ORIGINAL ARTICLE

Anti-hair loss effect of a shampoo containing caffeine and adenosine

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Abstract

Background: Hair loss is a widespread health problem that affects numerous individuals and is associated with age, lack of sleep, stress, endocrine problems, and other problems. Caffeine exerts various pharmacological effects, particularly after ingestion. The caffeine-induced inhibition of phosphodiesterases can increase intracellular cAMP concentrations, ultimately resulting in stimulatory effects on cell metabolism and proliferation. Hence, caffeine has been confirmed to inhibit hair loss caused by premature termination of the hair growth phase. Adenosine also improves hair loss by stimulating hair growth and thickening hair shafts. However, further empirical evidence is required to comprehensively assess the efficacy of hair loss treatment and prevention using a formulation of caffeine and adenosine in specific proportions in shampoos.

Objectives: This study aimed to evaluate a shampoo with caffeine and adenosine as a daily scalp care product for hair loss in 77 subjects aged 18–60 years.

Methods: The overall and local hair densities were assessed using professional cameras and dermoscopes at different magnifications and distances. Five hairs that came off the participant's head were randomly selected to measure hair diameter. The self-assessment questionnaires were filled on third month of product use.

Results: The combination of caffeine and adenosine in the shampoo significantly enhanced hair density compared to that of the baseline. The results revealed a significant reduction in hair loss. The hair diameters of the subjects did not change significantly. Most of the participants (71.05%) were satisfied with their hair after using the product.

Conclusions: Shampoos containing caffeine and adenosine have been demonstrated to exert therapeutic benefits for reducing hair loss.

KEYWORDS
adenosine, caffeine, hair loss, shampoo

1 | INTRODUCTION

In present-day China, due to the pressure of living environments and irregular living habits such as lack of sleep, heavy smoking, and drinking, hair loss has gradually become a serious disorder. The latest survey focused on hair loss that was conducted by the National Health Commission of China in 2021 revealed that approximately 250 million individuals in China suffer from hair loss. Although hair loss may not be considered a life-threatening disease, it can cause various psychosomatic problems,[1] including feelings of low self-esteem, anxiety, and depression.

Numerous factors are associated with hair loss, including increased sensitivity of scalp follicles to dihydrotestosterone, autoimmune response, hormonal disorders, genetic problems, environmental factors, medications, nutritional deficiencies, and stress.[2–4] Androgenetic alopecia (AGA), also known as seborrheic alopecia or patchy baldness, is one of the common types of hair loss. Hair follicles are dynamic microorgans, and each hair follicle is a regenerative system that physiologically undergoes a continuous cycle of anagen, catagen, and telogen phases. The anagen phase is the active phase of the hair follicle and is the most important determinant of hair length and thickness. The transition from the anagen phase to the catagen phase is mediated by key hair growth regulatory factors, including insulin-like growth factor 1 (IGF-1) that maintains growth[5] and transforming growth factor-β2 (TGF-β2) that promotes hair growth.[6] Thus, higher expression levels of IGF-1 and lower expression levels of TGF-β2 are beneficial for maintaining the anagen phase. However, in patients with AGA, the hair growth cycle can undergo changes in the degree to which the anagen phase becomes shorter and the telogen phase is prolonged, and this can lead to a reduction in the diameter of the hair follicles.

Currently, only two Food and Drug Administration-approved drugs (topical minoxidil and oral finasteride) are commonly used to treat hair loss. However, these two medications require long-term application to observe obvious improvements due to their limited clinical efficacy. Additionally, minoxidil and finasteride can cause various side effects. Experimental studies have demonstrated that the short-term use of minoxidil may lead to alopecia areata, whereas long-term use can result in scalp itching and flaking.[7] Similarly, the use of finasteride may lead to decreased libido (1.9%) and erectile dysfunction (1.3%), and certain individuals may experience allergic reactions and abnormal liver function.[8] Therefore, when patients have doubts regarding these two conventional therapies, scalp-related products containing natural substances can be considered as an alternative for treating hair loss. According to available clinical data, the use of melatonin, rosemary oil, saw palmetto, pumpkin seed oil, caffeine, and adenosine has been demonstrated to effectively decrease hair loss and enhance hair density[2]; however, a number of clinical studies have reported that most of these substances are associated with scalp itching.[2,9–14]

Caffeine, an alkaloid methylxanthine, can promote metabolic activity and cell proliferation by inhibiting phosphodiesterase[13,15] and providing higher energy levels. Though a hair organ culture model (HOCM), caffeine has been demonstrated to regulate the growth cycle of hair follicles, reverse testosterone-induced hair follicle growth, stimulate hair growth, and promote proliferation of keratinocytes in the dermal layer at certain concentrations, and this also extends the duration of the growth phase and counteracts the testosterone-induced increased expression of transforming growth factor-beta 2 (TGF-β2) protein in male hair follicles.[16,17] A separate clinical study demonstrated that the administration of a 0.2% topical caffeine solution via scalp injection improved hair growth during hair loss treatment.[18]

Adenosine is a purine nucleoside consisting of adenine molecules attached to ribofuranose.[19] Adenosine stimulates hair growth by upregulating fibroblast growth factor-7 (FGF-7).[20] A recent clinical study revealed that participants treated with a scalp treatment solution containing adenosine exhibited an increase in hair thickness and improvement in hair loss, and no adverse effects caused by the adenosine lotion were observed throughout the course of the trial.[11]

The mechanisms of action of caffeine and adenosine in the context of hair loss have been well studied in recent years,[18,19,21–23] and both have exhibited significant improvements in hair loss in clinical trials. However, data regarding the efficacy of these combined products are insufficient. Therefore, the applicability of scalp care products containing caffeine and adenosine to a wider population with hair loss warrants further study.

In this study, we aimed to explore the anti-hair loss effects of shampoos containing a combination of caffeine and adenosine. Hair density, hair loss count, and hair diameter were measured to achieve our goal. This study provides implications for the formulation optimization of anti-hair shampoos and insights into the effect of the combination of caffeine and adenosine on reducing hair shedding.

2 | MATERIALS AND METHODS

2.1 | Study design

A total of 84 participants with hair loss were recruited for this study. Following a 2-week washout period, they were randomly assigned and single-blinded to the experimental and control groups. Referring to previous research,[24–26] the participants were asked to consistently use the test shampoo three times each week for three consecutive months with two pumps (approximately 10 g) each use. Hair-related physical parameters were measured at baseline (T0) and at the end of the first (T1), second (T2), and third (T3) months.

This clinical study was conducted between July and October of 2022. All participants eligible for the efficacy study were formally informed of the purpose of the study, behavioral patterns, and possible side effects. All the participants signed an informed consent form before participating in the study. The recruitment, treatment, collection of biological materials, and use of personal data were conducted in accordance with the ethical guidelines detailed in the Declaration of Helsinki and in compliance with other national and international regulations and guidelines involving human subjects.

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2.2 | Participants

Based on the inclusion and exclusion criteria, a total of 84 healthy Asian individuals aged 20–60 years were enrolled in this study based on the inclusion and exclusion criteria. However, seven participants dropped out of the study for personal reasons, leaving a final total of 77 participants who successfully completed the study.

The inclusion criteria included signed informed consent, both sexes, age over 18 years, self-perceived thinning hair, Ludwig grade I-1, I-2, and I-3 for females and Norwood Type 2, 2A, 3, and 3A for males, no hair growth treatment in the previous month, regular use of the products for 14 weeks, avoidance of other products with similar intended use, and the ability to effectively communicate with the attending researchers to understand and comply with the requirements of this clinical application study.

The exclusion criteria included serious androgenetic alopecia, baldness, inflammatory scarring alopecia, or other scalp/hair disorders, pregnant or lactating women, serious internal or chronic diseases and known neoplastic diseases, use of oral and/or topical anti-hair loss products that may affect test results within 1 month, individual hypersensitivity to any component of the cosmetic products, infections of the hair-covered scalp skin, cognitively impaired and/or unable to give informed consent, or any other condition that in the opinion of the investigators may adversely affect the ability of the individual to complete the study or that may pose a significant risk to the individual.

2.3 | Formulation of the test product

The product was provided by UNILIPO Company (Beijing, China) and contained effective ingredients of 0.4% caffeine and 0.2% adenosine. The control product was a shampoo without caffeine and adenosine but with the same ingredients as the efficacious shampoo.

2.4 | Hair loss assessment methods

Overall hair density photographic equipment (Tianjin, China) was used. The head of each participant was positioned on the camera and illuminated using a white fill-in lamp. They were instructed to face downwards with the centerline of their head positioned 60 cm away from the fill-in lamp. A photograph was taken using a mobile phone positioned 20 cm perpendicular to the centerline of the head of each participant.

To assess local hair density, a smart scalp hair analysis system (HT-B30S, Shenzhen, China) was used for the analysis. At each time point, the dermatoscopic lens included in the device was securely and vertically attached to the scalp. Photographs were taken at 50× magnification for the same area in the middle of the participant's vertex. The local hair density was then measured in hairs/cm^2 and identified as "Visit X-P Subject Number."

For hair loss count, the hair of the participants was systematically divided into two sections that included the top of the head and the sides of the scalp. This division was accomplished using an equal combing method, where the entire head of hair was thoroughly combed. To ensure accuracy, the participant was required to wear a bib while the researcher combed their hair consistently from the forehead to the back of the head, from the front left side to the back left side, and from the front right side to the back right side. This combing process was repeated 60 times, with equal combing distributed evenly across the three areas (20 times each on the left, right, and top sides of the head). Hair removed from the combs and bibs was promptly collected and placed into designated self-locating bags that were each marked with a unique identifier for subsequent analysis.

Hair diameter was measured using a high-precision electronic spiral Micrometer Model 211-101 (Triple Measure, Tokyo, Japan). After combing, five randomly selected hair samples were collected at each time point. The hair was positioned between the two anvil holders of the micrometer close to the root area. The differential cylinder of the device was adjusted to be 0.5 cm closer to the hair, and then, ratchet rotation was activated. When a "click" sound was heard, this indicated that the measurement was completed, and the diameter value was recorded. The average value of five measurements was used as the final result.

Additionally, the participants were asked to complete a satisfaction questionnaire regarding the effectiveness of the product for preventing hair loss by the end of the 3rd month of product use. For each participant, answers were recorded on a 5-point scale (1 = definitely not, 2 = probably not, 3 = neutral, 4 = probably, and 5 = definitely), and the results were expressed as percentages of participant satisfaction. Satisfaction scores were calculated using the following formula: (participants with > three ratings)/(total number of participants). At all visits, participants were asked questions regarding concomitant treatments and adverse events.

2.5 | Statistical analysis

Statistical analyses were performed using SPSS v26 (IBM). The Shapiro–Wilk test was used to determine the normality of the data distribution. After testing for normal distribution, Tukey's multiple comparisons or paired-sample t-tests were performed. Statistical significance was set at a p-value (probability of error) < 0.05.

3 | RESULTS

3.1 | Overall hair density analysis and local hair density analysis

Figure 1A indicates an increase in overall hair density in the experimental group compared to that of baseline (T0) after 3 months (T3) when using the shampoo containing caffeine and adenosine.
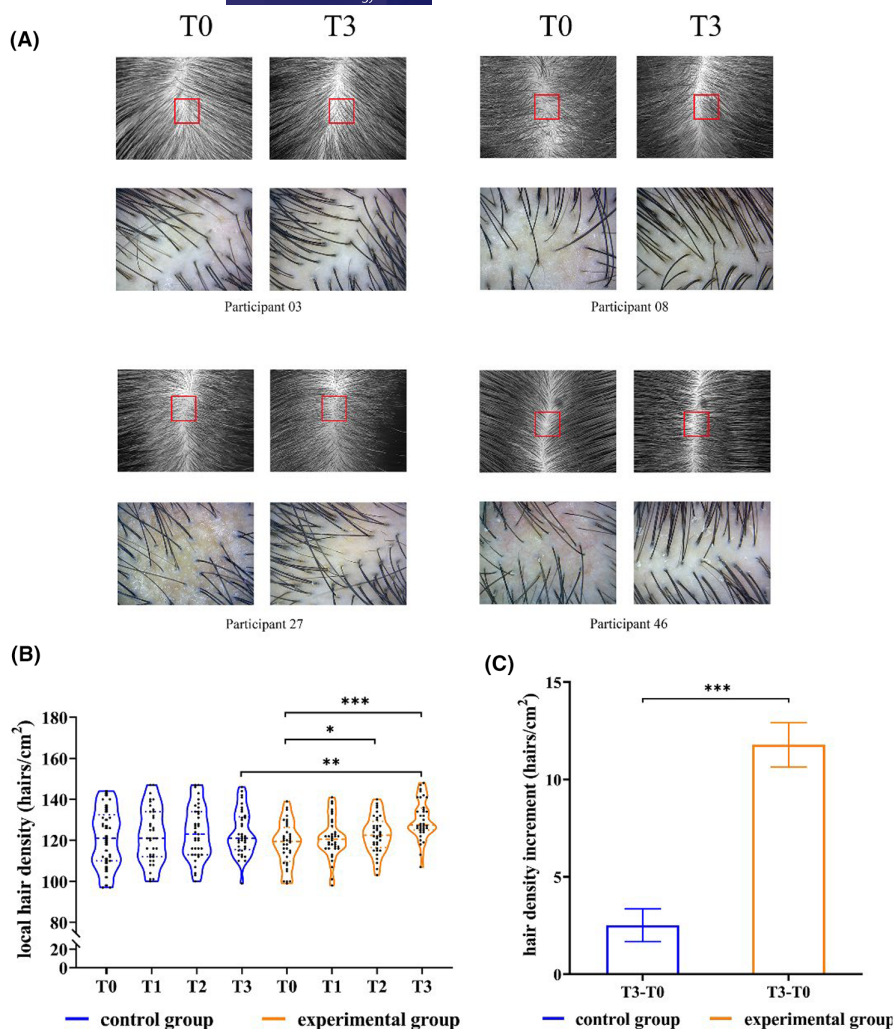
FIGURE 1 Effect of shampoos containing caffeine and adenosine on hair density. (A) Representative images of local hair density in the experimental group; (B) changes in hair density at baseline (T0) and at the end of the first (T1), second (T2), and third month (T3); (C) the increment (T3-T0) of the mean hair density. Data are mean ± standard error of the mean (SEM). *Statistically significant difference (Tukey's multiple comparison test; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$).

Moreover, images obtained using the Smart Scalp Hair Analysis System indicated an obvious increase in local hair density in the experimental group at the final visit compared to baseline. Specifically, the mean hair density of the experimental group increased from 118.25 hairs/cm^2 at baseline to 130.03 hairs/cm^2 at the 3-month mark, thus revealing a significant increase (Figure 1B). No significant changes in hair density were observed in the control group during the experiment (Figure 1B). Specifically, after 3 months of using the shampoos, the increment (T3-T0) in the mean hair density in the experimental group was significantly higher than that in the control group (Figure 1C).

3.2 | Hair loss count analysis

The mean number of hair loss episodes in the experimental group was 27.19 at baseline. After using a shampoo containing caffeine and adenosine for 1 month, it significantly decreased to 18.69, and it continued to decline until reaching 17.53 at the end of the third month (Table 1). In comparison, the mean number of hair losses in the control group was 24.97 at baseline, and it fluctuated throughout the entire experimental period with 19.68 in the first month,

20.51 in the second month, and 19.94 in the end of the third month, with no significant differences between each follow-up time point (T1, T2, and T3) and T0 (Table 1).

3.3 | Hair diameter

The average hair diameter in the experimental group measured 70.48 μm at baseline and exhibited a fluctuating trend (approximately 70 μm) following the use of caffeine and adenosine-containing scalp shampoos (Figure 2). However, no significant differences were observed between the experimental groups. Similar to the experimental group, the hair diameter of the control group also existed in a fluctuating state (approximately 67 μm), and there was no significant difference between the different observation points (Figure 2).

3.4 | Subjective evaluation

Figure 3 presents the findings of a questionnaire survey conducted to assess the anti-hair loss efficacy of shampoos containing caffeine

TABLE 1 Comparison of the amount of hair loss at each follow-up time point (T1, T2, and T3) and T0.

Hair loss (Number)				
	T0	**T1**	**T2**	**T3**
Control group	24.97 ± 3.11	19.68 ± 2.74	20.51 ± 4.01	19.94 ± 2.17
Experimental group	27.19 ± 2.80	18.69 ± 2.02	18.14 ± 3.07	17.53 ± 2.41
Pairwise comparison				
	T0 vs. T1		**T0 vs. T2**	**T0 vs. T3**
Control group	$p = 0.068$		$p = 0.212$	$p = 0.085$
Experimental group	$p < 0.001$***		$p < 0.001$***	$p < 0.001$***

Note: Data are mean $\pm$ SEM (paired-samples t-test; ***$p < 0.001$).
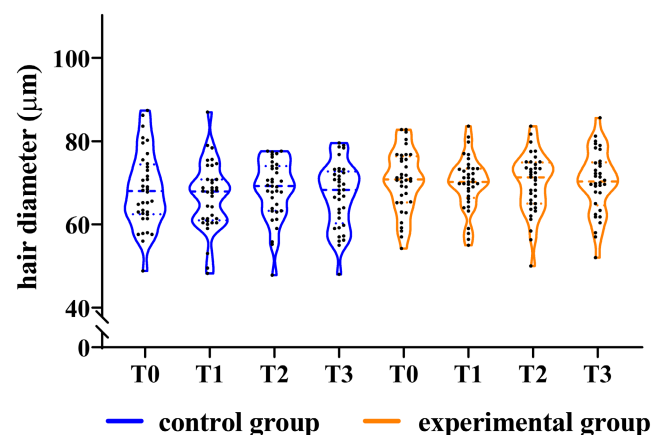
FIGURE 2 Changes in hair diameter at baseline (T0) and at the end of the first (T1), second (T2), and third (T3) months (Tukey's multiple comparison test).

and adenosine. Overall, participants in the experimental group expressed high satisfaction with the tested shampoo, with 71.05% of participants in the experimental group reporting satisfaction compared to 65.79% of participants in the control group. Furthermore, the experimental group reported higher levels of satisfaction, particularly regarding hair regrowth and renewal. Specifically, 26.32% and 21.05% of the participants in the experimental group expressed satisfaction with hair regeneration and renewal, respectively, whereas the corresponding figures for the control group were 18.42% and 15.79%, respectively. This observation demonstrates that the caffeine and adenosine in this shampoo exerted a relatively obvious effect on hair growth. However, the satisfaction of the experimental group with hair texture was slightly lower than that of the control group. This discrepancy could potentially be attributed to the natural decline in sebum secretion from summer to autumn during the experiment as well as the strong de-oiling effect of the shampoo in the experimental group (Figure 1A) that caused some subjects to feel that their hair became dry. The experimental and control groups exhibited identical levels of satisfaction regarding hair thickness and density. Both groups were highly satisfied with the texture of the shampoo (73.68%), thus indicating that the texture of the new formula was well received by the public.

Additionally, no adverse skin reactions (from a clinical dermatological perspective) such as burning, itching, or redness were observed during the test period. Therefore, the product is neither highly stimulating nor sensitive.

4 | DISCUSSION

Although hair loss does not affect physical health, it seriously affects the mental health and quality of life of patients. Early treatment can significantly delay the progression of hair loss and improve patient quality of life. Therefore, we proposed a viable method for treating hair loss. In the present study, we developed a novel combination of hair wash-and-care products to reduce hair loss. The core ingredients of this shampoo product are caffeine and adenosine that have been reported to increase the number of hairs, thus increasing the thickness or density of hair.[27] However, relevant studies have used limited testing methods and small numbers of participants.[26,28,29] Therefore, it is crucial to evaluate the anti-hair loss effects of caffeine and adenosine using various clinical metrics. In our study, we combined previous studies examining the effects of caffeine and adenosine on hair loss prevention and selected simple and rapid evaluation methods.

This study aimed to evaluate the effects of a scalp wash containing a combination of caffeine and adenosine on hair improvement in a population aged 18–60 years. The results revealed that the overall and local hair density increased significantly in the experimental group compared to that of the baseline. No significant changes were observed in the control group throughout the experimental period. This is similar to the results of previous experiments[26] that demonstrated that a combination of caffeine and adenosine exerted an enhanced effect on hair density. Similarly, by analyzing the data regarding the amount of hair loss in the participants, we observed that the amount of hair loss in the experimental group was significantly different compared to that of the baseline. In the experimental group, the amount of hair loss was significantly reduced after 1 month of product use and remained stable thereafter. Increased hair density indicates that more hair follicles are activated and the hair roots become firmer, thus reducing the amount
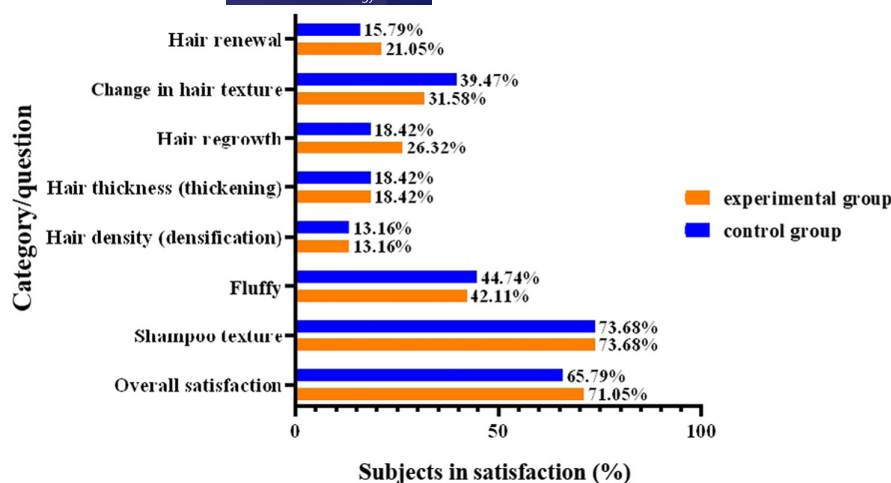
FIGURE 3 Participant questionnaire results. Product satisfaction attribute scores at the end of the third month.

of hair loss. Furthermore, it can be considered that the continuous use of the product can maximize its effectiveness.[30] Compared to the baseline, the hair diameter of the participants in both groups did not change significantly, and that of the experimental group decreased slightly during the experiment. This result is at odds with the discovery of an anti-hair loss mechanism, and this may be due to the short treatment period. The same result was also reported in a previous study,[31] and this is consistent with the seasonal variation in hair growth parameters in studies of specific time periods.[32,33] Moreover, according to the self-satisfaction survey of the experimental group, the participants reported significant improvements in hair quality and expressed high satisfaction with the shampoos used throughout the study. Therefore, the scalp shampoo containing caffeine and adenosine exerted a significant anti-hair loss effect, and the texture of the newly formulated shampoo was well accepted by the public.

5 | CONCLUSIONS

The shampoo containing 0.4% caffeine and 0.2% adenosine exhibited efficacy in regard to reducing hair loss and for hair density enhancement after 3 months compared to the baseline. Participants reported high levels of satisfaction with the shampoo texture. No adverse events related to the test products were reported. The results of this study support the use of adenosine and caffeine in combination with shampoos.

AUTHOR CONTRIBUTIONS

Haowei Chen, Jie Tan, and Fang Wang performed the research. Fang Wang, Huabing Zhao, Xihong He, Dongxiao Chen, Xinyan Liu, and Qingying Shi designed the research study. Haowei Chen, Jie Tan, Fang Wang, and Dongxiao Chen contributed essential reagents or tools. Haowei Chen, Huabing Zhao, Fanglu Yu, Congcong Wang, and Qingying Shi analyzed the data. Fanglu Yu wrote the original draft. Huabing Zhao and Dongxiao Chen reviewed and edited the draft. All authors have read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing financial interests or personal relationships that may have influenced the work reported in this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

This study was approved by the ethic committee of Tianjin University of Science & Technology. Subjects were consented by an informed consent process that was reviewed by Tianjin University of Science & Technology. The study was performed in accordance with the ethical guidelines detailed in the Declaration of Helsinki, and it complied with other national and international regulations and guidelines involving human subjects.

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