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The effect of an oral product containing Amla fruit (*Phyllanthus emblica* L.) on female androgenetic alopecia: A randomized controlled trial

Marzieh Akhbari [a], Alireza Firooz [b], Roja Rahimi [c], Meysam Shirzad [a,d], Niusha Esmaealzadeh [c,e], Laila Shirbeigi [a,*]

[a] Department of Traditional Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran
[b] Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Traditional Pharmacy, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran
[d] Persian Medicine Network (PMN), Universal Scientific Education and Research Network (USERN), Tehran, Iran
[e] Traditional Persian Medicine and Complementary Medicine (PerCoMed) Student Association, Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Ethnopharmacological relevance: Amla (*Phyllanthus emblica*) fruit has been emphasized as a hair tonic in Traditional Persian Medicine (TPM) and recommended for hair loss orally and topically.
Aim of the study: This study aimed to investigate the effect of an oral product containing Amla fruit on Female Androgenetic Alopecia (FAGA).
Materials and methods: This study was a triple-blind, randomized, controlled clinical trial. Sixty women with FAGA were randomly assigned into two groups of thirty. The intervention group received ten cc Amla syrup thrice a day for 12 weeks. The second group received a placebo with the same dose and duration. Hair growth parameters were analyzed using TrichoScan before and after 12 weeks of intervention. Physician and patient satisfaction were assessed using the CGI-I and PGI-I questionnaires, respectively.
Results: Twenty-seven participants in the intervention group and 25 in the placebo group completed the trial. Based on our findings, the anagen-to-telogen ratio increased significantly in the intervention group compared with the group who received placebo ($F = 10.4$, $P = 0.002$). Physician and patient satisfaction increased in the amla group compared with placebo at 12th weeks of intervention ($P<0.001$), ($P<0.001$). The formula had no remarkable side effects. Only one case of mild constipation was reported in one of the participants after one month of consuming Amla syrup.
Conclusion: The results of this study demonstrated that Amla syrup could help treat androgenic hair loss in women and increase the anagen phase. Further studies are needed to evaluate this potential treatment for FAGA.

1. Introduction

Female androgenetic alopecia (FAGA) is one of the most common causes of non-scarring hair loss in women (Carmina et al., 2019). FAGA is usually diagnosed clinically, characterized by diffuse hair thinning over the central scalp while the frontal hairline is preserved (Starace et al., 2020). The occipital and parietal regions may also be involved (Price, 2003).

The three-point Ludwig scale (Ludwig, 1977) is used for grading FAGA as follows: 1) Stage I: mild decrease in hair density on the crown with a hardly noticeable increase in part width; 2) Stage II: moderate decrease in hair density on the crown with a perceptible increase in part width; and 3) Stage III: severe decrease in hair density on the crown with almost no perceptible part width, and thinning of the frontal hairline (Ludwig, 1977; Levy and Emer, 2013). Diagnostic criteria in trichoscopy include a typical progressive follicular miniaturization and an increased telogen phase (Starace et al., 2020). Different etiologies have been suggested for FAGA, including abnormal changes in sex hormones, inflammatory processes, and decreased growth factors in Dermal Papilla Cells (DPCs) (Yano et al., 2001; Trüeb, 2002; Magro et al., 2011; Starace et al., 2020).

Although not life-threatening, FAGA is associated with psychological

* Corresponding author.
E-mail addresses: mentalhealth8981@gmail.com (M. Akhbari), Firozali@sina.tums.ac.ir (A. Firooz), rojarahimi@gmail.com (R. Rahimi), shirzadmd@gmail.com, shirzad@tums.ac.ir (M. Shirzad), Niushaesmaealzadeh@yahoo.com (N. Esmaealzadeh), l.shirbeigi@yahoo.com (L. Shirbeigi).

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burdens and can negatively impact the quality of life, self-confidence, and interpersonal and social relationships. Moreover, it can lead to anxiety and depression (Sawant et al., 2010; Russo et al., 2019).

Treatment of androgenic alopecia (AGA) with FDA-approved drugs, such as finasteride and minoxidil is associated with numerous side effects (Blumeyer et al., 2011; Padois et al., 2011; Traish et al., 2011; Kaliyadan et al., 2013). Alternatively, plant-based products are increasingly gaining popularity due to several mechanisms of action and fewer side effects (Kaushik et al., 2011).

As a holistic medical system with thousands of years of prolific history, Traditional Persian Medicine (TPM) describes various herbal medicines for preventing and treating hair loss (Hajimehdipoor et al., 2019). Amla, with the scientific name of *Phyllanthus emblica* L. is one of these remedies. A deciduous tree native to tropical and southern Asia, Amla fruit has been used for nutritional and medicinal purposes. *P. emblica* is well known for its nutrients and contains various phytochemical compounds, including tannins, mosaic acid, amino acids, alkaloids, flavonoid glycosides, phenolic glycosides, and terpenoids (Jain et al., 2016; Saini et al., 2022). In vivo studies have demonstrated hair growth-enhancing activities of Amla because it contains compounds that effectively increase the size of hair follicles and prolong the anagen phase (Purwal et al., 2008; Jadhav et al., 2009). According to ancient Persian medicine textbooks, Amla fruit is hair tonic and has been recommended to prevent hair loss orally and topically (Aghili-Alavi-Shirazi, 2001). Also, it has been utilized in Ayurveda, Siddha, Unani systems in India, Tibetan as hair tonic (Dasaroju and Gottumukkala, 2014; Saini et al., 2022). Amla fruit is used in traditional formulations for enriching hair growth and pigmentation (Saini et al., 2022).

Although various complementary and alternative treatments exist for hair loss, few are supported by clinical trial studies (Hosking et al., 2019). Even though sources of traditional medicine and animal and laboratory studies have shown the effect of Amla on hair growth as well as prevention and treatment of hair loss, to our knowledge, no clinical trial study has been conducted on the effect of orally-consumed Amla fruit on FAGA. Thus, this study was conducted to investigate the effect of Amla syrup on FAGA compared with placebo.

2. Materials and methods

2.1. Trial design and participants

This study was designed as a triple-blind, randomized, controlled trial. After receiving a code of ethics from the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1400.414), the protocol of this clinical trial was registered in the Iranian Registry of Clinical Trials (IRCT20201010048979N2). All participants signed the informed consent form before participating in this study.

This trial was conducted on women with FAGA from September 2021 to February 2022 at the Dermatology and Leprosy Research Center affiliated with Tehran University of Medical Sciences. Among the 91 participants evaluated for eligibility, 60 met the criteria for entering the study and were randomly allocated to either the intervention or placebo group. At the end of the study, eight participants (three in intervention and five in placebo) were excluded from the study (Fig 1). Volunteers who met the inclusion criteria were examined by a dermatologist and randomly allocated to either placebo or intervention groups.

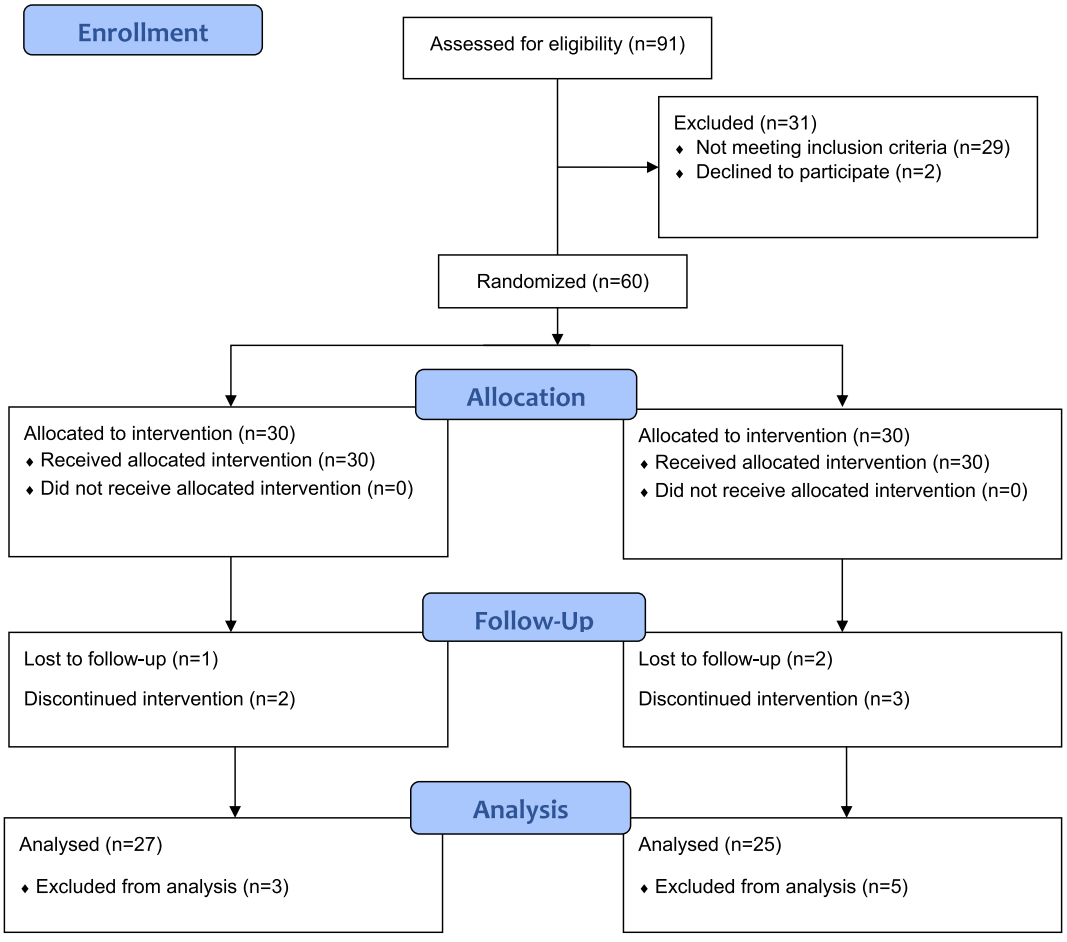

Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram for study methods.

2.2. Inclusion and exclusion criteria

Inclusion criteria comprised women aged 18-60, with more than six months duration of types 1 and 2 hair loss, according to Ludwig Scoring (Ludwig, 1977) Exclusion criteria included using any topical product or treatment to prevent hair loss or stimulate hair growth, including finasteride, minoxidil, platelet-rich plasma, biotin, and also laser therapy in the previous two months; use of 5α-Reductase inhibitors in the last two months; use of antiandrogens such as spironolactone, cimetidine, and cyproterone acetate over the last two months; use of systemic steroids for more than 14 days during the previous two months; any active disease in the head region, including scalp infection in the last six months; history of any cancer or autoimmune diseases; history of hair transplantation; pregnancy and breastfeeding; history of underlying disorders including diabetes mellitus, hypothyroidism, polycystic ovary syndrome; and history of any acute illness in the previous two months.

2.3. Randomization and blinding

Participants were randomly allocated to intervention and placebo groups. Due to gradual recruitment and to maintain balance in the groups, subjects were randomly selected based on the table of random numbers using the permuted block randomization method with blocks of four.

Amla and placebo syrups were delivered in similar packaging and were completely alike in appearance, color, and smell and could be distinguished only through the specific codes labeled on syrup bottles by the pharmacist. The patient, the researcher prescribing the drug, and the data analyst were not aware of the assigned codes.

2.4. Drug preparation

Amla was purchased from a reputable medicinal plant market and sent to the Herbarium of the Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran, for identification. The herbarium code PMP-3608 was received for the sample.

To prepare Amla syrup, 30 g of *P. emblica* fruit was coarsely ground and boiled in 500 ml water for 30 min. It was then strained, and 100 g of honey was added to the obtained extract and boiled to a volume of 240 ml. At the end of the concentration process, 5 ml of rose water was added to the syrup to improve the taste and smell of the formulation. To prepare the placebo, 100 g honey was added to 300 ml water and boiled to a volume of 240 ml. Again, 5 ml rose water was added to the syrup at the end of the concentration process. The edible brown color matched the color of the placebo with that of the Amla syrup.

2.5. Measurement of gallic acid with Reverse Phase High Performance Liquid Chromatography

The Reverse Performance High Performance Liquid Chromatography (RP-HPLC) was performed using Agilent Technologies HPLC device (1260 infinity II series, USA). The LC-C18 column was from Phenomenex (Luna®) (250 × 4.6 mm, 5 lm) and the detector was UV. The volume of each injection was 50 µl which was detected at λ = 270 nm. Mobile phase consisted of 1% acetic acid in double-distilled water (phase A, 90%) and acetonitrile, (Merk, Germany) (phase B, 10%) with a flow rate of 1 ml/min.

10 ml of Amla syrup was mixed with 10 ml of HCL (2M, diluted in methanol) and boiled for 1 h prior to the injection (acid hydrolyzation), and then neutralized with 12 ml NaOH (2M). The results were measured according to the gallic-acid, dissolved in methanol, (Merk, Germany) calibration curve. All experiments were repeated in triplicates in three different days (Bahramsoltani et al., 2022).

2.6. Total phenolic determination of syrup

The total phenolic content was determined quantitatively using the Folin Ciocalteu assay, with Gallic acid as the standard. One mL of Amla syrup and 1 mL of gallic acid solution in dilutions of 25, 50, 75, 100, 125, and 150 µg per mL of gallic acid were transferred to 25 ml volumetric flasks containing 9 ml of distilled water and shaken well after adding 1 ml of Folin Ciocalteu reagent. After 5 min, 10 mL sodium bicarbonate solution was added to each balloon, and the volume was adjusted with distilled water. After 90 min, the absorbance was determined at 650 nm versus a blank. A calibration curve was drawn based on the standard concentrations of gallic acid solutions, and the total phenolic content was calculated (Singleton et al., 1999).

2.7. Total flavonoid determination of syrup

The total flavonoid content was measured by aluminum chloride colorimetric assay. 1 mL syrup was added to 1 mL quercetin standard solution in dilutions of 25, 50, 75, 100, and 150 µg per mL in separate 10 mL volumetric flasks. Then, 4 ml of distilled water and 0.3 ml 5% sodium nitrite solution were added to each and shaken well. After 5 min, 0.3 ml 10% aluminum chloride solution was added to each flask and shaken well. After five more minutes, 2 ml 1 M sodium chloride solution was added, and the volume was adjusted with distilled water. The solution was then shaken well, and the absorbance was determined at 510 nm versus a blank. A calibration curve was drawn based on the standard concentrations of quercetin solutions, and the total flavonoid content was calculated (Zhishen et al., 1999).

2.8. Microbial control of syrup

Necessary tests were conducted to evaluate the presence and risk of microbial contaminants, including the total count of aerobic microorganisms, molds and yeasts, coliforms, Escherichia coli, Salmonella, and anaerobic microorganisms. The results indicated that microorganisms were within the permissible range (Council of Europe, 2014).

2.9. Sample size and statistical analysis

To achieve a power of 80%, α = 0.05, assuming a 20% dropout, the sample size was estimated to be 30 people in each group. The collected data was analyzed using R-4.2.2 software using Chi-square, Independent Samples Test, and covariance analysis (ANCOVA).

2.10. Research tools

Hair loss parameters, including the percentage of hair in the anagen phase, the percentage of hair in the telogen phase, the number of hair strands, and the average hair thickness, were calculated using TrichoScan (FotoFinder Systems GmbH). The Clinical Global Impression of – Improvement scale (CGI-I) and Patient Global Impression of Improvement (PGI-I) questionnaires were used at the end of the 6th and 12th weeks to evaluate physician and patient satisfaction, respectively. Drug side effects were assessed using the Common Terminology Criteria for Adverse Events Version 5 (CTCAE_5) questionnaire.

2.11. Intervention and data collection

The intervention group received a syrup-containing Amla fruit product, while the second group received a placebo medicine. The administered dose was ten ccs of syrup thrice daily for 12 weeks. Hair loss was evaluated using TrichoScan prior to intervention and 12 weeks after the end of the intervention. Physician and patient satisfaction were assessed at the end of the 6th and 12th weeks of intervention using the CGI-I and PGI-I questionnaires, respectively. Gastrointestinal and dermatological drug side effects were assessed using the CTCAE5

questionnaire. Phone follow-ups were made once every two weeks to remind the user of the drug and to check for possible side effects.

2.12. Ethical considerations

Participants were provided with a comprehensive explanation of the intervention, after which they signed the informed consent form. Also, subjects were informed that they could withdraw from the study at any trial stage. Participants did not pay for visits or medicine. The information obtained from participants was kept entirely confidential.

3. Results

3.1. Total phenols, flavonoid and gallic acid identification of Amla syrup

The amount of gallic acid was equal to 0.7611 ± 0.16 mg/ml of the syrup. Based on the results, the total phenol in Amla syrup was 306.95 ± 0.586 mg of gallic acid per milliliter of syrup. Total flavonoid content was 1.5 ± 0.067 mg quercetin per milliliter of syrup.

3.2. Participant sample and characteristics

The similarity of the two study groups in terms of the distribution of demographic and clinical variables was investigated using statistical tests prior to intervention. The results of the similarity assessment showed no significant difference between the two groups in terms of demographic variables except for age and marital status (P<0.05). The percentage of married participants in the placebo group was almost two times more than the intervention group. Moreover, the intervention and placebo groups had an average age of 33.2 (9.2) and 41.8 (10.5), respectively, which was significantly different (P<0.05). Therefore, the effect of age was controlled as a confounding variable in evaluating the treatment effect (Table 1).

Prior to intervention, the hair growth parameters of the two groups were evaluated using TrichoScan and compared using statistical tests. No significant difference was found between the intervention and placebo groups in the anagen-to-telogen ratio, the ratio of the villus to terminal hair, the number of hairs, hair thickness, and other variables at the beginning of the study (Table 2).

3.3. Outcomes

After 12 weeks of the intervention, hair quality, and quantity were re-measured with TrichoScan and statistically compared between groups. Moreover, participant and physician satisfaction with treatment results was also evaluated and compared. ANCOVA and Mann-Whitney statistical tests were used to analyze data. It should be noted that in cases where the data did not follow a normal distribution, logarithmic values were used to normalize the distribution.

According to the results, Amla syrup significantly affected the anagen percentage, telogen percentage, and anagen-to-telogen ratio.

Table 1
Baseline characteristics of study groups.

Demographic variable		Group		P-value
		Intervention (n = 30)	Placebo (n = 30)	
Age (years) (Mean ± SD)		33.1 ± 9.2	41.8 ± 10.5	<0.05[a]
Marital status N(%)	Single	18(67%)	9(33%)	<0.05[b]
	Married	12	21	
Type of Hair loss N (%)	I	18(50%)	18(50%)	1[b]
	II	12(50%)	12(50%)	
Duration of Hair loss (months) Mean ± SD		17.4 ± 9.6	18.2 ± 9.5	0.73[a]

[a] Independent sample *t*-test
[b] Chi-square.

Table 2
Baseline clinical characteristics of participants.

Variable	Group		p-value
	Intervention group (n = 27) (Mean± SD)	**Placebo group (n = 25) (Mean± SD)**	
Anagen percentage	73.84 ± 8.88	75.93 ± 6.69	0.309[a]
Telogen percentage	*26.14 ± 8.91*	24.36 ± 6.85	0.391
Anagen to telogen ratio	3.26 ± 1.45	3.46 ± 1.31	0.575
Terminal percentage	78.24 ± 13.70	80.01 ± 13.33	0.615
Vellus percentage	21.81 ± 13.71	19.99 ± 13.33	0.603
Vellus to terminal ratio	0.32 ± 0.30	0.29 ± 0.29	0.561
Hair count	112.56 ± 18.07	116.16 ± 24.39	0.519
Mean thickness	0.064 ± 0.014	0.066 ± 0.013	0.463

[a] Independent sample *t*-test.

Anagen percentage in the intervention and placebo groups was 77.22 ± 8.28 and 70.97 ± 8.08, respectively (F = 24.7, P<0.001), indicating the intervention's significant effect on this variable's improvement. After treatment in the intervention and placebo groups, the telogen percentage was 23.14 ± 8.23 and 29.32 ± 7.94, respectively (F = 12.6, P = 0.001). The average anagen-to-telogen ratio was 4.00 ± 2.11 in the intervention group and 2.70 ± 1.13 in the placebo group (F = 10.4, P = 0.002).

In order to achieve a better estimate of the effect size, Cohen's d index was calculated. The effect size obtained from Amla syrup was in the range of 0.04-0.7. The largest effect size was related to physician satisfaction, and the lowest was terminal percentage (Table 3). Regarding drug side effects, only one case of constipation was reported in one of the participants after one month of consuming Amla syrup, which was resolved with dietary recommendations.

4. Discussion

To our knowledge, this study was the first randomized controlled

Table 3
Outcomes investigated in this trial.

Variable	Group		p-value	Cohen's d
	Intervention group (n = 27) (Mean± SD)	**Placebo group (n = 25) (Mean ± SD)**		
Anagen percentage	77.22 ± 8.28	70.97 ± 8.08	.001[a]	0.21
Telogen percentage	23.14 ± 8.23	29.32 ± 7.94	.001[a]	0.22
Anagen to telogen ratio	4.00 ± 2.11	2.70 ± 1.13	0.002[a]	0.29
Vellus percentage	24.23 ± 17.79	27.88 ± 15.25	0.063[a]	0.09
Terminal percentage	75.39 ± 17.63	72.10 ± 15.24	0.22[b]	0.04
Vellus to terminal ratio	0.49 ± 0.93	0.47 ± 0.43	0.43[a]	0.65
Hair count	119.18 ± 44.40	110.00 ± 26.27	0.382[a]	0.05
Mean thickness	0.06 ± 0.01	0.06 ± 0.01	0.244[a]	0.20
Patient satisfaction	2.67 ± 0.73	4.40 ± 0.64	<0.001[a]	0.45
Physician satisfaction	2.81 ± 0.68	4.12 ± 0.33	<0.001[a]	0.73

[a] ANCOVA test.
[b] Mann-Whitney test.

clinical trial to investigate the effect of an oral product containing Amla fruit on FAGA. Our findings indicated that Amla syrup significantly increases the ratio of anagen phase to telogen phase in FAGA compared with placebo. Moreover, physician and patient satisfaction were significantly higher in the Amla group in comparison with the placebo group.

In normal hair cycling, ~90% of follicles are in anagen phase, 9% in telogen phase, and 1% in catagen phase at any given time (Burg et al., 2017). FAGA is characterized by an increased telogen/anagen ratio and a shortened hair cycle (Starace et al., 2020). Considering the need for long-term treatment and side effects of conventional drugs such as finasteride and minoxidil (Blumeyer et al., 2011; Kaliyadan et al., 2013), safe herbal drugs that can lead to an increase in anagen phase can be beneficial. Various preclinical studies have shown that Amla can increase the anagen phase and hair growth with different mechanisms (Luanpitpong et al., 2011; Kumar et al., 2012; Jang et al., 2018; Wongrakpanich et al., 2022).

The main compounds of Amla include tannins, alkaloids, polyphenols, vitamins, and minerals. A number of *P. emblica* compounds, including gallic acid, ellagic acid, emblicanin A & B, phyllembein, quercetin, and ascorbic acid, have been reported to be biologically effective and to nourish hair (Khan, 2009; Dasaroju and Gottumukkala, 2014).

Few studies have investigated the effect of Amla on hair parameters. A clinical trial on the topical effect of Amla fruit extract in combination with other herbal extracts on hair parameters in healthy individuals found significant improvement in hair density, hair growth rate, and terminal and vellus hair density. Nevertheless, in contrast with our findings, they found no significant change in the ratio of anagen to telogen (Majeed et al., 2020). Another clinical study on topical herbal products containing *P. emblica* extract for sixteen weeks indicated more effective slowing of hair loss progression and enhancement of hair growth compared with placebo or 3% minoxidil (Yu et al., 2017).

In addition to containing beneficial compounds for the hair, the effect of Amla on FAGA can be ascribed to various mechanisms, including antioxidant and anti-inflammatory activities, as well as effects on hormones and stimulated proliferation of DPCs.

Inflammatory processes are increasingly suggested as an integral part of the pathogenesis of AGA. The continuous inflammatory process and changes in the connective tissue of hair follicles may lead to permanent hair loss in AGA (Trüeb, 2002; Magro et al., 2011). Hazra et al. have investigated the anti-oxidant properties of Amla with different assays. Hydroxyl radicals and superoxide anions can damage tissues due to their high reactivity. Amla could notably inhibit their activity compared with standard phytochemicals ($p<0.01$), mannitol and quercetin, respectively. Furthermore, Amla could significantly ($p<0.001$) suppress radicals of nitric oxide in comparison with curcumin (Hazra et al., 2010). The anti-inflammatory effect of Amla was studied by Santoshkumar et al. in both acute inflammation, induced by Carrageenan, and chronic inflammation, induced by Rexin pellets in a rat model. In this study, the anti-inflammatory effect of Amla fruit was examined in comparison with diclofenac by comparing the paw inflammation volume before and after administration of the drugs. The inflammation was significantly suppressed by 540 mg/kg of Amla powder, comparable to diclofenac (Santoshkumar et al., 2013). Moreover, clinical studies have also found evidence that Amla ameliorates systemic inflammation and oxidative stress in both healthy individuals and those with underlying disorders, including metabolic syndrome, obesity, and diabetes (Santoshkumar et al., 2013; Usharani et al., 2013, 2019; Khanna et al., 2015; Kapoor et al., 2020).

Regarding hormonal mechanisms, some studies suggest that AGA is an androgen-dependent process in which testosterone is converted into active dihydrotestosterone (DHT) by the 5α-reductase enzyme. DHT binds to androgen receptors in the hair follicle and initiates a process that curtails the anagen phase. This will eventually cause transformation of terminal hair to vellus hair and result in hair loss (Dhariwala & Ravikumar, 2019).

In a study conducted on alcoholic extracts of 17 Thai plants traditionally used to treat hair loss, *P. emblica* was demonstrated to be a potent inhibitor of 5α-reductase, with a finasteride equivalent 5α-reductase inhibitory activity value of 18.99 ± 0.40 mg finasteride equivalent per 1g crude extract, promoting hair growth in C57BL/6 mice (Kumar et al., 2012). Moreover, another study reported that *P. emblica* extract decreases the expression of 5α reductase in human DPCs in a dose-dependent manner (Jang et al., 2018).

Among the different types of cells that regulate hair follicles, DPCs play a crucial role in the proliferation and differentiation of hair follicles and in regulating the hair cycle in each phase (Yang and Cotsarelis, 2010). The results of a preclinical study showed that Amla extract can stimulate proliferation of DPCs in a concentration-dependent manner (Luanpitpong et al., 2011). It has been demonstrated that *P. emblica* extract increases the expression of Insulin-Like Growth Factor 1 (IGF-1) and Vascular Endothelial Growth Factor (VEGF), which accelerates the differentiation and growth of DPCs in a dose-dependent manner (Jang et al., 2018). Furthermore, investigating transformants containing an aqueous extract of *P. emblica*, researchers found that the obtained aqueous extract of *P. emblica* enhances mRNA expression levels of genes that promote hair growth, including VEGF, IGF-1, and HGF in HaCaT keratinocyte cells (Wongrakpanich et al., 2022). These factors stimulate keratinocytes to proliferate and differentiate into the hair shaft during the anagen phase (Herman and Herman, 2016; Madaan et al., 2018).

In the current study, no remarkable side effect was observed after administration of Amla syrup, however one case of mild constipation was reported one month after consuming Amla. This case may be due to the significant content of tannins in Amla syrup which act as anticholinergic agent (Nowicka and Wojdyło, 2019). Moreover, tannins are reported to have inhibitory effect on chloride channels (Wongsamitkul et al., 2010). and therefore, could induce constipation in some individuals. Nevertheless, this complication is mostly observed in high doses (Serrano et al., 2009; Hussain et al., 2019).

Collectively, the mentioned evidence elucidates the mechanisms by which Amla syrup can prevent hair loss and strengthen hair growth. These include stimulation of growth factors that enhance the proliferation of DPCs and inhibition of 5α reductase. Moreover, *P. emblica* contains hair nutrients and exerts antioxidant and anti-inflammatory effects.

Overall, our results showed that compared with a placebo, Amla could be effective on FAGA via increasing the anagen phase and decreasing the telogen phase without serious side effects. Further studies should be conducted to compare Amla's effect with common oral androgenic alopecia drugs.

We acknowledge that the present study's limitations included not comparing intervention with a standard hair loss treatment such as finasteride, and not having a long-term follow-up.

5. Conclusion

This study was conducted to investigate Amla syrup's effect on FAGA. The results showed that this fruit could increase the ratio of anagen to telogen hairs compared with a placebo. We suggest Amla as a safe oral drug for FAGA. Indeed, further studies are needed to provide more robust evidence regarding the efficacy and safety of Amla.

CRediT authorship contribution statement

Marzieh Akhbari: Data acquisition, writing-original draft, writing–review & editing. Laila Shirbeigi: Conceptualization, methodology, review & editing, supervision, and project administration. Alireza Firooz: Patient recruitment and selection and data interpretation. Roja Rahimi: Formulation of the medication, review & editing. Meysam Shirzad: Investigation, review & editing. Niusha Esmaealzadeh: writing–review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Abbreviations

TPM	Traditional Persian Medicine
FAGA	Female Androgenetic Alopecia
AGA	Androgenic Alopecia
CGI-I	Clinical Global Impression of Improvement
PGI-I	Patient Global Impression of Improvement
CTCAE_5	Common Terminology Criteria for Adverse Events Version 5
RP-HPLC	Reverse Phase Haigh-Performance Liquide Chromatography
DHT	Dihydrotestosterone
DPCs	Dermal Papilla Cells
IGF-1	Insulin-Like Growth Factor 1
VEGF	Vascular Endothelial Growth Factor

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Marzieh Akbari MD, MPH was borne in 1977 in Kashan, Iran. She has a medical degree from Tehran University of Medical Sciences in 2003, MPH of mental health (Tehran University of Medical Sciences, 2014), and now she is a PhD Student in traditional Persian medicine, Tehran university of Medical sciences, Tehran, Iran.

Alireza Firooz was born in 1965 In Tehran, Iran. He is a Professor and director of Dermatology of Center for Research and Training in Skin Diseases and Leprosy of Tehran University of Medical Sciences. His research interests are Evidence based dermatology, Clinical trial, Skin biometrology, and Cutaneous leishmaniasis. His other positions are Director, Pharmaceutical, Cosmeceutical, and Hygienic Products Clinical Evaluation Lab (DermaLab), Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, Tehran, Iran, Founder and Ex-Director, Clinical Trial Center, Tehran University of Medical Sciences, Tehran, Iran, editor-in-Chief, Journal of Dermatology and Cosmetic.

Roja Rahimi was born in 1980 in Shiraz, Iran. She is professor of Traditional Pharmacy, School of Persian Medicine, Tehran University of Medical Sciences (TUMS), Iran. She has PhD in Traditional Pharmacy from Tehran University of Medical Sciences. Her research interests are Discovery of pharmacological activities of medicinal plants and phytochemicals along with their possible mechanisms of action Design of in vitro, animal and human studies for evaluation of activities claimed for natural products in Persian medicine, and Formulation and standardization of natural medicines. She was Top Young Researcher, Rhazi Festival, Iran (2008), Top Young Researcher, Avicenna Festival, Iran (2013), and Top 1% Scientist in Pharmacology and Toxicology (2015, 2016, 2017, 2022). She has a total of 180 publications, 5 books in persian, and 8 book chapters in English. Her H-index in scopus is 50.

Meysam Shirzad was born in 1978. He has a PhD in traditional Persian medicine (2013). He is an assistant professor at School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran, since 2014.

Niusha Esmaealzadeh is a Pharm.D., Ph.D. candidate of Traditional pharmacy. Her work focuses on standardization and evaluation of Persian medicine plants. She is also interested in different ways of lifestyle modification for raising patients' quality of life. She has been recently awarded for her E-poster presentation at 22nd international Congress of the international society for Ethnopharmacology (ISE SFEC-2023), Imphal, India.

Laila Shirbeigi is an associate professor of School of Persian Medicine of Tehran University of Medical Sciences (TUMS). Her Scopus ID is 57016683300 and with h-index 5 (33 published articles, mostly in the field of skin disease and Traditional Persian Medicine). Dr. Shirbeigi ORCiD ID is: 0000-0002-6503-8582. She is born in 1975/27/10 in Tehran- Iran. She defended her Ph.D. thesis in the field of integrative dermatology at 2014/12/03. Her field of study is herbal traditional Persian medicine and dermatologic diseases.