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# Herbal Hair Nutrients

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## Current State of Science Review focusing on characterization, efficacy and safety of *Polygon(i)um Multiflorum Thunb* for healthy hair

By Claudia Kelley, MPH, MS, HD, RD, CDE, CNSD\*\*  
Assistant Professor Clinical Nutrition Science; Southern California University of Health Sciences, Whittier CA 90604  
Nutrition, Dietetics and Complementary Medicine Consultant

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\*\*For reprint requests, contact [skckelley@comcast.net](mailto:skckelley@comcast.net)

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# *Polygonium multiflorum*

## Overview

*Polygonium multiflorum* root tuber is used in Traditional Chinese Medicine (TCM) as a tonic and an anti-aging remedy, particularly for hair loss and premature graying of hair. It is also known by the Chinese name He Shou Wu (Heshouwu) or Fo-Ti. Over the centuries, its reputation has bordered on the mythical for its power to produce longevity, increase vigor and promote fertility.

In recent years, preparations of the *Polygonium multiflorum* root have also become popular in the Americas, especially as ingredient of dietary supplements promoting hair growth. This application is not only supported by experimental studies based on the biological mode of action of its individual constituents, but also by clinical research demonstrating the efficacy and safety of *Polygonium multiflorum* root extract in the prevention of age-related hair loss while improving hair thickness and appearance.

## Introduction

### *Polygonium multiflorum*

The herb *Polygonium multiflorum* belongs to the *Polygonaceae* family, which includes approximately 150 different species of weedy herbs native to northern temperate regions.

The dried root of *Polygonium multiflorum* (PMr) is well known as *Heshouwu*, or in the U.S., as *Fo-Ti*. It is considered one of the most popular traditional medicinal herbs in China, and is officially listed in the Chinese Pharmacopoeia.<sup>1</sup> It is frequently used as a tonic and purgative in China and Japan. The main active constituents of the herb have been reported to be hydroxyanthraquinones, stilbenes, other phenolic compounds and their glycosides.<sup>2</sup>

PMr preparations have a bitter, astringent taste and act on the liver, heart and kidneys channels.<sup>3</sup> They have been used traditionally for rheumatoid arthralgia, itching, skin infection, aching of the loins and knees, traumatic injuries, and as anti-aging remedy, particularly for hair loss and premature graying of hair. Over the centuries, PMr's reputation has bordered on the mythical for its power to produce longevity, increase vigor and promote fertility.<sup>4</sup>

Indeed, preclinical studies have shown that PMr may promote blood flow to the brain,<sup>5</sup> thereby promoting the delivery of nutrients and hair-growing factors.

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**Table 1: Summary of Uses for *Polygonium multiflorum***<sup>6</sup>

○ Aging retardant	○ Interferon inducent
○ Antidepressant	○ Lymphatic decongestant
○ Antilipemic	○ Lymphocyte stimulant
○ Antioxidant	○ Musculoskeletal restorative
○ Cardio protector	○ Premature graying and hair-loss
○ Detoxicant	○ Reproductive restorative
○ Immune enhancer	

### **Hair Loss: Prevalence, Biology and History**

Hair loss has been attributed to aging, but may also be caused by hereditary factors, disease, or scalp disorders. It is estimated to effect more than 80% of American men and 25% of American women.<sup>7</sup>

Throughout history, people have sought remedies for hair loss. In Assyria, in 1500 BCE, common law dictated hairstyles according to social position and occupation. Baldness, considered an unsightly human defect, was hidden by wigs. Ancient Egyptian remedies included chopped romaine lettuce applied to the scalp and an ointment made of juniper berries (*Juniperus communis*) and two unidentified plants kneaded together into a paste with oil and heated. Hippocrates applied pigeon dung to his scalp to try to "sprout" hair.<sup>7</sup>

The first professional barbers shops opened in Rome around 303 BCE. Roman cures for hair loss included perfumed ointments made from crushed myrtle berries, bear grease, and hippopotamus fat; salves containing the urine of young foals; and liniments made from sulfur and tea. By the 1790s, powdering hair with heavily scented bleached and pulverized wheat flour was considered stylish. Members of the upper classes in colonial America wore powdered wigs to hide their receding hairlines.<sup>7</sup> American and European folk medicine recommended the use of rosemary (*Rosmarinus officinalis*), sage (*Salvia officinalis*) and olive oil (*Olea europaea*) scalp massages to promote hair growth.<sup>8</sup>

Hair is the fastest growing tissue in the human body: the average rate of growth is about one-half inch a month. Optimal hair growth occurs from age 15 to 30, slows down from age 40 to 50, and is progressively lost by about age 50. Most men lose hair to some degree by age 35 and are more likely to lose their hair than are women. The life cycle of hair is divided into anagen (active growth), catagen (transitional), and telogen (resting) phases. On a healthy scalp, 90% to 95% of hair follicles are growing, less than 1% is undergoing involution, and 5% to 10% are resting. The prognosis for encouraging hair growth is favorable if treatment begins before the growth stops altogether.<sup>7</sup>

Many genes appear to be involved in hair loss.<sup>9</sup> If even only one parent has it, the odds are in favor of the child eventually experiencing hair loss. Although women carry the genes that determine pattern baldness just as men do, they do not usually become bald themselves. Rather, they pass on the characteristic to their sons.<sup>10</sup>

## Biochemical Background of Hair Loss

Hair loss affects 80 percent of American men. Male pattern baldness (hair loss at the top of the head, called *androgenetic alopecia*) appears most frequently in men over age 40 and is considered a normal part of aging. Male pattern hair loss, which often begins during early adulthood, eventually results in a receding hairline or balding at the crown of the head. Androgenetic alopecia is believed to be due to the conversion of testosterone into dihydrotestosterone (DHT).<sup>10,11,12</sup>

Hair loss among women is usually less severe than in men and typically occurs over the crown of the scalp. Approximately two-thirds of women experience hair loss after menopause. The extent of the hair loss is determined by hormones, heredity, vitamin deficiencies, and age.<sup>7,13,14</sup>

Several diseases, including prolonged infections, may cause baldness. A gradual loss of hair can be caused by stress, malnutrition, endocrine disorders, drug poisoning, and other diseases. Hair loss caused by disease can be temporary or permanent, depending on the severity and duration of the disease. Certain drugs (antidepressants, blood thinners, hypertension and arthritis medications, and anabolic steroids) may also cause hair loss.<sup>15,16</sup> A growing concern about the side effects of pharmaceutical drugs has led to an increased interest in herbal medicine.

### The Sex Hormone Connection

Androgens, such as testosterone or DHT, are the main regulator of normal human hair growth. *Androgenetic alopecia* is believed to be due to the conversion of testosterone into DHT by the enzyme 5-alpha-reductase. Genetics determines the age at which hair follicles begin producing DHT. Once formed, DHT seems to facilitate male hair loss—especially in the front or top of heads.<sup>17</sup> On the other hand, hair loss in women seems to be associated by a relative lack of estrogen.<sup>14</sup>

### From Testosterone to Dehydrotestosterone (DHT): A Common Process in Aging Men

Testosterone is converted into its water-soluble form DHT by the enzyme 5-alpha-reductase. DHT is responsible for secondary male sex characteristics, such as larger muscles and facial hair. However, the formation of DHT has also been attributed to male pattern hair loss and human benign prostatic hyperplasia (BPH), which are frequently observed in aging men. Not surprisingly, 5-alpha-reductase inhibitors have received clinical approval for the treatment of BPH and androgenetic alopecia.<sup>18,19</sup>

### Estrogen Protection Against Hair Loss in Women

Hair loss among ageing women—while not as pronounced as in men—is common, especially with the onset of undergoing menopause. The reason for hair thinning in females appears to be unrelated to DHT-levels, as they have been reported to decline with age in women.<sup>14,20</sup> Instead, hair loss in women seems to be associated with a relative lack of estrogen.<sup>11,13,14,21</sup>

Several studies have shown that administration of estrogen (combined with or without certain nutrients) to the women affected, leads to symptomatic improvement, as seen by fewer numbers of hairs lost and increased subjective hair thickness.<sup>14,22</sup>

Pre-clinical studies suggest that the consumption of phytoestrogens, such as those found in soy or PMr,<sup>23</sup> may also have beneficial effect on preventing hair loss.<sup>24</sup>

## ***Polygonium multiflorum* – Studies Investigating its Potential**

### **Phytochemical Composition of *Polygonium multiflorum***

The analysis of PMr's biologically active ingredients reveals that it contains anthraquinones and stilbene derivatives. The anthraquinones found in the root are emodin, physcion, chrysophanol, rhein and chrysophanol anthrone; and the stilbene compounds are 2,3,5,4'-tetrahydroxystilbene 2-O-B-d-glucopyranoside and its 2''- and 3''-O-monogalloyl esters.<sup>25</sup> Additionally, gallic acid, 3-O-galloyl procyanidin B-2, catechin, epicatechin, 3-O-galloylcatechin, 3-O-galloylepicatechin and a hydroxylated acetophanone glycoside named *polygoacetophenoxide* have been isolated. The root also contains about 3.7% of lecithin.<sup>25,26</sup>

Raw PMr seems to possess a higher concentration of the anthraquinone constituents than cured products.<sup>27</sup> These constituents have stimulant laxative effects, which probably accounts for its use in constipation.<sup>28</sup>

### **Pre-Clinical Research with *Polygonium multiflorum***

Due to its popularity in Asian countries, a lot of research has been published there; however, so far, only few studies have also been published in English literature:

Some preliminary evidence suggests that the isolated stilbene glycoside constituents in raw PMr may have liver protectant effects, including inhibition of alanine aminotransferase (ALT) and aspartate aminotransferase (AST).<sup>29</sup> However, the anthraquinones in PMr may subsequently be converted in the gastrointestinal tract into anthrones and cause hepatitis.<sup>30,31</sup>

On the contrary, scientific research with the dried extract of PMr has widely demonstrated its antioxidative effect. In experimental studies, the administration of PMr not only protected isolated rat heart mitochondria against lipid peroxidation,<sup>32</sup> but also showed protective effects against carbon tetrachloride induced hepatotoxicity in rats.<sup>33</sup> Dried PMr also showed evidence it might increase the levels of superoxide dismutase (SOD), serotonin, norepinephrine, dopamine, and decrease levels of monoamine oxidase-B (MAO-B);<sup>29</sup> these are believed to be markers for anti-aging effects. Other authors also observed prominent antioxidative properties, in particular with regard to cardiovascular diseases.<sup>33,34,35</sup> The cardio protective effect of PMr is likely due to Ca<sup>2+</sup>-ATPase inhibitory activity,<sup>34</sup> but might also be attributable to its beneficial effects on blood lipids, namely by increasing high-density lipoprotein (HDL) cholesterol, reducing total cholesterol, free cholesterol, triglycerides, and retard atherosclerosis.

Other research suggests that PMr possesses pronounced anti-inflammatory properties,<sup>36</sup> and promotes blood flow to the brain,<sup>5</sup> which facilitates the delivery of nutrients. In animals, 2 weeks of PMr administration also seemed to be

neuroprotective, as evidenced by a reduction in ischemic damages seen in animals with artificially induced stroke.<sup>5</sup> Recent in-vitro evidence also suggests PMr has approximately 0.3% of the estrogen activity of natural estrogen (17-beta-estradiol) and is approximately equivalent to the estrogen activity found in soy and red clover.<sup>37</sup> Based on the observations that PMr was able to increase serum ceruloplasmin levels, reduce thymus gland atrophy, and inhibit atrophy of adrenal glands, while enhancing nonspecific and cellular immunity, and antagonizing the immunosuppressive effects of prednisolone or hydrocortisone,<sup>29</sup> its use as vitality agent may be supported.

Research in other areas, such as its efficacy for other age-related disorders like memory loss or atherosclerosis, appear promising.

Table 2: Available research evidence supporting the following properties of *Polygonium multiflorum*:

▪ Antioxidant	▪ Hepatoprotectant
▪ Anti-inflammatory agent	▪ Hypotensive agent
▪ Anti-ischemia agent	▪ Agent for neurodevelopmental disorders
▪ Blood sugar lowering agent	▪ Nootropic agent
▪ Cardio protectant	▪ Phytoestrogen
▪ Cholinergicum	

### **Clinical Research with *Polygonium multiflorum* for Healthy Hair**

In a double blind, placebo-controlled study lasting over 6 months, a standardized extract of PMr was able to demonstrate its beneficial effect on hair quality. The study employed 33 pre- and postmenopausal women (40-60 years of age) and investigated the effect of PMr (n=26) or placebo (n=7) on hair thickness, perceived appearance and hair loss.<sup>38</sup> After establishing baseline scores, the participants were asked to take PMr or a dummy pill twice daily (am and pm) for 6 months. After taking the product for 3 and 6 months, the surveys administered to the active treatment revealed a significant improvement of hair loss (97%) and perceived hair appearance (76.9%). Additionally, 77% of women in the PMr-group reported “thicker hair”, which was rated as “significant” and “dramatic” improvement. This finding was confirmed by the independent evaluation of hair pictures taken at baseline and trial end, which showed that more than 18% of the women who received PMr demonstrated improvements of equal or more than “2”. Since only minor side effects were reported by some women, it appears that the administration of PMr for 6 months is helpful for improving hair growth and quality in pre- and postmenopausal women.

In another study employing forty-eight 30-60 year old men (n=24) and women (n=24) with differing origins of hair loss (age-related, stress- and medication induced, and postpartum) received a standardized extract of PMr twice daily.<sup>39</sup> After 1 month of treatment, 91% of men and 87% of women reported symptomatic improvement. Additionally, none of the study participants reported any side effects during the treatment period.

## **How does *Polygonium multiflorum* contribute to Promoting Hair Growth?**

PMr has long been used in Traditional Chinese Medicine (TCM) as an energizing agent, as a tonic or anti-aging remedy, particularly for hair loss, hair thinning and premature graying of hair. According to TCM, PMr is believed to strengthen the kidney and liver, tonify the blood, work as a mild laxative, strengthen cartilage and bone, regulate blood pressure, prevent hardening of the arteries and blackens hair.<sup>3,7</sup>

Some authors note that PMr has shown promise as a hair and color restorative and is capable of inducing terminal hair to grow instead of vellus hair (the fine baby hair growth associated with use of *minoxidil*).<sup>7</sup> Indeed, recent studies show that PMr or its phytochemical constituents possess several biological properties to prevent age-related hair loss and promote thick, vibrant hair growth in men and women.

### ***Polygonium multiflorum* and 5-Alpha-Reductase**

Several natural components have been reported to possess alpha-reductase inhibiting properties.<sup>40,41</sup> For example, extracts from the herb Saw Palmetto have long been known to possess 5-alpha-reductase inhibiting properties.<sup>42,43</sup>

In fact, experimental studies showed that the phenolic substances contained in PMr appear to be very potent inhibitors of this particular enzyme,<sup>44,45</sup> which is responsible to convert testosterone to DHT and therefore, the purported cause of hair loss in men.<sup>46</sup>

### ***Polygonium multiflorum* and Estrogenic Activity**

As indicated earlier, a relative lack of estrogen appears to be primarily responsible for hair loss in women. Thus, it is not surprising that the use of phytoestrogen components has been shown to improve and prevent hormone-related hair loss.<sup>47</sup>

Indeed, several studies have demonstrated the estrogenic properties of PMr<sup>48,49,50</sup> and its constituents.<sup>51</sup>

### ***Polygonium multiflorum* and Hair Nutrient Provision**

Newest research with PMr extracts has shown that it may possess neuroprotective and memory-enhancing effects.<sup>52,53,54,55</sup> Animal studies also suggest that its use might be beneficial for the prevention of Alzheimer's disease.<sup>56,57</sup> One possible reason for PMr's nootropic effect might be related to its antioxidative properties,<sup>58,59,60</sup> but also the observed improvement of blood flow—and therefore, nutrients—to the brain and the facilitation of detoxification processes might account for the underlying mechanism of action.

### **Other Possible Mechanisms of Action**

Studies involving the stilbene components of PMr demonstrated inhibitory effect on the enzyme breaking down the hair and skin pigment *melanin*,<sup>61</sup> which might prevent hair graying.

Biochemical investigations have determined that nitric oxide (NO) contributes to DHT-mediated hair-loss,<sup>62</sup> which might be prevented by the antioxidative compounds found in PMr.

### **Dosing and Reported Side Effects**

Clinical studies to promote hair growth have utilized a daily dose of 1300mg-1800mg standardized PMr extract (with or without the addition of other nutrients). During the treatment period of 1-6 months, only mild side effects were reported.<sup>38,63</sup>

However, non-standardized PMr products may show other undesirable effects, which has become more obvious since the introduction of the voluntary reporting of dietary supplement related side effects.

### **Safety and Toxicity Data**

The major constituents of PMr are polyphenols and anthraquinones. After intestinal metabolism, anthraquinones are transformed in anthrones, which are highly reactive substances and may cause hepatotoxicity when absorbed.<sup>64,65,66,67,68</sup>

### **Hepatotoxicity Reported with the use of *Polygonium Multiflorum*-Containing Products**

Several cases of hepatitis have recently been described in the medical literature, which may have been attributed to the use of PMr. As indicated earlier, PMr is known in the U.S. as Fo-Ti or *Heshouwu*, and available in different products, such as dried powders, standardized extracts, or a combination of the two with and without added herbs or nutrients.

As of September 2006, five reports of suspected adverse reactions associated with PMr have been published, all of which involved the liver.<sup>30,31,69,70,71</sup> Most patients reported taking PMr for hair loss: four patients had taken a proprietary Chinese medicine prepared from PMr,<sup>31</sup> and one patient consumed a standardized extract blend. All the patients had recovered or were recovering after stopping product use.

*Note: The herbal proprietary blend and the product containing a standardized PMr extract both contain certain amounts of raw PMr, which might account for the adverse events (see: "Quality Products in the Market Place" section).*

### **Possible Interactions with Medications and Other Dietary Supplements**

Although, so far, no interactions with other herbs or dietary supplements have been reported with PMr, some potential drug interactions are theoretically possible. Due to the hypoglycemic property of PMr and its constituents,<sup>27,72</sup> people taking insulin or oral hypoglycemic agents, such as glimepiride (Amaryl), glipizide (Glucotrol), glyburide (Diabeta, Micronase), tolazamide (Tolinase), tolbutamide (Orinase), should exercise caution and monitor their blood sugar readings very closely.

Due to the potential laxative effect of PMr, its concomitant use with other laxatives may increase the risk of fluid and electrolyte depletion.<sup>73,74</sup> This holds especially true for potassium.<sup>29</sup> Theoretically, the overuse of anthraquinone laxatives (e.g., PMr) might increase the risk of hypokalemia and *digoxin* cardio-toxicity.<sup>73,74</sup>

### **Other Safety Considerations and Contraindications**

Due to the anthraquinone content of PMr and their stimulant laxative effect, the herb should be avoided by people with frequent diarrhea episodes, acute intestinal inflammation (Crohn's disease, ulcerative colitis, appendicitis) or obstruction, ulcer, abdominal pain of unknown origin, nausea, and vomiting. Patients with a known (or a history of) liver disease should exercise caution due to the above hepatotoxicity reports.

Since safety data are lacking, it is also advisable for pregnant and lactating women to avoid the herb—especially since anthraquinone constituents may cross into breast milk and might cause loose stools in some breast-fed infants.<sup>74</sup>

### **Quality: Products in the Market Place**

PMr is either used raw (uncured) or processed (cured) by repeated steaming and sun drying. Raw PMr contains the anthraquinone derivatives, chrysophanol and emodin, along with a small amount of rhein. These constituents have stimulant laxative effects, which probably accounts for its use in constipation;<sup>28</sup> however, they may also possess hepatotoxic properties.<sup>65,75</sup> Curing PMr reduces these constituents by 42-96%.<sup>27</sup> Therefore, reputable manufacturers are treating their PMr with heat and steam under 60~70 centigrade during production for extraction and sterilization processing.<sup>76</sup>

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