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Effects of Nano-cerium Oxide on the Levels of DHT, TGF-β, and IGF-1 in the Local Skin of AGA Model Mice and Efficacy Observation

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Abstract: ***Objective:*** ***Explore the improvement effect of nano-cerium oxide on mice with androgenetic alopecia.*** ***Methods:*** ***First, the backs of mice were depilated and an androgenetic alopecia model was established by treating them with 5mg/kg testosterone propionate. C57BL/6 mice were randomly divided into 5 groups: the blank group, the model group, the roller microneedle group, the nano-cerium oxide group, and the minoxidil group. Corresponding treatment substances were introduced into the depilated areas respectively. The ratio of terminal hairs to vellus hairs (T/V) in mice was observed through HE histological examination. The contents of dihydrotestosterone (DHT), transforming growth factor-β (TGF-β), and insulin-like growth factor-1(IGF-1) in skin tissues were determined by enzyme-linked immunosorbent assay (ELISA).*** ***Results:*** ***Compared with the model group, the drug - treated groups could increase the T/V ratio in mice, elevate the protein expression level of IGF-1, and decrease the protein expression level of TGF-β in mice as well as the content of DHT in mouse skin.*** ***Conclusions:*** ***Nano-cerium oxide has a certain ability to alleviate androgenetic alopecia. It can increase the ratio of terminal hair to vellus hair, providing some theoretical guidance for the development of drugs for the prevention and treatment of androgenetic alopecia.***

Keywords: Nano-cerium oxide, Androgenetic alopecia (AGA), Dihydrotestosterone (DHT), Transforming growth factor-β (TGF-β), Insulin - like growth factor-1 (IGF-1)**.**

1. Introduction

Androgenetic alopecia (AGA), influenced by androgens, is a common non-cicatricial hair loss disorder that occurs during and after puberty. It is also the most prevalent type among all hair loss diseases. Its main characteristics include the miniaturization of androgen - sensitive hair follicles, the shortening of the growth cycle, and the stagnation of the telogen phase. In China, the prevalence rate is approximately 21.3% in men and 6.0% in women [1]. In recent years, androgenetic alopecia (AGA) has shown a trend of becoming more prevalent among younger people, attracting much attention. For young individuals, hair loss can cause self - esteem issues due to its negative impact on appearance, and it can easily trigger psychological problems. Moreover, due to the progressive nature of this disease, it may eventually lead to baldness. Therefore, it is necessary to control the progression of the disease as early as possible through various treatment methods. The pathogenesis of AGA generally includes the following aspects: abnormal androgen metabolism, disorder of the hair follicle growth cycle, inflammatory and immune responses, and genetic factors [2]. In response to the pathogenesis of AGA, experts and scholars have developed many treatment methods, including oral and topical medications for hair growth, laser hair growth therapy, scalp injection of autologous platelet-rich plasma for hair growth, and hair transplantation [3], However, none of these treatment methods are completely risk - free. They all have more or less some side effects and complications. Therefore, it is of great importance to find a new type of drug that is safe, effective, has few side effects, can effectively balance the environment around the hair follicles, and is convenient to use. Rare earths are known as the "gold" of industry, and many metal elements extracted from them have been developed for applications in various industries. Baotou City, Inner Mongolia Autonomous Region, has a rare earth reserve accounting for 31.67% of the global total, and is thus known as the "Capital of Rare Earths". Cerium, extracted from rare earth raw materials, is applied in many fields, including the medical field, in the form of nano-cerium oxide (CeO2). Its applications in the medical field include: antioxidant effect, anti - inflammatory effect [4], anti - tumor effect, antibacterial effect, tissue repair and regeneration [5], drug carrier, disease diagnosis, etc. Its antioxidant, anti - inflammatory properties, ability to stimulate the proliferation of hair follicle cells, and induction of angiogenesis can have certain effects in the treatment of AGA. Based on the mechanism of action of nano-cerium oxide, I designed this experiment. By observing the hair growth of AGA model mice before and after drug administration, and detecting the levels of dihydrotestosterone (DHT), transforming growth factor-β (TGF-β), and insulin - like growth factor-1 (IGF-1), we can evaluate the therapeutic effect of nano-cerium oxide, providing a theoretical basis for the development of new drugs or daily hair-growth shampoos.

2. Materials and Methods

2.1 Animal

Thirty male C57BL/6 mice at 4 weeks of age, at the SPF grade, with a body weight of 20-22g, were purchased from SinoBest (Suzhou) Biotechnology Co., Ltd., and the license number is SCXK (Su) 2022-0006.

2.2 Experimental Consumables

0.01μg/ml nano-cerium oxide solution (Baotou Xinyuan Rare Earth High-tech Materials Co., Ltd.); 5% Minoxidil Tincture (Zhejiang Wansheng Pharmaceutical Co., Ltd.; Approval Number of National Medicine: H20010714); Testosterone

Propionate Injection (Guangzhou Baiyunshan Mingxing Pharmaceutical Co., Ltd.; Specification: 25mg:1ml); Isoflurane (Shandong New Time Pharmaceutical Co., Ltd.). Injectable-grade soybean oil; 4% paraformaldehyde; HE reagents (absolute ethanol, xylene, hematoxylin-eosin staining solution, immunohistochemical solution, ammonia water, neutral gum); Mouse Dihydrotestosterone (DHT) ELISA Kit (Product Number SUB20628, Jiubang Biotechnology Co., Ltd.); Mouse Transforming Growth Factor-β (TGF-β) ELISA Kit (Product Number SUB20861, Jiubang Biotechnology Co., Ltd.); Mouse Insulin - like Growth Factor-1 (IGF-1) ELISA Kit (Product Number SUB20780, Jiubang Biotechnology Co., Ltd.)

2.3 Experimental Grouping, Modeling and Drug Administration

Thirty C57BL/6 mice were randomly and equally divided into 5 groups, namely the blank group, the model group, the roller microneedle group, the nano-cerium oxide group, and the minoxidil group. Before modeling, all mice were adaptively raised in an environment with a temperature of (22±2) °C and a humidity of (45±10) % for one week, with free access to food and water. After one week, the modeling was carried out. The mice were anesthetized systemically by inhaling isoflurane. A 2x3 cm area was selected and depilated using depilatory cream. Mice in the blank group and non - blank groups were subcutaneously injected with normal saline and 5mg/kg·d testosterone propionate respectively (for ease of operation, testosterone propionate was diluted 4:1 with soybean oil). This injection lasted for 4 weeks. During the modeling period, the hair growth was observed every 4 days. After 4 weeks, in the mice injected with testosterone propionate, the depilated area showed thinner and sparser hair, and increased skin oil secretion. After successful modeling, mice in the roller microneedle group were given microneedle stimulation to the hair follicles. Mice in the minoxidil group were smeared with 5% minoxidil tincture, and then the skin was rolled with a roller microneedle to help with drug delivery. Mice in the nano - cerium oxide group were smeared with 0.01 μg/ml nano - cerium oxide solution, and then the skin was rolled with a roller microneedle to help with drug delivery. The treatment was carried out once a day for 4 weeks.

2.4 HE Histological Observation

After 28 days of treatment, the mice were sacrificed rapidly. Skin samples approximately 1cm×1cm in size were taken from the alopecia area on the back of each mouse in each group. These samples were thoroughly rinsed in normal saline to remove residual blood, spread on filter paper, air - dried at room temperature, wrapped in aluminum foil, and then placed in centrifuge tubes containing 4% paraformaldehyde solution for tissue fixation. After 24 to 48 hours of fixation, the skin tissues were taken out and dehydrated successively in 75%, 85%, 90%, 95%, 100% ethanol, xylene 1, and xylene 2. Subsequently, the skin tissues were embedded in an embedding machine. The wax blocks obtained after embedding were subjected to dewaxing of paraffin sections, hematoxylin - eosin staining, and dehydration and mounting. Under a 200-fold microscopic field of view, the morphological changes of the mouse hair follicles were observed. The ratio of terminal hairs to vellus hairs in the skin of mice in each group was counted using Image J to evaluate the drug effect.

2.5 Determine the Contents of DHT, TGF-β and IGF-1 in Skin Tissues by ELISA Method.

Prepare tissue homogenates from the tissues of each mouse collected through dissection. Determine the contents of DHT, TGF-β, and IGF-1 in the tissues of mice in each group according to the methods described in the ELISA kit instructions. Record the data and calculate their average values.

2.6 Statistical Analysis

Bar charts were plotted using GraphPad Prism, and one - way ANOVA in the software was employed to conduct significance comparisons of the data. A P - value of less than 0.05, denoted by ✲, indicated statistical significance.

3. Results and Analysis

3.1 Morphological Analysis of Hair Follicles

Compared with the model group, in the blank group, terminal hairs accounted for a larger proportion of the total hair quantity within the visual field, and the hair follicle density was higher, with almost no vellus hairs in the visual field, showing a significant difference. Compared with other groups, the model group had a lower overall hair follicle density and fewer hair follicles, with vellus hairs accounting for a relatively large proportion of the total hair, indicating successful modeling. For the minoxidil group, in the microscopic field of view, terminal hairs accounted for a larger proportion of the total hair quantity, while vellus hairs accounted for a smaller proportion. Among all the composition groups, the nano - cerium oxide group had the highest ratio of terminal hairs/vellus hairs. It had a high hair follicle density, with mostly terminal hairs and fewer vellus hairs in the visual field. See Figure 1 and Figure 2 for details.

Figure 1: Results of HE staining of mouse dorsal tissues

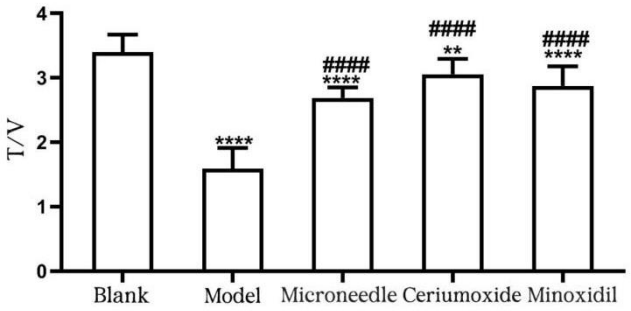

Figure 2: Ratio of terminal hairs to vellus hairs in HE - stained dorsal tissues of mice

Notes: * indicates comparison with the blank group, *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001; # indicates comparison with the model group, #P < 0.05, ##P < 0.01, ###P < 0.001, ####P < 0.0001.

3.2 The Contents of DHT, TGF-β and IGF-1 in Mouse Skin

According to the data of the contents of DHT, TGF-β, and IGF-1 in skin tissues obtained from this ELISA, after modeling, the contents of DHT and TGF-β in the skin tissues of mice in the model group, microneedle group, minoxidil group, and nano-cerium oxide group were significantly increased compared with those in the blank group, while the content of IGF-1 decreased. After drug administration, the contents of DHT and TGF-β in the skin tissues of mice in the microneedle group, minoxidil group, and nano-cerium oxide group decreased to varying degrees compared with those in the model group, while the content of IGF-1 increased. See Table 1, Figure 3; Table 2, Table 4; Table 3, Figure 5.

Table 1: Content of DHT in the dorsal tissues of mice

Group	DHT (nmol/L)
Blank	119.06±2.39
Model	177.22±4.98*
Microneedl	89.50±9.17*#
Cerium oxide	75.13±2.29*#&
Minoxidil	83.69±2.91*#&$

Notes: *indicates a statistically significant difference compared with the blank group; #indicates a statistically significant difference compared with the model group; &indicates a statistically significant difference compared with the roller microneedle group; $indicates a statistically significant difference compared with the cerium oxide group.

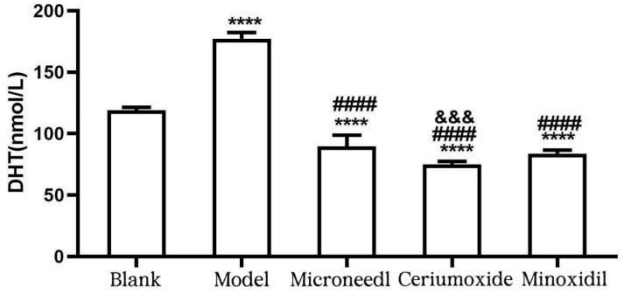

Figure 3: Bar chart of DHT content in the dorsal tissues of mice

Notes: * indicates comparison with the blank group, *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001; # indicates comparison with the model group, #P<0.05, ##P<0.01, ###P<0.001, ####P<0.0001; & indicates comparison with the roller microneedle group, &P<0.05, &&P<0.01, &&&P<0.001, &&&&P<0.0001; $ indicates comparison with cerium oxide, $P<0.05, $$P<0.01, $$$P<0.001, $$$$P<0.0001.

Table 2: Content of TGF-β in the dorsal tissues of mice

Group	TGF-β (pg/mL)
Blank	100244.44±1592.88
Model	175925±5198.02*
Microneedl	155688.89±2583.29*#
Ceriumoxide	112938.89±5417.41*#&
Minoxidil	134050±12484.30*#&$

Notes: *indicates a statistically significant difference compared with the blank group; #indicates a statistically significant difference compared with the model group; &indicates a statistically significant difference compared with the roller microneedle group; $indicates a statistically significant difference compared with the cerium oxide group.

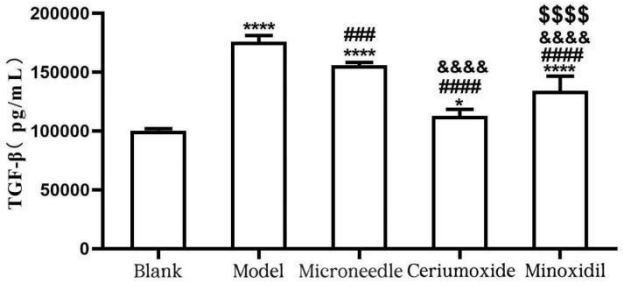

Figure 4: The content of TGF - β in the dorsal tissues of mice

Notes: * indicates comparison with the blank group, *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001; # indicates comparison with the model group, #P<0.05, ##P<0.01, ###P<0.001, ####P<0.0001; & indicates comparison with the roller microneedle group, &P<0.05, &&P<0.01, &&&P<0.001, &&&&P<0.0001; $ indicates comparison with cerium oxide, $P<0.05, $$P<0.01, $$$P<0.001, $$$$P<0.0001.

Table 3: Content of IGF-1 in the dorsal tissues of mice

Group	IGF-1 (ng/mL)
Blank	308.05±2.49
Model	248.85±1.075*
Microneedl	375.57±1.03*#
Ceriumoxide	561.59±1.84*#&
Minoxidil	460.73±0.85*#&$

Notes: *indicates a statistically significant difference compared with the blank group; #indicates a statistically significant difference compared with the model group; &indicates a statistically significant difference compared with the roller microneedle group; $indicates a statistically significant difference compared with the cerium oxide group.

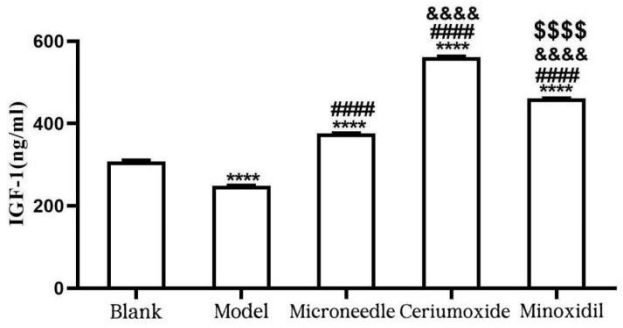

Figure 5: The content of IGF-1 in the dorsal tissues of mice

Notes: *indicates comparison with the blank group, *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001; # indicates comparison with the model group, #P<0.05, ##P<0.01, ###P<0.001, ####P<0.0001; & indicates comparison with the roller microneedle group, &P<0.05, &&P<0.01, &&&P<0.001, &&&&P<0.0001; $ indicates comparison with cerium oxide, $P<0.05, $$P<0.01, $$$P<0.001, $$$$P<0.0001.

4. Discussion

AGA is caused by the increased expression of androgen receptor genes and/or type II 5α-reductase genes in the hair

follicles of the balding area, which leads to an enhanced effect of androgens on susceptible hair follicles. In the case of AGA, the dermal component cells in susceptible hair follicles contain specific type II 5α-reductase, which can convert testosterone, an androgen circulating in the blood to this area, into dihydrotestosterone (DHT). After DHT binds to the androgen receptor (AR) in the hair follicles, it activates a series of intracellular signaling pathways [6], DHT can upregulate the expression of certain cell cycle inhibitory proteins, such as p27Kip1. p27Kip1 is able to inhibit the activity of cyclin-dependent kinases (CDKs), thereby preventing hair follicle cells from transitioning from the G1 phase to the S phase, leading to a slowdown in the proliferation of hair follicle cells and causing the hair follicles to enter the regression phase prematurely. After DHT binds to the AR, it alters the microenvironment in which hair follicle stem cells reside, reducing the secretion of some growth factors that promote the activation of hair follicle stem cells, such as insulin-like growth factor-1 (IGF-1). As a result, hair follicle stem cells are less likely to be activated and enter a new growth phase, leading to an extended resting phase and increased hair loss [7]. In addition to this, after DHT binds to the AR, it activates the apoptotic signaling pathways within cells. For example, it induces the apoptosis of outer root sheath cells by activating proteins from the caspase family [8]. As the continuous apoptosis of outer root sheath cells occurs, the volume of the hair follicle gradually decreases. The originally thick terminal hair follicles gradually transform into fine vellus hair follicles. In the pathological process of AGA, it can be observed that hair follicles gradually change from large ones capable of producing thick and long hair to small ones that can only produce fine and soft hair. This is the manifestation of follicular miniaturization [9]. During the process of follicular miniaturization, the lipid synthesis of hair follicle cells decreases, which may affect the normal physiological functions of the hair follicles, such as intercellular signal transduction and barrier function. At the same time, the synthesis of keratin also changes, leading to a decrease in the quality of hair, making it finer and softer. A large amount of DHT binding to androgen receptors can increase the protein expression of TGF-β. The overexpression of TGF-β inhibits the development of hair follicles [10], In the normal hair follicle growth cycle, the balance of TGF-β levels is crucial for maintaining the normal state of hair follicles. However, when the level of TGF-β abnormally increases, it can induce hair follicles to enter the regression phase prematurely from the growth phase. TGF-β exerts its effects by activating intracellular signaling pathways, such as the Smad signaling pathway. Specifically, after TGF-β binds to receptors on the cell membrane, it causes the receptors to be phosphorylated, thereby activating Smad proteins. The phosphorylated Smad proteins can then transfer to the cell nucleus and regulate the expression of a series of genes. These genes include some that are related to cell cycle arrest, such as p15INK4B and p21Cip1. They can inhibit the activity of cyclin-cyclin-dependent kinase (cyclin-CDK) complexes, slowing down the proliferation of hair follicle cells, leading to the stagnation of hair follicle growth and entry into the regression phase. Hair follicle stem cells play a key role in the cyclical regeneration of hair follicles, and TGF-β can inhibit the activity of hair follicle stem cells [11], Reduce its proliferation and differentiation. It achieves this goal by regulating the microenvironment in which hair follicle stem cells reside. TGF-β can induce changes in the extracellular matrix (ECM) components surrounding hair follicle stem cells, such as increasing the deposition of collagen and fibronectin. These changes make the microenvironment of hair follicle stem cells more rigid, which is not conducive to the proliferation and differentiation of stem cells. At the same time, TGF-β can also directly act on hair follicle stem cells, inhibiting some signaling pathways that promote the proliferation and differentiation of stem cells, such as the Wnt/β-catenin signaling pathway. This reduces the activity of hair follicle stem cells and hinders the hair follicles from entering a new growth phase [12]. The normal growth and maintenance of hair follicle function depend on an adequate blood supply. TGF-β can induce apoptosis of microvascular endothelial cells in the hair follicles of the scalp in AGA patients, leading to vascular regression [13], For example, TGF-β can inhibit the expression and activity of angiogenesis-promoting factors such as vascular endothelial growth factor (VEGF). VEGF is a key regulator of angiogenesis, capable of stimulating the proliferation, migration, and lumen formation of endothelial cells. By suppressing the expression of VEGF, TGF-β reduces the formation of new blood vessels around the hair follicles, leading to insufficient blood supply to the hair follicles. Insufficient blood supply deprives the hair follicles of necessary nutrients and oxygen, affecting the normal metabolism and function of hair follicle cells, which in turn leads to hair loss [14]. On the contrary, the positive expression of IGF-1 can inhibit the onset of AGA. For example, DHT can cause hair follicle cell cycle arrest, while IGF-1 can restore the normal progression of the cell cycle by promoting the expression of cyclins and activating cyclin-dependent kinases, reducing the phenomenon of shortened hair follicle growth phase caused by DHT. There is also a mutual regulatory relationship between IGF-1 and TGF-β. The Smad signaling pathway is the main intracellular pathway through which TGF-β exerts its effects. IGF-1 can activate the PI3K-Akt signaling pathway, leading to the phosphorylation of Akt and the inhibition of Smad protein activity. This prevents TGF-β-induced hair follicle cell cycle arrest and apoptosis, maintaining the normal growth of hair follicles [15]. The newly formed blood vessels can provide the hair follicles with sufficient nutrients (such as glucose, amino acids, etc.) and oxygen, which is crucial for the growth of hair follicles and the maintenance of their normal physiological functions. If the blood supply to the hair follicles is insufficient, it can lead to hair follicle atrophy and hair loss. IGF-1 ensures a good blood supply to the hair follicles by promoting angiogenesis [16], thereby helping to prevent hair loss. In view of the above-mentioned mechanisms, this experiment evaluated the therapeutic effect of nano-cerium oxide on androgenetic alopecia in mice by measuring the growth of hair follicles and the concentrations of DHT, TGF-β, and IGF-1 in the body. Androgenetic alopecia models were established in mice by injecting testosterone. Histological observations with HE staining revealed a low proportion of terminal hair and reduced hair follicle density, indicating the successful establishment of the mouse model ($P<0.01$). The experimental results showed that, through morphological observation of hair follicles, all treatment groups could effectively improve the reduction and decrease of hair follicles caused by testosterone, and increase the ratio of terminal hair to vellus hair in mice, with the nano-cerium

oxide group showing better therapeutic effects than the other two groups. In the ELISA measurement of the content of DHT, TGF-β, and IGF-1 in mouse skin tissue, the treatment groups could all reduce the content of DHT and TGF-β, and increase the content of IGF-1 compared with the model group, especially the nano-cerium oxide group, which showed the most significant effect.

5. Conclusion

The results of this experiment show that nano-cerium oxide alleviates androgenetic alopecia by reducing the DHT produced by mouse skin cells, decreasing the metabolic production of TGF-β protein, and increasing the expression of IGF-1. This in turn inhibits the activation of genes related to the transformation of terminal hair into vellus hair in mice, ultimately achieving the goal of relieving androgenetic alopecia. The therapeutic effect on androgenetic alopecia in mice is significant, which is similar to the clinical effect of minoxidil. We speculate that it has similarities with the mechanism of action of minoxidil, such as: extending the anagen phase of hair follicles [17], promoting the proliferation and differentiation of hair follicle cells, dilating blood vessels [18], facilitating the transport and release of growth factors, reducing the sensitivity of androgen receptors [19], and regulating the activity of androgen enzymes, etc. This has explored its potential as an anti-hair loss and hair growth drug, providing a reference for the clinical application of nano-cerium oxide in AGA.

References

[1] Wang TL, Zhou C, Shen YW, Wang XY, Ding XL, Tian S, Liu Y, Peng GH, Xue SQ, Zhou JE, Wang RL, Meng XM, Pei GD, Bai YH, Liu Q, Li H, Zhang JZ. Prevalence of androgenetic alopecia in China: a community-based study in six cities. Br J Dermatol. 2010 Apr;162(4):843-7. doi: 10.1111/j.1365-2133.2010.09640.x. Epub 2009 Jan 22. PMID: 20105167.

[2] Lolli F, Pallotti F, Rossi A, Fortuna MC, Caro G, Lenzi A, Sansone A, Lombardo F. Androgenetic alopecia: a review. Endocrine. 2017 Jul;57(1):9-17. doi: 10.1007/s12020-017-1280-y. Epub 2017 Mar 28. PMID: 28349362.

[3] Pozo-Pérez L, Tornero-Esteban P, López-Bran E. Clinical and preclinical approach in AGA treatment: a review of current and new therapies in the regenerative field. Stem Cell Res Ther. 2024 Aug 15;15(1):260. doi: 10.1186/s13287-024-03801-5. PMID: 39148125; PMCID: PMC11328498.

[4] Cui W, Chen S, Hu T, Zhou T, Qiu C, Jiang L, Cheng X, Ji J, Yao K, Han H. Nanoceria-Mediated Cyclosporin A Delivery for Dry Eye Disease Management through Modulating Immune-Epithelial Crosstalk. ACS Nano. 2024 Apr 30;18(17):11084-11102. doi: 10.1021/acsnano.3c11514. Epub 2024 Apr 17. PMID: 38632691.

[5] Chen S, Wang Y, Bao S, Yao L, Fu X, Yu Y, Lyu H, Pang H, Guo S, Zhang H, Zhou P, Zhou Y. Cerium oxide nanoparticles in wound care: a review of mechanisms and therapeutic applications. Front Bioeng Biotechnol. 2024 May 20;12:1404651. doi: 10.3389/fbioe.2024.1404651. PMID: 38832127; PMCID: PMC11145637.

[6] Dhurat R, Sharma A, Rudnicka L, Kroumpouzos G, Kassir M, Galadari H, Wollina U, Lotti T, Golubovic M, Binic I, Grabbe S, Goldust M. 5-Alpha reductase inhibitors in androgenetic alopecia: Shifting paradigms, current concepts, comparative efficacy, and safety. Dermatol Ther. 2020 May;33(3):e13379. doi: 10.1111/dth.13379. Epub 2020 Apr 24. PMID: 32279398.

[7] Panchaprateep R, Asawanonda P. Insulin-like growth factor-1: roles in androgenetic alopecia. Exp Dermatol. 2014 Mar;23(3):216-8. doi: 10.1111/exd.12339. PMID: 24499417.

[8] Liu Y, Yang S, Tan L, Li X, Long D, Lu J, Wang D. Necrosulfonamide promotes hair growth and ameliorates DHT-induced hair growth inhibition. J Dermatol Sci. 2024 Aug;115(2):64-74. doi: 10.1016/j.jdermsci.2024.04.004. Epub 2024 Apr 26. PMID: 39043505.

[9] Fu D, Huang J, Li K, Chen Y, He Y, Sun Y, Guo Y, Du L, Qu Q, Miao Y, Hu Z. Dihydrotestosterone-induced hair regrowth inhibition by activating androgen receptor in C57BL6 mice simulates androgenetic alopecia. Biomed Pharmacother. 2021 May;137:111247. doi: 10.1016/j.biopha.2021.111247. Epub 2021 Jan 29. PMID: 33517191.

[10] Ceruti JM, Leirós GJ, Balañá ME. Androgens and androgen receptor action in skin and hair follicles. Mol Cell Endocrinol. 2018 Apr 15;465:122-133. doi: 10.1016/j.mce.2017.09.009. Epub 2017 Sep 12. PMID: 28912032.

[11] Lu GQ, Wu ZB, Chu XY, Bi ZG, Fan WX. An investigation of crosstalk between Wnt/β-catenin and transforming growth factor-β signaling in androgenetic alopecia. Medicine (Baltimore). 2016 Jul;95(30):e4297. doi: 10.1097/MD.0000000000004297. PMID: 27472703; PMCID: PMC5265840.

[12] Calvo-Sánchez MI, Fernández-Martos S, Carrasco E, Moreno-Bueno G, Bernabéu C, Quintanilla M, Espada J. A role for the Tgf-β/Bmp co-receptor Endoglin in the molecular oscillator that regulates the hair follicle cycle. J Mol Cell Biol. 2019 Jan 1;11(1):39-52. doi: 10.1093/jmcb/mjy051. PMID: 30239775; PMCID: PMC6359924.

[13] Deng Z, Chen M, Liu F, Wang Y, Xu S, Sha K, Peng Q, Wu Z, Xiao W, Liu T, Xie H, Li J. Androgen Receptor-Mediated Paracrine Signaling Induces Regression of Blood Vessels in the Dermal Papilla in Androgenetic Alopecia. J Invest Dermatol. 2022 Aug;142(8):2088-2099.e9. doi: 10.1016/j.jid.2022.01.003. Epub 2022 Jan 14. PMID: 35033537.

[14] Hou C, Miao Y, Wang J, Wang X, Chen CY, Hu ZQ. Collagenase IV plays an important role in regulating hair cycle by inducing VEGF, IGF-1, and TGF-β expression. Drug Des Devel Ther. 2015 Sep 25;9:5373-83. doi: 10.2147/dddt.s8912. PMID: 26451090; PMCID: PMC4590320.

[15] Ahn SY, Pi LQ, Hwang ST, Lee WS. Effect of IGF-I on Hair Growth Is Related to the Anti-Apoptotic Effect of IGF-I and Up-Regulation of PDGF-A and PDGF-B. Ann Dermatol. 2012 Feb;24(1):26-31. doi: 105021/ad.2012.24.1.26. Epub 2012 Feb 2. PMID: 22363152; PMCID: PMC3283847.

[16] Delafontaine P, Song YH, Li Y. Expression, regulation, and function of IGF-1, IGF-1R, and IGF-1 binding proteins in blood vessels. Arterioscler Thromb Vasc Biol. 2004 Mar;24(3):435-44. doi: 10.1161/01.ATV. 0000105902.89459.09. Epub 2003 Nov 6. PMID: 14604834.
[17] Messenger AG, Rundegren J. Minoxidil: mechanisms of action on hair growth. Br J Dermatol. 2004 Feb; 150(2):186-94. doi: 10.1111/j.1365-2133.2004.05785.x. PMID: 14996087.
[18] Rossi A, Cantisani C, Melis L, Iorio A, Scali E, Calvieri S. Minoxidil use in dermatology, side effects and recent patents. Recent Pat Inflamm Allergy Drug Discov. 2012 May;6(2):130-6. doi: 10.2174/187221312800166859. PMID: 22409453.
[19] Jain R, De-Eknamkul W. Potential targets in the discovery of new hair growth promoters for androgenic alopecia. Expert Opin Ther Targets. 2014 Jul;18(7):787-806. doi: 10.1517/14728222.2014.922956. Epub 2014 May 30. PMID: 24873677.

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