minoxidil (1) induces cell growth factors such as VEGF, HGF, IGF-1 and potentiates HGF and IGF-1 actions by the activation of uncoupled SUR on the plasma membrane of dermal papilla cells, (2) inhibits of TGF beta induced apoptosis of hair matrix cells by opening the Kir 6.0 channel pore coupled with SUR on the mitochondrial inner membrane, and (3) dilates hair follicle arteries and increases blood flow in dermal papilla by opening the Kir 6.0 channel pore coupled with SUR on the plasma membrane of vascular smooth muscle cells.

Human hair follicles contain two forms of ATP-sensitive potassium channels, only one of which is sensitive to minoxidil.
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Hair disorders cause psychological distress but are generally poorly controlled; more effective treatments are required. Despite the long-standing use of minoxidil for balding, its mechanism is unclear; suggestions include action on vasculature or follicle cells. Similar drugs also stimulate hair, implicating ATP-sensitive potassium (K(ATP)) channels. To investigate whether K(ATP) channels are present in human follicles, we used organ culture, molecular biological, and immunohistological approaches. Minoxidil and tolbutamide, a K(ATP) channel blocker, opposed each other's effects on the growing phase (anagen) of scalp follicles cultured in media with and without insulin. Reverse transcriptase-polymerase chain reaction identified K(ATP) channel component gene expression including regulatory sulfonylurea receptors (SUR) SUR1 and SUR2B but not SUR2A and pore-forming subunits (Kir) Kir6.1 and Kir6.2. When hair bulb tissues were examined separately, epithelial matrix expressed SUR1 and Kir6.2, whereas both dermal papilla and sheath exhibited SUR2B and Kir6.1. Immunohistochemistry demonstrated similar protein distributions. Thus, human follicles respond biologically to K(ATP) channel regulators in culture and express genes and proteins for two K(ATP) channels, Kir6.2/SUR1 and Kir6.1/SUR2B; minoxidil only stimulates SUR2 channels. These findings indicate that human follicular dermal papillae contain K(ATP) channels that can respond to minoxidil and that tolbutamide may suppress hair growth clinically; novel drugs designed specifically for these channels could treat hair disorders