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Original Research Article

Data mining on varieties, therapeutic uses and medicinal characteristics of Traditional Chinese Medicine preparations for treating hair loss

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Abstract

Purpose: *To review the varieties, therapeutic uses, and medicinal characteristics of traditional Chinese medicine (TCM) preparations for treating hair loss, and to provide a reference for research and development of new drugs.*
Methods: *For this review, literature from the last 50 years pertaining to the treatment of hair loss via TCM were collected mainly from China National Knowledge Infrastructure database and Wanfang Data Resource System database. Information on Chinese traditional patent medicines and ethnomedicines for treating hair loss was drawn from books.*
Results: *A total of 322 preparations were identified, including 135 preparations made by medical institutions, 108 Chinese traditional patent medicines, 60 preparations produced by doctors themselves, and 19 ethnomedicines. The forms of dosage included decoctions, pills, capsules, tablets, granules, tinctures, liniments, and powders. These preparations are traditionally used in the treatment of skin and subcutaneous tissue diseases. A total of 400 medicinal materials were used in preparations, including 339 from plants, 40 from animals, 14 from minerals. The most commonly used Chinese medicinal materials in order of frequency were Rehmannia glutinosa (Gaertn.) DC., Fallopia multiflora (Thunb.) Haraldson, Angelica sinensis (Oliv.) Diels, Ligustrum lucidum W.T. Aiton and Ligusticum chuanxiong Hort.*
Conclusion: *TCM preparations for treating hair loss are abundant in variety. They are mainly decoctions, and primarily botanical medicinal materials. Most of the preparations are composed of Chinese medicinal materials for 'toning the kidneys' and 'nourishing the liver'. They are used mainly in the treatment of seborrheic alopecia and alopecia areata.*

Keywords: *Hair loss, Traditional Chinese medicine, TCM, Preparation, Variety characteristics, Medicinal, Data mining*

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INTRODUCTION

Pathological hair loss is a common and frequently occurring dermatological abnormality. It is refractory and may take a variety of forms, including seborrheic alopecia, alopecia areata, and total alopecia. Though not life-threatening, it can be seen at any age, and most commonly among the young and middle-aged. Its recurrence and lingering and refractory

characteristics may significantly alter a person's physical appearance, leaving them great mental trauma and anguish. Normally, sebum is secreted by the sebaceous glands through the hair follicles. When sebum secretion increases and accumulates in large quantities, it will cause a mechanical compression on the root of the hair, which consequently affects hair growth. What's more, a large amount of sebum secretion will impede the normal growth of the hair follicle orifice epidermis, resulting in excessive keratosis of the hair follicle orifice, the formation of embolism, and eventually hair loss [1]. Today, hair loss is becoming increasingly common, and those affected tend to be younger. Thus, people are paying more attention to preventing hair loss.

Seborrheic alopecia and alopecia areata are the two common types of hair loss. Seborrheic alopecia has a genetic component and is androgen-dependent. It falls into the category of "insect bite alopecia" in TCM and occurs mostly in males and rarely in females, usually between the ages of 20 and 30 [2]. The main clinical symptoms are polydandruff, greasy hair, and marked itching. At the same time, the hair on the patients' head and forehead gradually becomes thinner, and with hair loss eventually appearing. Patients generally pay no attention to the early stage of seborrheic alopecia nor to later hair follicle atrophy, making treatment more difficult [3]. Alopecia areata is a sudden, non-inflammatory, non-scarring type of hair loss known as "demon-licked head" in TCM. It manifests in localized, circular, and patchy hair loss with clear borders and is related to stress and immune abnormalities. It typically lasts a long time and recurs easily. In addition, it has a serious impact on the psychology of those affected [4].

The most common modern medicines and methods for clinical treatment of hair loss include minoxidil, finasteride, dutasteride, ketoconazole, prostaglandins, laser therapy, and hair transplantation [5]. Although they all have a certain level of effectiveness, the chance of recurrence is pretty high. Traditional Chinese medicine, with a history of thousands of years' practice, has proved to be quite effective in treating hair loss. As early as in Qin, Han, and Sui dynasties, a basic understanding about etiology and pathogenesis of hair loss was already formed. The detailed recording of hair loss treatment can be traced back to Kuangyin Zhao, the founding emperor of the Song Dynasty [6].

Traditional medicinal preparations enjoy a good reputation of rich varieties, definite curative effect, easy administration, high quality and low price in the long history of its development. In this paper, the traditional medicinal preparations include preparations of medical institutions, Chinese traditional patent medicines, preparations produced by doctors themselves, and ethnomedicines. Preparations of medical institutions are preparations designed and used by medical institutions with approved fixed prescription according to their clinical needs. Chinese traditional patent medicines are made from herbs under the guidance of TCM theory as a means of preventing and treating diseases. They are processed into certain dosage forms according to prescription and preparation technology. Preparations produced by doctors themselves are empirically tested prescriptions prepared by physicians on the basis of abundant clinical experience. Finally, ethnomedicines are used by ethnic minorities under the guidance of the theory and practice of their own traditional medicine.

In recent years, with the State's support for TCM, Chinese medical culture has been well disseminated. As a pillar industry of TCM industry, Chinese traditional patent medicines have been well used in the treatment of various diseases. This essay summarizes and analyzes the past 50 years' research on the varieties, therapeutic uses, and medicinal characteristics of TCM preparations for treating hair loss, hence providing a reference for research and development of new drugs.

METHODS

From the databases of *China National Knowledge Infrastructure database*, *Wanfang Data Resource System database*, and other data resource systems, 221 TCM preparations for clinical treatment of hair loss were collected from medical literature spanning the past 50 years. Other 85 Chinese traditional patent medicines and 16 ethnomedicines for treating hair loss were collected from the *Pharmacopoeia of the People's Republic of China (Part 1 of the 2015 edition), Departmental Standard, Newly Edited National Chinese Traditional Patent Medicines, Preparations of Ethnic Medicine Formulas*, *Drug Standards of the Ministry of Health of the People's Republic of China: Uighur Medicine Fascicule*, *Drug Standard of the Ministry of Health of the People's Republic of China: Tibetan Medicine*, *Prescriptions of Dai Medicine*, and *Tibetan Medicine Standards*. Excel software was used to set up a database in order to analysis the varieties, therapeutic uses, and medicinal characteristics of these 322 preparations.

RESULTS

Variety characteristics

Names of preparations

A total of 18 naming methods are used, 43.79 % of which are "main treatment + dosage form," such as *Zhiyi Tuofakang* Electuary; 16.46 % are "efficacy + dosage form," such as *Bushen Yangxue* Capsule; 13.66 % are "main drug name + dosage form," such as *Tianma Shouwu* Tablet; 4.35 % are "main drug name + main treatment + dosage form," such as *Shouwu Shengfa* Pill; and 3.42 % are "main drug name + efficacy + dosage form," such as *Qitian Fuzheng* Capsule. The names of most preparations are related to the main treatment and efficacy thus they are clear and easy to remember, but it is easy to find the same or similar names elsewhere; for instance, "*Shengfa* Decoction" appears eight times, and "*Shengfa* Drink" also appears eight times. These identical or similar names come mainly from preparations of medical institutions and preparations produced by doctors themselves. The data are shown in Table 1.

Categories of preparations

Among the 322 preparations, 135 (41.93 %) are preparations from medical institutions, 108 (33.54 %) are Chinese traditional patent medicines, 60 (18.63 %) are preparations produced by doctors themselves, and 19 (5.90 %) are ethnomedicines. Chinese traditional patent medicines account for a small portion, the reason for this perhaps being that hair loss has not been given adequate attention by practitioners of Chinese medicine. However, preparations from medical institutions account for the majority. This can provide a basis for the follow-up development of new Chinese traditional patent medicines.

Dosage forms

A total of 19 dosage forms are identified, including decoctions (34.78%), pills (13.66%), capsules (9.32 %), tablets (7.14 %), granules (6.83 %), tinctures (5.28 %), liniments (4.66 %), and powders (4.04 %). For the treatment of hair loss, modern medicine generally suggests external dosage forms, while traditional Chinese medicine prefers oral administration.

In traditional Chinese medicine, it is believed that the health of one's body can be improved by adjusting one's internal constitution. Decoctions are the most widely used dosage forms. It is easy to prepare, quickly absorbed, and can quickly exert its efficacy, which together fully embody the characteristics of TCM. The data are shown in Table 2.

Table 1: Statistics of naming characteristics of preparations for treating hair loss

Naming characteristics	Number of preparations (n)	Percent (%)
Main treatment + dosage form	141	43.79
Efficacy + dosage form	53	16.46
Main drug name + dosage form	44	13.66
Main drug name + main treatment + dosage form	14	4.35
Main drug name + efficacy + dosage form	11	3.42
Fufang + main drug name + dosage form	10	3.11
Total number of medicinal flavors + main treatment + dosage form	9	2.80
Number of medicinal flavors of characteristic medicines + name of characteristic medicines + dosage form	8	2.48
Use of exaggerated, boastful, unrealistic terms	8	2.48
Fufang + main drug name + main treatment + dosage form	5	1.55
Zhongyao + dosage form	5	1.55
Others	4	1.24
Total number of medicinal flavors + main drug name + dosage form	3	0.93
Number of medicinal flavors of characteristic medicines + name of characteristic medicines + main treatment + dosage form	2	0.62
Total number of medicinal flavors + dosage form	2	0.62
Fufang + main treatment + dosage form	1	0.31
Implicative good effect + dosage form	1	0.31
Total number of medicinal flavors + efficacy + dosage form	1	0.31
Total (n)	322	100.00

[a] "Fufang" is the Latin alphabetical transcription of the first two Chinese characters in the Chinese name of the preparation; [b] "Zhongyao" is the Latin alphabetical transcription of the first two Chinese characters in the Chinese name of the preparation

Table 2: Statistics of dosage forms of preparations for treating hair loss

Dosage form	Number of preparations (n)	Percentage (%)
Decoction	112	34.78
Pill	44	13.66
Capsule	30	9.32
Tablet	23	7.14
Granule	22	6.83
Tincture	17	5.28
Liniment	15	4.66
Powder	13	4.04
Oral solution	9	2.80
Mixture	7	2.17
Paste	7	2.17
Syrup	5	1.55
Gel	4	1.24
Lotion	3	0.93
Pellet	3	0.93
Wine preparation	3	0.93
Injection	2	0.62
Spray	2	0.62
Medicated tea	1	0.31
Total (n)	322	100.00

Number of medicinal flavors

Number of medicinal flavors refers to the total number of Chinese medicinal materials contained in the preparations. It ranges from 1 to 28, with an average of 9.30 ± 4.63 medicinal flavors. 94.72% of the preparations contain flavors within 15, and 41.61 % within 8, indicating that the number of medicinal flavors of the preparations for treating hair loss is moderate. The data are shown in Table 3.

Approval number

A preparation can be produced by multiple pharmaceutical manufacturers using different approval number according to the *National Medical Products Administration of the People's Republic of China*. There are 108 preparations (33.54%) with 1,539 approval numbers, and the average approval number of each preparation is 14.25. The top ten preparations with the most approval numbers are *Liuwei Dihuang* Pill (653), *Shengmai* Drink (270), *Wuji Baifeng* Pill (211), *Shouwu Yanshou* Tablet (84), *Qibao Meiran* Pill (24), *Chuzhi Shengfa* Tablet (23), *Qibao Meiran* Granule (17), *Bantu* Pill (16), *Erzhi* Pill (14), and *Zibu Shengfa* Tablet (11).

The first few preparations are used to regulate the physiological state or tissue associated with hair loss after oral administration, and then indirectly play the role of treating hair loss. It shows that treating hair loss with traditional Chinese medicine not only targets the hair loss site itself, but also aims to adjust the state of the whole body to improve local lesions. This reflects the difference between TCM and modern medicine in the treatment of hair loss.

Table 3: Statistics on number of medicinal flavors of preparations for treating hair loss

Number of medicinal flavors (n)	Number of preparations (n)	Percentage (%)
12	46	14.29
13	27	8.39
7	26	8.07
10	25	7.76
9	22	6.83
4	20	6.21
8	20	6.21
11	19	5.90
1	18	5.59
14	18	5.59
6	17	5.28
15	14	4.35
3	13	4.04
2	11	3.42
5	9	2.80
17	5	1.55
16	4	1.24
21	2	0.62
18	1	0.31
19	1	0.31
20	1	0.31
22	1	0.31
26	1	0.31
28	1	0.31
Total (n)	322	100.00

Provinces with high production of preparations for treating hair loss

The top ten provinces in terms of the number of units producing preparations for treating hair loss are Guangdong (21), Hubei (15), Jiangsu (15), Shanxi (15), Sichuan (13), Hunan (13), Zhejiang (12), Beijing (11), Henan (11), and Shandong (11). The units refer to any company, hospital, pharmaceutical factory and research institute that produce preparations.

Due to the impact of geographical location and living environment, the degree of hair loss varies from region to region. The more developed the region is, the more obvious the phenomenon of hair loss is. For example, Guangdong, one of the most developed provinces in China, ranks first in the number of units producing preparations for treating hair loss. Perhaps the more developed the region is, the greater the pressures in people's lives are, which then result in the prevalence of hair loss from overwork or irregular working hours and hence, a higher demand for treatment.

Therapeutic features

These preparations could be classified into three levels in the treatment of diseases. The first level is the direct treatment of hair loss, with clinical treatments of seborrheic alopecia, alopecia areata, and prematurely graying hair being the most common. The second level is the treatment of hair-loss-related diseases; for instance, hair loss caused by nervous system diseases could be treated by improving blood circulation. The third level is the treatment of diseases irrelevant to hair loss. The composition of TCM preparations is complex that they may have direct or indirect effects in the treatment of hair loss, and some of them can also treat other diseases. The categories and frequencies of diseases are shown in Table 4.

Medicinal characteristics

Common Chinese medicinal materials

A total of 400 Chinese medicinal materials are used in the 322 preparations with 339 botanical medicinal materials accounting for 84.75%, 40 animal medicinal materials accounting for 10.00%,

Table 4: Statistics of therapeutic uses of preparations for treating hair loss

Category	Diseases (number of preparations (n))	Total (n)	Percentage (%)
Skin and subcutaneous tissue diseases	Hair loss (93), Seborrheic alopecia (86), Alopecia areata (66), premature hair-graying (57), Androgenic alopecia (35), Total alopecia (10), Pruritus capitis (8), male pattern alopecia (6), Female pattern alopecia (6), postoperative and postpartum alopecia (6), alopecia universatis (4), Folliculitis (3), climacteric alopecia (2), Desquamation (2), leucoderma (2), Neurological alopecia (1), progressive alopecia (1)	388	57.23
Nervous system diseases	Dizzy head (29), Dizzy vision (28), Tinnitus (27), Insomnia (16), Amnesia (14), General lassitude (12), Headache (6), hearing loss (4)，Hypopsia (3), Hypofunction of brain (3), neurasthenia (2), anorexia (1), climacteric syndrome (1)	146	21.53
Mental and behavioral disorders	Lumbar debility (33), parched mouth and scorched tongue (7), pale complexion (4), Unhealthily thin (4), limb numbness (3), Restless sleeping at night (2), lack of *qi* and no desire to speak (1), weak lower limbs (1), Progeria (1)	56	8.26
Circulation system diseases	Spontaneous sweating and night sweating (6), Hyperlipidemia (5), hypertension (3), coronary heart disease (3), hemorrhage (2), cerebrovascular embolism (1)	20	2.95
Digestive system diseases	Loss of appetite (6), constipation (6), diarrhea (2), vomiting (2), dyspepsia (1), abdominal distension (1)	18	2.65
Urogenital diseases	Spermatorrhea and enuresis (6), premature ejaculation (4), menstrual disorder (2), polyuria at night (2), porbid leucorrhea (2), prolapse of uterus (1)	17	2.51
Blood and hematopoietic organ diseases	Cardiopalmus (8), cerebral arteriosclerosis (2), deficiency of blood (2), hemoptysis (2)	14	2.06
Musculoskeletal system and connective tissue diseases	Limp sinews and bones (4), Osteoporosis (2), Chill and cold limbs (1), Loose teeth (1)	8	1.18
Respiratory system diseases	Shortness of breath (4), cough and expectoration (1), bloody sputum (1), chest pain (1)	7	1.03
Immune system diseases	Anemia (2), immune hypofunction (1), leukocytopenia (1)	4	0.59

14 mineral medicinal materials accounting for 3.50%, 6 other medicinal materials accounting for 1.50%, and 1 chemical raw medicine accounting for 0.25%. China is among the countries with the richest medicinal plant resources in the world, and it has a long history of discovering, using, and cultivating medicinal plants. Botanical medicinal materials are often used to treat hair loss in TCM because they have the advantages of few side effects, stable and long-lasting functioning and wide-range impact. The most commonly used 20 botanical medicinal materials, 5 animal medicinal materials, and 3 mineral medicinal materials are shown in Table 5. The high frequency of these medicinal materials used in preparations reflected their good effect for treating hair loss, which can provide reference for new drug development.

Table 5: Chinese medicinal materials used in the preparations for treating hair loss

Classification	No.	PinYin	Latin name	Family	Live Form	Part used	Clinical attending	Chemical composition	Pharmacological action	Frequency	Reference
Botanical medicinal materials	1	Dihuang	*Rehmannia glutinosa* (Gaertn.) DC.	Scrophulariaceae	Herb	Root tuber	Cardiovascular disease, diabetes, hypertension, senile dementia, cerebral infarction, oral ulcer	Glycosides, carbohydrates, amino acids, organic acids	Anti-inflammatory, sedative, anti-hypertension, anti-hyperglycemic, cardiotonic, diuretic, protect liver, anti-radiation, regulate immunity, anti-aging, anti-tumor	180 (6.11%)	[7]
	2	Heshou wu	*Fallopia multiflora* (Thunb.) Haraldson	Polygonaceae	Herb	Root tuber	Hyperlipidemia, vascular dementia, hair loss, senile pruritus, bronchial asthma	Chrysophanol, emodin, rhein, emodin methyl ether	Promote hematopoiesis, enhance immunity, anti-hyperlipidemic, anti-atherosclerosis, protect liver, anti-aging, anti-myocardial ischemia, anti-bacteria, anti-virus	166 (5.64%)	[8]
	3	Danggui	*Angelica sinensis* (Oliv.) Diels	Umbelliferae	Herb	Root	Muscle pain, arthralgia, neuralgia, chronic tracheitis, chronic pelvic inflammation, emmeniopathy, hypertension, rhinitis	Ligustilide, angelica ketone, carvacrol, ferulic acid, angelica polysaccharide, amino acid	Promote hematopoiesis, enhance immunity, anti-myocardial ischemia, anti-arrhythmia, anti-hypertension, anti-thrombosis, anti-hyperlipidemic, protect liver, analgesia, anti-tumor, anti-bacteria	143 (4.86%)	[9]
	4	Nvzhenzi	*Ligustrum lucidum* W.T.Aiton	Oleaceae	Shrub or tree	Fruit	Chronic bronchitis, chronic atrophic gastritis, hepatitis, hyperlipidemia, menopausal syndrome, infertility, arrhythmia, senile constipation	Oleanolic acid, stearic acid, glycosides, volatile oils, polysaccharides, amino acids	Protect liver, regulate immunity, anti-hyperlipidemic, anti-atherosclerosis, anti-aging, anti-fatigue, anti-inflammation, anti-bacteria, promote hair follicle growth	110 (3.74%)	[10]
	5	Chuanxiong	*Ligusticum chuanxiong* Hort.	Umbelliferae	Herb	Rhizome	Coronary heart disease, atherosclerosis, soft tissue injury, rheumatoid arthritis, nervous headache	Ligustrazine, ligustilide, senkyunolide, ferulic acid, visfatin	Expand coronary arteries, improve microcirculation, anti-thrombosis, sedation, spasmolysis, bacteriostasis, regulate immunity, cholagogic	100 (3.40%)	[11]
	6	Fuling	*Poria cocos* (Schw.) Wolf	Porphyridae	Fungi	Sclerotium	Cardiac edema, arrhythmia, schizophrenia, alopecia areata	Poria cocos polysaccharide, triterpenoids, choline, histidine	Diuresis, protect liver, sedation, anti-hyperglycemia, anti-tumor	96 (3.26%)	[12]
	7	Danshen	*Salvia miltiorrhiza* Bunge	Moschidae	Labiatae	Root and Rhizome	Coronary heart disease, cervical spondylosis, essential hypertension, cerebral arteriosclerosis, concussion	Tanshinone, salvianic acid a, salvianic acid	Expand coronary arteries, improve microcirculation, protect liver, sedation, analgesia, anti-bacteria, anti-inflammatory, anti-allergic, anti-hypertension	93 (3.16%)	[13]

Table 5: Chinese medicinal materials used in the preparations for treating hair loss **(continued)**

Classification	No.	PinYin	Latin name	Family	Live Form	Part used	Clinical attending	Chemical composition	Pharmacological action	Frequency	Reference
	8	Mohanlian	*Eclipta prostrata* (L.) L.	Compositae	Herb	Aerial part	Coronary heart disease, hypertension, gastritis, esophagitis	Triterpenoid saponins, flavonoids, thiophenes, nicotinic acid, amino acids, vitamins	Regulate immunity, protect liver, anti-aging, antioxidant, anti-tumor, anti-inflammatory, promote hair growth, anti-bacteria, hemostasis	89 (3.02%)	[14]
	9	Gancao	*Glycyrrhiza uralensis* Fisch.	Leguminosae	Herb	Root and Rhizome	Arrhythmia, gastrointestinal spasm, acute and chronic pharyngitis, cough, acute and chronic hepatitis, peptic ulcer	Glycyrrhizic acid, alkaloids, polysaccharides, ferulic acid	Anti-arrhythmia, anti-ulcer, spasmolysis, analgesia, antitussive, anti-bacteria, anti-inflammatory, anti-allergic, anti-diuretic, anti-hyperlipidemic, protect liver	32 (2.02%)	[15]
	10	Cebai	*Platycladus orientalis* (L.) Franco	Cupressaceae	Tree	Branch and leaf	Internal haemorrhage, hair loss, cough, insomnia	Thujene, thujone, fenchone, flavonoids, organic acids, resins	Hemostasis, antitussive, expectorant, antiasthmatic, anti-bacteria, sedation	78 (2.65%)	[16]
	11	Gouqizi	*Lycium barbarum* L.	Solanaceae	Shrub	Fruit	Sexual dysfunction, neurasthenia, senile dementia, optic atrophy, hypertension	Betaine, polysaccharide, carotene, riboflavin, amino acids, vitamins	Enhance immunity, anti-aging, anti-fatigue, anti-tumor, anti-hyperglycemia, anti-hyperlipidemia, protect liver, anti-radiation	75 (2.55%)	[17]
	12	Sang	*Morus alba* L.	Moraceae	Shrub or tree	Fruit and leaf	Influenza, bronchitis, hypertension, dry eye, keratitis	Molting hormone, moracetin, rutin, quercetin, scopolamine	Anti-hyperglycemic, anti-hypertensive, anti-hyperlipidemic, anti-bacteria, anti-thrombotic, anti-aging, anti-filaria	75 (2.55%)	[18]
	13	Shaoyao	*Paeonia lactiflora* Pall.	Ranunculaceae	Herb	Root	Autoimmune diseases, cardiovascular and cerebrovascular diseases, neurodegenerative diseases	Paeoniflorin, albiflorin, benzoyl paeoniflorin, oxypaeoniflorin	Analgesia, sedation, anti-convulsion, anti-inflammation, anti-ulcer, protect liver, anti-hypertension, regulate immunity, anti-tumor	74 (2.51%)	[19]
Botanical medicinal materials	14	Tusizi	*Cuscuta chinensis* Lam.	Convolvulaceae	Herb	Seed	Abortion, fetal irritability, tinnitus, chronic glomerulonephritis	Flavonoids, coumarin, steroid terpenoids, resins, carbohydrates, organic acids, fatty acids	Enhance immunity, anti-aging, anti-hypertension, cholesterol-lowering, promote hematopoiesis	67 (2.28%)	[20]
	15	Huangqi	*Astragalus membranaceus* (Fisch.) Bunge	Leguminosae	Herb	Root	Neurasthenia, anemia, arrhythmia, myocarditis, anal prolapse, chronic bronchitis	Glycosides, polysaccharides, flavonoids, choline, amino acids, carotene	Enhance immunity, anti-fatigue, anti-stress, anti-hypoxia, anti-radiation, protect liver, anti-ulcer	65 (2.21%)	[21]
	16	Zexie	*Alisma plantago-aquatica* L.	Alismataceae	Herb	Stem tuber	Diarrhea, hypertension, fatty liver, coronary heart disease, edema	Triterpenoids, volatile oils, alkaloids, asparagine, fatty acids, resins	Diuresis, anti-hypertension, anti-hyperlipidemic, anti-atherosclerosis, protect liver	49 (1.66%)	[22]

Table 5: Chinese medicinal materials used in the preparations for treating hair loss **(continued)**

Classification	No.	PinYin	Latin name	Family	Live Form	Part used	Clinical attending	Chemical composition	Pharmacological action	Frequency	Reference
	17	Shanzha	*Crataegus pinnatifida* Bunge	Rosaceae	Tree	Fruit	Dyspepsia, postpartum abdominal pain, dysmenorrhea, hypertension, coronary heart disease	Citric acid, chlorogenic acid, quercetin, flavonoids, triterpenoids	Anti-hyperlipidemic, anti-ischemic, anti-hypertension, regulate immunity, anti-bacteria, anti-tumor, anti-fatigue	43 (1.46%)	[23]
	18	Heizhima	*Hibiscus trionum* L.	Malvaceae	Herb	Seed	Cough, liver disease, hair loss	Carbohydrates, vitamins, lecithin	Strengthen the stomach, protect liver, promoting erythrocyte growth, promote hair growth	41 (1.39%)	[24]
	19	Dangshen	*Codonopsis pilosula* (Franch.) Nannf.	Campanulaceae	Herb	Root	Dyspepsia, chronic gastroenteritis, peptic ulcer, chronic hepatitis, chronic bronchitis, coronary heart disease	Sterols, codonopsis glycosides, codonopsis polysaccharides, codonopsis lactones, volatile oils, alkaloids, flavonoids	Anti-ulcer, enhance immunity, anti-stress, anti-shock, anti-ischemia, anti-thrombosis, anti-convulsion	40 (1.36%)	[25]
	20	Baizhu	*Atractylodes macrocephala* Koidz.	Compositae	Herb	Rhizome	Cirrhotic ascites, primary liver cancer, acute enteritis	Atractylol, atractylone, atractylenolide, glycosides, polysaccharides, flavonoids	Diuresis, anti-hyperglycemia, protect liver, anti-coagulation, anti-hypertension, anti-tumor, anti-bacteria	38 (1.29%)	[26]
Animal medicinal materials	21	Chantui	*Cryptotympana pustulata* Fabricius	Cicadidae	-	Shell	Cough, nephritis, urticaria, insomnia	Chitin, protein, amino acids, organic acids, phenols	Sedation, hypnotic, anti-convulsive, antipyretic, anti-inflammatory, anti-allergic, immunosuppression	13 (0.44%)	[27]
	22	Muli	*Ostrea gigas* Thunberg	Ostreidae	-	Shell	Insomnia, chronic otitis media, uterine leiomyoma, breast hyperplasia	Calcium carbonate, calcium phosphate, calcium sulfate	Sedation, analgesia, anti-convulsion	9 (0.31%)	[28]
	33	Lurong	*Cervus nippon* Temminck	Cervidae	-	Little horn	Primary hypotension, hemopathy, brain trauma	Estradiol, estrone	Promote sexual function, anti-fatigue, anti-aging, enhance immunity, anti-arrhythmia	7 (0.24%)	[29]
	24	Wugong	*Scolopendra subspinipes mutilans* L.Koch	Scolopendridae	-	Dry body	Neuralgia, tuberculosis, nephritis, hepatitis	Centipede venom, fat oil, cholesterin, formic acid	Sedation, anti-convulsive, anti-inflammatory, anti-bacteria, analgesic, anti-hypertension	7 (0.24%)	[30]
	25	Ejiao	*Equus asinus* L.	Equidae	-	Dry skin	Hemoptysis of pulmonary tuberculosis, hematuria, dysfunctional uterine bleeding	Collagen, amino acids	Anti-coagulation, anti-shock, anti-fatigue, enhance immunity, anti-radiation	5 (0.17%)	[31]

Table 8: Chinese medicinal materials used in the preparations for treating hair loss **(continued)**

Classification	No.	PinYin	Latin name	Family	Live Form	Part used	Clinical attending	Chemical composition	Pharmacological action	Frequency	Reference
Mineral medicinal materials	1	Huashi	Speckstone	-	-	-	Inhibited urination, watery diarrhea, eczema	[Mg3(Si4O10)(OH)2]	Diuresis, anti-bacteria, hemostasis, protection gastric mucosa	7 (0.24%)	[32]
	2	Mingfan	Alums	-	-	-	Hypertension, enteritis, otitis media	KAl(SO4)2·12H2O	Anti-bacteria	2 (0.07%)	-
	3	Zheshi	Haematitum	-	-	-	Pulmonary edema, cerebral edema	Fe2O3	Sedation, excite intestinal smooth muscle	1 (0.03%)	-

Ethnomedicines

Nineteen ethnomedicines for treating hair loss are identified, including 6 Dai medicinal preparations, namely *Baodongdian Wufa* Formula, *Hejie Tuofa* Formula, *Haoming Rongfa* Formula, *Weizi Wufa* Formula, *Mameng Gufa* Decoction, and *Wuyuecha Shengfa* Formula; 5 Uyghur medicinal preparations, namely *Gujing Maisiha* Tablet, *Fufang Siyadan Shengfa* Tincture, *Qubai Aili Lesiya* Powder, *Fufang Siyadan Shengfa* Oil, and *Qubai Yitierfeili Aman* Honey Paste; 4 Buddhist medicinal preparations, namely *Zhi Xuexu Tuofa* Formula, *Zhusun Sangshen* Porridge, *Shouwu* Porridge, and *Yinghua Shengfa* Formula; 3 Tibetan medicinal preparations, namely *Sanwei Dujuantang* Powder, *Zangyao Huantong Shengfa* Liquid, and *Wufa* Paint; 1 Zhuang medicinal preparation, namely *Zhuangyao Gufa Meiran* Decoction.

National essential medicines and protected varieties of TCM

Among the 322 preparations, there are 4 national essential medicines, namely *Tangcao* Tablet, *Shengmai* Drink, *Liuwei Dihuang* Pill, and *Wuji Baifeng* Pill. There is 1 protected variety of TCM, namely *Fufang Siyadan Shengfa* Tincture.

Common Chinese traditional patent medicines

Qibao Meiran Pellet

Qibao Meiran Pellet is a TCM preparation with unique therapeutic advantages of *blackening the beard and hair*. The preparation consists of 7 Chinese medicinal materials: *Fallopia multiflora (Thunb.) Haraldson, Poria cocos (Schw.) Wolf, Achyranthes bidentata Blume, Angelica sinensis (Oliv.) Diels, Lycium barbarum* L., *Cuscuta chinensis* Lam., and *Psoralea corylifolia* L. In dermatology, they are used to treat premature gray hair, hair loss, leucoderma, and cutaneous pruritus [33]. *Qibao Meiran* Pellet can be used to treat all types of hair loss with *liver and kidneys deficiency syndrome*, according to the syndrome differentiation of TCM. Yougui Wang [34] used *Qibao Meiran* Pellet to treat hair-loss patients and the effect was remarkable after 2-4 courses. Liru Wang [35] treated 60 patients with climacteric alopecia using *Qibao Meiran* Pellet together with *Erxian* Decoction, and the effect was also good. Yongjun Tang [36] used *Qibao Meiran* Pellet to treat alopecia areata patients with *liver and kidneys deficiency syndrome*, and the total effective rate was 87.88 % with no obvious adverse reactions. The results showed *Qibao Meiran* Pellet could up-regulate the level of CD4+ cells and down-regulate the level of CD8+ cells by regulating T cells subsets in peripheral blood to improve the immune system.

Yangxue Shengfa Capsule

Yangxue Shengfa Capsule is composed of *Fallopia multiflora* (Thunb.) Haraldson, *Rehmannia glutinosa (Gaertn.) DC., Angelica sinensis (Oliv.) Diels, Cynanchum otophyllum C.K. Schneid., Cuscuta chinensis Lam., Gastrodia elata Blume, and Notopterygium incisum K.C.Ting ex H.T.Chang.* They have demonstrated good results in treating alopecia areata, total alopecia, seborrheic alopecia, and postpartum alopecia. Yanli Wu [37] found that *Yangxue Shengfa* Capsules not only promoted hair growth in normal rats and guinea pigs, but also promoted hair growth in a rat model of hair loss duplicated by thallium. Furong Chen [38] found that *Yangxue Shengfa* Capsule could promote hair growth in C57BL/6 mice by increasing VEGF expression, hair follicle number and skin blood vessels. Dong Sai [39] found that *Yangxue Shengfa* Capsule could significantly increase the content of zinc which can regulate metabolism *in vivo* to promote hair growth.

Huoxue Bushen Mixture

Huoxue Bushen Mixture is composed of *Astragalus membranaceus* (Fisch.) Bunge, *Codonopsis pilosula* (Franch.) Nannf., *Poria cocos* (Schw.) Wolf, *Rehmannia glutinosa* (Gaertn.) DC., *Scrophularia ningpoensis* Hemsl., and *Epimedium brevicornu* Maxim. Modern pharmacological studies have confirmed that all of these Chinese medicinal materials can improve immune system.

Among them *Rehmannia glutinosa* (Gaertn.) DC. can protect the pituitary-adrenal cortex system, and it has significant clinical efficacy in the treatment of autoimmune diseases [40]. Shangpu Gao [41] found that *Huoxue Bushen* Mixture could up-regulate VEGF expression to accelerate blood vessel neogenesis and hair growth. Studies show that the ratio of estrogen to androgen (E2/T) in female pattern alopecia is significantly decreased, so the initiating factor of female pattern alopecia may be the imbalance between estrogen and androgen [42]. *Huoxue Bushen* Mixture can effectively correct the imbalance between estrogen and androgen, and is probably one of the mechanisms to treat female pattern alopecia [43].

Fufang Siyadan Shengfa Tincture

Fufang Siyadan Shengfa Tincture, a Uygur medicine produced in Xinjiang province, is made up of dry seeds from *Nigella damascena* L., *Amygdalus persica* L. and *Punica granatum* L. It is a brownish-black clear liquid with a slightly pungent odor and, it has a remarkable effect on male pattern alopecia, alopecia areata, seborrheic alopecia, and other types of hair loss of unknown origin. According to the theory of Chinese medicine, it can regulate the patients' constitution and local alopecia areata, and hence play an active role in treating hair-loss both at the manifestation and the root cause [44]. *Fufang Siyadan Shengfa* Tincture has been shown to increase to a certain extent the number of hair follicles in the skin of rats, which may be related to its ability to increase skin blood flow, improve local microcirculation, and strengthen follicle nutrition, thereby promoting hair growth [45].

Chuzhi Shengfa Capsule

Chuzhi Shengfa Capsule can treat seborrheic alopecia by reducing body oil secretion with minimal side effects. This preparation consists of *Angelica sinensis* (Oliv.) Diels, *Paeonia suffruticosa* Andr., *Ligusticum chuanxiong* Hort., *Dictamnus dasycarpus* Turcz., *Cryptotympana pustulata* Fabricius, *Rehmannia glutinosa* (Gaertn.) DC., *Sophora flavescens* Aiton, *Kochia scoparia* (L.) Schrad., *Saposhnikovia divaricata* (Trucz.) Schischk., *Fallopia multiflora* (Thunb.) Haraldson, *Bombyx mori* L., and *Scolopendra subspinipes mutilans* L.Koch[46].

Bushen Yangxue Capsule

Bushen Yangxue Capsule can effectively treat alopecia areata with *kidney and blood deficiency syndrome*. This preparation consists of *Fallopia multiflora* (Thunb.) Haraldson, *Rehmannia glutinosa* (Gaertn.) DC., *Cuscuta chinensis* Lam., *Ligustrum lucidum* W.T.Aiton, *Lycium barbarum* L., *Cynanchum otophyllum* C.K.Schneid., *Psoralea corylifolia* L., *Placenta Hominis, Morus alba* L., *Astragalus membranaceus* (Fisch.) Bunge, *Polygonatum sibiricum* F.Delaroche, *Angelica sinensis* (Oliv.) Diels, and *Ligusticum chuanxiong* Hort. The therapeutic effect of *Bushen Yangxue* Capsule on alopecia areata may lie in its function of regulating the nerve, endocrine, and immune systems. The capsule has been found to increase the content of T cells subsets in serum, improving the ratio of TH to TS, and directly regulate T cell-mediated autoimmune response, thereby eliminating the cause of disease and promoting hair growth. It can also promote the hematopoietic function of bone marrow and increase the volume or circulation of the peripheral blood, so as to effectively improve the condition of blood deficiency. What's more, it has demonstrated an ability to improve hemorheological indices, activate blood, and increase local microcirculation perfusion to provide adequate nutrition for hair growth, thereby promoting hair growth [47].

Huolisu Oral Solution

Huolisu Oral Solution has the effect of promoting hair growth. This preparation consists of *Fallopia multiflora* (Thunb.) Haraldson, *Lycium barbarum* L., *Polygonatum sibiricum* F.Delaroche, *Astragalus membranaceus* (Fisch.) Bunge, *Epimedium brevicornu* Maxim., and *Salvia miltiorrhiza* Bunge [48]. *Astragalus membranaceus* (Fisch.) Bunge has good immunomodulatory effect and helps to dilate blood vessels and improve blood circulation. *Epimedium brevicornu* Maxim. enhances immune function and has an observable sedative effect used for improving patients' mental state, thereby inhibiting hair loss. *Fallopia multiflora* (Thunb.) Haraldson promotes adrenal cortex function and regulates the endocrine system. *Lycium barbarum* L. supplements hair protein. *Salvia miltiorrhiza* Bunge improves microcirculation in alopecia areata patients and increases blood supply for capillaries around hair follicles. These five Chinese medicinal materials are all beneficial to hair growth and have a definite effect on alopecia areata [49].

Jingwu Capsule

Jingwu Capsule can treat insomnia, dreaminess, tinnitus, amnesia, hair loss, and premature hair-graying caused by mental tension and chronic fatigue. This preparation consists of *Fallopia multiflora* (Thunb.) Haraldson, *Polygonatum sibiricum* F.Delaroche, *Ligustrum lucidum* W.T.Aiton, and *Eclipta prostrata* (L.) L. *Fallopia multiflora* (Thunb.) Haraldson is the main Chinese medicinal material for promoting hair growth. Pharmacological study found that *Fallopia multiflora* (Thunb.) Haraldson has the effects of promoting hematopoiesis, enhancing immune function, and anti-aging. *Polygonatum sibiricum* contains a variety of anthraquinone compounds that can enhance immunity and energy, and has the effect of anti-aging. *Ligustrum lucidum* W.T.Aiton has many effects such as anti-oxsidation, anti-fatigue, and promoting adrenal cortex function. *Eclipta prostrata* (L.) L. has immunomodulatory, antioxidant and hepatoprotective effects. *Jingwu*

Capsule has definite curative effects and is quite safe for clinical use in treating alopecia areata [50].

Gushen Shengfa Pill

Gushen Shengfa Pill is composed of *Rehmannia glutinosa* (Gaertn.) DC., *Lycium barbarum* L., *Notopterygium incisum* K.C.Ting ex H.T.Chang, *Fallopia multiflora* (Thunb.) Haraldson, *Ligusticum chuanxiong* Hort., *Chaenomeles sinensis* (Dum.Cours.) Koehne, *Ligustrum lucidum* W.T.Aiton, *Angelica sinensis* (Oliv.) Diels, *Morus alba* L., *Salvia miltiorrhiza* Bunge, *Codonopsis pilosula,* (Franch.) Nannf. and *Hibiscus trionum* L. It has been used for the treatment of alopecia areata, total alopecia, and alopecia universatis. In recent years, scholars have found that alopecia areata is a T cell-mediated organ-specific autoimmune disease involving hair follicles, and the regulation of alopecia areata by T-lymphocyte factors has become a subject of great interest among researchers [51]. *Gushen Shengfa* Pill up-regulates Th2 cytokines such as IL-4 and IL-10, and down-regulates Th1 cytokines such as IL-12 and IFN-γ to promote balance in Th1/Th2, thus alleviating illness, controlling disease activities, improving sleep quality, and promoting hair growth [52].

Shengfa Tablet

Shengfa Tablet is listed in the seventeenth volume of *China-TCM Prescription Preparation*. It is composed of twelve Chinese medicinal materials, namely *Fallopia multiflora* (Thunb.) Haraldson, *Ligustrum lucidum* W.T.Aiton, *Rehmannia glutinosa* (Gaertn.) DC., *Eclipta prostrata* (L.) L., *Morus alba* L., *Ipomoea batatas* (L.) Lam., *Paeonia suffruticosa* Andr., *Alisma plantago-aquatica* L., *Poria cocos* (Schw.) Wolf, *Ophiopogon japonicus* (Thunb.) Ker Gawl., *Diospyros lotus* L., and *Ribes nigrum* L. It is used to treat premature hair-graying, hair loss, alopecia areata, total alopecia, and seborrheic alopecia. Inhibition of melanin production is the direct cause of premature hair-graying. Tyrosinase gene family, however, could play a major role in regulating melanin synthesis [53]. Within the concentration range of 0.25-1 g·L-1, the water extract of *Shengfa* Tablet can increase the activity of tyrosinase, promote the synthesis of melanin, and up-regulate the expression of MITF, TYR and P-CREB protein in a concentration-dependent manner, suggesting that the water extract of *Shengfa* Tablets may promote melanin synthesis through PKA-MITF-TYR signaling pathway [54].

DISCUSSION

This study has identified a wide variety of TCM preparations available for treating hair loss. Out of the 322 preparations, the majority (41.93%) are produced by medical institutions, providing important resources for the development of new medicines. Decoctions, liquids made from the extracted juice of boiled or soaked medicinal materials, are the earliest and most widely used dosage form in TCM due to their easy preparation and quickness to take effect, therefore becoming the main form of clinical treatment for hair loss, accounting for 34.78% of all dosage forms. This study found that the number of medicinal flavors vary from 1 to 28, with the most common being 12, indicating that the number of medicinal flavors of the preparations for treating hair loss is moderate. These preparations are mainly used to treat skin and subcutaneous tissue diseases, of which seborrheic alopecia and alopecia areata are the most common diseases. It has been found that most preparations could also be used to treat premature hair-graying. In addition, this study also identified out the most commonly used botanical, animal, and mineral medicinal materials in preparations, providing a reference for the development of new preparations for treating hair loss.

All the top 40 Chinese medicinal materials are from plants, comprising 84.75 % of the total. China is among the richest nations in terms of medicinal plants, and it has a long history of discovering, using and cultivating medicinal plants. Botanical medicinal materials, with their advantages of minimal side effects, stability, and lasting and wide-ranging curative effects, are often used in various TCM preparations. Ethnomedicines account for a small proportion, but their effects are broad and profound; it is expected that increasing attention will be given to ethnomedicines in future research. Most of the preparations are primarily composed of Chinese medicinal materials for *toning the kidneys* and *nourishing the liver*. The three most frequently used Chinese medicinal materials are *Rehmannia glutinosa* (Gaertn.) DC., *Fallopia multiflora* (Thunb.) Haraldson, and *Angelica sinensis* (Oliv.) Diels. Their underlying mechanism may be the improvement of microcirculation, regulation of the endocrine system, and an increase in immune function,

thereby nourishing hair follicles and promoting hair growth.

The results have showed that most TCM preparations are used to treat seborrheic alopecia and alopecia areata, indicating a prevalence of these two diseases. From the data of World Health Organization, hair loss occurs in one out of every six people in China, with the affected population increasingly tending to be younger and younger. The proportion of those suffering from hair loss among youths in post-80s and post-90s has exceeded 35 %. There are about 250 million people afflicted by hair loss in China in 2019, including approximately 163 million males and 88 million females [55].

The prevalence rate of seborrheic alopecia has been found to be 21.3 % in males, 6.0 % in females, and the total prevalence rate of alopecia areata 0.27 %. This survey also found that the number of people afflicted by hair loss is increasing at least 15 % every year. Research on hair loss has attracted extensive attention in recent years. However, most of the studies focus on the prescription analysis based on their effectiveness and, unfortunately, lack a discussion on chemical composition and the mechanism of preparations, perhaps due to the complexity of the composition of preparations. In the future, deeper research into this area is needed.

CONCLUDING REMARKS

In recent years, as the number of hair loss increases year by year, there is a huge consumer market in hair loss health industry. However, due to the complex factors that cause hair loss and numerous types of hair loss, the treatment for hair loss has always been one of the great challenges in medical research. Up till now, seborrheic alopecia is the most common type of hair loss, and the effective medical methods include drug therapy, diet therapy, laser therapy and hair transplantation. But the current treatment methods have obvious deficiencies, whereas the new treatment methods with good efficacy and less side effects are not yet developed. Traditional Chinese medicine has a long history and exhibits unique advantages in hair loss treatment. It not only has oral and external preparations, but also advocates improving hair loss symptom by regulating drugs and diet. Acupuncture is also used to promote hair growth by stimulating blood circulation of scalp. Through the summary and analysis of traditional Chinese medicine preparations for the treatment of hair loss, we hope to find effective medicinal materials or preparations for the development of new drugs.

DECLARATIONS

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Conflict of interest

There is no conflict of interest to disclose.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Xiaoli Li conducted the research, performed data analysis, and wrote the manuscript; You Zhou, Ming Sun, and Mengdie Cao collected and organized the data; Min Xu and Ke Fu analyzed the data; Zhang Wang conceived and designed the study.

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