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ANNURCA APPLE EXTRACT - A BREAKTHROUGH IN ALOPECIA PHYTOTHERAPY: A LITERATURE REVIEW

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ABSTRACT

Aim: Baldness is one of the most common cosmetic problems of our time. It negatively affects self-esteem and mood, which causes a deterioration in the quality of life. For years, scientists have been trying to discover a remedy to stop hair loss. The **aim** of this paper is to review the current reports about action of polyphenols contained in annurca apples on baldness available on PubMed and Google Scholar, including in vitro, animal, and clinical studies.

Methods: The research method was a critical analysis of scientific articles available in the Pubmed and Google Scholar databases. The team reviewed content from 2004 to 2023. paying special attention to the latest news. By systematizing and verifying the content, 24 most reliable publications were selected and the work was based on them.

Results: Current treatments have many disadvantages, ranging from low effectiveness to burdensome side effects. Therefore, it is worth looking into the achievements of natural medicine. A promising discovery seems to be an extract from the substances contained in the Annurca apple extract (AAE). This fruit holds high levels of polyphenols, including procyanidin B-2 (PCB2), which has been linked to hair growth promotion.

Conclusions: In this work, we checked the effectiveness of Annurca apple supplementation in the treatment and prevention of baldness in scientific sources. Available research shows that including annurca apple extract in the diet is a promising alternative to previously known baldness treatment methods. Further research and meta-analyses are needed to clearly assess the effectiveness of the preparations. However, it is a promising alternative to previously known treatment methods for baldness.

Keywords: annurca apple extract, annurca polyphenol extract, baldness, phytotherapy, procyanidin B-2.

INTRODUCTION

Hair loss, also known as alopecia, is a widespread cosmetic defect [11], known to significantly affect self-

esteem [2]. Its pathogenesis has been associated with various, mutually modulating factors (eg., genetics, hormonal changes, nutritional deficiencies, and stress) [20]. Many attempts have been made to find an effective treatment for alopecia. Currently, various pharmacological methods are known [14], depending on the etiology and type of alopecia. In the advanced stage, hair transplant procedures are used [12]. However, persistence and the numerous side effects of the proposed therapies are increasingly prompting research into alternative cures [17]. Recently, there has been growing interest in the potential benefits of natural remedies for hair loss [9], one of which is the annurca apple extract (AAE). The annurca apple, native to Southern Italy, is known for its high concentration of polyphenols, particularly procyanidin B2 (PCB2) [23]. Polyphenols are plant compounds with antioxidant properties, and PCB2 has been specifically linked to hair growth promotion. In the further part of the article, we will present in more detail the current state of knowledge about the anti-fall effect of AAE on hair.

METHODS

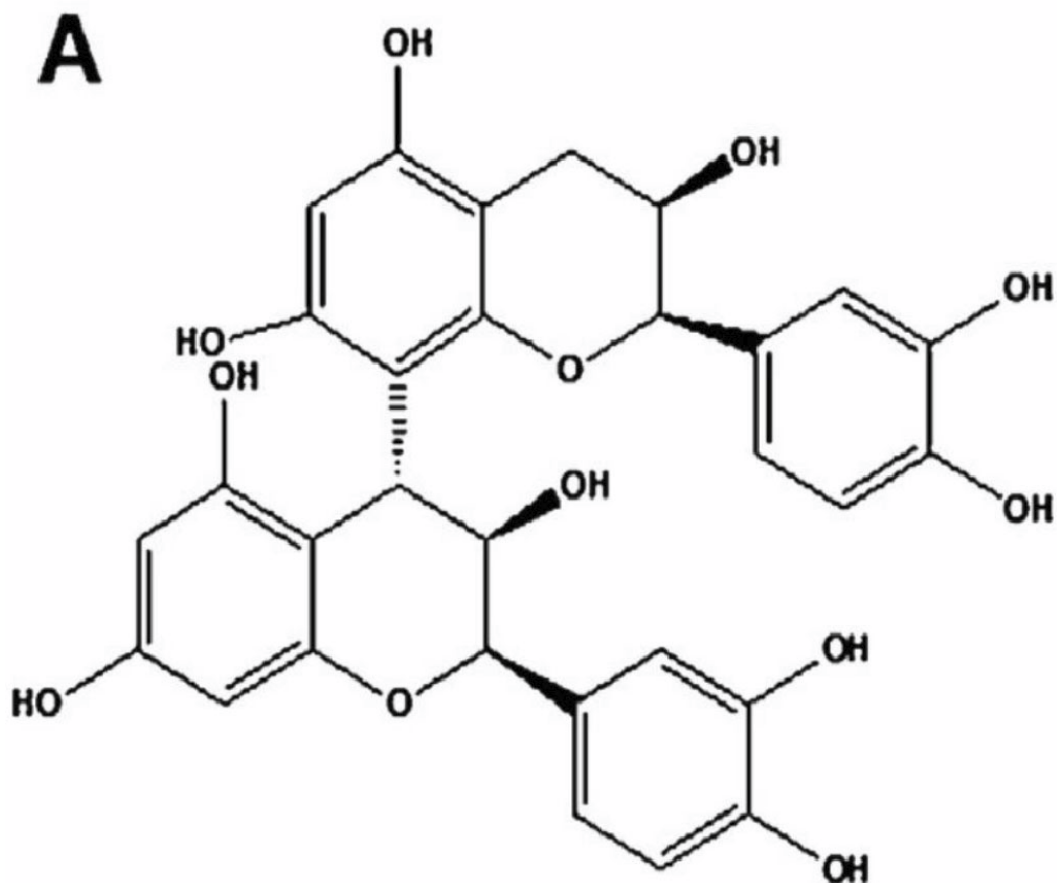
When collecting the database for this article, the team took into account the most recent and most reliable articles. 30 articles were selected and then subjected to detailed analysis and substantive evaluation. They were assessed in terms of relevance to the current state of knowledge, publication date, citation index and IF of the journal. Additionally, possible conflict of interest and financing of the work were taken into account. Of these, 24 articles were selected and became the basis for this publication.

CONTENT OF THE REVIEW

ANNURCA APPLE

The 'Annurca' apple, scientifically known as *Malus pumila* Mill. cv. 'Annurca', is a variety of apple native to the Campania region of Italy [21]. It is highly regarded for its unique characteristics and rich cultural history. It has been cultivated for centuries and is deeply rooted in local traditions, cuisine, and festivals [5]. It is protected by the European Union's Protected Geographical Indication (PGI) status [4], highlighting its importance and uniqueness. Thanks to the high content of polyphenols, catechin, epicatechin, and excellent taste [8], it is called the "queen of apples". This rich composition makes the annurca apple extract considered a dietary supplement supporting diseases of the cardiovascular [24], digestive [7] and immune systems [18]. It has also been shown to kill free radicals and lower the level of cholesterol in the blood [24]. In this article, we will pay special attention to substances that stimulate hair growth and inhibit their loss. One of these stores is PCB2, a flavonoid known for its wide action.

PROCYANIDIN B2



(A) The chemical structure of procyanidin B2 (PCB2) [9]

Procyanidin B-2 (PCB2) is a natural flavonoid compound that belongs to the class of proanthocyanidins. It is commonly found in various plant sources, such as grape seeds, cocoa beans, and apples [3]. Numerous scientific studies have investigated the potential health benefits of PCB2 i.a. its strong antioxidant properties. Oxidative stress plays an important role in the pathogenesis of various chronic diseases, including cardiovascular diseases, cancer, and neurodegenerative disorders [16]. By neutralizing free radicals, PCB2 may contribute to reducing the risk of these conditions. Moreover, PCB2 has demonstrated antimicrobial properties [19]. It may inhibit the growth of certain bacteria, fungi, and viruses, suggesting its potential in combating infections. It is presumed that by inhibiting a protein called transforming growth factor-beta 1 (TGF- β 1), PCB2 may prolong the anagen phase, leading to longer hair growth [13]. Inflammation can damage hair follicles and inhibit hair growth [22]. PCB2 has anti-inflammatory effects, which can help to protect hair follicles and promote hair growth [3].

PRESENTATION OF PREVIOUS RESEARCH RESULTS

1. *In vitro* studies

The *in vitro* study involved the use of human keratinocytes, the primary cell type found in the outermost layer of the skin. The cells were treated with annurca apple polyphenolic extract and the effects on keratin expression and accumulation were observed. Keratin is a key protein in hair and skin, contributing to their structure and function. The results showed that the extract supplementation led to a significant upregulation of keratin expression, resulting in keratin accumulation within the cells [23].

2. *In vivo* studies

One study's results showed that annurca apple polyphenols could indeed stimulate keratin production in hair follicles [1]. This was achieved by inhibiting the pentose phosphate pathway (PPP) and amino acid oxidation. The PPP is a metabolic pathway parallel to glycolysis and plays a significant role in producing NADPH, serving as a cofactor in anabolic reactions, and ribose 5-phosphate, a component of nucleotides. By inhibiting this pathway, the polyphenols could redirect the metabolic flux towards the production of keratin. In addition, the polyphenols also inhibited amino acid oxidation. This may cause more amino acids to be available for keratin synthesis, further promoting hair growth.

Another study was performed on mice, which were orally administered AAE once a day for 21 days. The

results revealed a significant improvement in the overall condition of hair in mice treated with the extract. Furthermore, the expression levels of genes responsible for encoding hair growth factors, including vascular endothelial growth factor A (VEGF-A) and fibroblast growth factor 7 (FGF-7), were measured using quantitative reverse transcription polymerase chain reaction (qRT-PCR). The study showed that the expression of genes encoding both growth factors significantly increased in the group treated with the extract. Moreover, the study confirmed that treatment with AAE suppressed the expression of the gene encoding the enzyme 5 α -reductase type 1, which is involved in the conversion of testosterone to dihydrotestosterone (DHT) and is responsible for hair loss. The levels of cytokeratin 5 and 10 proteins, which are epithelial cell markers, essential for the structural integrity of hair, were also analyzed histologically. The levels of both proteins were increased in the skin tissues of those in the extract-treated group [15]. In addition, the results of the study also presented a significant increase in the number of hair follicles in the anagen phase (the active growth phase of hair follicles) compared to the control group.

This suggests that AAE may stimulate the transition of hair follicles from the telogen phase (the resting phase) to the anagen phase, thereby promoting hair growth [15]. The researchers also observed an increase in the expression of β -catenin and lymphoid enhancer-binding factor-1 (LEF1) in the dermal papilla cells of the treated group. These proteins are known to play a crucial role in hair development and growth cycle. According to the results of this research, it can be supposed that the extract stimulates hair growth also at the molecular level [15].

3. Clinical research

The clinical study involved a double-blind, placebo-controlled clinical trial with 250 subjects, both men and women, suffering from pattern baldness. The subjects were randomly assigned to receive either an oral supplement of AAE or a placebo for two months. The effects on hair growth, density, and weight, and keratin content were assessed. The results of the study showed that AAE supplementation led to significant improvements in hair growth and skin health. The subjects who received AAE showed an increase in hair density and weight, and an increase in keratin content of about 35% more than the untreated group. The study confirmed that in addition to affecting the condition of the hair, AAE also has a positive effect on the skin.

[23].

The latest randomized double-blind placebo-controlled clinical trial from 2023 on patients with androgenetic alopecia showed the effectiveness of AAE in stimulating growth and inhibiting hair loss [5]. The study included 80 people with alopecia, divided into 2 groups: 40 people took the extract as a nutraceutical supplement and 40 people took a placebo. Each group received a 180-day treatment, taking 2 capsules a day. After this period, the volunteers did not take any supplements for 30 consecutive days. The supplement significantly affected hair loss: hair density and weight increased significantly, and hair loss noticeably decreased over time ($p < 0.001$). In addition, its pleasant taste and good dermal and gastric tolerance of the product were observed, confirming its compliance with use: the product had no significant effect on gastrointestinal disturbances and abdominal pain ($p = 0.41$ and $p = 0.25$, respectively).

DISCUSSION AND CONCLUSION

The described properties of annurca apple extract are not yet well known, and there are relatively few reliable scientific reports available on the influence of AAE on the problem of baldness. Nevertheless, dietary supplements based on AAE containing PCB2 seem to be promising. They can effectively support hair growth and improve skin quality. Regular supplementation has been found to increase the density, weight and keratin content of hair. The data published so far also suggest that the use of AAE may be a real alternative to current methods of treating pattern baldness because it does not cause side effects associated with pharmaceutical therapies, such as sexual dysfunction, cardiovascular, immunological and endocrine disorders.

Additionally, preparations derived from annurca apples can be a supporting element of more complex therapies. Further research is ongoing to better understand the molecular basis of procyanidin-induced growth-promoting effects at the skin level. While research into AAE and its potential effects on hair loss is promising, it should be noted that this research is still in its early stages. Further comprehensive studies are needed to confirm these findings and determine the optimal dose and form of administration for the treatment of hair loss. Nevertheless, AAE, known for its high PCB2 content, shows potential as a natural alternative in the fight against hair loss. Additional research will help better understand its effectiveness, optimal dosing, and safety profile. The possibility of artificial synthesis of compounds that determine hair growth, including PCB2, would be important to increase availability and reduce production costs. In artificial industrial production, it would be possible to control the composition of products more precisely and increase the content of active substances. Variable weather and breeding conditions influence the health properties of annurca apples. Artificial synthesis would solve this problem.

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