ORIGINAL ARTICLE

CONTENTS

Effect of topically applied simvastatin plus Luteolin on enhancing the development of hair in male mice

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ABSTRACT

Aim: The aim of this study to examine the effect of simvastatin and Luteolin in regrowing hair and stop hair loss in male mice.

Materials and Methods: 25 adult male mice, weighing 25–35 g and aging 6-7 weeks, were employed. Male mice had their coat hairs on their dorsal skin, which was then carefully trimmed by an electrical machine and colored with a dye. Mice were divided into five equal groups (5 mice in each group) as follows: sham group (ethanol-treated group); Minoxidil-treated group; simvastatin-treated group; Luteolin-treated group; simvastatin and Luteolin coadministration group. The drugs were applied on the skin once daily for three weeks.

Results: We demonstrated that the tissue levels of total antioxidant capacity (TAC), vascular endothelia growth factor (VEGF) and keratinocyte growth factor (KGF) in the Minoxidil-treated group, simvastatin-treated group, Luteolin-treated group, and simvastatin and Luteolin coadministration group were considerably greater than those of the sham (ethanol) groups. Furthermore, these groups revealed significant increases in hair growth, hair count, and hair follicle diameters.

Conclusions: these results have identified that simvastatin and Luteolin significantly reduced hair loss due to their anti-inflammatory and antioxidant capabilities.

KEY WORDS: simvastatin, Luteolin, effect of topically, Simvastatin and Luteolin

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INTRODUCTION

The skin of a fetus is coated in lanugo hairs throughout pregnancy. This hair is usually lost throughout the eighth month of growth. The first three or four months of the additional uterine life are finished before a second generation of lanugo hairs begins to form. Two forms of hair, known as vellus and terminal hairs, occur after all lanugo hairs have vanished [1]. Vellus hairs are brief (under 2 cm), thin (less than 0.1 mm), and occasionally colored. Except for the skin on the palms, soles, volar side of the fingers, penile glans, and labia minora et majora, all skin is covered with vellus hairs (only on the internal side) [1]. Hairs are converted to terminal hairs in some locations under the effect of several local and systemic stimuli. Terminal hairs are long (> 2 cm), thick (up to 0.6 mm), pigmented, and modulated [2]. One of the traits that distinguish mammals is the hair follicle, which functions as a special miniorgan. Human hair has a variety of purposes, including defense from the environment, sebum, apocrine sweat, pheromone synthesis, and thermoregulation. The individual's social and sexual interactions are significantly influenced by their hair as well. The hair root is located inside the follicle, and the piece of the hair shaft that extends beyond the level of the epidermis is known as the hair shaft. Vellus hairs lack a medulla, while terminal hairs are made up of a cortex, cuticle, and medulla [3]. The medulla, which is located in the center of the hair shaft, is made up of a few rows of incompletely keratinized cells. The cortex, which provides the hair with strength, is composed of numerous rows of fusiform cells that have undergone full keratinization. The cuticle, which is made up of a single row of flat, keratinized cells organized like roof tiles, covers the cortex. The follicle houses the root of the hair. Sheaths of connective tissue and epithelial cells make up the hair follicle. There are two layers to the epithelial sheath, which is in close proximity to the hair root [1]. Three sublayers make up the inner layer: (a) the cuticle, which is identical to and in close contact with the hair cuticle; (b) the Huxley's layer, which is made up of a few rows of square cells; and (c) the Henle's layer, which is made up of one row of polygonal, flattened cells. With the spinous layer within and the basal layer and basal lamina outside, the outer epithelial layer is thought to represent a down growth of the epidermis. The vitreous membrane is a thicker portion of the basal lamina. An extension of the dermis, the connective tissue sheath contains two layers: an inner papillary layer and an outer reticular layer. The cells toward the bottom of the hair root are larger and have a high capacity for cell division and differentiation. The so-called "hair matrix" is made up of these cells. The

Fig. 1. A photograph showing hair removal at the dorsal area
Picture taken by the authors

Fig. 2. A photograph showing the dorsal area stained with Hoffmann dye
Picture taken by the authors

cells that make up the hair matrix divide as they ascend up the follicle and either becomes hair cells or cells that make up the inner epithelial sheath. Melanocytes, which create the color of the hair, are found among matrix stem cells. The enzyme phenol-oxidase catalyzes the pigment's synthesis from the amino acid tyrosine, which is then converted to dopaquinone by the enzyme dopa. Dopaquinone undergoes two more transformations: either a spontaneous conversion to indolequinone or a change involving the amino acid cysteine. Only the dark pigment, melanin, is produced when indolequinone is polymerized. The yellow pigment, pheomelanin, is produced when indolequinone and dopaquinone are polymerized with the addition of cysteine. Melanin or pheomelanin from melanocyte dendritic elongations is ingested by matrix cells throughout their development process (by phagocytosis). Hair takes on its color in the following ways: black if melanin predominates, and yellow or red if pheomelanin predominates [1]. The dermal papilla is the area of the connective tissue root sheath that is directly in touch with the hair matrix. It significantly influences how hair grows. Topical Minoxidil has been the standard

Table 1. Types of 25 mice groups

Study group	Concentrations
Sham group	100 % of ethanol
Minoxidil-treated group	5 % of Minoxidil solution
Luteolin-treated group	0.5 % of Luteolin solution [8]
Simvastatin-treated group	0.8 % of simvastatin solution [9]
Luteolin- and simvastatin-coadministered group	0.5 % of Luteolin solution and 0.8 % of simvastatin solution

Source: compiled by the authors of this study

therapy for treating and rogenetic alopecia and is also used off-label to treat other hair loss problems. Despite being widely used, minoxidil's precise mode of action is still not entirely known. Due to the minimal risk of negative sexual effects, several publications with strong data back up the safety of finasteride and dutasteride in both men and women with androgenic alopecia (AGA) [4]. The PGF2 analogs latanoprost and bimatoprost are known to enhance hair growth by extending the anagen phase among prostaglandins (PG) [5]. In this study we use Luteolin and Simvastatin. Luteolin has pleotropic mechanisms. The mechanism that can show a beneficial effect on Luteolin in treating hair fall is the antioxidant mechanism. It can be employed for the management of cancer and inflammatory diseases. Simvastatin can induce hair growth by many mechanisms: vasculogenesis, immunomodulatory, anti-inflammatory, blocking induction of nitric oxide (NO) synthesis. Mice were chosen as experimental model for our study due to easy availability and suitability for this type of research [6-8].

AIM

The aim of this study to examine the effect of simvastatin and Luteolin in regrowing hair and stop hair loss in male mice.

MATERIALS AND METHODS

A twenty-five of Wister Albino mice aged and weighted 6-7 weeks and 25-35 grams respectively were obtained from the Centre for Control and Pharmaceutical Research, Iraq. The animals were maintained in the animal laboratory of the Faculty of Sciences, University of Kufa, Iraq. They kept in cages under the conditions of a 20-25 °C and 60-65 % of the humidity with a 12 hr. light: 12 dark cycles.

ETHICS STATEMENT

The present study was conducted at University of Kufa, College of Medicine and obtained approval from the Bioethics Committee at the same University with a license number, AEC: 65 October 2022

EXPERIMENTAL PROTOCOL

After a period of acclimatization, diethyl ether was applied as an aesthetic agent at the area where the hairs were being removed. The hairs of mouse in the dorsal area were then removed using electrical clipper. After removal of the hair, a pink color of the skin was appeared indicating the rest phase signal. A photograph was captured for each mouse using digital camera, Fig. 1 [6]. A Hoffmann dye was used to stain the dorsal area to differentiate between the black area (no hair growth) and the white area (hair is growing). This dye is useful to calculate the ratio between the two areas [7]. A photograph for each mouse was taken, Fig. 2.

STUDY DESIGN

A total of 25 mice were randomly divided into five groups with five animals in each as follows: the sham group or ethanol applied group; Minoxidil-treated group; Luteolin-treated group; simvastatin-treated group; Luteolin- and simvastatin-coadministered group, table 1. A 0.3 ml of each drug prepared was applied once daily on the skin for three weeks.

PHOTOGRAPHIC ANALYSIS

MATLAB 2015 software was used to analyze the photos. This program was calculated the ratio between the black area (hair mice covering the dorsal region) and the white area (the hair-growing components that were stripped of their hair) [10].

PREPARATION OF DRUGS

The medications were prepared immediately by dissolving the drugs in specified volumes of a 100% of ethanol (simvastatin 0.002 mg in 0.3 ml and Luteolin 0.001 mg in 0.3 ml).

HISTOLOGICAL SECTIONS ANALYSIS

In the end of the experiment, hair in the dorsal region were removed, a 5 mm of the skin was cut. The piece of

skin from each mouse was put in a 10% of formalin and visualized under microscope by independent pathologist who blinded to the study groups [11].

ASSESSMENT OF THE TISSUE LEVELS OF TAC, VEGF AND KGF

After the experiment was finished, the small skin fragments were cut and washed in cold a phosphate buffer saline (PBS). The pieces of skin were then weighed, and a PBS containing a 1 % of protease inhibiter cocktail, 1% Triton X100 was added in a ratio of 1:10 w/v for each sample. These samples were homogenized ultrasonic processor. The homogenates were centrifuged for 15 minutes at 14000 rpm and 4°C. Supernatants were employed to examine the concentrations of total antioxidant capacity (TAC), vascular endothelial growth factor (VEGF) and keratinocyte growth factor (KGF) [12].

STATISTICAL ANALYSIS

Analysis of data was performed using SPSS version 26 software. Data were expressed as mean ± standard error of mean unless otherwise stated. For comparison among the study groups, a one-way ANOVA followed by post-hoc test. Chi-square test was used to analyze the histological data among the study groups.

ETHICAL APPROVAL

The study was approved by the Bioethics Committee of the University of Kufa and its representation in the Faculty of Medicine (Approval: AEC: 65 October 2022). The entire procedure was carried out in accordance with the Committee's recommendations.

RESULTS

EFFECT OF TREATMENT ON HAIR GROWTH

In comparison to the sham group (ethanol), there was a marked increase in hair growth (p-value <0.05) in Minoxidil-treated group, Luteolin-treated group, simvastatin-treated group, and their combination group (Luteolin and simvastatin), Fig.3. This combination revealed a significant increase in hears growth as compared with Minoxidil-treated group.

EFFECT OF TREATMENT ON THE NUMBER AND DIAMETER OF HAIR FOLLICLES

The results showed a substantial increase in the number of hair follicles (p≤0.05) in Minoxidil-treated group, Luteolin-treated group, simvastatin-treated group, and their combination group (Luteolin and simvastatin) as compared with the sham (ethanol group), Fig.4. Treatment with combination revealed a marked increase in diameter of the hair follicles in comparison with Minoxidil-treated group, Fig. 5.

EFFECT OF TREATMENT ON LEVELS OF TAC

The present study demonstrated that tissue levels of TAC were considerably elevated in Minoxidil-treated group, Luteolin-treated group, simvastatin-treated group, and their combination group as compared with the sham (ethanol group), furthermore, the combination (Luteolin and simvastatin) was significantly greater than that of the Minoxidil-treated group, Fig.6.

EFFECT OF TREATMENT ON VEGF

In combination with the sham (ethanol group), treatment with Minoxidil, Luteolin, simvastatin or Luteolin and simvastatin coadministration resulted in a marked increase in the levels of VEGF. This combination of Luteolin and simvastatin showed a statistically significant increase in the levels of VEGF as compared to the Minoxidil-treated group, Fig.7.

EFFECT OF TREATMENT ON THE LEVELS OF KGF

The current study revealed that treatment with Minoxidil, Luteolin, simvastatin or Luteolin and simvastatin coadministration resulted in a marked increase in the levels of KGF as compared to the sham (ethanol group), Fig. 8. Treatment with combination (Luteolin and simvastatin) increased the levels of KGF in comparison with mice treated with Minoxidil, Fig. 8.

DISCUSSION

Alopecia can be described as loss of hair from a specific area of the head or body with the head being more involved some people experience psychological anxiety due to hair loss [9-13]. Recently, an attention has made to some of preparations that are being investigated in preclinical studies for their significant effects as antioxidant and anti-inflammatory properties in comparison to traditional ones such as minoxidil. Minoxidil is topically formulated drug that is widely used for treatment of androgenic alopecia, however, multiple side effects like skin irritation, abnormal hair growth and poorly understood mechanisms have increased the search for safe and effective preparations [14, 15]. The antioxidant and anti-inflammatory effects of simvastatin and

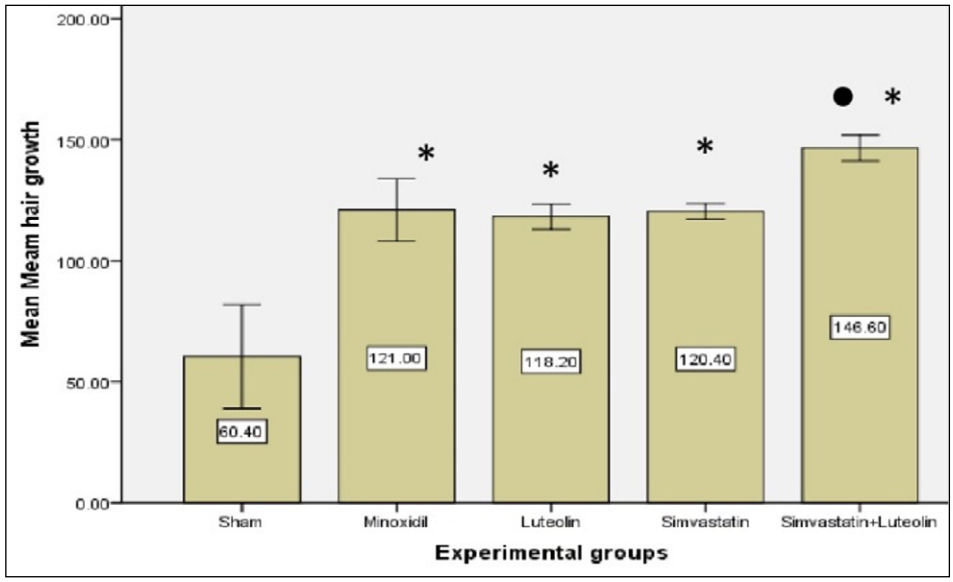

Fig. 3. Shows the average hair growth ratio using MATLAB software among the study groups.
Data are expressed as Mean ± SD,
*p-value<0.05 vs. sham (ethanol group),
·p-value<0.05 vs. Minoxidil group
Picture taken by the authors

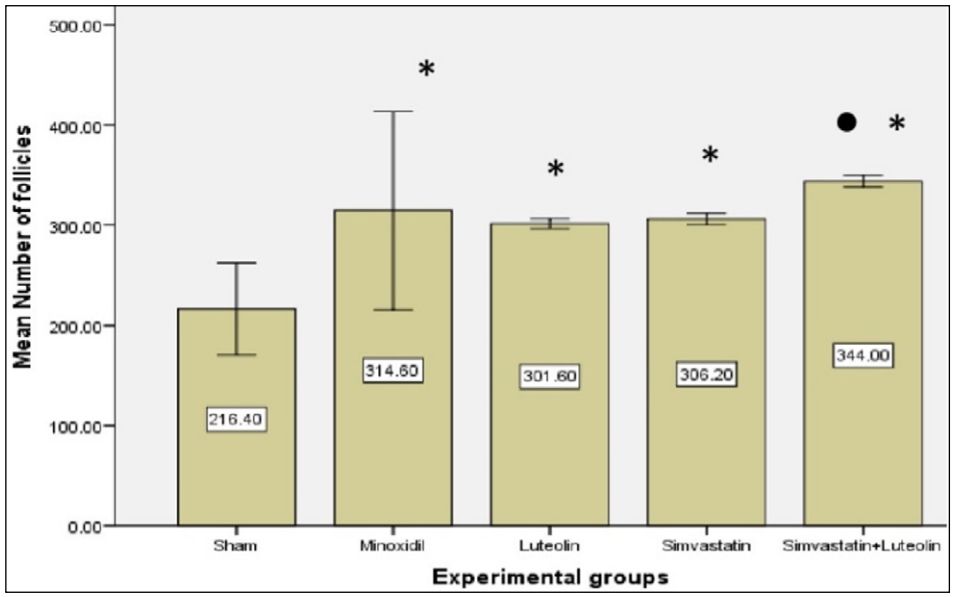

Fig. 4. Average number of hair follicles of hair follicles among the experimental groups.
Data are expressed as Mean ± SD,
*p-value<0.05 vs sham (ethanol group),
·p-value<0.05 vs. minoxidil group
Picture taken by the authors

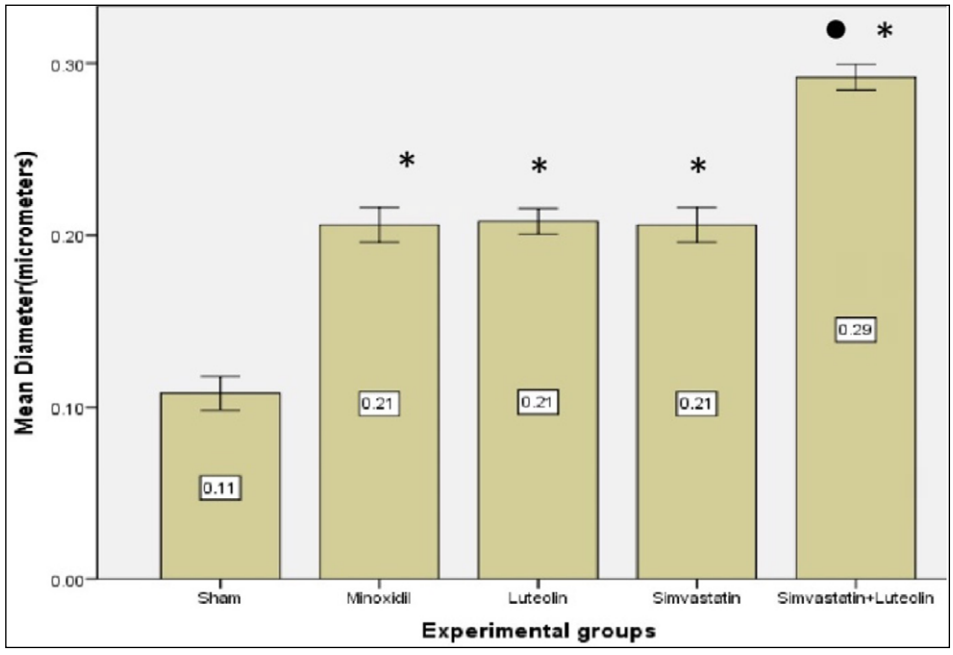

Fig. 5. Mean diameter (in micrometers) of the hair follicles among the study groups.
Data are expressed as Mean ± SD,
*p-value<0.05 vs. sham (ethanol group),
·p-value<0.0 5 vs. Minoxidil group
Picture taken by the authors

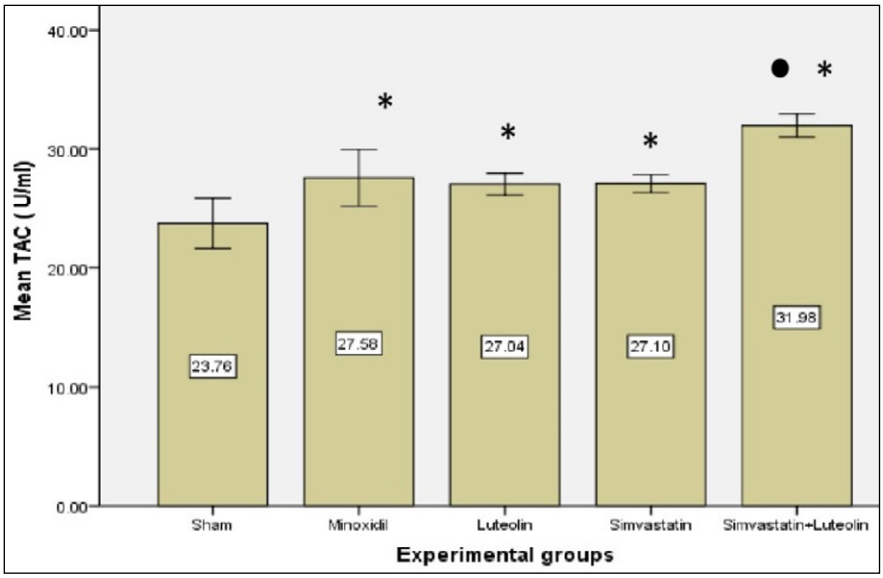

Fig. 6. Mean levels of TAC (in U/ml) among the study groups
Data are expressed as Mean ± SD,
*p-value<0.05 vs. sham (ethanol group),
·p-value<0.05 vs. Minoxidil group
Picture taken by the authors

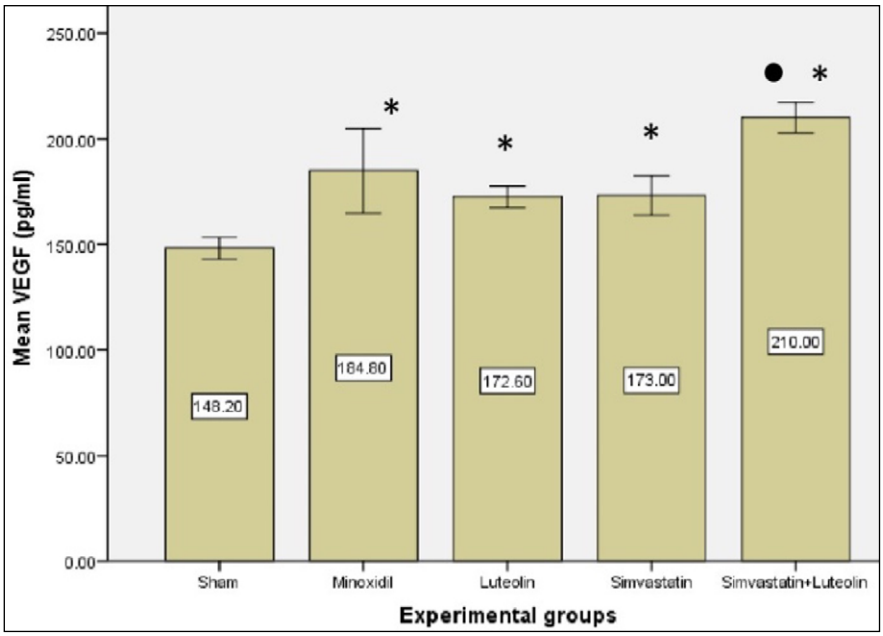

Fig. 7. Levels of VEGF (pg/mL) among the experimental groups
Data are expressed as Mean ± SD,
*p-value<0.05 vs. sham (ethanol group),
·p-value<0.05 vs. Minoxidil group
Picture taken by the authors

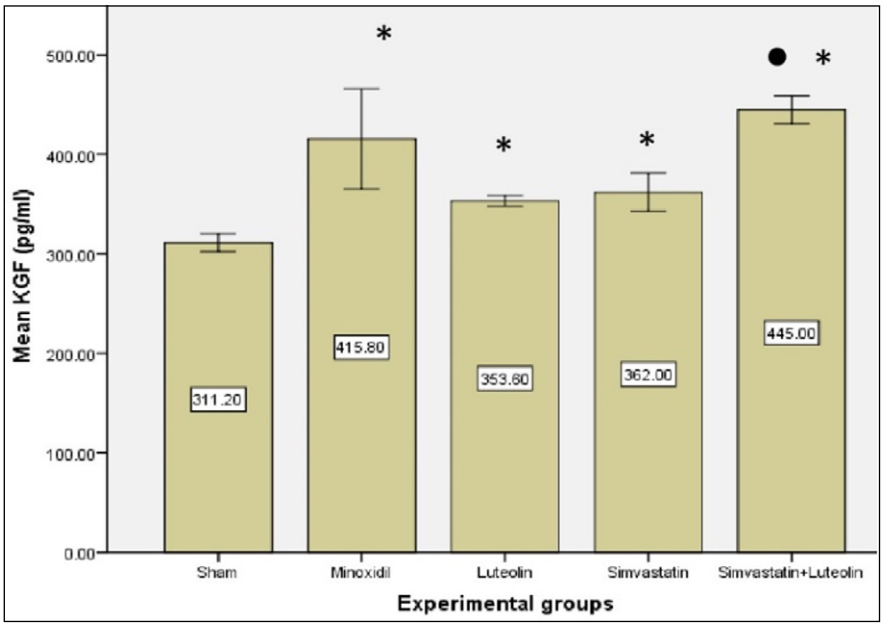

Fig. 8. levels of KGF (pg/ml) among the experimental groups
Data are expressed as Mean ± SD,
*p-value<0.05 vs. sham (ethanol group),
·p-value<0.05 vs. Minoxidil group
Picture taken by the authors

luteolin could be preliminary ground for restoration of microenvironment that is crucial for hair growth and addressing the reasons for alopecia. Supporting this hypothesis was evident by reports showing the role of antioxidant rich foods in mitigating androgenic alopecia while the risk of this condition is aggravated by ingesting of proinflammatory food [16]. Targeting these two pathways by simvastatin and luteolin may not only enhance hair growth but also provide alternative to existing medications with fewer unwanted effects.

Luteolin has pleotropic mechanisms, particularly the antioxidant effect that has been found to play a beneficial role in hair loss simvastatin is lipid lowering agent having vasculogenesis, immunomodulatory, anti-inflammatory effects suggesting its potential to induce hair growth. The present study shows that treatment with simvastatin resulted in an increase in the hair growth and number of follicles as compared to the sham. These results seem to be consistent with other research which found that statins reduced hair loss in patients with alopecia Areata via their immunomodulatory properties [17-18]. In addition, simvastatin treatment increased the diameter of hair follicles suggesting its role in increasing hair growth. The current study demonstrated that treatment with simvastatin elevated the levels of TAC in tissues of the skin as compared to the sham group. Simvastatin has been found to decrease the production of free radicals, TNF-α and elevate the antioxidant capacity of the human abdominal aortic aneurysm wall tissue, probably through inhibiting NF-kB activity [19-20]. The present study showed that treatment with simvastatin markedly increased the level of VEGF in comparison with the sham group. It has been reported that simvastatin treatment increased the VEGF levels at mRNA levels and protein levels, and improved wound healing in a mouse model of diabetes [21]. Indeed, administration of anti-VEGF monoclonal antibody reversed the effect of simvastatin in wound healing in diabetic mice suggesting a role of VEGF in modulating hair growth [21]. In a rat model of brain injury, there is a correlation between therapeutic improvement and VEGF upregulation with simvastatin [22]. Furthermore, simvastatin improved a burn wound healing via ameliorating the wound closure percentage, epithelial thickness, collagen remodeling and VEGF expression [23]. The current study showed that treatment with simvastatin notably increased levels of KGF as compared to the sham group. High concentrations were found following injection simvastatin and mesenchymal stem cells in oleic acid induced lung injury suggesting its role as catalyst in increasing the levels of KGF [24]. The current research demonstrates that Luteolin treatment enhanced the growth of hair, number of hair and diameter of hair follicles. Consistent with the literature, Luteolin-loaded Nanoemulsion has been found to increase hair growth [25]. This type of flavonoids has antioxidants properties may be able to both slow hair loss and promote hair growth [26]. The present study reveals that high levels of TAC in the skin tissues as compared with the sham group. These results are in line of previous studies showing that Luteolin increased levels of TAC following intestinal ischemia-reperfusion injury in mice [27]. Luteolin-treated while cleaved caspases 3, NF-B, and MIP-1 levels were decreased, CNTF expression was upregulated, and cAMP and TAC levels significantly increased in the experimental autoimmune encephalomyelitis group [28]. The current study demonstrated high levels of VEGF in mice treated with Luteolin as compared to the sham group. The study showed the primary components of Methanolic shallot extract have been determined to be phenolic chemicals. Quercetin and Luteolin Reduced NO generation and release from shallot extract results in anti-inflammatory action. SRD5A1 and SRD5A2 expression were reduced by shallot extract in DU-145 cell lines. SHH, SMO, GIL1, CTNNB1, and VEGF expressions, however, were elevated in hHFDPC. These results show that shallot extract inhibits androgen and inflammatory pathways to promote hair development. Additionally, the VEGF, Sonic Hedgehog, and Wnt/-catenin pathways were also active [29]. The current study shows that treatment with Luteolin resulted in high levels of KGF as compared with sham group. KGF in the dermal papillae is crucial for the growth of hair. It regulates the migration, proliferation, differentiation, and survival of keratinocytes [30]. The current investigation revealed that the combination of simvastatin and Luteolin showed notable increases in hair growth and diameters of follicles and increased tissue levels of TAC, VEGF, and KGF after three weeks of treatment. To best our knowledge, no studies have examined the effect of this combination on hair growth and further studies need to be done. It is unclear what potential mechanisms might underlie the combined effects of these drugs but may be through their antioxidant and anti-inflammatory properties.

CONCLUSIONS

Simvastatin and Luteolin solution significantly promote hair growth, increase hair counts and hair follicle diameter, and elevate the levels of TAC, VEGF, and KGF. Taken together, these results show that simvastatin and Luteolin reduce hair loss that could be by their effects as anti-inflammatory and antioxidant capabilities.

REFERENCES

1. Jankovic SM, Jankovic SV. The control of hair growth. Dermatology Online Journal. 1998;4(1):4-9. doi:10.5070/d36gz420mw. DOI
2. Jahoda CAB, Reynolds AJ. Dermal-epidermal interactions-follicle-derived cell populations in the study of hair-growth mechanisms. J Invest Dermatol. 1993;101(1):33S-38S. doi: 10.1111/1523-1747.ep12362577. DOI
3. Kosti A. Osnovi Normalne Histologije. [Basics of Normal Histology]. Belgrade: NauNa Knjiga. 1950, pp.709-715. (Slovenian)
4. Choi YM, Diehl J, Levins PC. Promising alternative clinical uses of prostaglandin F2 analogs: Beyond the eyelashes. J Am Acad Dermatol. 2015;72:712-6. doi:10.1016/j. jaad.2014.10.012. DOI
5. Liu L, Zhao S, Li F et al. Effect of 5- reductase inhibitors on sexual function: A meta-analysis and systematic review of randomized controlled trials. J Sex Med. 2016. doi:10.1016/j.jsxm.2016.07.006. DOI
6. Bitto A, Minutoli L, Altavilla D et al. Simvastatin enhances VEGF production and ameliorates impaired wound healing in experimental diabetes. Pharm Res. 2008;57(2):159-169. doi:10.1016/j.phrs.2008.01.005. DOI
7. Hoffmann R. Tricho Scan: A novel tool for the analysis of hair growth in vivo. Journal of Investigative Dermatology Symposium Proceedings. 2003;8(1):109–115. doi:10.1046/j.1523-1747.2003.12183.x. DOI
8. Ueda H, Yamazaki C, Yamazaki M. Inhibitory effect of perilla leaf extract and Luteolin on mouse skin tumor promotion. Biological and Pharmaceutical Bulletin. 2003;26(4):560-563, doi:10.1248/bpb.26.560. DOI
9. Feingold KR, Man MQ et al. Cholesterol synthesis is required for cutaneous barrier function in mice. J Clin Invest. 1990;86(5):1738-45. doi: 10.1172/JCI114899. DOI
10. Hadi NR, Al-Dhalimi MA, Fadheel KJ. Effect of topical Minoxidil solution in promoting hair growth in male mice. Kufa Med. Journal. 2011;14(1):246.
11. Fischer TW, Trüeb RM, Hänggi G et al. Topical melatonin for treatment of androgenetic alopecia. Int J Trichology. 2012;4(4):236-45. doi: 10.4103/0974-7753.111199. DOI
12. Wenjuan Li, Zhang Ch, Ren A et al. Shikonin Suppresses Skin Carcinogenesis via Inhibiting Cell Proliferation. PLoS One. 2015;10(5):e0126459. doi: 10.1371/journal.pone.0126459. DOI
13. Nalluri R, Harries M. Alopecia in general medicine. Clin Med (Lond). 2016;16(1):74-8. doi: 10.7861/clinmedicine.16-1-74. DOI
14. Fiedler-Weiss VC. Topical minoxidil solution (1% and 5%) in the treatment of alopecia areata. J Am Acad Dermatol. 1987;16(3):745-8. doi: 10.1016/s0190-9622(87)80003-8. DOI
15. 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. DOI
16. Bazmi S, Sepehrinia M, Pourmontaseri H et al. Androgenic alopecia is associated with higher dietary inflammatory index and lower antioxidant index scores. Front Nutr. 2024;11:1433962. doi: 10.3389/fnut.2024.1433962. DOI
17. Babakhani A, Hashemi P, Ansari JM et al. In vitro differentiation of hair follicle stem cell into keratinocyte by simvastatin. Iranian Biomedical Journal. 2019;23(6):404-411. doi: 10.29252/ibj.23.6.404. DOI
18. Evers BM, Farooqi MS, Shelton JM et al. Hair growth defects in insigdeficient mice caused by cholesterol precursor accumulation and reversed by simvastatin. Journal of Investigative Dermatology. 2010;130(5):1237-1248. doi: 10.1038/jid.2009.442. DOI
19. Karimi B, Ashrafi M, Shomali T, Yektaseresht A. Therapeutic effect of simvastatin on DMBA-induced breast cancer in mice. Fundamental and Clinical Pharmacology. 2019;33(1):84-93. doi: 10.1111/fcp.12397. DOI
20. Piechota-Polanczyk A, Goraca A, Demyanets S et al. Simvastatin decreases free radical's formation in the human abdominal aortic aneurysm wall via NF-κB. European Journal of Vascular and Endovascular Surgery. 2012;44(2):133-137. doi: 10.1016/j.ejvs.2012.04.020. DOI
21. Bitto A, Minutoli L, Altavilla D et al. Simvastatin enhances VEGF production and ameliorates impaired wound healing in experimental diabetes. Pharm Res. 2008;57(2):159-169. doi: 10.1016/j.phrs.2008.01.005. DOI
22. Wu H, Lu D, Jiang H et al. Simvastatin-mediated upregulation of VEGF and BDNF, activation of the PI3K/Akt pathway, and increase of neurogenesis are associated with therapeutic improvement after traumatic brain injury. J Neurotrauma. 2008;25(2):130-139. doi: 10.1089/neu.2007.0369. DOI
23. Ansari JM, Ramhormozi P, Shabani R et al. Simvastatin combined with bone marrow mesenchymal stromal cells (BMSCs) improve burn wound healing by ameliorating angiogenesis through SDF-1α/CXCR4 pathway. Iranian Journal of Basic Medical Sciences. 2020;23(6):751-759. doi: 10.22038/IJBMS.2020.39782.9465. DOI
24. Yang Y, Zhu Y, Fan X. Mesenchymal stem cells joint simvastatin therapy improves oleic acid induced acute lung injury in rats. Int J Clin Experiment Med. 2017;10(2):2590-2597.
25. Shin K, Choi H, Song SK et al. Nanoemulsion Vehicles as Carriers for Follicular Delivery of Luteolin. ACS Biomaterials Science and Engineering. 2018;4(5);1723-1729. doi: 10.1021/acsbiomaterials.8b00220. DOI
26. Altamimi MA, Hussain A, Alshehri S et al. Development and evaluations of transdermally delivered Luteolin loaded cationic Nanoemulsion: In vitro and ex vivo evaluations. Pharmaceutics. 2021;13(8). doi: 10.3390/pharmaceutics13081218. DOI

27. El-Deeb OS, Ghanem HB, El-Esawy RO, Sadek MT. The modulatory effects of Luteolin on cyclic AMP/Ciliary Neurotrophic factor signaling pathway in experimentally induced autoimmune encephalomyelitis. IUBMB Life. 2019;71(9):1401-1408. doi: 10.1002/iub.2099. DOI
28. Ruksiriwanich W, Khantham C, Muangsanguan A et al. Phytochemical Constitution, Anti-Inflammation, Anti-Androgen, and Hair Growth-Promoting Potential of Shallot (Allium ascalonicum L) Extract. Plants. 2022;11(11). doi: 10.3390/plants11111499. DOI
29. Herman A, Herman AP. Mechanism of action of herbs and their active constituents used in hair loss treatment. Fitoterapia. 2016;114:18-25. doi: 10.1016/j.fitote.2016.08.008. DOI
30. Junlatat J, Sripanidkulchai B. Hair growth-promoting effect of Carthamus tinctorius floret extract. Phytotherapy Research. 2014;28(7):1030-1036. doi: 10.1002/ptr.5100. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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