IFSCC 2025 full paper (IFSCC2025-854)

"A Randomized Clinical Trial Assessing the Noninferiority of an Alcohol-Free Adenosine Formula Versus 2% Minoxidil in Mild Alopecia"

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1. Introduction

Minoxidil remains the first line topical drug for androgenetic alopecia (AGA) because it can lengthen the anagen phase and enlarge miniaturized follicles [1,2]. Most commercial lotions, however, dissolve the drug in a mixture of ethanol and propylene glycol (PG). These solvents enhance penetration but may trigger irritant or allergic contact dermatitis. In patch test series, local reactions to the vehicle are several fold more common than true minoxidil allergy and are a leading reason patients discontinue treatment [3,4]. Long term adherence therefore depends as much on cosmetic feel and scalp comfort as on pharmacological potency [5,6].

Adenosine offers a different mode of action. In cultured dermal papilla cells it increases intracellular cAMP and up regulates fibroblast growth factor 7 and vascular endothelial growth factor, signals linked to anagen maintenance [7,8]. Clinical trials also have shown that adenosine lotion can match minoxidil for hair density gain while causing fewer adverse events and receiving higher patient satisfaction scores [9,10,11]. Building on these observations, we created an ethanol free, water, propanediol and urea adenosine formula. Water, propanediol and urea form a humectant matrix that slows evaporation, reduces sting and leaves no sticky residue, aiming to improve day to day usability [12].

China has the world's largest potential AGA population. A six city survey reported a prevalence of 21 % in men and 6 % in women, with onset often in the late twenties and a steep rise after age 30 [13]. Yet few domestic studies have examined tolerability or efficacy of new vehicles in East Asian hair and scalp types, which differ from Caucasian hair in diameter, density and sebum profile [14,15]. We therefore carried out a 24 week, randomized, double blind trial in Chinese adults with mild, early stage alopecia to test whether the alcohol free adenosine formula can deliver minoxidil equivalent efficacy with superior local comfort.

2. Materials and Methods

All volunteers signed written informed consent and were told how their personal data would be anonymized.

Eligible subjects were Chinese men or women aged 18-60 years with hair 5-40 cm long, a telogen rate above 15 % on Phototrichogram, mild hair loss (score 2-3 on the AlviArmani scale) and at least 10 shed hairs in the 60 times combing test [16].

After a two week wash out period during which only a usual shampoo without anti hair loss claims was allowed, 81 subjects entered the study. 40 applied a 2 % minoxidil topical solution twice daily and 41 used the alcohol-free adenosine-based formula twice daily. with baseline alopecia grade and telogen rate balanced between groups.

Clinic visits were scheduled every four weeks for six months; at each visit hair density and combing test shedding were graded by the same expert, scalp images were captured with a DermoGenius Ultra device, and TrichoScan® software calculated hair growth rate and the anagen hair ratio [2].

Statistical analysis was performed with SPSS 25.0. Continuous variables were summarized as n, mean, SD, median, minimum and maximum; percentage change from baseline was reported; significance was set at two sided $p < 0.05$; normally distributed data were analyzed by ANOVA followed, when significant, by Dunnett's post hoc comparison with baseline, while non normal data were tested with the Wilcoxon signed rank test.

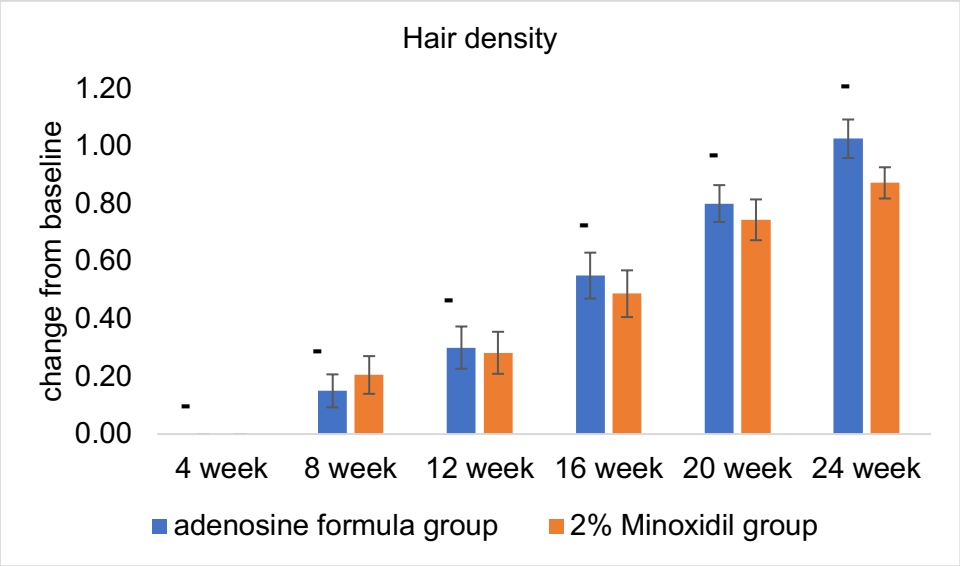
3. Results

Among the 81 participants, 79 of them completed all visits, 39 received 2 % minoxidil (mean ± SD 46.69 ± 9.09 years old ; 17 male : 22 female) and 40 applied the alcohol-free adenosine formula (mean ± SD 46.38 ± 7.26 years old ; 19 male : 21 female).

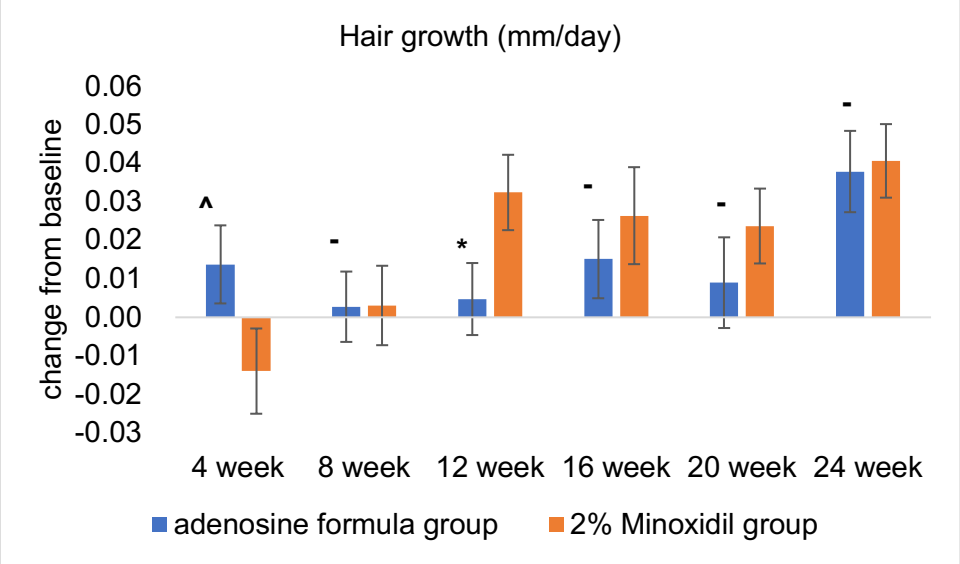
Table 1. Mean ± SE change from baseline at each study visit (weeks 0–24) for hair-density, hair-growth rate and anagen ratio in the two treatment groups

	adenosine formula group n=40			2% Minoxidil group n=39			
Hair density	change from base-line	SE	p-value in groups	change from base-line	SE	p-value in groups	p-value between groups
- 4 week	0.00	0.00	1.0000	0.00	0.00	1.0000	1.0000
- 8 week	0.15	0.06	0.0143	0.21	0.07	0.0047	0.5493
- 12 week	0.30	0.07	0.0005	0.28	0.07	0.0009	0.8715
- 16 week	0.55	0.08	<0.0001	0.49	0.08	<0.0001	0.6022
- 20 week	0.80	0.06	<0.0001	0.74	0.07	<0.0001	0.5839
- 24 week	1.03	0.07	<0.0001	0.87	0.05	<0.0001	0.1492
Hair growth (mm/day)							
- 4 week	0.014	0.010	0.3674	-0.014	0.011	0.7842	0.0331

- 8 week	0.003	0.009	0.7339	0.003	0.010	0.9999	0.9805
- 12 week	0.005	0.009	0.9332	0.032	0.010	0.0692	0.0268
- 16 week	0.015	0.010	0.2672	0.026	0.013	0.1941	0.4312
- 20 week	0.009	0.012	0.6426	0.024	0.010	0.2870	0.2834
- 24 week	0.038	0.011	0.0013	0.041	0.010	0.0122	0.8364
Anagen ratio %							
- 4 week	2.70	1.63	0.1811	-2.38	2.28	0.8519	0.0402
- 8 week	-0.64	1.49	0.8297	0.72	1.90	0.9996	0.5673
- 12 week	0.66	1.60	0.7470	6.68	1.74	0.0410	0.0056
- 16 week	3.31	1.64	0.0738	4.57	2.26	0.2764	0.6283
- 20 week	2.10	1.97	0.4973	6.74	1.78	0.0387	0.0621
- 24 week	5.88	1.77	0.0023	7.37	1.79	0.0188	0.5426



(a)



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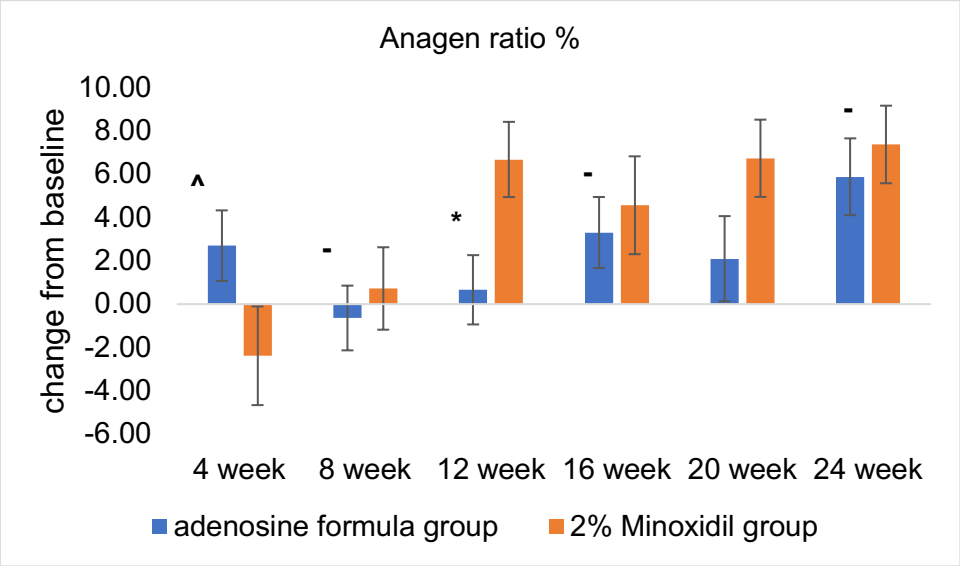

(c)

Chart 1. Values are expressed as mean change ± standard error (n = 39 for 2 % minoxidil; n = 40 for alcohol-free adenosine). p-values refer to the between-group comparison at each time-point (two-sided α = 0.05). Abbreviations: ^ Sig higher than 2% Minoxidil group, * Sig lower than 2% Minoxidil group, - On parity with 2% Minoxidil group

Mean change-from-baseline plots showed that hair density remained virtually unchanged at week 4 (adenosine 0.00 ± 0.00, minoxidil 0.00 ± 0.00) and then rose in parallel: by week 12 the improvement had reached 0.30 ± 0.07 for adenosine and 0.28 ± 0.07 for minoxidil, and by week 24 it stood at 1.03 ± 0.07 versus 0.87 ± 0.05, respectively; at no time-point did the between-group p-value fall below the 0.05 threshold.

Hair-growth rate showed that adenosine led at week 4 (0.014 ± 0.010 mm /day versus -0.014 ± 0.011 mm /day for minoxidil, $p < 0.05$), but lagged behind at week 12 (0.005 ± 0.009 versus

0.032 ± 0.010 mm /day, $p < 0.05$), and showed no significant difference from minoxidil at any later visit, consistent with a roughly four-week delay between the two treatment kinetics. Both curves settled at week 24 on virtually identical gains (adenosine 0.038 ± 0.011 mm /day, minoxidil 0.041 ± 0.010 mm /day; $p = 0.84$).

The anagen ratio behaved similarly, the nominal divergence occurred at week 4 (adenosine 2.70 ± 1.63 %, minoxidil 2.38 ± 2.28 %, $p < 0.05$), confirming the transient “dread-shed” unique to minoxidil [11]. A between-group difference emerged at week 12, where minoxidil out-performed adenosine ($p < 0.05$); at following visit the two curves were statistically indistinguishable, by week 24 a rise of 5.88 ± 1.77 % versus 7.37 ± 1.79 % for minoxidil ($p = 0.54$) confirming parity effficacy of the study.

4. Discussion

This study provides one of the densest time-series data sets yet published for non-surgical hair-growth therapy, with six consecutive monthly assessments across a full 24 weeks. A search of PubMed shows that a few minoxidil or adenosine trials report outcomes at monthly intervals; most restrict analysis to baseline and a single end-point [5,16,17]. Our continuous profile therefore fills a methodological gap and offers a more precise picture of treatment kinetics.

The trial is also had its 50 : 50 in gender distrubution ratio. Most controlled studies are either male-only or female-only [18,19], yet men and women differ in the relative weight of genetic, hormonal and inflammatory drivers of hair loss [14,15]. By showing that both sexes arrive at the same 24-week endpoint yielding results applicable to both.

Data in Asian scalps are still limited; Chinese hair’s larger mean diameter (≈ 70 μm) and faster growth (≈ 1.3-1.4 cm / month) may amplify visible gains from anagen prolonging agents [9,10]. Our Chinese cohort therefore extends external validity to a large number of mild alopecia population[8].

Anti-alopecia therapy succeeds when it achieves three concurrent goals: (i) moves resting follicles rapidly from telogen to anagen, (ii) allows the new vellus fibres to mature into terminal shafts, and (iii) keeps follicles in anagen long enough to maintain coverage. Minoxidil and adenosine reach these goals through different entry points on the same growth circuit, a fact that explains the distinct month-to-month shapes in our data yet the identical 24-week endpoints.

Minoxidil acts first on goal (i). Once converted to its sulphate, it opens ATP-sensitive potassium channels in dermal-papilla cells, shortens the telogen phase and pushes a cohort of hairs abruptly into anagen [16,20]. This forced exit produces the familiar week-2-to-4 shedding burst that we captured at visit 1 and which clinical series have placed in up to half of new users [21]. It also raises local prostaglandin E_2, boosting matrix-cell proliferation and helping goal (ii) along [5]. Adenosine enters the pathway upstream of minoxidil: binding to A_2B receptors elevates intracellular cAMP, up-regulates FGF-7 and VEGF, and down-modulates TGF-β [7,8,11]. These trophic signals do not trigger shedding but instead act on goals (ii) and (iii), thickening shafts and prolonging anagen. Consequently, the hair growth and density adenosine formula

group in our study rose slowly during the first 8 weeks yet never dipped, and by 24-week its cumulative effect on all three goals matched that of minoxidil.

The two routes therefore illustrate complementary kinetics: minoxidil delivers a fast start at the cost of transient loss, whereas adenosine offers a shed-free, steady ascent. When plotted over 24 weeks, the early advantage of minoxidil and the later catch-up of adenosine converge on the same follicular set-point, echoing earlier Japanese and Iranian trials [9,10] and supporting the molecular logic of using either agent to satisfy all three anti-hair-loss requirements.

5. Conclusion

This double-blind, 24-week Chinese study confirms that an alcohol-free adenosine formula is non-inferior to 2 % minoxidil, achieves similar improvements in density, growth and anagen ratio, and avoids both the early shedding spike and vehicle-related irritation. Because the cohort was sex-balanced and ethnically relevant, the results extend current evidence to both genders and to Asian hair types. The main limitation is temporal: curves had only converged at week 24. Future work should track outcomes through a full 48-week cycle and test larget sample sizes in hormonally complex female-pattern hair loss to determine whether pathway synergy can deliver longer-lasting benefit [17].

Because the cohort included equal numbers of men and women, the data add sex-balanced evidence to a field still dominated by single-gender trials [13]. They also extend the literature to Asian scalps, which differ from Caucasian hair in shaft diameter and baseline growth rate [9,10]. Participants reported earlier cosmetic satisfaction with adenosine, reinforcing its value for daily quality of life. Taken together, these findings position alcohol-free adenosine as a gentle, adherence-friendly first-line or switch option for patients-especially women or sensitive-scalp users-who are reluctant to start or to persist with conventional minoxidil lotions.

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