



ARCHIVES OF PHARMACEUTICAL SCIENCES AND BIOTECHNOLOGY JOURNAL

VOLUME 4 ISSUE 2, JUNE 2024

ISSN 2971 – 611X

©ALL RIGHTS RESERVED

**Published by the Faculty of Pharmaceutical Sciences, Kaduna State University,
Kaduna**



BROMELAIN AND FINASTERIDE COMBINATION THERAPY INDUCES HAIR REGROWTH IN ALOPECIA PARTICIPANTS

Kolawole Olatunde¹, Oghenetega T. Oweh^{2*}, Chisom, C Adim³ and Awhin, P. Ejiro⁴

¹American society for Microbiology

²Department of Medical Biochemistry, Kaduna State University, Kaduna, Nigeria

³Department of Microbiology, University of Port Harcourt, Rivers, Nigeria

⁴Department of Medical Biochemistry, Delta State University, Delta State, Nigeria

Corresponding author: **Oghenetega T. Oweh^{2*}**, Tel: +234-806-4017-444,

E-mail: oghenetega.owe@kasu.edu.ng ORCID Number: <https://orcid.org/0000-0002-0051-9975>

ABSTRACT

Background: Loss of hair or alopecia is a growing issue of concern in the world, which creates an immense mental and emotional impact on the individual. Existing therapies are with severe side effects due to long term use. Therefore, the need to look for alternative natural remedies to complement current options.

Aim: To investigate the anti-inflammatory activity of bromelain, its potential synergistic impact with finasteride in the management of hair loss resulting from inflammation due to follicular damage.

Method: The study was a randomized, double-blind placebo-controlled study involving 24 participants divided into three groups: bromelain + finasteride, finasteride only and non-active cream. Topical bromelain and finasteride gel were used in combination, finasteride was used singly, and a third group applied a non-active cream twice daily for 12 consecutive weeks.

Results: Our results revealed that the bromelain + finasteride group had a positive increase of 22% in hair count, 18% increase in thickness and a 24% increase in hair density more than the other groups. Furthermore, the IL-1 and TNF- α concentrations were lower in the bromelain + finasteride group, 145.52 ± 1.2 to 42.46 ± 0.8 (30%) and $115 \div 15 \pm 0.8$ to 28.71 ± 0.7 (25%) indicating the anti-inflammatory role of bromelain. On self-completion questionnaires, participants demonstrated high level of satisfaction with a mean score of 8.5 out of 10.

Conclusion: The results support the need for bromelain to be used as an additional treatment in alopecia, in addition to other multi-target strategies that may enhance effective yield for patients who have not responded to traditional treatments.

Key words: Alopecia, Bromelain, Finasteride, Hair Regrowth, Inflammation

The possible benefit from using bromelain in combination with such treatments is that it targets a different biological pathway than both minoxidil and finasteride. For example, while minoxidil's vasodilation might stimulate increased blood flow and thus nourishing hair roots [12], unrelieved scalp inflammation could damage hair follicles, which in turn could be prevented by bromelain [13]. Much has been written about the effects of finasteride and minoxidil in reversing the balding process with their side effects [14]. Nonetheless, there is little evidence on the possibility of the combination of bromelain, and finasteride in reversing baldness and boosting the hair growth process. This paper thus aims at establishing the effects of using bromelain alongside finasteride on hair regeneration.

MATERIALS AND METHODS

Study Description and Participant

The study adopted a randomized, experimental and control clinical trial that involved twenty-four (24) participants all aged between 20 to 45 years, with moderate to severe alopecia areata attending a particular clinic. All participants were screened for prior treatments, with a requirement that they had not used any hair regrowth therapies within the past six months. Participants with history of previous hair regrowth therapy were excluded from the study. The participants with varying forms of alopecia were evenly distributed into the three groups by stratified randomization. The participants were distributed into three groups A, B and C. Group A applied bromelain and finasteride, group B applied finasteride only and group

C applied a non-active cream respectively twice daily for 12 weeks as shown in Table 1 below. Ethical approval was gotten and consent formed signed by the participants after understanding the research. Participants with recent history of the usage of any hair regrowth therapies within the past six months were excluded from the study. All participants were asked to do a routine hair washing every three days. This will minimize the likelihood of accumulation of the various products and ensure optimal scalp health. Adherence was monitored through daily logs and weekly interviews to maintain treatment fidelity, an essential factor in ensuring the internal validity of the study.

Table 1: Participants and Different Treatment

Group	Treatment	Subjects
A	Bromelain and Finasteride	8
B	Finasteride	8
C	Non active cream	8
Total		24

Hair Count and Thickness

The method described by Trüeb, [15] that involved the use of digital trichoscopy and high-resolution scalp photography was adopted, modified and used in quantifying hair regrowth and hair density.

Inflammatory markers

Tumour necrosis factor-alpha (TNF- α) and interleukin-1 (IL-1) were measured using enzyme-linked immunosorbent assay (ELISA), spectrophotometry, and modified Westergren method, respectively.

Hair Quality and Satisfaction score

We estimated the hair quality and satisfaction of the participant by using a patient-reported outcomes on hair loss severity and satisfaction with hair appearance.

Data Analysis

The data generated from the study were presented using statistical analysis such as percentages, mean and Analysis of variance (ANOVA). ANOVA was used to compare hair count, thickness, and density between the three groups at different time points. A mixed-model approach was considered to account for repeated measures, allowing for the evaluation of changes over time within each participant and between groups. Statistical significance was set at $p < 0.05$.

Hair Count, Thickness and Density

Participants in group A had a significant increase ($p < 0.05$) in hair count compared to both groups B and C. At the end of week 12, the mean percentage increase in hair count was 22% in group A, compared to 15% in group B, and 3% in group C (Figure 1). A similar trend was observed in hair thickness, with participants in group A experiencing an average of 18% increase in hair shaft diameter by week 12, compared to a 10% increase among the participants in group B and 2% in the group C participants (Table 2). The observed difference was significant at ($p < 0.05$) when compared to the other groups. Table 3 showed a significant increase ($p < 0.05$) in hair density of group A participants compared to groups B and C participants at the end of week 12.

RESULTS

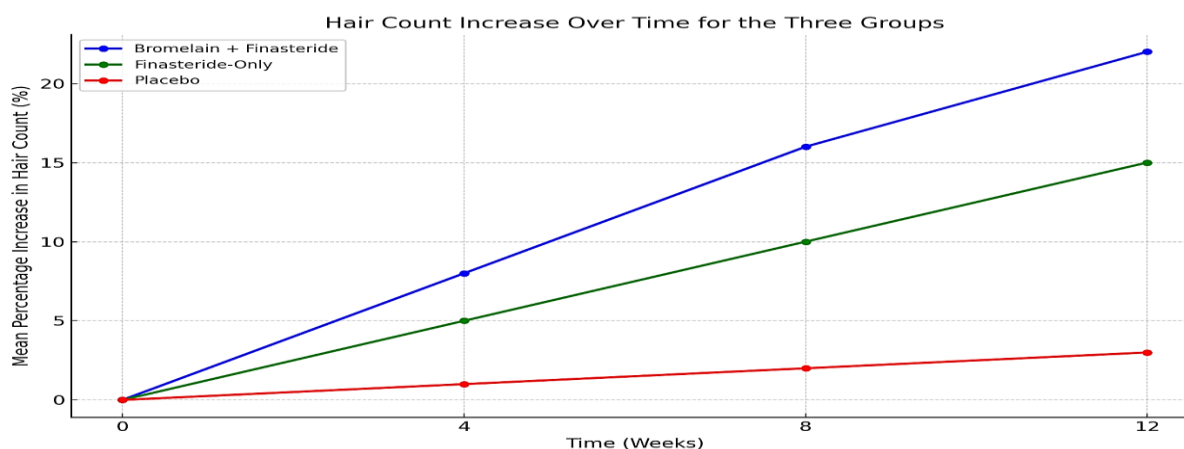


Figure 1: Changes in Hair Count Increase over time for the three Groups

Table 2: Hair Thickness Changes over Time (Mean Percentage Increase)

On	Group A	Group B	Group C
Week 0	0	0	0
Week 4	6 ^a	4 ^b	1 ^c
Week 8	12 ^a	8 ^b	1.5 ^c
Week 12	18 ^a	10 ^b	2 ^c

Values are expressed in mean percentages. Different alphabetical superscript represents statistical significance $p < 0.05$ within the group. Group A= Bromelain + Finasteride, Group B= Finasteride-Only and Group C= Placebo

Table 3: Hair Density Changes over Time (Mean Percentage Increase)

Time (Weeks)	Group A	Group B	Group C
Week 0	0	0	0
Week 4	7 ^a	5 ^b	1 ^c
Week 8	15 ^a	9 ^b	1.5 ^c
Week 12	24 ^a	13 ^b	2 ^c

Values are expressed in mean percentages. Different alphabetical superscript represents statistical significance $p < 0.05$ within the group. Group A= Bromelain + Finasteride, Group B= Finasteride-Only and Group C= Placebo

Inflammatory markers

Participants in group A demonstrated a significant decrease $p < 0.05$ in inflammatory markers, with IL-1 and TNF- α levels decreasing by 30% and 25%, respectively, by the end of the study. In contrast, group B participants had a 15% and 10% reduction in these markers, while the group showed no significant changes (Table 4 and 5).

Table 4: Percentage Reduction in Inflammatory Markers (IL-1)

IL-1(pg/mL)	Group A	Group B	Group C
Week 0	145.52 $\pm$ 1.2 ^a	138.23 $\pm$ 1.3 ^a	141.21 $\pm$ 0.6 ^a
Week 4	115.23 $\pm$ 0.1 ^b	98.23 $\pm$ 0.9 ^b	139.23 $\pm$ 0.9 ^a
Week 8	85.75 $\pm$ 1.6 ^c	67.46 $\pm$ 1.5 ^c	138.21 $\pm$ 1.7 ^a
Week 12	42.46 $\pm$ 0.8 ^d	20.75 $\pm$ 0.2 ^d	138.11 $\pm$ 0.4 ^a

Values are expressed in Mean $\pm$ SEM. Different alphabetical superscript represents statistical significance $p < 0.05$ within the group. Group A= Bromelain + Finasteride, Group B= Finasteride-Only and Group C= Placebo

Table 5: Percentage Reduction in Inflammatory Markers (TNF- α)

TNF- α (pg/mL)	Group A	Group B	Group C
Week 0	115.15 $\pm$ 0.8 ^a	120.20 $\pm$ 0.9 ^a	118.01 $\pm$ 1.2 ^a
Week 4	71.01 $\pm$ 1.6 ^b	98.23 $\pm$ 0.3 ^b	115.31 $\pm$ 0.6 ^a
Week 8	39.32 $\pm$ 0.2 ^c	67.46 $\pm$ 1.2 ^c	118.23 $\pm$ 0.4 ^a
Week 12	28.71 $\pm$ 0.7 ^d	12.75 $\pm$ 0.8 ^d	116.41 $\pm$ 1.5 ^a

Values are expressed Mean $\pm$ SEM. Different alphabetical superscript represents statistical significance $p < 0.05$ within the group. Group A= Bromelain + Finasteride, Group B= Finasteride-Only and Group C= Placebo

Hair Quality Scores

Eighty percent (80%) of the participants in group A reported "good" or "excellent" hair quality by week 12, compared to 60% in group B and 10% in group C (Table 6).

Table 6: Patient-Reported Hair Quality Scores (Percentage of Participants)

Quality Score	Group A	Group B	Group C
Excellent	40	25	5
Good	40	35	5
Fair	15	30	20
Poor	5	10	70

Values are expressed in mean percentages. Group A= Bromelain + Finasteride, Group B= Finasteride-Only and Group C= Placebo

Patient Satisfaction

Satisfaction with the overall treatment was higher among the participants in group A with an average satisfaction score of 8.5 out of 10 compared to 6.5 in the group B participants and 3.0 in the group C participants (Table 7).

Table 7: Mean Satisfaction Scores (Scale of 1-10)

Group	Mean Satisfaction Score
A: Bromelain + Finasteride	8.5
B: Finasteride-Only	6.5
C: Placebo	3

Values are expressed as mean score

Adverse Reactions

Mild scalp irritation was noted in 25% of participants in group A and 12.5% in group B (Table 8).

Table 8: Incidence of Adverse Reactions

Adverse Reaction	Group A	Group B	Group C
Mild Scalp Irritation	2 (25%)	1 (12.5%)	0
Allergic Reaction	0	0	0

Values are expressed in percentages. Group A= Bromelain + Finasteride, Group B= Finasteride-Only and Group C= Placebo

DISCUSSION

The result from our study shows that the combination of bromelain and finasteride significantly enhances hair regrowth, as evidenced by the primary outcomes: 22% increase in hair count, 18% increase in hair thickness and 24% increase in the hair density by week 12. These results provide evidence for the assumption that bromelain has synergistic effects that could help to extend finasteride's therapeutic potential. This agrees with recent literature showing that inflammation serves as a major factor increasing hair loss especially in conditions such as alopecia areata and in androgenetic alopecia [16]. Interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF- α) decreases were detected in the bromelain +

finasteride group, which indicates that bromelain has strong possibilities of being used as an anti-inflammatory agent in hair regrowing treatments.

This is supported by the study of Kaufman *et al.* [17] who reported the effects of finasteride in males with androgenetic alopecia, also revealed that it decreases DHT stimulated hair follicle density and diameter. However, the present study builds upon these concepts by opening the possibility of also lowering inflammation at the scalp level with bromelain to enhance follicle conditions for even more regrowth. The reduction of IL-1 and TNF- α among participants taking the bromelain and finasteride combination provides sufficient evidence in support of this claim thus



propounding the importance of bromelain in the prevention of inflammation induced hair loss.

Supporting this claim is a finding on the link between inflammation and hair follicle miniaturization that was revealed in other studies. For example, the study by Kaufman *et al* [17], shows finasteride in the treatment of men with androgenetic alopecia: results of two placebo-controlled studies showed that, in addition of increasing hair density and thickness, decrease in DHT was important. However, the present study builds upon that knowledge by proposing that additional benefits can be gleaned from bromelain by alleviating inflammation of the scalp where more can be achieved in terms of regrowth. This assertion is supported by the reduction of IL-1 and TNF- α among the participants under the bromelain and finasteride combination and pushes the potential of bromelain in the prevention of inflammation and consequent hair shedding.

An opposing argument to this view might be based on issues about bromelain's absorbance in case of direct application on the hair and skin. A few research has revealed the penetrating capacity of enzymes such as proteolytic enzymes like bromelain particularly when used in localized application as it is in alopecia treatments. Waldman [18] has observed that bromelain works depends on the method taken to administer it. Interestingly, in conditions that can be treated with systemic inflammation, bromelain taken orally has been found to have large anti-inflammatory properties, however, studies on its use when applied topically is still a topic of contention due to the scalp's skin barrier, which may limit the absorption. Therefore, although the present work revealed potent anti-

inflammatory effects when bromelain was administered concomitantly with finasteride, such therapeutic effects should be further tailored in terms of delivery system.

The present study's topical application of bromelain directly negates this counter argument on the bioavailability of bromelain when used tropically by showing precisely measurable improvements in hair count, thickness, and density. By comparison, the hair count grew by approximately 22% in the bromelain formulation group, while the finasteride group saw a 15% increase and the placebo only a 3% increase. This is an indication that the bromelain +finasteride formulation was at least able to penetrate the scalp sufficiently enough to affect the hair. Moreover, inflammation was significantly reduced in the affected region, supporting the suggestion that bromelain as a proteolytic and anti-inflammatory based drug was successfully delivered to the site. While topical bioavailability always remains as a reasonable concern, the results herein stated show that bromelain can still play its part fully in the management of alopecia by virtue of compounds in combination treatment if the bromelain is formulated properly for optimal penetration and absorption.

The further consequences of these observations are vast: the chances to achieve better outcomes would be higher when using multi-targeted approaches to manage intricate diseases including alopecia areata. Combined treatment modalities particularly those that target inflammation, hormones and vasculature have been described to improve outcome due to the convergence of the respective pathways, as depicted by Rossi *et al.* [19] where platelet rich plasma (PRP) was added to mainstream alopecia

therapy. Like PRP, bromelain acts on other pathways that play a role in loss of hair and may be beneficial in the broader control of alopecia. The bromelain formulation approach addresses one of the most fundamental issues of present-day therapies: the fact that a significant percentage of patients are unresponsive to minoxidil or finasteride individually. Thus, the present investigation provides evidence that the combined use of bromelain and finasteride will reduce the variability of patients' reactions by addressing the multifactorial nature of diseases that cause hair loss.

Since this study illustrates marked enhancements in primary end point measures, coupled with comparative patient satisfaction scores of 8.5/10 on average this study corroborates other findings that bromelain could be incorporated in conventional therapeutic regimens to enhance treatment results. No serious allergic reactions or permanent scalp side effect observed for the period observed and from the mild irritation reported. In addition, the decrease in the severity and incidence of other adverse effects adds to the possibility of this combination therapy in regular clinical practice.

Nevertheless, the present research has limitations that deserve to be mentioned, most important of which is the small number of the participants, twenty-four in total. There were statistically significant differences between participants in the various groups recorded in the

REFERENCE

1. Pucheu-Haston, C. M. (2017). Integumentary system. In Atlas of Feline Anatomy For Veterinarians (pp. 9-21). Teton NewMedia.
2. Jafferany, M. (2022). Handbook of psychodermatology. Springer International Publishing.
3. Rossi A, D'Arino A, Pigliacelli F, Caro G, Muscianese M, Fortuna MC. &Carlesimo M (2019). The diagnosis of androgenetic alopecia in children: considerations of pathophysiological

results but due to the trial size, it is evident that more diverse cohorts are required for clearer generalization of outcomes. Furthermore, the study has not been performed over long term more than 12 weeks and thus, increased duration of such treatments is necessary with bromelain to demonstrate the advantages in long-term treatment and possible side effects. This is especially important because alopecia treatments are usually applied repeatedly to make the result permanent; as it has been noted in the long-term finasteride trials [17].

CONCLUSION

AND

RECOMMENDATIONS

This study provides supportive data for the use of bromelain supplement along with finasteride for hair regrowth treatment as it significantly reduces inflammation of the scalp and also favourably supported hair growth, specifically the count, thickness, and density. This study suggests that the desired therapeutic impact is attainable with bromelain if formulated well. Further studies should be directed at the details of the application of this concept, expanding the sample size, and evaluating the outcome of the use of this combination therapy in the long term. If the promising observations of this study can be reproduced in larger trials, bromelain might be of great value as a new therapeutic option for alopecia, finally providing hope for those who failed conventional treatments.

plausibility. Australas. J. Dermatol.; 60(4):E279–E283. doi:

10.1111/ajd.13079

4. Cranwell W, & Sinclair R. (2016). Male Androgenetic Alopecia. Nih.gov; MDText.com, Inc.
5. Kaiser M, Abdin R, Gaumond SI, Issa NT, & Jimenez JJ. (2023). Treatment of Androgenetic Alopecia: Current Guidance and Unmet Needs. Volume 16, 1387–1406.



6. Islam, S. M. (2022). Safety and efficacy of dutasteride for male Androgenetic Alopecia (Doctoral dissertation, Brac University).
7. Nestor MS, Ablon G, Gade A, Han H, & Fischer DL. (2021). Treatment options for androgenetic alopecia: Efficacy, side effects, compliance, financial considerations, and ethics. *Journal of Cosmetic Dermatology*, 20(12).
8. Müller Ramos P, Melo DF, Radwanski H, de Almeida RFC, & Miot HA. (2023). Female pattern hair loss: therapeutic update. *Anais Brasileiros de Dermatologia*, 98(4).
9. Bottega R, Persico I, De Seta F, Romano F, & Di Lorenzo G. (2021). Anti-inflammatory properties of a proprietary bromelain extract (Bromeyal) after in vitro simulated gastrointestinal digestion. *International Journal of Immunopathology and Pharmacology*, 35, 205873842110346.
10. Morgun, E. I., & Vorotelyak, E. A. (2020). Epidermal stem cells in hair follicle cycling and skin regeneration: a view from the perspective of inflammation. *Frontiers in cell and developmental biology*, 8, 581697.
11. Chakraborty AJ, Mitra S, Tallei TE, Tareq AM, Nainu F, Cicia D, Dhama K., Emran TB, Simal-Gandara J, & Capasso R. (2021). Bromelain a Potential Bioactive Compound: A Comprehensive Overview from a Pharmacological Perspective. *Life*, 11(4), 317.
12. Suchonwanit P, Thammarucha S, Leerunyakul K. Minoxidil and its use in hair disorders: a review. *Drug Des Devel Ther.* 2019;13:2777-2786. doi:10.2147/DDDT.S214907.
13. Chobotova, K., Vernallis, A. B., & Majid, F. A. A. (2010). Bromelain's activity and potential as an anti-cancer agent: Current evidence and perspectives. *Cancer letters*, 290(2), 148-156.
14. Nestor, M. S., Ablon, G., Gade, A., Han, H., & Fischer, D. L. (2021). Treatment options for androgenetic alopecia: Efficacy, side effects, compliance, financial considerations, and ethics. *Journal of cosmetic dermatology*, 20(12), 3759-3781.
15. Trüeb RM. (2015). The impact of oxidative stress on hair. *International Journal of Cosmetic Science*, 37, 25–30.
16. Tamashunas NL, & Bergfeld WF. (2021). Male and female pattern hair loss: Treatable and worth treating. *Cleveland Clinic Journal of Medicine*, 88(3), 173–182.
17. Kaufman KD, Olsen EA, Whiting D, Savin R, DeVillez R, Bergfeld W, Price VH, Van Neste D, Roberts JL, Hordinsky M, Shapiro J, Binkowitz B, & Gormley GJ. (1998). Finasteride in the treatment of men with androgenetic alopecia. *Journal of the American Academy of Dermatology*, 39(4), 578–589.
18. Waldman S. (2017). An Analysis on Whether or Not Baldness Can Be Reversed An Analysis on Whether or Not Baldness Can Be Reversed. 10. <https://touro scholar.touro.edu/cgi/viewcontent.cgi?article=1010&context=sjlcas>
19. Rossi A, Anzalone A, Fortuna MC, Caro G, Garelli V, Pranteda G, & Carlesimo M. (2016). Multi-therapies in androgenetic alopecia: review and clinical experiences. *Dermatologic Therapy*, 29(6), 424–432.



APPENDIX

Informed Consent Form

Title of Study: Bromelain and Finasteride Combination Therapy Induces Hair Regrowth in Alopecia Participants

Section	Details
Principal Investigators	Kolawole Olatunde ¹ , Oghenetega T. Oweh ^{2*} , Chisom Adim ³ , Awhin P. Ejoro ⁴
Affiliations	¹ American Society for Microbiology ² Department of Medical Biochemistry, Kaduna State University, Kaduna, Nigeria ³ Department of Microbiology, University of Port Harcourt, Rivers State, Nigeria ⁴ Department of Medical Biochemistry, Delta State University, Delta State, Nigeria
Purpose of the Study	This study aims to investigate the anti-inflammatory activity of bromelain and its potential synergistic effect with finasteride in the management of hair loss due to follicular inflammation.
Procedures	Participants will be randomly assigned to one of three groups: - Bromelain + Finasteride treatment - Finasteride-only treatment - Non-active cream (placebo) The treatment will be applied twice daily for 12 weeks. Hair regrowth, thickness, and density will be measured using digital tracheoscopy and high-resolution scalp photography. Blood samples may be collected for inflammatory marker analysis.
Potential Risks	Mild scalp irritation may occur in some participants. No serious adverse reactions are expected.
Benefits	Participants may experience hair regrowth and improved hair density. The study will contribute to research on alternative hair loss treatments.
Confidentiality	All personal and medical information will be kept confidential. Data will be anonymized for research purposes.
Voluntary Participation	Participation is voluntary. You may withdraw at any time without consequences.
Contact Information	For further inquiries, please contact: <i>Oghenetega T. Oweh</i> (Lead Investigator) Department of Medical Biochemistry, Kaduna State University Email: [Insert Email] Phone: [Insert Contact]
Consent Statement	I have read and understood the study details. My questions have been answered. I voluntarily agree to participate.
Participant Name & Signature	
Date	
Researcher's Signature	