

Systematic Review

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Is There Scientific Evidence that Panax Promotes Hair Growth?

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ABSTRACT

In cosmetology, although the use of natural products can be considered as a fancy, research related to the hair growth has been considered. Some synthetic products, as minoxidil and finasteride have been used to stimulate the hair. However, several important side effects have been reported with these drugs. Natural products are gaining popularity mainly due to, in general, their fewer side effects and better formulation strategies. Hair loss is a dermatologic disorder and urges the necessity of alternative treatments with hair growth promoting potential, as the medicinal plants. Among the medicinal plants used to treat the hair loss and to promote the hair growth, there is the *Panax ginseng*. The purpose of this study was to review the published researches concerning the use of *Panax ginseng* in investigations involving the hair growth using the PubMed database. Eight studies have reached the inclusion criteria to be analyzed. Considering the selected papers, there is a predominance of experimental procedures with the compound ginsenoside. The aim of the works was mainly related to investigation on the molecular and cellular mechanisms responsible for hair growth in presence of *Panax ginseng* or a compound related to this natural product. The number of publications in PubMed with the keyword *Panax ginseng* involving hair growth is about 0.43 %. The results indicate that *Panax ginseng* has stood out as a promising natural source with relevant effects in treatment of hair loss, despite the small number of publications selected involving the keywords “*Panax ginseng*” AND “hair loss”. Putting together the findings, it is concluded that the use of *Panax ginseng* and its chemical products could be an important strategy to manage the loss hair.

KEYWORDS: *Panax ginseng*; Hair loss; Hair growth; Ginsenoside.

INTRODUCTION

In cosmetology are considered studies and applications of the beauty treatments. Skin care, cosmetics, hairstyling, manicures/pedicures and electrolysis are subjects related to the cosmetology. Trichology is that branch of dermatology involved with scientific investigations of the health of hair and scalp.¹

Healthy skin is an excellent barrier maintaining balance between the internal and external environment of the body. In the skin are found several structures with different functions, as the hair.² Hair loss, in general, is an undesirable disorder in which the hair falls out from skin areas where they are usually present, such as the scalp and the body. This loss interferes with the many useful biologic functions of the hair, including sun protection (mainly to the scalp) and dispersal of sweat gland products. As hair cover to the scalp has psychological importance in our society, patients with hair loss suffer tremendously. In cosmetology, although the use of natural products can be considered as a fancy, research related to the hair growth has been considered.³

The causes of hair loss are controversial and there is no agreement about the main factors that cause the loss of hair, which is a universal complaint. It affects the both genders and depends on the race since the humankind existed.^{3,4} Among the factors that can contribute to the hair loss include (i) genetic predisposition, (ii) hormonal factors, (iii) disease states and (iv) the use of chemotherapeutic agents.⁵

Various medical treatments aimed at arresting the progression of the hair loss have become available (i) surgical treatments are constantly being refined and (ii) medications, such as minoxidil and finasteride, that are the only two drugs approved by the Food Drug Administration (FDA), USA for hair growth in men.

The treatment of hair loss depends on the knowledge of its etiology and of the progression of this undesirable condition. Angiogenesis (through endogenous substances), androgen antagonism, vasodilatation through potassium channel opening 5- α reductase inhibition and modulation of hair cycle are some of the non-surgical therapeutic strategies for the hair growth promotion.^{6,7}

Minoxidil is the only drug available for women with androgenetic alopecia. Besides having hair growth promotion effect, therapy with the synthetic drug has become questionable due to their occasional lack of efficacy, safety and their potential side effects.³

Integrative and complementary practices involve several procedures in healthcare. These practices are related to the disease prevention and health promotion.^{8,9} Some of them are related to the Traditional Chinese Medicine, as phytotherapy and acupuncture.⁸ In the phytotherapy are used medicinal plants in different forms. The utilization of natural products, as the medicinal plants in the art of healing is an ancient form of treatment of different diseases.⁹

In cosmetology, research related to the use of herbal medicines for hair growth has been considered.⁵ Moreover, Patel et al³ have pointed out that various medicinal plants have been used for care of the hair and hair growth potential activity. Considering the hair loss (alopecia), Patel et al³ reported that there

are various causes for this loss and the phenomenon related to this, it is still poorly known. Natural products are gaining popularity mainly due to, in general, their fewer side effects. Herbal medicines have been widely used for alopecia treatment since ancient times as reported in Ayurveda, Chinese and Unani systems of medicine.

Kumar et al¹⁰ reported that the hair grows from follicles of the dermis and it is found exclusively in mammals. Zhang et al¹¹ described that the hair is a complex filamentous biomaterial that has a structure with many layers including, from outside in, the cuticle, the cortex and the medulla, all bound by the cell membrane.

In mammals, hair plays a vital role in thermal insulation and for social and sexual communication, both visually and as a means for dispersing scents secreted by skin glands. Humans are relatively hairless compared to other mammals and human hair has no known significance for survival of species. However, it remains an important cosmetic asset.¹²

Among the medicinal plants used to treat the hair loss and to promote the hair growth, there is the *Panax ginseng*. *Ginseng radix* is the steamed and dried root of *Panax ginseng*.¹³⁻¹⁵

Panax ginseng is traditionally used as an important medicinal herb worldwide for more than 5,000 years.¹⁶ It is a semishade perennial plant originally from the Eastern Asia regions. It belongs to the family *Araliaceae*, and is known to possess various pharmacological effects, such as anti-inflammatory, antioxidation, antitumor, antidiabetic and antihepatotoxicity.^{17,18} In addition, Matsuda et al¹⁹ have reported that *Panax ginseng* is able (i) to improve the constitutional tendencies to poor body condition, (ii) to promote appetite, (iii) to increase vitality and (iv) to reduce over sensitivity to cold. It contains several chemical components, as ginsenosides, essential oil, sesquiterpenes, polyacetylenes, polysaccharides, peptidoglycans, steroid, choline, vitamin- B, C, E, fatty acid, carbohydrates, and amino acids. Moreover, it is reported that a 70% methanolic extract from red ginseng seems to have superior activity to that of the white ginseng in a hair growth-promoting assay using mouse vibrissal follicles in organ culture. The activity is credited to the saponin component of ginseng.

Studies revealed that ginseng acts as a 5- α reductase inhibitor.^{6,7} Ginsenosides Ro enhances *in vivo* hair re-growth based on their inhibitory activity against 5- α reductase in the androgenetic alopecia model.²⁰

As authors have demonstrated the possibility of medicinal plants act in the process involving the hair loss and/or hair growth,^{21,22} the purpose of this study was to review the published researches concerning the use of *Panax ginseng* in investigations involving the hair growth. Considering the findings described in the literature, it is hypothesized an improvement in the hair growth due to the *Panax ginseng*.

METHODS

Search Strategy and Selection of the Studies

This systematic review of scientific studies followed the guidelines of the *Transparent Reporting of Systematic Reviews and Meta-Analyses* (PRISMA statement).²³ One database was systematically searched for experimental trials *in vivo* and *in vitro*. The papers were searched in the PubMed, (<http://www.ncbi.nlm.nih.gov/pubmed>) on February 14th, 2016. The search was performed using the keyword (i) “*Ginseng radix*”, (ii) “hair loss”, (iii) “hair growth”, (iv) “*Ginseng radix*” AND “hair growth”, (v) “*Ginseng radix*” AND “hair loss”, (vi) “Medicinal plants” AND “hair growth”, (vii) “Medicinal plants” AND “hair loss”, (viii) “*Panax ginseng*”, (ix) “*Panax ginseng*” AND “hair growth” and (x) “*Panax ginseng*” AND “hair loss”.

Inclusion and exclusion criteria

A systematic selection of the articles was carried out by three independent examiners based on the following inclusion criteria: (i) Biological activity: hair growth activity of *Panax ginseng*; (ii) Plant material: extract from *Panax ginseng*; (iii) Study design: experimental trials *in vitro* and/or *in vivo* (with *Panax ginseng*); (iv) Language: articles written in English. In addition, ethnobotanical and ethnopharmacological surveys, case reports, expert opinion or consensus statements were excluded, as those have used *Panax ginseng* mixed with other product.

RESULTS

Table 1 shows the number of publications found in the

PubMed involving the keywords that were searched. It is possible to verify a strong interest in studies involving “hair loss” and “hair growth”, with more than three thousands papers. It is also observed that about 0.43% and 0.19% of the articles with the keyword “*Panax ginseng*” are related to “hair growth” and “hair loss”, respectively.

Keyword	Number of publication
" <i>Ginseng radix</i> "	266
" <i>Ginseng radix</i> " AND "hair growth"	1
" <i>Ginseng radix</i> " AND "hair loss"	0
"hair growth"	3,162
"hair loss"	3,627
"Medicinal plants" AND "hair growth"	8
"Medicinal plants" AND "hair loss"	7
" <i>Panax ginseng</i> "	2,083
" <i>Panax ginseng</i> " AND "hair growth"	9
" <i>Panax ginseng</i> " AND "hair loss"	4

Table 1: Number of publications (database PubMed) involving *Panax ginseng* and hair growth/hair loss.

According to a previously set strategy, literature searches involving the keywords “*Ginseng radix*” AND “hair growth”, “*Ginseng radix*” AND “hair loss”, “*Panax ginseng*” AND “hair growth”, “*Panax ginseng*” AND “hair loss”, “medicinal plants” AND “hair growth” and “medicinal plants” AND “hair loss” resulted in 29 articles. Eight publications met the inclusion criteria and were included in the final review after thorough analysis (Figure 1).

It is possible to see in Table 2 the aim, the experimental model used and the plant material or the chemical compound

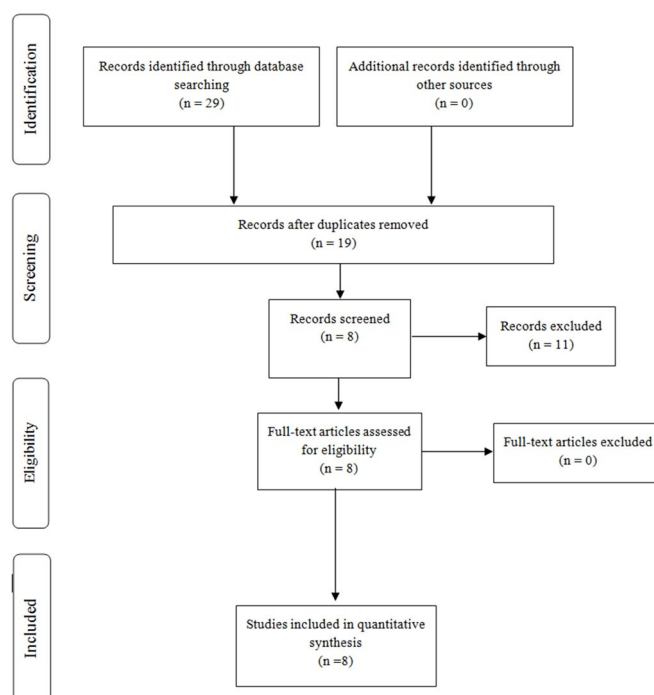


Figure 1: Flow diagram of the search strategy comprising the identification of potentially relevant material, and preliminary screening and final selection of the studies included in this review (based on PRISMA statements).

related to the *Panax ginseng* ginsenoside.^{13,20,21} of the selected papers. There is a predominance of experimental procedures with the compound. Only one study¹⁴ does not specify what part of the plant/chemical compound that was used. The aim of these selected works was mainly related to investigation on the molecular and cellular mechanisms responsible for hair growth in presence of a chemical component of the *Panax ginseng*.

It is possible to see in Table 3 the results and conclusion of the selected studies. Despite the different protocols and procedures, the results indicated a hair growth due the treatment with *Panax ginseng*. According the majority of the studies^{13-15,24} the *Panax ginseng* seemed to be effective in the treatment of hair growth.

DISCUSSION

In cosmetology, several subjects are related to the study and application of the beauty treatments have been considered; such as skin care, cosmetics, hairstyling, manicures and pedicures, and electrology. Concerning to the cosmetology, trichology is involved with scientific investigations of the health of hair and scalp.¹ The skin is a barrier in the body to maintain the balance between the internal and external environment of the body, and the hair is found in it.² Hair loss, in general, is an undesirable disorder and strategies to avoid the hair loss and to promote the hair growth are desirable. Among these strategies, the use of medicinal products would be considered.¹⁹⁻²¹

Reference	Aim	Experimental procedure	Plant material/chemical component
(13)	To investigate the molecular and cellular mechanisms responsible for HG promoting effect of GRe <i>in vitro</i> and <i>in vivo</i> .	Investigation of the HG in animals. Isolation and culture of C57BL/6 mouse vibrissa HF. Cell culture and western blot analysis. High quality mRNA extract and NGS. MA datasets and systemic analysis.	GRe
(26)	To investigate the synergistic effect of each <i>Eclipta alba</i> (L.) Hassk, <i>Asiasarum sieboldii</i> (Miq.) F. Asiasari radix, and <i>Panax ginseng</i> for HG potential on nude mice, as these mutant mice genetically lack hair.	Chromatographic analysis. Toxicity studies. Treatment protocol of extracts on nude mice. Measurement of hair density and length. Evaluation of hair existing area. Histologic assessment of HG. BrdU immunohistochemistry.	Dried roots (<i>Panax ginseng</i>)
(15)	To identify the molecules through which Rg3 stimulates HG. The thymidine incorporation for measuring cell proliferation was determined.	Culture of human dermal papillae cells. Thymidine incorporation assay. RNA isolation. MA. Real-time PCR. Immunohistochemistry. Image acquisition and protein quantification.	Ginsenoside Rg3
(14)	To investigate the hair growth efficacy and safety of KRG in AA comparing corticosteroid ILI alone patient group with ILI with KRG taking patient group using Folliscope 2.5 for 12 weeks.	Phototrichogram. Expert panel assessment of global photographs.	Korean red ginseng
(24)	To determine how ginsenosides prevent HL and investigate the effects of ginsenosides on cell genesis in different phases of adult HF, using BrdU as a marker for dividing cells.	BrdU labeling. Immunohistochemical staining.	Ginsenosides Rb1 and Rd
(25)	To evaluate the effects of FPG on proliferation and apoptosis of human hair DPCs.	Cells and growth condition. Cell viability assay. Immunoblot analysis. HG activity <i>in vivo</i>	Ginsenoside Re (5.99%) was revealed as the major component of the extract.
(19)	This report deals with the HG promoting effect of <i>Ginseng Radix</i> on vibrissal HF (excised from the upper lip region of mice) in order to explore resources involved in the acceleration and promotion of HG.	Organ culture of mouse vibrissal HF. Measurement of length of vibrissal HF.	Red Ginseng or white ginseng and ginsenosides
(27)	To investigate the effect of the water fraction of <i>Panax ginseng</i> on apoptosis and the formation of medullary cell in the HF of irradiated mice	Adult N:GP(s) mice with HF synchronously in the middle of the HG cycle received doses of gamma-radiation. HF were analyzed either 12 hours after irradiation with 2 Gy in the experiment on the apoptosis, or 3 days after 3 Gy in the experiment on the forming medulla. The number of medullary cells per unit length (100 microns) was measured by H and E staining. Apoptosis was detected by a non ISEL technique and H and E stain applied to histologic sections.	Water fraction of <i>Panax ginseng</i>

BrdU – 5-bromo-2' deoxyuridine, NGS – next-generation sequencing, ILI – intra-lesional injection, KRG – Korean red ginseng, HF – hair follicles, HG – hair growth, HL – hair loss, Gy – gray, H – hematoxylin, E – eosin, ISEL – isotopic in situ DNA end-labeling, GRe – ginsenoside Re, MA – Microarray, N:GP(s)

Table 2: Information about the aim, experimental procedure and plant material or chemical component related to the *Panax ginseng* used on the selected studies.

Reference	Results	Conclusion
(13)	Topical treatment of GRe increased the hair shaft length and hair existent time, comparable to the minoxidil. GRe stimulated hair shaft elongation in the <i>ex vivo</i> cultures of vibrissa HFIs isolated from C57BL/6 mouse. Systemic transcriptome analysis by next generation sequencing demonstrated that TGF- β -pathway related genes were selectively down-regulated by treatment of GRe <i>in vivo</i> , and the same treatment suppressed TGF- β induced phosphorylation of ERK in HeLa cells.	GRe is the effective constituent in the ginseng on hair promotion <i>via</i> selective inhibition of the HG phase transition related signaling pathways, TGF- β signaling cascades.
(26)	The hair density and length of <i>Eclipta alba</i> treated mice were increased. HG area was visible in <i>Eclipta alba</i> treated mice. Mice treated with <i>Asiasari radix</i> and <i>Panax ginseng</i> had hair loss. Histomorphometric observation of nude mice skin samples revealed an increase in number of HFIs. The presence of follicular keratinocytes was confirmed by BrdU labeling, S-phase cells in HFIs.	<i>Eclipta alba</i> extract and/or phytochemicals strongly displayed incomparability of hair growth promotion activity than others. Thus, the standardized <i>Eclipta alba</i> extract can be used as an effective, alternative, and complementary treatment against HL.
(15)	Reverse transcription polymerase chain reaction showed dose-dependent increases in VEGF mRNA levels on treatment with Rg3. Immunohistochemical analysis showed that expression of VEGF was up-regulated by Rg3 in human DP cells and in mouse HFIs. CD8 and CD34 were also up-regulated by Rg3 in the mouse HFIs.	It may be concluded that Rg3 might increase HG through stimulation of HF stem cells and it has the potential to be used in HG products.
(14)	At the 12 th week after initiation, the result of expert panel assessment of global photographs showed improvement. The hair density and hair thickness, measured by Follicscope 2.5, also showed a tendency of some improvement.	The efficacy of KRG in the treatment of AA and recommend KRG as a useful complementary food for gaining efficacy of treatment for AA was observed.
(24)	Treatment with ginsenosides Rb1 and Rd increased cell proliferation in both anagen and telogen of HFIs. Investigation of p63 demonstrated that up-regulation of p63 expression in the matrix and outer root sheath might be one of the mechanisms by which ginsenosides Rb1 and Rd promote cell proliferation in HFIs.	Ginsenoside promotes hair growth through p63 induction in follicular keratinocytes and indicates that ginsenosides Rb1 and Rd might be developed as a therapeutic agent for the prevention of HL.
(25)	FPG extract significantly increased the proliferation of DPCs in dose and time dependent manners. FPG extract also enhanced Bcl-2 expression and decreased Bax expression compared with control. Significant elongations of anagenphase during hair cycle after application of FPG were evaluated by photographical and histological observations	FPG extract improves the cell proliferation of human DPCs through anti apoptotic activation. Topical administration of FPG extract might have hair regeneration activity for the treatment of HL.
(19)	<i>Panax ginseng</i> , ginsenoside-Rb1 (G-Rb1) exhibited activity, but ginsenoside-Rg1 (G-Rg1) and -Ro (G-Ro) were ineffective. Additionally, 20(S)-ginsenoside-Rg3 (20(S)-G-Rg3) formed by the processing of red ginseng from the crude root of <i>Panax ginseng</i> <i>Panax ginseng</i> also showed HG promoting activity.	These results indicate that <i>Ginseng Radix</i> possesses hair growth promoting activity, and its bioactive components are partially attributable to the ginseng saponin components.
(27)	Ginseng administration before irradiation resulted in a suppression of apoptosis, as shown by a reduced number of cells stained with ISEL for fragmented DNA, both i.p. (0.3 mg/head) and p.o. (2 mg/ml of drinking water) treatment. Ginseng treatment increased the number of medullary cell per unit length as compared with the vehicle treated mice.	The water fraction of ginseng can exert a potent effect on the recovery of the HFIs by its combined effects on proliferation and apoptosis of the cells in the HF.

BrdU – 5-bromo-2'-deoxyuridine, NGS – Next-generation sequencing, ILI – Intra-lesional injection, KRG – Korean red ginseng, HFIs – Hair follicles, HG – Hair growth, HL – hair loss, Gy – gray, H – hematoxylin, E – eosin, ISEL – Isotopic *in situ* DNA end-labeling, GRe – ginsenoside Re, VEGF – Vascular endothelial growth factor, ISEL – Isotopic *in situ* DNA end-labeling, TGF- β – transforming growth factor beta, ERK – Extracellular-signal-regulated kinases, FPG – Fructus *Panax ginseng*, DPC – Dermal papilla cells.

Table 3: Results and conclusion of findings reported on the selected studies.

The utilization of natural products, as the medicinal plants is an ancient form of treatment of different diseases.²⁸ This consideration justifies more studies about the mechanism of action and the efficacy of these natural products to be validated scientifically.²⁹ Various medicinal plants have been used for care of the hair and they promote hair growth.³ It is also observed that about 0.43% and 0.19% of the articles with the keyword “*Panax ginseng*” are related to “hair growth” and “hair loss”, respectively (Table 1). Eight studies have reached the inclusion criteria to be analyzed (Figure 1).

In almost all of these investigations, the conclusions indicated that *Panax ginseng* or some chemical compound seemed to be effective in the treatment of hair growth.^{13,19,24,27} Begum et al²⁶ had shown some results about hair growth indicating possible effects of the various medicinal plant extracts, and among them, the *Panax ginseng*.

Due to, in general, their fewer side effects and better formulation strategies, the natural products are gaining popularity. *Panax ginseng* have stood out as a promising natural source with relevant effects in treatment of hair loss,^{13,15} despite the small number of publications in the PubMed database involving the keyword *Panax ginseng* AND “hair loss”, as shown in Table 1.

The chemical components of the plant used were similar in most of studies using the dried roots (Table 2), namely ginsenoside who is the major bio-active ingredients included in *Panax ginseng*. The aim of these selected works was mainly investigate the molecular and cellular mechanisms responsible for hair growth. As it was shown in Table 2, different experimental procedures were used.

The main findings of the selected papers reveal the importance of the *Panax ginseng* in improving hair growth. There-

fore it might be developed as a therapeutic agent for the prevention of alopecia. The studies on the hair follicle, demonstrate that it undergoes successive cyclic periods of growth, involving an (i) active growing phase (anagen) during which the previous hair is shed, (ii) a small transitional regressive phase (catagen) and (iii) a dormant resting phase (telogen),¹⁰ which allows the follicle to produce different types of hair in response to hormonal changes. Each strand of hair on the human body is at its own stage of development. Once the cycle is complete, it restarts and a new strand of hair begins to form.

The findings with *Panax ginseng* are important due to the fact that minoxidil and finasteride used for treatment of androgenic alopecia may have side effects.³⁰ The associated adverse events with the use of these synthetic compounds include erythema, scaling, pruritus, gynaecomastia, dermatitis, itching or skin rash. In consequence, due to these undesirable side effects, alternative products have been investigated to treat the alopecia, as the natural products.³¹

The current study has several limitations that must be considered in the interpretation of the findings in this review. It is suggested to take care in generalizing these results due to the analyzed publications have methodological variations concerning to the experimental procedure utilized, and design of the protocols. In addition, although we have tried to retrieve the articles following the selected keywords, it was not retrieved all the papers identified for inclusion, including articles that were not published in English and articles published in journals that were not indexed in the PubMed database.

The findings reported in this study are also relevant considering that the management of alopecia is a target of a steadily growing multi-billion dollar market worldwide. Great opportunities are associated with pharmaceutical hair loss management, but still there is no radical improvement in the availability of specific therapies. In this case, the results with *Panax ginseng* could be important to have alternative chemical products to manage the loss hair.

CONCLUSION

Putting together the findings described in this study and considering the results in the publications, it is possible to conclude and to suggest that the use of *Panax ginseng* could be suitable to try to improve the hair growth. However, it is important to consider the limited number of publications available in the PubMed involving searches evaluating the hair growth effect of *Panax ginseng*.

CONFLICTS OF INTERESTS: None.

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