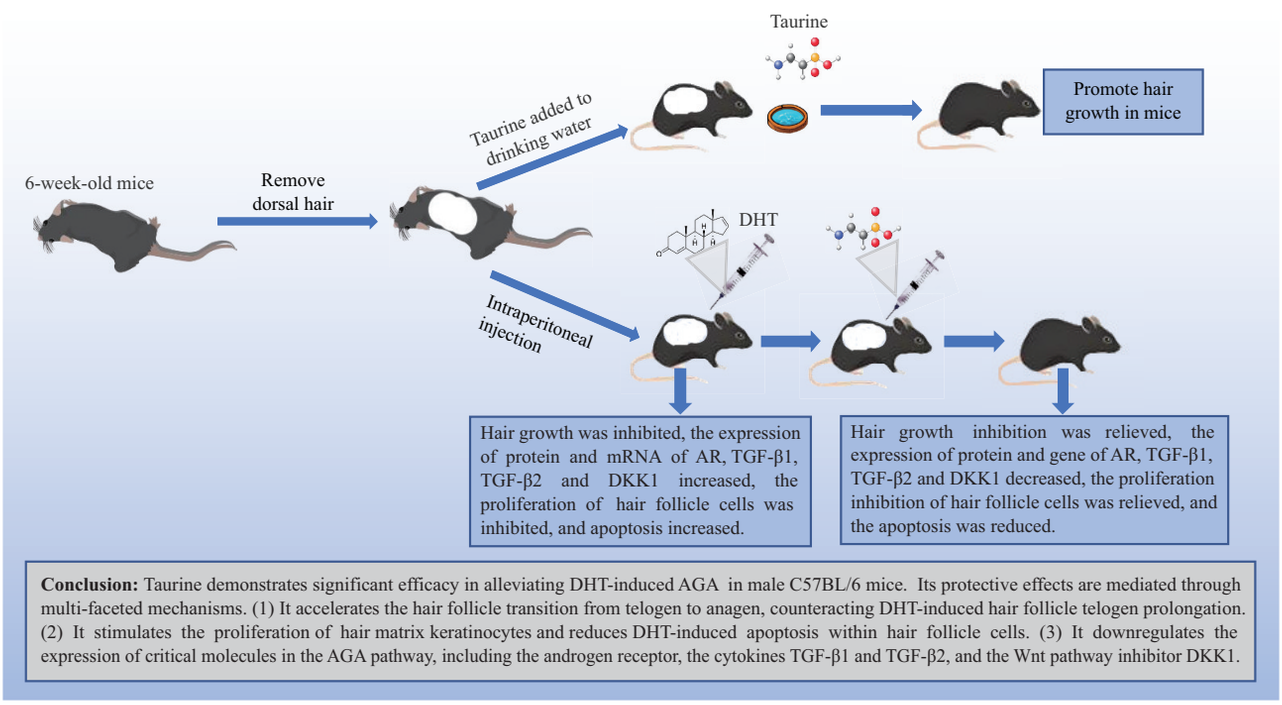
PIBB 生物化学与生物物理进展
Progress in Biochemistry and Biophysics
2025, 52(11): 2854~2868
www.pibb.ac.cn

Taurine Alleviates Androgenetic Alopecia in Male C57BL/6 Mice by Modulating Hair Follicle Cycle and Related Signaling Pathways*

WU Jin-Qiang[1,2], GUO Guo-Guo[1], ZHANG Xin-Ting[1], LIU Jin-Jia[1], WANG Ji-Xiang[1], HE Xiao-Yan[2]**, WANG Hai-Dong[2]**

([1]*Basic Medicine College, Changzhi Medical College, Changzhi* 046000, China;
[2]*College of Veterinary Medicine, Shanxi Agricultural University, Taigu* 030801, China)

Graphical abstract



Abstract **Objective** This study aimed to comprehensively investigate the potential protective effects and underlying mechanisms of taurine against dihydrotestosterone (DHT)-induced androgenetic alopecia (AGA) in male C57BL/6 mice, with a

* This work was supported by grants from The National Natural Science Foundation of China (31772690), the Natural Science Foundation of Shanxi Province (201701D121106), and PhD Research Startup Foundation of Changzhi Medical College (BS202308).

** Corresponding author.
HE Xiao-Yan. Tel: 86-354-6288160, E-mail: sxndhxy@163.com
WANG Hai-Dong. Tel: 86-354-6288160, E-mail: wanghaidong@sxau.edu.cn

Received: May 29, 2025 Accepted: September 19, 2025

focus on hair follicle cycle modulation, cellular proliferation/apoptosis, and key related signaling pathways. **Methods** Six-week-old female C57BL/6 mice were initially used to assess the hair growth-promoting potential of taurine. After acclimatization, they were randomly assigned to three groups (*n*=8): control (regular drinking water), taurine (drinking water containing 1% taurine), and minoxidil (topical 2% minoxidil, positive control). For the AGA study, male C57BL/6 mice were randomly divided into five groups (*n*=8): control (physiological saline), DHT (model group, 1 mg/d DHT), DHT+low-dose taurine (1 mg/d DHT+2 mg/d taurine), DHT+high-dose taurine (1 mg/d DHT+10 mg/d taurine), and DHT+minoxidil (positive control, 1 mg/d DHT+topical 2% minoxidil). One day before treatment initiation, dorsal hair was shaved with scissors, and residual hair was removed using a depilatory cream. DHT and taurine were administered *via* daily intraperitoneal injection. Hair regrowth was assessed by photographing the depilated area at regular intervals and quantified using a four-point grading system (0−3). Dorsal skin samples were collected on day 14 for histological analysis (H&E staining), immunofluorescence staining (Ki67 for proliferation, TUNEL for apoptosis), ELISA (DHT quantification), RT-qPCR, and Western blot analysis to evaluate the expression of key genes and proteins (androgen receptor (AR), transforming growth factor (TGF)-β1, TGF-β2, Dickkopf-1 (DKK1)). **Results** In female mice, taurine supplementation significantly accelerated hair growth, with effects comparable to minoxidil. This was evidenced by an earlier transition from pink (telogen) to black (anagen) skin and increased hair growth scores. Histological analysis showed that taurine increased hair follicle count and dermal thickness. Immunofluorescence confirmed enhanced keratinocyte proliferation in the hair matrix. In the DHT-induced AGA model, DHT significantly extended the telogen phase, inhibited hair growth, increased skin DHT content, and induced hair follicle miniaturization. Taurine treatment, particularly at the high dose, effectively counteracted these effects: it promoted the telogen-to-anagen transition and improved hair growth scores. Histomorphometric analysis showed that taurine significantly restored DHT-induced reductions in dermal thickness, hair follicle count, hair bulb depth, and follicle size. Taurine treatment also reduced apoptosis and promoted the proliferation of hair follicle cells, as demonstrated by Ki67 and TUNEL assays. Crucially, RT-qPCR and Western blot analyses revealed that DHT significantly up-regulated the expression of AR, TGF-β1, TGF-β2, and DKK1 at both mRNA and protein levels in dorsal skin. Taurine administration markedly down-regulated the expression of these pathogenic factors, bringing them closer to the levels observed in the control group. **Conclusion** Taurine demonstrates significant efficacy in alleviating DHT-induced AGA in male C57BL/6 mice. Its protective effects are mediated through multi-faceted mechanisms. (1) Promoting hair follicle cycle progression: it accelerates the transition from telogen to anagen, counteracting DHT-induced prolongation of the telogen phase. (2) Modulating cellular dynamics: it stimulates the proliferation of hair matrix keratinocytes and reduces DHT-induced apoptosis within hair follicle cells. (3) Suppressing androgen-driven pathogenic pathways: it downregulates the expression of critical molecules in the AGA pathway, including AR, the cytokines TGF-β1 and TGF-β2, and the Wnt pathway inhibitor DKK1. Given its favorable safety profile and multi-targeted action, taurine emerges as a promising novel therapeutic candidate or adjunct for treating AGA. Further investigation into its clinical potential and precise molecular mechanisms is warranted. This study provides a robust preclinical foundation for considering taurine supplementation or topical application in hair loss management strategies.

Key words taurine, androgenetic alopecia, dihydrotestosterone, C57BL/6 mice, hair follicle

DOI：10.3724/j.pibb.2025.0264 **CSTR**：32369.14.pibb.20250264

Androgenetic alopecia (AGA), being the most common type of hair loss worldwide, significantly impairs the quality of life and mental health of patients[1-3]. According to statistics, approximately 80% of men and 50% of women will be affected by AGA during their lifetime[4]. AGA exhibits marked gender and racial differences, with a higher incidence rate among Caucasians compared to Asian populations[5-6]. In men, AGA typically manifests as receding hairlines and hair thinning in the frontal and temporal regions. In women, the hairline remains stable, but there is obvious hair thinning in the frontal region[7-9].

The pathogenesis of AGA mainly involves the conversion of testosterone to dihydrotestosterone (DHT) by 5α-reductase. DHT has a high affinity for the androgen receptor (AR), which in turn triggers a series of biological effects[10]. Notably, DHT stimulates the production of transforming growth factor (TGF)-β in dermal papilla cells, inhibits the proliferation of keratinocytes induces apoptosis, and upregulates the expression of the secreted glycoprotein Dickkopf-1 (DKK1). This promotes the transition of hair follicles from the anagen to catagen phase, ultimately resulting

in hair follicle miniaturization and hair loss[11-13]. Presently, the treatment options for AGA are relatively limited[14]. Conventional therapies such as topical minoxidil and oral finasteride have certain efficacy, but cause significant side effects, require long-term use, and exhibit high relapse rates upon discontinuation[3]. Thus, there is an urgent need to explore safe and effective new treatment methods.

Taurine, an abundant sulfur-containing amino acid in living organisms, exerts diverse biological activities including antioxidant, anti-inflammatory, and regulation of cell osmotic pressure[15-17]. In recent years, studies have shown that taurine holds promise for treating various stress-related diseases[18-19]. Additionally, previous studies have found that taurine has a resistance effect against chemically-induced hair loss[20]. Given that lymphocyte infiltration and fibrosis often accompany the process of hair follicle miniaturization, and taurine can regulate these pathological processes[21-22], we speculate the taurine may ameliorate AGA.

In this study, C57BL/6 mice were established to explore the effect of taurine on hair growth and its resistance to male alopecia and its mechanism, thereby offering new ideas and theoretical basis for the treatment of AGA.

1 Methods and materials

1.1 C57BL/6 mice treatments

Six-week-old C57BL/6 mice (male and female) were procured from Sipeifu Biotechnology Co., Ltd. (Beijing, China) and acclimatized for one week under specific-pathogen-free (SPF) conditions (22±2)℃ , 50%±5% humidity, 12-h light/dark cycle). To assess the potential of taurine to promote hair growth, a total of 24 female mice were randomly allocated to 3 groups (n=8): control (regular drinking water), taurine (drinking water containing 1% taurine) and minoxidil (topical 2% minoxidil, positive control) [23]. Dorsal hair was shaved using scissors, and residual hair was removed using a depilatory cream (Veet, France) one day before treatment. To investigate taurine's resistance effects against AGA, a DHT-induced AGA model was established. Following random allocation, a total of 40 male mice were randomly divided into 5 groups (n=8): control (physiological saline), DHT (model group, 1 mg/d DHT), DHT+low-dose taurine (1 mg/d DHT+2 mg/d taurine), DHT+high-dose taurine (1 mg/d DHT+10 mg/d taurine), and DHT+ minoxidil (positive control, 1 mg/d DHT+topical 2% minoxidil) [24-25]. Dorsal hair was shaved using scissors, and residual hair was removed using a depilatory cream one day before treatment. DHT and taurine were daily intraperitoneally injected. In the positive control group, 2% minoxidil was diluted with 95% alcohol and evenly applied to the back once a day. No significant difference in food intake or body weight between groups was observed, and no adverse clinical signs occurred.

On day 14 of treatment, mice were euthanized. Dorsal skin tissues were obtained for histological analysis, RNA/protein extraction, and ELISA. All animal care and experimental protocols complied with the Animal Management Rule of the Ministry of Health, People's Republic of China (Documentation No. 55, 2001) and the Guide for the Care and Use of Laboratory Animals published by the United States National Institutes of Health (Publication No. 85−23, Revised 1996), and the Global Research Animal Guide. All animal operations were carried out in accordance with the Guidelines for the Care and Use of Laboratory Animals of Shanxi Agricultural University and were approved by the Animal Medicine Committee of Shanxi Agricultural University (SXAU-EAW-2022M.PQ.003010003).

1.2 Hair regrowth assessment

As the depilation on the back skin of C57BL/6 mice induces hair follicles to enter the anagen[26], the changes within the depilation area on the dorsal skin were compared, and photographs were taken at regular intervals using a standardized camera setup, with 4 biological replicates and 2 technical replicates. ImageJ software was used to assess the hair regrowth using a four-point grading system reflecting progressive hair follicle activity based on dorsal skin color: 0 (pink skin, no hair regrowth), 1 (grey skin, initial hair growth), 2 (dark grey skin, advanced hair growth), and 3 (black skin, fully grown hair). The hair regrowth score was calculated as:

Score=((area of pink)×0+(area of grey)×1+(area of dark grey)×2+(area of black)×3)/total area[27].

1.3 Dorsal skin histological analysis and immunofluorescence staining

Dorsal skin samples were fixed in Bouin's solution (24 h), gradient ethanol dehydration, xylene transparency, and paraffin embedding. Serial sections

(6 μm) were subjected to hematoxylin and eosin (H&E) staining to evaluate basic morphological characteristics among treatments under an optical microscope. The hair follicle size, number, dermal thickness and hair bulb depth in the whole visual field were quantitatively analyzed by ImageJ software, and 3 visual fields were detected for each index.

To examine the impact of taurine on the proliferation and apoptosis of hair follicle cells, immunofluorescence staining with Ki67 and TUNEL was performed on the prepared sections. Fluorescence images were captured using a fluorescence microscope, and the results were quantified utilizing Image-Pro Plus software, and 3 visual fields were detected for each index.

1.4 ELISA assay

After the mouse skin was cut to a suitable size, a certain amount of PBS buffer was added, and 9 ml of homogenate was added to 1 g of tissue (on ice). Homogenize the tissue with a homogenizer at 4℃, 2 000*g* and centrifuge for 20 min. The supernatant was collected. DHT content in mice skin homogenates samples were measured by using ELISA kits (mlbio, China). The coefficient of variation (CV)% range of all sample groups is below 10%. The detection range is 1.25−40 nmol/L, and the sensitivity is that the minimum detection concentration is less than 0.1 nmol/L. Biological repetition was 3 times and technical repetition was 3 times.

1.5 RT−qPCR analysis

To explore mRNA expression levels of genes potentially influenced by taurine, total RNA was isolated from mouse samples using TRIzol (TIANGEN, China). HiScript III RT SuperMix for qPCR (+gDNA wiper) (Vazyme, China) was utilized for cDNA synthesis. Gene sequences for *AR, TGF-β1, TGF-β2, DKK1*, and *β-actin* were obtained from the NCBI GenBank database. Primers were designed utilizing Primer5.0, and their sequences are presented in Table 1. The application system is Thermo Fisher. ChamQ Universal SYBR qPCR Master Mix was employed for RT-qPCR, and the reaction system is shown in Table 2. The reaction conditions were 95℃ for 10 min, then 40 cycles of 95℃ for 15 s, 56−60℃ for 30 s, and 72℃ for 15 s. The relative mRNA expression level was determined by $2^{-\Delta\Delta C_t}$ method. Biological repetition was 3 times and technical repetition was 3 times.

Table1 Primer sequences

Gene	Sequence	Product size/bp	Annealing temperature/℃
AR	F: 5'-TGTGCCAGCAGAAACGATTG-3'	109	60
	R: 5'-GCTTACGAGCTCCCAGAGTCA-3'		
TGF-β1	F: 5'-ACCGCAACAACGCCATCT-3'	205	60
	R: 5'-CCAAGGTAACGCCAGGAAT-3'		
TGF-β2	F: 5'-TCACTGTCAGGCGACACTTC-3'	143	57
	R: 5'-TGAGGCTTCACGTGCATTAG-3'		
DKK1	F: 5'-TGAGGGCGGGAACAAGTA-3'	149	58
	R: 5'-TTCGGCAAGCCAGACAGA-3'		
β-Actin	F: 5'-GCTGTCCCTGTATGCCTCT-3'	222	58
	R: 5'-GATGTCACGCACGATTTCC-3'		

Table 2 The reaction system of RT−qPCR

Reagents	Volume/μl
2×ChamQ universal SYBR qPCR master mix	5
Forward primer	0.2
Reverse primer	0.2
cDNA	1
ddH_2O	3.6

1.6 Western blot

Skin tissue samples were subjected to total protein extraction using RIPA protein lysis buffer (Beyotime, China). Protein concentration was quantified utilizing an ND-1000 microplate reader. A 10% SDS-PAGE gel (Bioss, China) was utilized to separate the proteins, followed by their transfer onto a nitrocellulose membrane. Following a 1-h blocking step using 5% skim milk powder, the membrane underwent overnight incubation at 4℃ with primary antibodies (Table 3). After washing, the membrane was exposed to a horseradish peroxidase-conjugated secondary antibody for 1 h at 37℃. Protein bands

were detected utilizing ECL chemiluminescence (CWBIO, China) and analyzed using ImageJ software for grayscale intensity quantification. Biological repetition was 3 times and technical repetition was 3 times.

Table 3 Antibody information

Name	Host	Concentration	Manufacturer
Androgen receptor polyclonal antibody	Rabbit	1∶5 000	Proteintech
TGF-β1 polyclonal antibody	Rabbit	1∶2 000	Proteintech
TGF-β2 polyclonal antibody	Rabbit	1∶1 000	Proteintech
DKK1 polyclonal antibody	Rabbit	1∶500	Sangon Biotech
GAPDH polyclonal antibody	Rabbit	1∶5 000	Sangon Biotech
Goat anti-rabbit IgG	Goat	1∶20 000	Sangon Biotech

1.7 Data analysis

The RT-qPCR results were analyzed by the $2^{-\Delta\Delta C_t}$ method. The statistical results of immunofluorescence, RT-qPCR and Western blot were one-way ANOVA analyzed by SPSS17.0 statistical analysis software. Two-way ANOVA was used for hair regrowth assessment. Statistical significance was set at $^{*}P<0.05$, $^{**}P<0.01$.

2 Results

2.1 Taurine promotes hair growth in C57BL/6 female mice

To investigate taurine's impact on hair growth *in vivo*, we utilized C57BL/6 mice, and leveraged distinctive skin color changes during hair cycle, transitioning from pink (telogen) to black (anagen) [26,28], to visually monitor hair growth after depilation.

Taurine supplementation significantly accelerated hair growth compared with that in the control group (Figure 1a). By day 6, grayish areas started to appear in the taurine and minoxidil groups, whereas the control remained pink. On day 8, all the groups displayed gray skin, which was significantly lighter in the control group. On day 10, both the taurine and minoxidil groups exhibited dark gray skin, some even showing hair growth; however, in the control group, some of the mice presented dark gray skin, whereas others still presented light gray skin. At this time point, the difference in hair growth between the taurine group and the control group was most pronounced (Figure 1a, b). On day 12, taurine and minoxidil groups achieved nearly complete hair coverage, their skin turning black, whereas in the control group, some mice still had dark gray skin and only partial hair coverage. At day 14, taurine and minoxidil groups achieved complete hair coverage, whereas the control group achieved shorter hair with partially visible skin (Figure 1a). As shown in Figure 1b, c, the relative area under the curve (*AUC*) of taurine and minoxidil groups was 1.52- and 1.59-fold greater, respectively, than that of the control group. These results demonstrated that 1% taurine effectively accelerated the hair growth transition from telogen to anagen, leading to significant hair growth in C57BL/6 female mice.

2.2 Histological analysis of the effects of taurine on hair follicles

Histological analysis was performed on day 14, corresponding to the late anagen phase of the hair cycle in C57BL/6 mice[26]. Histological analysis of hematoxylin and eosin (HE) -stained dorsal skin sections revealed that, consistent with the observed acceleration of hair growth, taurine supplementation significantly increased hair follicle number and dermal thickness compared to the control group (Figure 2a). Compared with that in the control group, the number of hair follicles in the taurine group increased by 29%, whereas that in the minoxidil group increased by 47% (Figure 2b). Similarly, the dermal thickness in the taurine and minoxidil groups was 41% and 49%, respectively, greater than in the control group (Figure 2c).

2.3 Taurine enhances the proliferation of hair follicle stromal keratinocytes

Immunofluorescence staining revealed that, compared with the control group, both the taurine and the minoxidil groups presented significantly increased Ki67 expression, predominantly within hair matrix. These indicates that the follicle, especially

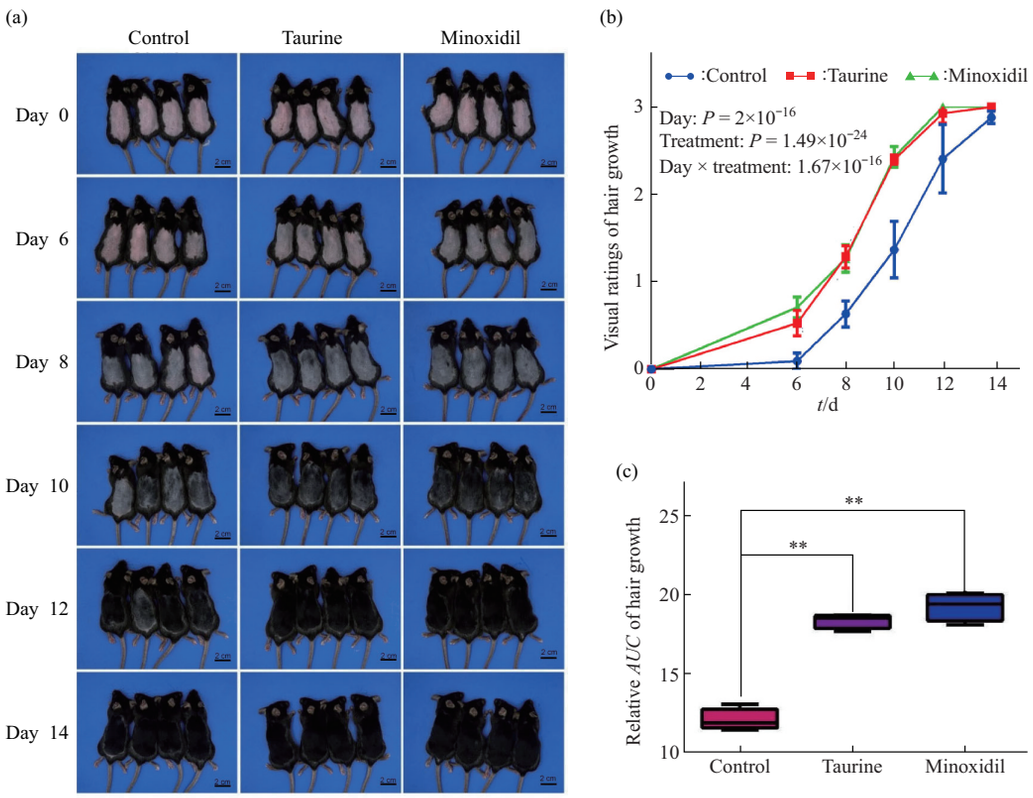


Fig. 1　Effect of taurine on hair growth in the dorsal skin of C57BL/6 female mice

(a) Hair growth images. (b) Visual scoring of hair growth. Two-way ANOVA: the main effect of days: $P=2\times10^{-16}$ the main effect of treatment group: $P=1.49\times10^{-24}$, the number of days×the interaction of treatment group: $P=1.67\times10^{-16}$. (c) Relative area under curve of hair growth in mice. Control: normal drinking water; Taurine: drinking water containing 1% taurine; Minoxidil: positive control, topical application of 2% minoxidil. **P<0.01.

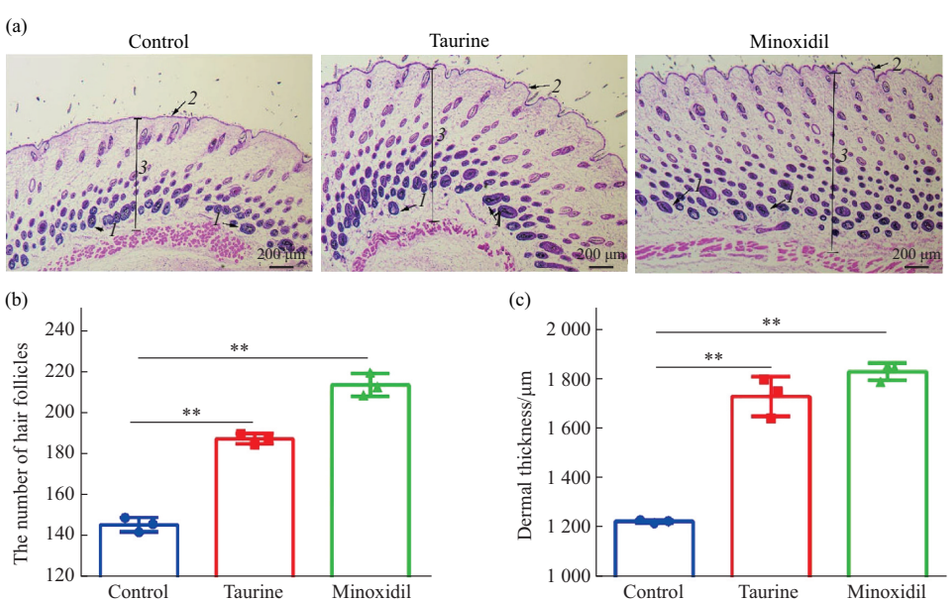


Fig. 2　Effects of taurine on the dorsal skin hair follicles of C57BL/6 female mice

(a) Hematoxylin and eosin (H&E) staining of dorsal skin sections on day 14 post-shaving. *1*: hair follicles; *2*: epidermis; *3*: dermis. (b) Number of hair follicles. (c) Dermal thickness. Control: normal drinking water; Taurine: drinking water containing 1% taurine; Minoxidil: positive control, topical application of 2% minoxidil. **P<0.01.

proliferative capacity of hair follicle stroma keratinocytes, is enhanced (Figure 3a). Compared with the control group, both the taurine and the minoxidil groups exhibited significant increases in Ki67 immunofluorescence intensity (22% and 28%, increased respectively; Figure 3b) and number of Ki67-positive cells (60% and 63%, increased respectively; Figure 3c).

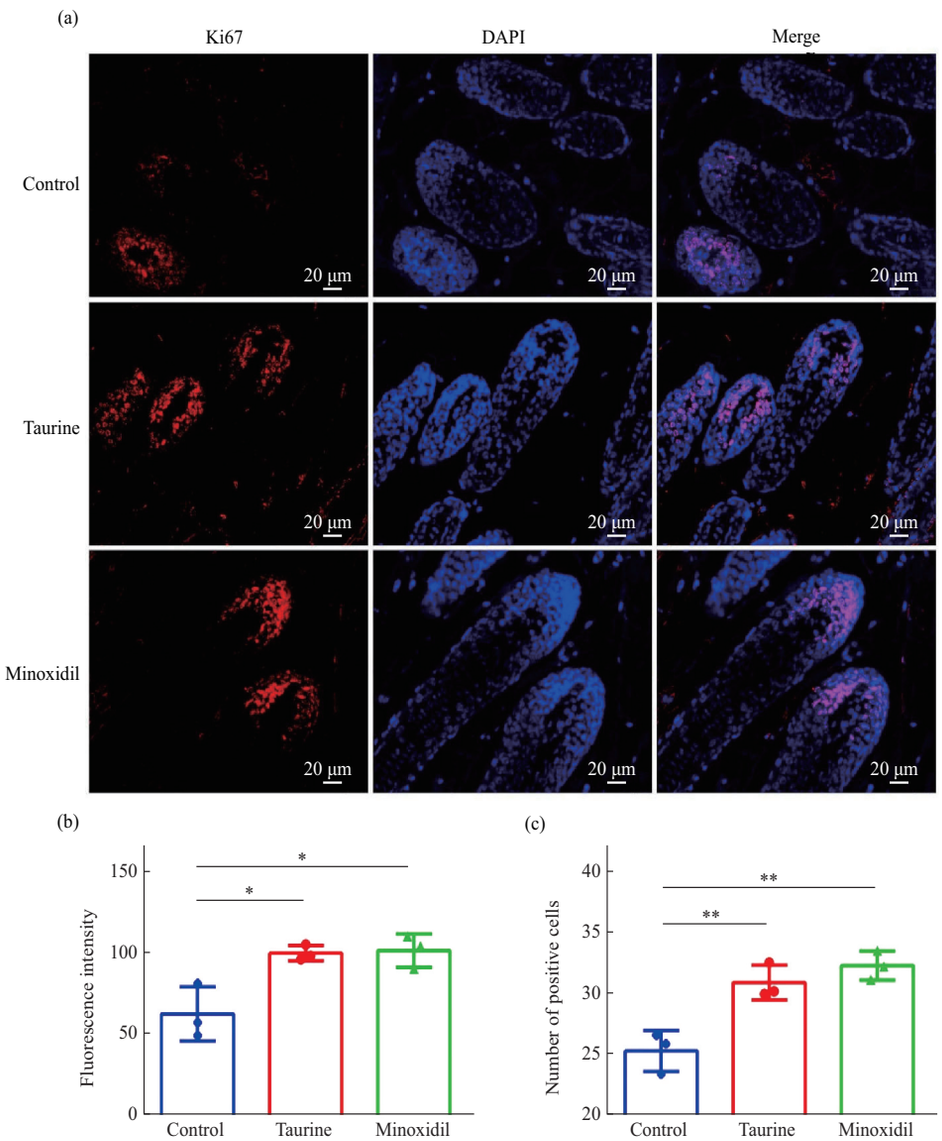


Fig. 3 Influence of taurine on hair follicle keratinocyte formation in C57BL/6 female mice

(a) Representative immunofluorescence images. (b) Fluorescence intensity of Ki67 staining. (c) Number of Ki67-positive cells. *P<0.05, **P<0.01.

2.4 Influence of taurine on dorsal skin hair growth in DHT−induced AGA model

To assess taurine's potential in mitigating AGA, we established a mouse model of AGA using male C57BL/6 mice. Hair growth progression in each treatment group was photographed at 0, 6, 10, 12, and 14 d after depilation. On day 0, all groups displayed pink skin. On day 6, negative control and positive control groups presented initial greying, while some mice treated with high-dose taurine also exhibited grey. Model and low-dose taurine groups remained pink. On day 10, negative control group displayed dark grey and partial hair regrowth. High-dose taurine and positive control groups showed mixed grey and dark grey areas. Low-dose taurine group appeared grey, while the model group showed light grey. On day 12, negative control, high-dose Taurine, and

positive control groups achieved near complete hair coverage with black skin. Low-dose taurine group appeared dark grey skin with partial hair regrowth, while the model group remained mostly grey, with some deeper grey. By day 14, all groups except the model exhibited complete hair coverage, while the model group displayed shorter hair with partially exposed skin uncovered (Figure 4a). In conclusion, mice in the model group experienced an extended telogen phase and significantly more inhibited hair growth than the negative control group. Conversely, treatment with taurine effectively counteracted the hair growth inhibitory effects caused by DHT. Additionally, the positive control group also showed a reversal of DHT-induced hair growth inhibition (Figure 4b, c).

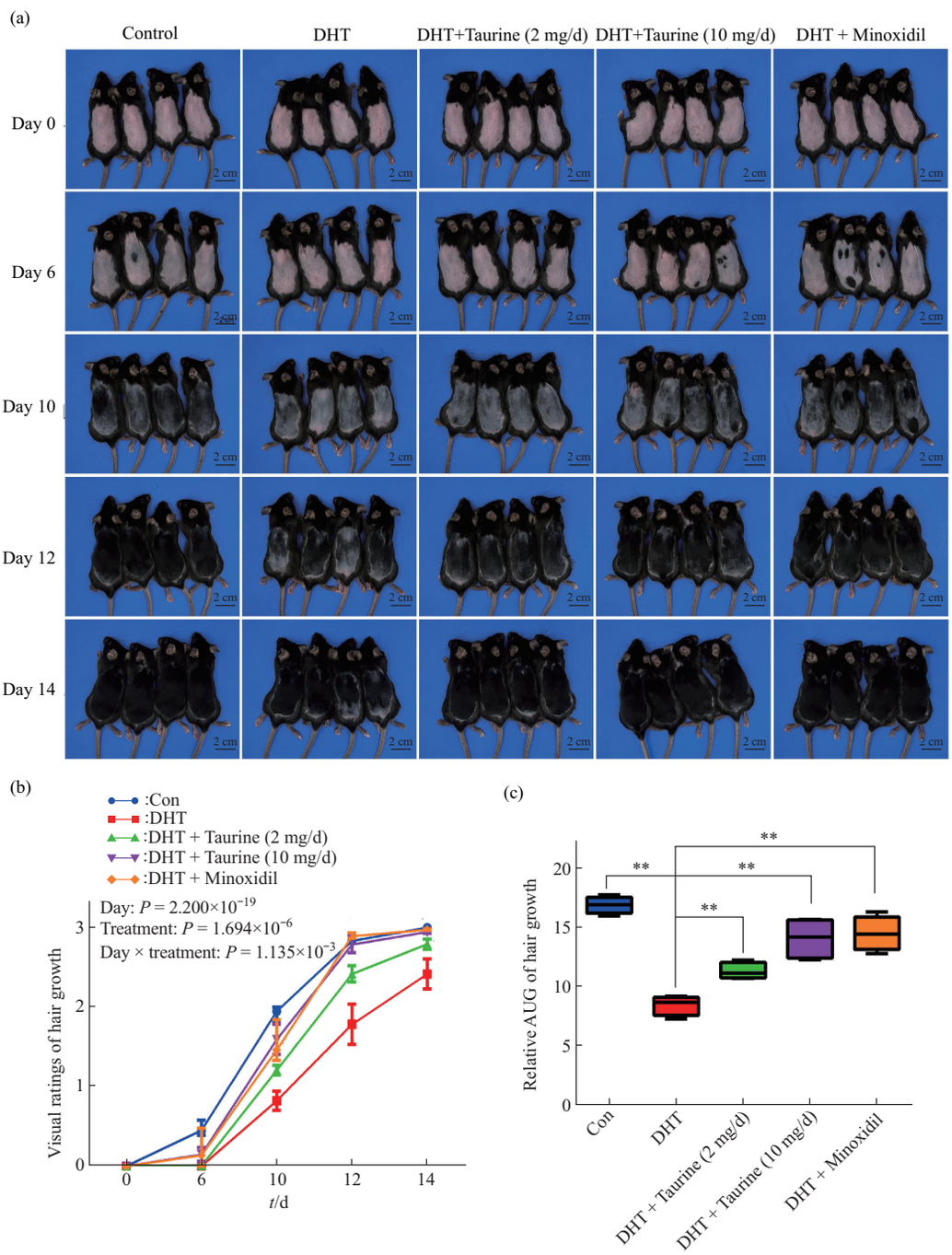


Fig. 4　Effects of taurine on hair growth in DHT−induced AGA C57BL/6 mice model

(a) Hair growth images. (b) Visual hair growth scoring. Two-way ANOVA: the main effect of days: P=2.200×10^{-19} the main effect of treatment group: P=1.694×10^{-6}, the number of days×the interaction of treatment group: P=1.135×10^{-3}. (c) Relative area under curve of hair growth in mice. **P<0.01.

2.5 Histological analysis of taurine's effects on AGA mouse hair follicles

Four histological parameters, including dermal thickness, hair follicle count, hair bulb depth, and hair follicle size, were evaluated in H&E-stained skin sections (Figure 5a). These parameters are established indicators of hair follicles from telogen to anagen phases[26,29]. In comparison to the DHT-induced AGA model group, all other groups (negative control, taurine treatment, and positive control) showed significant increases in all four parameters (Figure 5b−e). Taurine treatment promotes hair follicles from telogen to anagen phase, potentially counteracting DHT's inhibitory effects and promoting hair growth. Moreover, the high-dose taurine group showed a stronger ability to counteract DHT-induced hair growth inhibition compared to the low-dose taurine group, indicating a concentration-dependent effect. Hence, subsequent experiments were conducted using the high-dose taurine group.

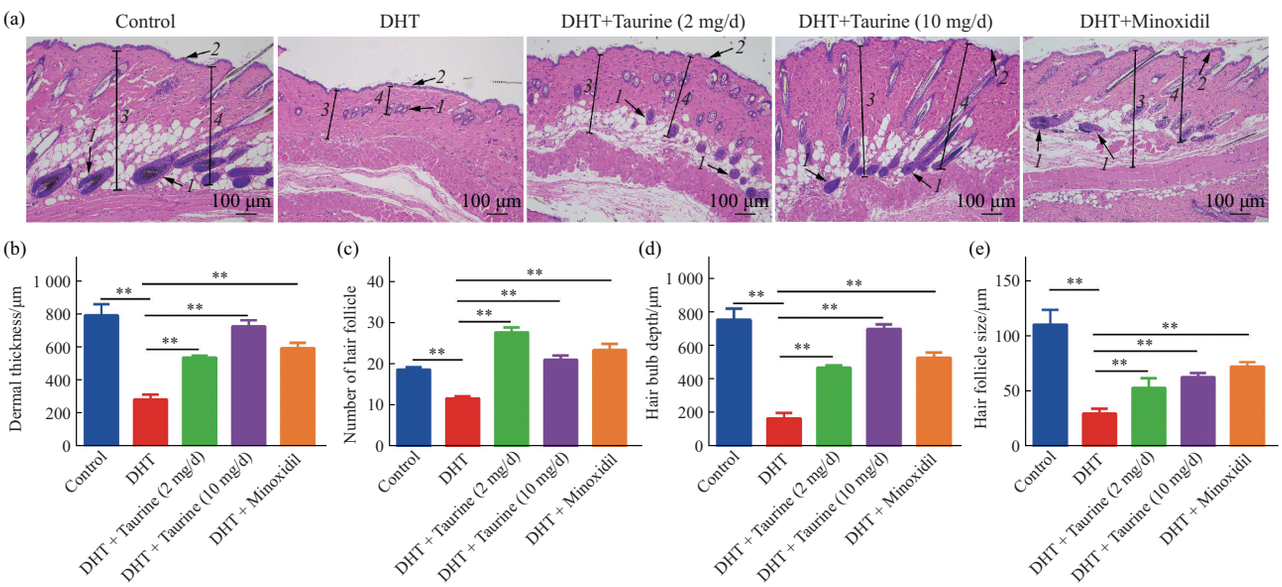


Fig. 5　Effects of taurine on hair follicles in DHT−induced AGA mice model

(a) HE staining of dorsal skin sections reveals morphological changes. *1*: hair follicle; *2*: epidermis; *3*: dermis layer; *4*: depth of hair bulbs. (b) Dermal thickness. (c) The quantity of hair follicle. (d) Hair bulb depth. (e) Hair follicle size. ***P*<0.01.

2.6 Model validation and taurine's impact on hair follicle cell proliferation and apoptosis

To ensure successful AGA model establishment, DHT content in mouse skin was quantified utilizing ELISA. The results revealed significantly higher DHT content (*P*<0.01) in model, taurine treatment, and positive control groups than the negative control group, confirming model validity (Figure 6a). To assess taurine's effects on hair follicle cell activity and death, immunofluorescence staining for Ki67 (proliferation marker) and TUNEL assay (apoptosis marker) were performed on AGA mouse skin sections (Figure 6). Immunofluorescence staining for Ki67 demonstrated a notable inhibition in cell proliferation within hair follicles of the model group, specifically in the proliferating cornified cells of hair follicle matrix. However, both taurine treatment and positive control groups showed a reversal of this inhibitory effect (Figure 6b). In comparison to the model group, the negative control, taurine treatment, and positive control groups exhibited 9.35, 7.10, and 8.10 times more positive cells, respectively (*P*<0.01, Figure 6c).

TUNEL analysis revealed that DHT treatment significantly increased cell apoptosis within hair follicles. However, taurine treatment and the positive control group significantly reduced the DHT-induced apoptosis in hair follicles compared to the model group (Figuer 6d). The model group exhibited 5.87, 5.20, and 2.75 times more apoptotic cells than the negative control, taurine treatment, and positive control groups, respectively (*P*<0.01, Figure 6e). The findings indicate taurine treatment effectively counteracts DHT's detrimental impact on hair follicle cell activity by reducing apoptosis and promoting proliferation.

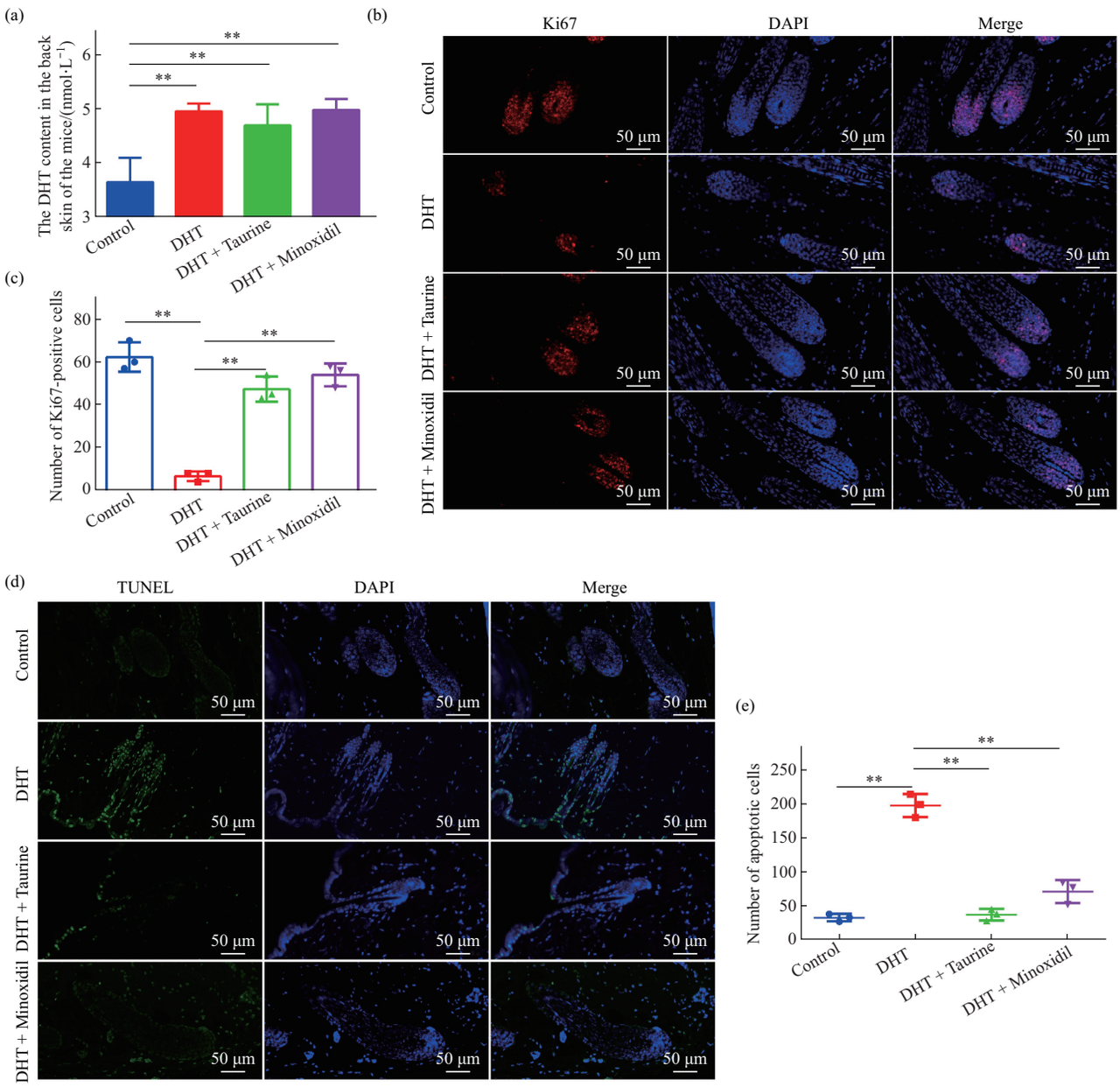


Fig. 6　Effects of taurine on proliferation and apoptosis of hair follicle cells in DHT−induced AGA mice model

(a) Detection results of DHT content in mouse skin. (b) Effect of taurine on the proliferation of cornified cells. (c) Number of Ki67-positive stained cells. (d) Effect of taurine on apoptosis. (e) Number of TUNEL-positive stained cells. $^{**}P<0.01$.

2.7　Effects of taurine on the expression of AR, TGF−β1, TGF−β2, and DKK1 genes and proteins

To elucidate how taurine counteracts AGA, we investigated the expression of *AR*, *TGF-β1*, *TGF-β2*, and *DKK1* genes and proteins within AGA model mice's dorsal skin. The model group exhibited notably elevated expression of these targets compared to the other groups. Notably, taurine administration or topical application of 2% minoxidil significantly ameliorated this condition, resulting in the restoration of their expression levels to near-normal levels (Figure 7).

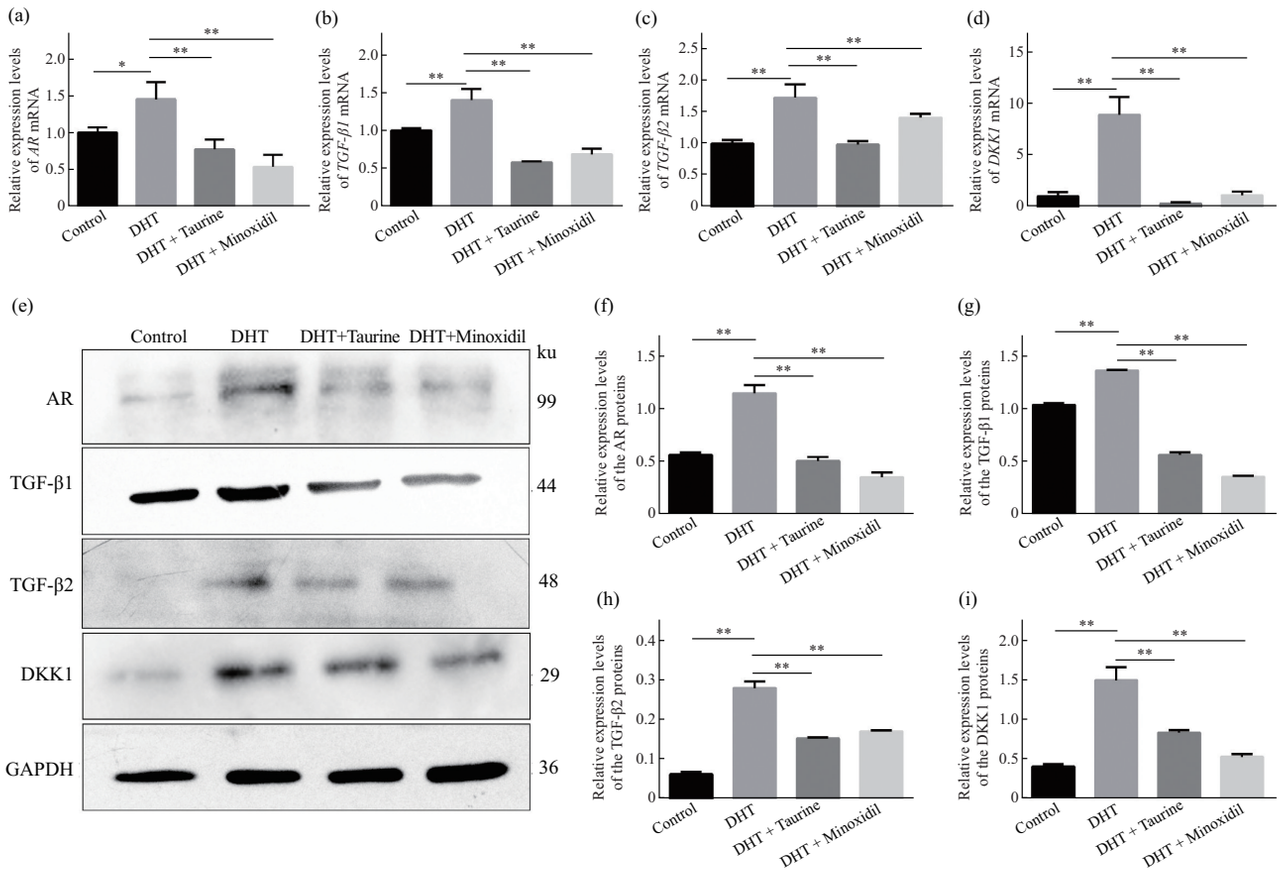


Fig. 7　Effects of taurine on gene and protein levels of AR, TGF−β1, TGF−β2, and DKK1 in DHT−induced AGA mice model

(a−d) RT-qPCR analysis of *AR*, *TGF-β1*, *TGF-β2*, and *DKK1* mRNA levels in dorsal skin. (e−i) Western blot results of protein expression levels. **P*<0.05, ***P*<0.01.

3　Discussion

AGA remains one of the most prevalent dermatological conditions, its pathogenesis-rooted in androgen dysregulation, follicular miniaturization, and cycle disruption-demands more effective, multi-targeted therapies[30]. Current treatments, such as minoxidil and finasteride, are limited by variable efficacy and side effects, highlighting the need for novel therapeutic agents[31]. In this study, we demonstrate that taurine, a naturally occurring sulfonic acid with established safety in humans[32-34], ameliorates DHT-induced AGA in C57BL/6 mice through a coordinated mechanism involving hair cycle acceleration, restoration of follicular homeostasis, and suppression of androgen-driven pathogenic pathways. These findings not only expand our understanding of taurine's biological functions but also position it as a promising candidate for translational development.

3.1　Taurine drives the transformation of hair follicles from telogen−to−anagen

The hair follicle cycle, a dynamic process of growth (anagen), regression (catagen), and rest (telogen), is tightly regulated by intrinsic and extrinsic signals[35]. A defining feature of AGA is the pathological prolongation of telogen, where follicles remain quiescent and fail to initiate anagen[36]. Our observations revealed that DHT-exposed mice exhibited persistent telogen with delayed hair regrowth, whereas taurine treatment-particularly at high doses-induced robust anagen entry, resulting in near-complete hair coverage by day 14. Histologically, taurine increased dermal thickness, follicle count, and hair bulb depth, which are hallmarks of anagen progression[29]. Maintaining a healthy hair growth cycle requires prolonging the anagen and promoting the transition from telogen to anagen[27]. Taurine treatment promoted this transition

in hair follicles. Besides, we investigated the effects of taurine in a C57BL/6 mouse model. Our findings demonstrated that supplementation with 1% taurine significantly accelerated hair growth, increased hair follicle number, and increased the dermal thickness, indicating a clear promotion of the anagen phase. Hair follicles are born obliquely within the dermis, which serves as a critical source of nutrients for their growth and development[37]. These findings suggest that taurine promotes the transition of hair follicles into the anagen phase, leading to increased follicle numbers and a thicker dermis, which are characteristic features of active hair growth[26, 29].

3.2 Taurine can resist AGA by promoting the proliferation of hair matrix keratinocytes and reducing the apoptosis of hair follicle cells

As is well-established, hair growth is intrinsically linked to keratinocytes, as the hair shaft comprises terminally differentiated keratinocytes [38]. A key mechanism underlying AGA involves DHT causes apoptosis of hair follicle keratinocytes, leading to hair loss [39]. In the AGA model of male C57BL/6 mice, our experimental results showed that DHT-exposed follicles exhibited reduction of proliferating keratinocytes and increase of apoptotic cells. Taurine reversed both effects, restoring proliferation and suppressing apoptosis to levels comparable to untreated controls, which further proved the resistance of taurine to AGA.

3.3 Taurine suppresses androgen−responsive pathogenic pathways *via* AR, TGF−βs, and DKK1

It is well-established that testosterone is converted to the most potent androgen DHT *via* 5α-reductase. Unlike testosterone, DHT cannot be aromatized into estrogen and exhibits a high affinity for AR. Indeed, the androgen-AR axis represents the primary driver of AGA: DHT binds AR with high affinity, triggering transcriptional programs that promote follicle miniaturization[10]. Our experimental results identify four key downstream effectors—AR, TGF-β1, TGF-β2, and DKK1—as targets of taurine, each playing distinct roles in AGA pathogenesis:

Androgen signaling is mediated by AR, a 110 ku ligand-activated nuclear receptor that regulates target gene expression by binding to androgen response elements[40]. AR overexpression in dermal papilla cells enhances androgen sensitivity, a characteristic feature of AGA[41-42]. Previous studies indicate increased DNA methylation in the AR promoter region in occipital scalp hair follicles compared to AGA-affected follicles. This hypermethylation likely reduces AR expression, explaining the resistance of occipital hair to miniaturization and alopecia[43]. Importantly, our study demonstrates taurine treatment reduces DHT-induced AR expression and decreases follicular androgen sensitivity , indicating its therapeutic potential against AGA.

TGF-β superfamily comprises several related proteins, including TGF-β, activins, inhibin, and BMP[44]. Mammals express three TGF-β isoforms: TGF-β1, TGF-β2, and TGF-β3. TGF-β signaling participates in hair follicle development and cycling[37]. Inui *et al*. [45-46] demonstrated that the synthetic androgen R1881 inhibits keratinocyte growth through TGF-β1-mediated pathways. TGF-β1 drives the anagen-to-catagen transition by inhibiting proliferation and promoting apoptosis, contributing to AGA pathogenesis[47]. Similarly, TGF-β2 inhibits epithelial proliferation and activates cysteine proteases, initiating a proteolytic cascade that induces epithelial cell death[48]. Moreover, TGF-β2 inhibits hair growth and promotes catagen entry[49-50]. Our findings indicate taurine suppresses DHT-induced overexpression of TGF-β1 and TGF-β2, concurrently reversing its inhibitory effects on keratinocyte proliferation and pro-apoptotic actions.

DKK1, a secreted glycoprotein of the dickkopf family[51], orchestrates follicular regression and cellular apoptosis. During catagen, follicular cells undergo apoptosis, driving follicular regression and hair loss[52-54]. DKK1 exerts dual functions in the hair cycle: it inhibits Wnt/β-catenin signaling *via* LRP5/6, impeding hair growth, while concurrently inducing keratinocyte apoptosis[12, 39, 51]. Thus, DKK1-mediated mechanisms likely contribute to AGA pathogenesis. Notably, taurine administration significantly reduced DKK1 expression, suggesting it may mitigate AGA by DKK1 inhibition.

4 Conclusion

In conclusion, our data suggest taurine demonstrates significant efficacy in alleviating DHT-induced AGA in male C57BL/6 mice. Its protective effects are mediated through multi-faceted mechanisms. (1) Promoting hair follicle cycle

progression: it accelerates the hair follicle transition from telogen to anagen, counteracting DHT-induced hair follicle telogen prolongation. (2) Modulating cellular dynamics: it stimulates the proliferation of hair matrix keratinocytes and reduces DHT-induced apoptosis within hair follicle cells. (3) Suppressing androgen-driven pathogenic pathways: it downregulates the expression of critical molecules in the AGA pathway, including the AR, the catagen-inducing cytokines TGF-β1 and TGF-β2, and the Wnt pathway inhibitor DKK1. Overall, its ability to potentially influence hair follicle cycle progression, cellular dynamics, androgen signaling and key regulatory pathways presents a compelling case for further investigation of taurine as a potential therapeutic candidate for AGA.

References

[1] Cai Y, Jia Z, Zhang Y, *et al*. Cell-free fat extract restores hair loss: a novel therapeutic strategy for androgenetic alopecia. Stem Cell Res Ther, 2023, **14**(1): 219

[2] Liu D, Xu Q, Meng X, *et al*. Status of research on the development and regeneration of hair follicles. Int J Med Sci, 2024, **21**(1): 80-94

[3] Kaiser M, Abdin R, Gaumond S I, *et al*. Treatment of androgenetic alopecia: current guidance and unmet needs. Clin Cosmet Investig Dermatol, 2023, **16**: 1387-1406

[4] Alessandrini A, Starace M, D'Ovidio R, *et al*. Androgenetic alopecia in women and men: Italian guidelines adapted from European dermatology forum/European academy of dermatology and venereology guidelines. G Ital Dermatol Venereol, 2020, **155**(5): 622-631

[5] Paik J H, Yoon J B, Sim W Y, *et al*. The prevalence and types of androgenetic alopecia in Korean men and women. Br J Dermatol, 2001, **145**(1): 95-99

[6] Wang T L, Zhou C, Shen Y W, *et al*. Prevalence of androgenetic alopecia in China: a community-based study in six cities. Br J Dermatol, 2010, **162**(4): 843-847

[7] Nestor M S, Ablon G, Gade A, *et al*. Treatment options for androgenetic alopecia: efficacy, side effects, compliance, financial considerations, and ethics. J Cosmet Dermatol, 2021, **20**(12): 3759-3781

[8] Bertone F, Sanii S, Menzinger S, *et al*. Alopécie androgénétique: où en est-on en 2024?. Rev Médicale Suisse, 2024, **20**(867): 653-658

[9] Piraccini B M, Alessandrini A. Androgenetic alopecia. G Ital Dermatol Venereol, 2014, **149**(1): 15-24

[10] Uemura M, Tamura K, Chung S, *et al*. Novel 5 alpha-steroid reductase (SRD5A3, type-3) is overexpressed in hormone-refractory prostate cancer. Cancer Sci, 2008, **99**(1): 81-86

[11] Zgonc Škulj A, Poljšak N, Kočevar Glavač N, *et al*. Herbal preparations for the treatment of hair loss. Arch Dermatol Res, 2020, **312**(6): 395-406

[12] Mahmoud E A, Elgarhy L H, Hasby E A, *et al*. Dickkopf-1 expression in androgenetic alopecia and alopecia areata in male patients. Am J Dermatopathol, 2019, **41**(2): 122-127

[13] Kwack M H, Kim M K, Kim J C, *et al*. Dickkopf 1 promotes regression of hair follicles. J Investig Dermatol, 2012, **132**(6): 1554-1560

[14] Shen Y L, Li X Q, Pan R R, *et al*. Medicinal plants for the treatment of hair loss and the suggested mechanisms. Curr Pharm Des, 2018, **24**(26): 3090-3100

[15] Huxtable R J. Physiological actions of taurine. Physiol Rev, 1992, **72**(1): 101-163

[16] Qaradakhi T, Gadanec L K, McSweeney K R, *et al*. The anti-inflammatory effect of taurine on cardiovascular disease. Nutrients, 2020, **12**(9): E2847

[17] Schaffer S W, Jong C J, Ramila K C, *et al*. Physiological roles of taurine in heart and muscle. J Biomed Sci, 2010, **17**(Suppl 1): S2

[18] Baliou S, Adamaki M, Ioannou P, *et al*. Protective role of taurine against oxidative stress (Review). Mol Med Rep, 2021, **24**(2): 605

[19] Castelli V, Paladini A, D'Angelo M, *et al*. Taurine and oxidative stress in retinal health and disease. CNS Neurosci Ther, 2021, **27**(4): 403-412

[20] Kim H, Chang H, Lee D H. Simulative evaluation of taurine against alopecia caused by stress in caenorhabditis elegans. Taurine 8. New York, NY: Springer, 2013: 267-276

[21] de Lacharrière O, Deloche C, Misciali C, *et al*. Hair diameter diversity: a clinical sign reflecting the follicle miniaturization. Arch Dermatol, 2001, **137**(5): 641-646

[22] Deloche C, de Lacharrière O, Misciali C, *et al*. Histological features of peripilar signs associated with androgenetic alopecia. Arch Dermatol Res, 2004, **295**(10): 422-428

[23] Yoshimura T, Manabe C, Inokuchi Y, *et al*. Protective effect of taurine on UVB-induced skin aging in hairless mice. Biomed Pharmacother, 2021, **141**: 111898

[24] Ommati M M, Heidari R, Ghanbarinejad V, *et al*. Taurine treatment provides neuroprotection in a mouse model of manganism. Biol Trace Elem Res, 2019, **190**(2): 384-395

[25] Hajhashemi V, Rajabi P, Mardani M. Beneficial effects of pumpkin seed oil as a topical hair growth promoting agent in a mice model. Avicenna J Phytomed, 2019, **9**(6): 499-504

[26] Müller-Röver S, Foitzik K, Paus R, *et al*. A comprehensive guide for the accurate classification of murine hair follicles in distinct hair cycle stages. J Investig Dermatol, 2001, **117**(1): 3-15

[27] Hwang S B, Park H J, Lee B H. Hair-growth-promoting effects of the fish collagen peptide in human dermal papilla cells and C57BL/6 mice modulating Wnt/β-catenin and BMP signaling pathways. Int J Mol Sci, 2022, **23**(19): 11904

[28] Kang J I, Yoon H S, Kim S M, *et al*. Mackerel-derived fermented fish oil promotes hair growth by anagen-stimulating pathways. Int J Mol Sci, 2018, **19**(9): E2770

[29] Yon J M, Park S G, Lin C, *et al*. Hair growth promoting effects of emodin in telogenic C57BL/6 mice. Korean J Vet Res, 2016, **56**(2): 97-101

[30] Randall V A, Thornton M J, Hamada K, *et al*. Androgens and the hair follicle. Ann N Y Acad Sci, 1991, **642**(1): 355-375

[31] Anjum M A, Zulfiqar S, Chaudhary A A, *et al*. Stimulation of hair regrowth in an animal model of androgenic alopecia using 2-deoxy-D-ribose. Front Pharmacol, 2024, **15**: 1370833

[32] Zhang M, Bi L F, Fang J H, *et al*. Beneficial effects of taurine on serum lipids in overweight or obese non-diabetic subjects. Amino Acids, 2004, **26**(3): 267-271

[33] Murakami S, Kondo Y, Nagate T. Effects of long-term treatment with taurine in mice fed a high-fat diet: improvement in cholesterol metabolism and vascular lipid accumulation by taurine. Adv Exp Med Biol, 2000, **483**: 177-186

[34] Sturman J A, Messing J M. High dietary taurine effects on feline tissue taurine concentrations and reproductive performance. J Nutr, 1992, **122**(1): 82-88

[35] Stenn K S, Paus R. Controls of hair follicle cycling. Physiol Rev, 2001, **81**(1): 449-494

[36] Paus R, Cotsarelis G. The biology of hair follicles. N Engl J Med, 1999, **341**(7): 491-497

[37] Lee J, Rabbani C C, Gao H, *et al*. Hair-bearing human skin generated entirely from pluripotent stem cells. Nature, 2020, **582**(7812): 399-404

[38] Schneider M R, Schmidt-Ullrich R, Paus R. The hair follicle as a dynamic miniorgan. Curr Biol, 2009, **19**(3): R132-R142

[39] Kwack M H, Sung Y K, Chung E J, *et al*. Dihydrotestosterone-inducible dickkopf 1 from balding dermal papilla cells causes apoptosis in follicular keratinocytes. J Investig Dermatol, 2008, **128**(2): 262-269

[40] Lolli F, Pallotti F, Rossi A, *et al*. Androgenetic alopecia: a review. Endocrine, 2017, **57**(1): 9-17

[41] Fujimoto N, Yeh S, Kang H Y, *et al*. Cloning and characterization of androgen receptor coactivator, ARA55, in human prostate. J Biol Chem, 1999, **274**(12): 8316-8321

[42] Inui S, Fukuzato Y, Nakajima T, *et al*. Androgen receptor co-activator hic-5/ARA55 as a molecular regulator of androgen sensitivity in dermal papilla cells of human hair follicles. J Investig Dermatol, 2007, **127**(10): 2302-2306

[43] Cobb J E, Wong N C, Yip L W, *et al*. Evidence of increased DNA methylation of the androgen receptor gene in occipital hair follicles from men with androgenetic alopecia. Br J Dermatol, 2011, **165**(1): 210-213

[44] Kitisin K, Saha T, Blake T, *et al*. TGF-beta signaling in development. Sci STKE, 2007, **2007**(399): cm1

[45] Inui S, Fukuzato Y, Nakajima T, *et al*. Identification of androgen-inducible TGF-beta1 derived from dermal papilla cells as a key mediator in androgenetic alopecia. J Investig Dermatol Symp Proc, 2003, **8**(1): 69-71

[46] Inui S, Fukuzato Y, Nakajima T, *et al*. Androgen-inducible TGF-beta1 from balding dermal papilla cells inhibits epithelial cell growth: a clue to understand paradoxical effects of androgen on human hair growth. FASEB J, 2002, **16**(14): 1967-1969

[47] Inui S, Itami S. Molecular basis of androgenetic alopecia: from androgen to paracrine mediators through dermal papilla. J Dermatol Sci, 2011, **61**(1): 1-6

[48] Hibino T, Nishiyama T. Role of TGF-beta2 in the human hair cycle. J Dermatol Sci, 2004, **35**(1): 9-18

[49] Soma T, Tsuji Y, Hibino T. Involvement of transforming growth factor-beta2 in catagen induction during the human hair cycle. J Invest Dermatol, 2002, **118**(6): 993-997

[50] Tsuji Y, Denda S, Soma T, *et al*. A potential suppressor of TGF-beta delays catagen progression in hair follicles. J Investig Dermatol Symp Proc, 2003, **8**(1): 65-68

[51] Papukashvili D, Rcheulishvili N, Liu C, *et al*. Perspectives on miRNAs targeting DKK1 for developing hair regeneration therapy. Cells, 2021, **10**(11): 2957

[52] Hirata H, Hinoda Y, Nakajima K, *et al*. Wnt antagonist *DKK1* acts as a tumor suppressor gene that induces apoptosis and inhibits proliferation in human renal cell carcinoma. Int J Cancer, 2011, **128**(8): 1793-1803

[53] Di M, Wang L, Li M, *et al*. Dickkopf1 destabilizes atherosclerotic plaques and promotes plaque formation by inducing apoptosis of endothelial cells through activation of ER stress. Cell Death Dis, 2017, **8**(7): e2917

[54] Morgan M B, Rose P. An investigation of apoptosis in androgenetic alopecia. Ann Clin Lab Sci, 2003, **33**(1): 107-112

牛磺酸通过调节毛囊周期及相关信号通路减轻雄性C57BL/6小鼠雄激素性脱发*

吴晋强[1,2] 郭果果[1] 张欣婷[1] 刘晋佳[1] 王吉祥[1] 赫晓燕[2]** 王海东[2]**

（[1] 长治医学院基础医学院，长治 046000；
[2] 山西农业大学动物医学学院，太谷 030801）

摘要 目的 研究牛磺酸对二氢睾酮（DHT）诱导的雄性C57BL/6小鼠雄激素性脱发（AGA）的潜在保护作用及其机制，重点研究毛囊周期调节、细胞增殖/凋亡及相关信号通路。**方法** 使用雌性C57BL/6小鼠来评估牛磺酸的毛发生长促进潜力。将6周龄雌性C57BL/6小鼠适应性饲养，然后随机分为3组（*n*=8）：对照组（普通饮用水）、牛磺酸组（含1%牛磺酸的饮用水）和米诺地尔组（外用2%米诺地尔，阳性对照组）。将6周龄雄性C57BL/6小鼠适应性饲养，然后随机分为5组（*n*=8）：对照组（生理盐水）、DHT（模型组，DHT 1 mg/d）、DHT+低剂量牛磺酸（DHT 1 mg/d+牛磺酸2 mg/d）、DHT+高剂量牛磺酸（DHT 1 mg/d +牛磺酸10 mg/d）、DHT+米诺地尔（阳性对照组，DHT 1 mg/d，局部应用2%米诺地尔）。使用剪刀剃去背毛，并在治疗前一天使用脱毛膏去除毛发。毛发再生通过定期拍摄脱毛区域并用四点分级系统（0~3）量化评估。在第14天采集背部皮肤样本，用于组织学分析（苏木精-伊红（HE）染色）、免疫荧光染色（Ki67用于检测毛囊细胞增殖，原位末端转移酶标记法（TUNEL）用于检测毛囊细胞凋亡）、酶联免疫吸附分析（ELISA）（DHT定量）、逆转录-实时定量聚合酶链式反应（RT-qPCR）和蛋白质印迹（Western blot，WB）分析，以评估关键基因和蛋白质（雄激素受体（AR）、转录生长因子(TGF)-β1、TGF-β2、Dickkopf相关蛋白1（DKK1））的表达。**结果** 在雌性小鼠中，补充牛磺酸能显著加速毛发生长，表现在小鼠皮肤较早从粉红色（毛发休止期）向黑色（毛发生长期）转变，以及毛发生长评分增加，其效果与米诺地尔相当。形态学分析结果显示：牛磺酸显著增加了毛囊数量和真皮厚度。免疫荧光证实，毛发基质中角质细胞增殖增强。在DHT诱导的AGA模型中，DHT显著延长休止期，抑制毛发生长，增加皮肤DHT含量，并诱导毛囊小型化。牛磺酸的治疗，特别是高剂量牛磺酸有效地抵消了这些影响：它促进了毛发由休止期向生长期转变，改善了毛发生长评分。形态学分析结果显示：牛磺酸显著恢复了DHT导致的真皮厚度、毛囊数量、毛球深度和毛囊大小的改变。Ki67和TUNEL分析表明，牛磺酸处理减少了毛囊细胞凋亡并促进了毛囊细胞的增殖。至关重要的是，RT-qPCR和WB分析表明，DHT在mRNA和蛋白质水平上显著上调了小鼠背部皮肤中AR、TGF-β1、TGF-β2和DKK1的表达。牛磺酸的施用显著下调了这些致病因子的表达，使它们更接近对照组的水平。**结论** 牛磺酸对DHT诱导的雄性C57BL/6小鼠AGA有明显的缓解作用。它的保护作用是通过多方面的机制介导的。a. 促进毛囊周期进展：它加速毛发从休止期向生长期转变，抵消DHT诱导的毛囊休止期延长。b. 调节细胞动力学：它刺激毛囊基质角质细胞的增殖，并减少了DHT诱导的毛囊细胞凋亡。c. 抑制雄激素驱动的致病途径：它下调AGA途径中关键分子的表达，包括AR、细胞因子TGF-β1和TGF-β2，以及Wnt途径抑制剂DKK1。鉴于其良好的安全性和多靶点作用，牛磺酸有望成为治疗AGA的新型候选药物或辅助药物，值得进一步研究其临床潜力和精确的分子机制。这项研究为考虑在脱发治疗策略中补充牛磺酸或局部应用牛磺酸提供了坚实的临床前基础。

关键词 牛磺酸，雄激素性脱发，双氢睾酮，C57BL/6小鼠，毛囊
中图分类号 Q5 **DOI**：10.3724/j.pibb.2025.0264 **CSTR**：32369.14.pibb.20250264

* 国家自然科学基金（31772690），山西省自然科学基金（201701D121106）和长治医学院博士科研启动基金（BS202308）资助项目。
** 通讯联系人。
赫晓燕 Tel：0354-6288160，E-mail：sxndhxy@163.com
王海东 Tel：0354-6288160，E-mail：wanghaidong@sxau.edu.cn
收稿日期：2025-05-29，接受日期：2025-09-19