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Review Article

Liver Damage Associated with *Polygonum multiflorum* Thunb.: A Systematic Review of Case Reports and Case Series

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Objective. To summarize the characteristics and analysis of relevant factors and to give references for prevention and further study of liver damage associated with *Polygonum multiflorum* Thunb. (HSW), we provide a systematic review of case reports and case series about liver damage associated with HSW. *Methods*. An extensive search of 6 medical databases was performed up to June 2014. Case reports and case series involving liver damage associated with HSW were included. *Results*. This review covers a total of 450 cases in 76 articles. HSW types included raw and processed HSW decoction pieces and many Chinese patent medicines that contain HSW. Symptoms of liver damage occur mostly a month or so after taking the medicine, mainly including jaundice, fatigue, anorexia, and yellow or tawny urine. Of the 450 patients, two cases who received liver transplantation and seven who died, the remaining 441 cases recovered or had liver function improvement after discontinuing HSW products and conservative care. *Conclusion*. HSW causes liver toxicity and may cause liver damage in different degrees and even lead to death; most of them are much related to long-term and overdose of drugs. Liver damage associated with HSW is reversible, and, after active treatment, the majority can be cured. People should be alert to liver damage when taking HSW preparations.

1. Introduction

Polygonum multiflorum Thunb. (He Shou Wu in Chinese pinyin, hereinafter referred to as HSW) is the root of Polygonum multiflorum, a member of Polygonaceae. As a Chinese herb, it was recorded most early in "Kaibao Bencao" published by the imperial court of the Song Dynasty (973-974 A.D.) [1]. In the Chinese Pharmacopoeia (2010), there are two forms of HSW decoction pieces: raw state (natural root) (Figure 1) and processed form, that is, radix polygoni multiflori preparata (boiled in black-bean liquid according to a traditional process) (Figure 2). The two forms have different properties: the raw HSW is used for detoxification, eliminating carbuncle, preventing malaria, and relaxing bowel,

whereas the processed HSW is used for nourishing liver and kidney, supplementing essence and blood, blackening hair, strengthening bones and muscles, eliminating dampness, and reducing lipid [2]. Modern pharmacological studies have shown that HSW have the effect of reducing blood lipid and antiarteriosclerosis [3–5], protecting liver [6, 7], enhancing immunologic [8, 9], improving memory, protecting nerve cells, and increasing intelligence [10, 11], antioxidation, antiaging [12, 13], and so forth.

HSW is popular in many countries, especially in China. Traditional Chinese herbal medicine ordinarily recommends the use of herbs in complex formulas, but HSW is also often taken as a single herb. While there are many HSW-containing

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FIGURE 1: Raw HSW.



FIGURE 2: Processed HSW.

products, the most well-known product is like Shou-Wu-Pian, which is usually consumed as an antiaging product, or as a tonic for dizziness with tinnitus, and also appears to be efficacious in the treatment of premature greying of hair, lumbago, spermatorrhea, leucorrhea, and constipation. With the wide application, liver damage associated with HSW has been reported in China, Korea, Japan, Britain, Italy, Australia, and other countries [14, 15]. To fully understand the characteristics and possible factors of hepatitis associated with HSW, we conduct a comprehensive review of the relevant published literatures; we hope that our findings can provide guidance for clinical medication and scientific research and thus can help to avoid hepatitis induced by HSW in the future.

2. Methods

2.1. Data Sources and Search Strategy. In June 2014, we searched the following Chinese-language electronic databases: Chinese Biomedical Literature Database (CBM, 1980–2014), Chinese Journal Full-Text Database (CNKI, 1980–2014), Weipu Journal Database (VIP, 1989–2014), and Wanfang Data (1990–2014) and two English-language databases PubMed and EMBASE (1989–2014). The search terms included *Polygonum multiflorum*, radix polygoni multiflori,

He Shou Wu, liver injury, liver damage, liver diseases, hepatitis, and liver failure in English or Chinese. These terms were searched as free-text in the title or the abstract. The references of relevant reviews and the included literatures were checked for possible identification of additional studies.

2.2. Study Selection. Case reports and case series are included in the review if they reported factual data on liver damage related to HSW. Clinical trials, reviews, commentaries, and other nonrelated literatures were excluded. Some clinical trials of HSW that reported liver damage were excluded for reasons originally given by Lao et al., specifically that they were too small to provide convincing evidence of rare complications [16]. Two authors (Xiang Lei and Jing Chen) independently examined the titles and abstracts of all papers found through the search to determine if they fulfilled the inclusion criteria outlined above. The full texts of potentially relevant articles were retrieved for detailed assessment. Differences can be resolved through discussion.

2.3. Data Extraction. After screening, articles were read in full and extracted by two independent reviewers (Xiang Lei and Jing Chen). Information on author, year of publication, number of patients, disease originally treated, gender, dose and dosage forms, course of taking HSW, clinical manifestations, length of hospitalization, outcome and family history, and recurrence of hepatitis related to HSW were extracted according to the designed data extraction table independently by two authors.

3. Results

3.1. Search Process and Result. The search identified 923 database records, which led to the retrieval of documentation on 103 studies for a full-text review. One additional reference was identified while searching reference lists of the included papers. 76 articles (59 case reports and 17 case series) met the inclusion criteria. In total, 450 cases of hepatitis associated with HSW were reported. The characteristics of the case reports and case series are shown in Tables 1 and 2. Because case series is summary report for multiple patients and because of the lack of description of the individual patient information, the following is mainly an analysis of case reports.

3.2. Gender and Age. In 450 cases, 224 (49.78%) were male and 226 (50.22%) were female. In 72 cases of case reports, patients ranged in age from 5 to 78 years, with a median of 36.5. The most commonly affected age group was 18-44 (37/72, 51.4%), followed by 45-59 (24/72, 33.3%), <18 (6/72, 8.3%), and >60 (5/72, 6.9%).

3.3. Reasons for Medication (Disease Originally Treated). In case series, the causes of consuming HSW products include grey hair, hair loss, hypertension, coronary heart disease, hyperlipidemia, osteoarthritis, insomnia, dizziness, and health care; the top diseases were gray hair and hair loss

TABLE 1: Patient details recorded from published case reports.

June et al.	Reference	Age/gender	Reasons for medication	HSW type	Administration and dosage	Duration of intake, day	Hospitalization, day	Outcome	Rechallenge?
Yun [18] 52.PF Health care P. HSW OAB, 5 g 2.0 12] 39/M NAA P. HSW uAB, 5 g 180 21] 39/M NAA P. HSW uAB, 10 g 40 22] 39/M Vitiligo P. HSW uAB, 10 g 30 22] 34/F Vitiligo P. HSW OAB, 10 g 30 22] 34/F Vitiligo P. HSW OAB, 10 g 30 22] 34/F Vitiligo P. HSW OAB, 10 g 30 22] 34/F Harl loss P. HSW OAB, 18 g 30 22] 34/F Grey harr HSW OAB, 18 g 60 22] 36/M Chordin caphritis P. HSW OAB, 28 g 60 23] 36/M Chordin caphritis P. HSW OAB, 28 g 60 24] Grey harr P. HSW OAB, 28 g 60 60 25/M Grey harr P. HSW OAB, 28 g	Liu et al. [17]	20/F	Grey hair	HSW	OAP, 15 g	42	10	Recovery	NA
1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,		52/F	Health care	P. HSW	OAP, 5 g	20	14	Recovery	NA
[21] 39/M Grey hair Ing-Wu-Phan Oral, 3 × c tablets 60 [22] 37/M Vitiligo P. HSW UAN, 10g 40 [23] 37/M Vitiligo P. HSW OAP, 10g 30 [24] 14/F Vitiligo P. HSW OAP, 10A 38 [24] 45/M Hair loss P. HSW Oral, 10A 60 [25] 45/F Grey hair HSW OAP, 10A 60 [25] 45/F Health care R. HSW OAP, 10A 60 [26] 40/F Health care R. HSW OAP, 10A 60 [27] 40/F Health care R. HSW OAP, 2g 60 [28] 52/F Grey hair R. HSW OAP, 2g 60 [29] 57/M Grey hair R. HSW OAP, 2g 60 [29] 57/M Grey hair R. HSW OAP, 2g 60 [29] 57/M Grey hair R. HSW	Miao and Yun [18]	61/F	Hyperlipidemia	R. HSW	SIW, 5 g	180	12	Recovery	NA
[21] 48/F NAA P HSW UnAb, 10g 40 [22] 14/F Virliggo P HSW OAP, 10g 30 ct al. [23] 33/F NAA P HSW OAP, 10g 30 ct al. [24] 45/A Hair loss P HSW OAP, 10g 30 ct al. [24] 45/F Grey hair HSW OAP, 10g 60 27] 40/F Grey hair P HSW OAP, 10g 60 27] 36/M Grey hair P HSW OAP, 13g 50 27] 50/F Grey hair R HSW OAP, 13g 50 1, [30] 50/F Grey hair R HSW OAP, 13g 57 1, [30] 56/F Grey hair R HSW OAP, 13g 57 1, [30] 56/F Haith care R HSW OAP, 12g 50 [31] 56/F Grey hair R HSW OCal, 2×10mL 20 [32] 26/F Haith care R HSW De	Zhao [19]	39/M	Grey hair	Jing-Wu-Pian	Oral, 3×6 tablets	09	18	Recovery	NA
[22] 37/M Vitiligo P. HSW OAR, 10g 30 [22] 34/F Vitiligo P. HSW Oral, NA 38 et al. 45/M Hari loss P. HSW OAR, NA 60 2hen 45/M Hari loss P. HSW OAR, NA 60 2hen 45/M Health care H. HSW OAR, P. NA 60 2h 50/M Gery hair P. HSW OAR, P. NA 60 2x/ Gery hair P. HSW OAR, P. NA 60 2x/ Grey hair P. HSW OAR, P. NA 11 3x/ Grey hair P. HSW OAR, P. S 60 1, [30] 5x/R Grey hair R. HSW OAR, P. NA 11 (31) 5x/R Grey hair R. HSW OAR, 2x 0m 60 (31) 5x/R Heath care R. HSW Oral, 2x 4 capsules 60 (31) 5x/R Heath care HSW Oral, 2x 4 capsules 60 <td>Tan [20]</td> <td>48/F</td> <td>NA</td> <td>P. HSW</td> <td>uNA, 10 g</td> <td>40</td> <td>30</td> <td>Recovery</td> <td>NA</td>	Tan [20]	48/F	NA	P. HSW	uNA, 10 g	40	30	Recovery	NA
te al. [23] 34F Vitiligo P. HSW Decoction, NA 66 45/M Hair loss P. HSW Orah, NA 66 45/M Hair loss P. HSW Orah, NA 66 24/M Grey hair HSW OAP, NA 60 11 [26] 40/F Health care R. HSW OAP, NA 60 12 [28] 56/M Grey hair P. HSW OAP, 15 g 30 22 [28] 56/M Grey hair P. HSW OAP, 15 g 30 22 [28] 56/M Grey hair P. HSW OAP, 15 g 30 23 [27] 28/M Grey hair R. HSW OAP, 28 g 60 24 [28] 57/M Grey hair R. HSW OAP, 28 g 60 25 [27] 28/M Grey hair R. HSW OAP, 28 g 60 25 [27] 28/M Grey hair R. HSW OAP, 28 g 60 25 [28] 40/F Health care R. HSW Decoction, 10-20 g 60 26 [28] 56/F Grey hair Nishen wufa Decoction, 10-20 g 60 27 [28] 56/F Grey hair Nishen wufa Decoction, 10-20 g 60 28 [34] 28/M Hair loss Niapgwe shengf Oral, 2× 4 capsules 60 28 [34] 28/M Hair loss Niapgwe shengf Oral, 1× 2 g 60 28 [35] 46/F Health care HSW ca Oral, 1× 3 g 60 28 [39] 51/F Grey hair SWW OAP, 1× 3 g 60 28 [39] 51/F Grey hair SWW OAP, 1× 3 g 60 28 [39] 51/F Grey hair SWW OAP, 1× 3 g 60 28 [39] 51/F Grey hair SWW OAP, 1× 3 g 60 29 [39] 51/F Grey hair SWW OAP, 1× 3 g 60 20 [39] 51/F Grey hair SWW OAP, 1× 3 g 60 21 [44] 34/M NA Health care R. HSW SWW OAP, 1× 3 g 60 21 [45] 34/M Health care R. HSW SWW OAP, 1× 3 g 60 21 [45] 34/M Health care R. HSW SWW OAP, 1× 3 g 60 21 [45] 56/M Hair loss R. HSW SWW OAP, 1× 3 g 60 21 [48] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 22 [41] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 23 [41] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 24 [42] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 25 [44] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 26 [44] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 26 [44] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 27 [44] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 28 [44] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 28 [44] 56/M Health care R. HSW SWW OAP, 1× 3 g 60 29 [45] 56/M Grey hair OAP, 1× 3 g 60 20 [46] 56/M Grey hair OAP, 1× 3 g 60 20 [47] 56/M Grey hair OAP, 1× 3 g 60 20 [48] 56/M Grey hair OAP, 1× 3 g 60 20 [48] 56/M Grey hair SWW OAP, 1× 3 g 60 20 [48] 56/M Grey ha	Liu et al. [21]	37/M	Vitiligo	P. HSW	OAP, 10g	30	35	Recovery	NA
te al. [23] 33/F NA SWW Oral, NA 60 Li [26] 43/F Grey hair HSW OAP, NA 90 Li [26] 50/M Grey hair HSW OAP, NA 60 27] 36/M Grey hair HSW OAP, 15g 60 28. [2mg [28] 52/F Grey hair PHSW OAP, 15g 30 28. [2mg [28] 53/F Grey hair PHSW OAP, 15g 30 28. [2mg [28] 53/F Grey hair PHSW OAP, 3g 775 28. [34] 56/F Grey hair PHSW OAP, 3g 775 28. [34] 56/F Grey hair R. HSW OAP, 3g 775 28. [34] 26/F Health care R. HSW OAP, 20 60 38. [34] 26/F Health care R. HSW OAP, 20 60 38. [34] 26/F Hair loss R. HSW OAP, 20 60 38. [34] 26/M Hair loss R. HSW OAP, 15-20 38. [34] 26/M Hair loss R. HSW OAP, 15-20 38. [34] 26/M Hair loss R. HSW OAP, 15-20 38. [34] 26/M Hair loss R. HSW OAP, 15-20 38. [34] 26/M Hair loss R. HSW OAP, 10-20 38. [34] 26/M Hair loss R. HSW OAP, 10-20 38. [34] 26/M Hair loss R. HSW OAP, 10-20 38. [34] 26/M Hair loss R. HSW OAP, 10-20 38. [34] 38/F Grey hair RSW tea Oral, 2× 0g 180 38. [34] 38/F Grey hair RSW tea Oral, 1-2 g 60 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 35/M Grey hair R. HSW OAP, NA 50 38. [34] 35/M Grey hair NA 50 38. [34] 35/M Health care R. HSW OAP, NA 50 38. [34] 35/M Health care R. HSW OAP, NA 50 38. [34] 35/M Health care R. HSW OAP, NA 50 38. [34] 35/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. HSW OAP, NA 50 38. [34] 34/M Health care R. H	Gao et al. [22]	14/F	Vitiligo	P. HSW	Decoction, NA	38	15	Recovery	NA
145/M Hair loss P.HSW OARP NA 90 14,76 Grey hair HSW OARP 8-10g 60 11,126 50/M Grey hair HSW OARP 10g 60 12,12 50/M Grey hair HSW OARP 15g 30 12,21 36/M Chronic nephritis P. HSW OARP 12g 30 12,21 36/M Grey hair P. HSW OARP 3g 75 amg [29] 28/F Grey hair R. HSW OAR 3g 75 1,30 57/M Grey hair R. HSW OAR, 3g 75 1,31 56/F Grey hair R. HSW OAR, 3g 75 1,34 56/F Health care R. HSW Decoction, 15-20g 90 1,34 56/F Health care R. HSW Decoction, 15-20g 90 1,34 Hair loss Yishen wufa Oral, 2×10m 20 90 1,45 Hair loss Yishen wufa Oral, 3×10m 20	Baňárová et al. [23]	33/F	NA	SWW	Oral, NA	09	NA	Recovery	NA
Time [25] 43/F Grey hair HSW OAR 8-10g 60 11 [26] 40/F Health care R. HSW OAR NA 60 22] 36/M Grey hair P. HSW OAR 15 30 12 [28] 36/M Chronic nephritis P. HSW OAR 15 30 12 [28] 50/F Grey hair R. HSW OAR 3 75 1 [30] 58/F Hair loss R. HSW OAR 3 75 [31] 56/F Hair loss R. HSW OAR 2 1 [31] 56/F Allergic rhintis R. HSW Decoction, 15–20 90 [31] 56/F Allergic rhintis R. HSW Decoction, 15–20 90 [34] 26/M Hair loss Yagken wufa Oral, 2×10 mL 20 [34] 26/M Hair loss Yagken wufa Oral, 3×10 mL 20 [34] 46/F Hair loss Yagken wufa Oral, 1.2 g 90 [34] 57/M	Gao [24]	45/M	Hair loss	P. HSW	OAP, NA	06	21	Recovery	NA
11 26 50 M Grey hair HSW Decoction, 10-20 g 60 27 36 M Chronic neptrins P. HSW Decoction, 10-20 g 60 28 52 Grey hair P. HSW OAP, 18 30 29 50 Grey hair P. HSW OAP, 28 50 21 30 57 Grey hair P. HSW OAP, 28 50 21 30 57 Grey hair R. HSW OAP, 38 75 21 56 Grey hair R. HSW OAP, 38 75 21 57 Grey hair R. HSW OAP, 38 75 21 57 Health care R. HSW Decoction 15-20 g 50 21 39 Grey hair R. HSW Decoction 15-20 g 60 22 Allegic chintis R. HSW Decoction 15-20 g 60 23 28 Hair loss Yangxue shengfa Oral, 2-x d capsules 60 24 28 Hair loss Yangxue shengfa Oral, 2-x d capsules 60 25 Allegic chintis R. HSW Oral, 2-x d capsules 60 26 Allegic chintis R. HSW Oral, 2-x d capsules 60 26 Allegic chintis R. HSW Oral, 2-x d capsules 60 27 Hair loss Yangxue shengfa Oral, 1-2 g 60 28 Allegid care HSW Oral, 2-x d capsules 60 27 Hair loss Yangxue shengfa Oral, 1-2 g 60 28 Allegid care HSW Oral, 2-x d capsules 60 29 Allegid care HSW Oral, 2-x d capsules 60 20 Allegid care HSW Oral, 2-x d capsules 60 20 Allegid care R. HSW Oral, 2-x d capsules 60 20 Allegid care R. HSW Oral, 2-x d capsules 60 20 Allegid care R. HSW Oral, 2-x d capsules 60 20 Allegid care R. HSW Oral, 2-x d capsules 60 21 Allegid care R. HSW SIW, NA Hair loss SiW, NA Hair loss SiW, NA Hair loss SiW, NA SiW, NA SiW, NA SiW, NA Hair loss SiW, NA	Kui and Chen [25]	43/F	Grey hair	HSW	OAP, 8–10 g	09	30	Recovery	NA
Lat Log) 40/F Health care R. HSW Decoction, 10–20g 60 [27] 36/M Chronic nephritis P. HSW OAP, 15g 30 ang [28] 50/F Grey hair R. HSW OAP, 2g 60 ang [29] 50/F Grey hair R. HSW OAP, 2g 60 1, [30] 57/M Grey hair R. HSW OAP, 2g 60 1, [31] 56/F Grey hair R. HSW OAP, 2x 10 mL 120 39/F Allegic rhinitis R. HSW Decoction, 10–20 g 60 [34] 26/M Health care R. HSW Decoction, 10–20 g 60 [34] 26/M Hair loss Yangxue shengfa Oral, 2x 4 capsules 60 [34] 26/M Hair loss Yangxue shengfa Oral, 2x 4 capsules 60 [35] 28/M Hair loss Yangxue shengfa Oral, 2x 4 capsules 60 [37] 46/F Health care HSW Oral, 2x 6 capsules 60 <tr< td=""><td>[20]:17</td><td>50/M</td><td>Grey hair</td><td>HSW</td><td>OAP, NA</td><td>09</td><td>30</td><td>Recovery</td><td>NA</td></tr<>	[20]:17	50/M	Grey hair	HSW	OAP, NA	09	30	Recovery	NA
[27] 36/M Chronic nephritis P. HSW OAP, 15g 30 [28] 50/F Grey hair P. HSW OAP, 2g 60 [30] 50/F Grey hair R. HSW OAP, 3g 75 [31] 56/F Hair loss R. HSW OAP, 3g 75 [31] 56/F Hair loss R. HSW OAP, 20 mL 10 [33] 56/F Allergic rhinitis R. HSW Decoction, 15–20g 30 [34] 56/M Health care R. HSW Decoction, 15–20g 30 [34] 28/M Hair loss Yangue shengfa Oral, 2×4 capsules 60 [34] 28/M Hair loss Yishen wufa Oral, 2×4 capsules 60 [35] 28/M Hair loss Yishen wufa Oral, 2×6 90 [37] 40/F Health care HSW Oral, 1×2 60 [38] 57/M Health care HSW Oral, 1×6 10 [39] 57/M <td>Snao and L1 [26]</td> <td>40/F</td> <td>Health care</td> <td>R. HSW</td> <td>Decoction, 10-20 g</td> <td>09</td> <td>50</td> <td>Recovery</td> <td>NA</td>	Snao and L1 [26]	40/F	Health care	R. HSW	Decoction, 10-20 g	09	50	Recovery	NA
Zeng [28] 57/F Grey hair P. HSW OAR, NA 14 ang [29] 50/F Grey hair R. HSW OAR, 3g 56 I. [30] 57/M Grey hair R. HSW OAR, 3g 75 [31] 56/F Grey hair Yishen wufa Oral, 2×10mL 120 [31] 56/F Allegic rhinitis R. HSW Decoction, 15–20g 60 [33] 28/M Allegic rhinitis R. HSW Decoction, 15–20g 60 [34] 26/M Hairl loss R. HSW Decoction, 10–20g 60 [34] 26/M Hair loss Yingage shengfa Oral, 2×4 epsules 60 [34] 26/M Hair loss Yishen wufa Oral, 3×10mL 20 [37] 50/F Hair loss Yishen wufa Oral, 1×2 g 90 [37] 47/F Hair loss Yishen wufa Oral, 2×6 g 60 [38] 46/F Health care HSW Oral, 2×6 g 180	Hu et al. [27]	36/M	Chronic nephritis	P. HSW	OAP, 15 g	30	37	Recovery	NA
[29] 50/F Grey hair R. HSW OAR, 2 g 60 [31] 56/F Hair loss R. HSW NA 75 [31] 56/F Hearl loss R. HSW NA 120 [31] 56/F Allergic rhinitis R. HSW Decoction, 10-20g 60 [34] 56/F Allergic rhinitis R. HSW Decoction, 10-20g 60 [34] 28/M Hair loss Yishen wufa Oral, 2 × 10mL 90 [34] 26/M Hair loss Yishen wufa Oral, 2 × 10ml 7 [34] 26/M Hair loss Yishen wufa Oral, 2 × 6 cps 90 [37] 50/F Hair loss Yishen wufa Oral, 1 × 2 90 [38] 57/M Health care HSW Oral, 1 × 2 60 [39] 51/F Gev hair HSW Oral, 1 × 6 90 [31] 54/F Health care HSW Oral, 2 × 10g 60 [41] 54/F	Zhen and Zeng [28]	52/F	Grey hair	P. HSW	OAP, NA	14	30	Recovery	NA
1 30 57/M Hair loss R. HSW NA NA 3 3 4 Allergic rhinitis R. HSW NA 1 1 1 1 1 1 1 1 1	1; ord 7hang [20]	50/F	Grey hair	R. HSW	OAP, 2 g	09	15	Recovery	NA
1. [30] 57/M Grey hair Yishen wufa NA 1 [31] 36/F Grey hair Yishen wufa Decoction, 15–20g 30 [33] 28/A Allergic rhintits R. HSW Decoction, 16–20g 60 [33] 28/A Health care R. HSW Decoction, 16–20g 60 [34] 28/M Hair loss Yingene shengfa Oral, 2×4 capsules 90 [34] 26/M Hair loss Yishen wufa Oral, 2×4 capsules 60 [34] 26/M Hair loss Yishen wufa Oral, 2×4 capsules 60 [37] 50/F Hair loss Yishen wufa Oral, 3×6 m 20 [37] 50/F Hair loss Yishen wufa Oral, NA 7 [38] 50/F Health care HSW Oral, 1-2 g 60 [38] 57/M Health care HSW Oral, 2× 6 180 [41] 53/F Orastpation HSW Oral, 1-2 g 6	Li aliu Zilalig [29]	28/F	Hair loss	R. HSW	OAP, 3 g	75	12	Recovery	NA
[31] 56/F Grey hair Yishen wufa Oral, 2 × 10 mL 120 [34] Allergic rhinitis R. HSW Decoction, 10–20g 30 [34] 28/M Health care R. HSW Decoction, 10–20g 60 [34] 26/M Hair loss Yangxue shengfa Oral, 2 × 4 capsules 60 [34] 26/M Hair loss Yangxue shengfa Oral, 2 × 4 capsules 60 [34] 26/M Hair loss Yangxue shengfa Oral, 2 × 4 capsules 60 [37] 28/M Hair loss Yangxue shengfa Oral, 2 × 4 capsules 60 [37] 46/F Hair loss Yaww Oral, AA 20 [37] 46/F Health care HSW Oral, AA 20 [38] 57/M Health care HSW Oral, 1-2 g 60 [41] 53/F Grey hair HSW Oral, NA 120 [44] 34/M Hair loss R. HSW SIW, NA 30 [44]	Chen et al. [30]	57/M	Grey hair	R. HSW	NA	1	20	Recovery	NA
39/F Allergic rhinitis R. HSW Decoction, 15–20g 30 [34] 28/M Health care R. HSW Decoction, 10–20g 60 [34] 28/M Grey hair P. HSW Decoction, 10–20g 60 [34] 26/M Hair loss Yishen wufa Oral, 2 × 4 capsules 60 [31] 28/M Hair loss Yishen wufa Oral, 2 × 4 capsules 60 [37] 46/F Hair loss Yishen wufa Oral, NA 7 [37] 50/F Hair loss Xishen wufa Oral, NA 7 [38] 57/M Health care HSW tea Oral, 1-2 60 [39] 51/F Grey hair SWW Oral, 1-2 20 [41] 53/F MA SWW Oral, 1-2 20 [44] 34/F Grey hair HSW Oral, 2 × 6 180 [44] 34/M Health care R. HSW NA HSW A [44] 34/M	Liu et al. [31]	$56/\mathrm{F}$	Grey hair	Yishen wufa	Oral, $2 \times 10 \text{ mL}$	120	21	Recovery	NA
[33] 28/M Health care R. HSW Decoction, 10–20 g 60 [34] 28/M Grey hair P. HSW NA, 10 pieces 90 [34] 26/M Hair loss Yangxue shengfa Decoction, 10–20 g 60 [37] 28/M Hair loss Yishen wufa Decoction, 4g 90 [37] 50/F Hair loss SWW Oral, 1–2 g 20 [37] 50/F Health care HSW tea Oral, 1–2 g 20 [38] 57/M Health care HSW tea Oral, 1–2 g 20 [39] 51/F Grey hair SWW Oral, 1–2 g 20 [41] 53/F Grey hair HSW OAP, 2×10 g 60 [41] 54/F Grey hair HSW OAP, NA 15 [41] 34/M Health care R. HSW SIW, NA 30 (4) [44] 34/M Health care R. HSW SIW, NA 5 36/M Health care	Cum [32]	39/F	Allergic rhinitis	R. HSW	Decoction, 15-20 g	30	28	Recovery	NA
[33] 28/M Grey hair P HSW NA,10 pieces 90 [34] 26/M Hair loss Yangxue shengfa Oral, 2 × 4 capsules 60 [37] 47/F Hair loss Yishen wufa Oral, 3 × 10 ml 20 [37] 50/F Hair loss SWW Oral, 3 × 10 ml 20 [37] 46/F Hair loss SWW Oral, 1-2 g 60 1. [38] 5/M Health care HSW tea Oral, 1-2 g 20 1 [39] 5/F Grey hair SWW Oral, 1-2 g 20 1 [41] 54/F Grey hair HSW Oral, 1-2 g 20 [41] 54/F Grey hair HSW Oral, NA 15 [4] 38/F Grey hair HSW Oral, NA 15 [44] 34/M Health care R. HSW SIW, NA 30 [44] 34/M Health care R. HSW SIW, NA 5 [44] 36/M Health care <td>Jan [22]</td> <td>72/F</td> <td>Health care</td> <td>R. HSW</td> <td>Decoction, 10-20 g</td> <td>09</td> <td>42</td> <td>Recovery</td> <td>NA</td>	Jan [22]	72/F	Health care	R. HSW	Decoction, 10-20 g	09	42	Recovery	NA
[34] 26/M Hair loss Yangxue shengfa Oral, 2 × 4 capsules 60 [37] 28/M Hair loss Yishen wufa Decoction, 4g 90 [37] 50/F Hair loss Yishen wufa Oral, 1-2 g 60 [37] 50/F Health care HSW Oral, 1-2 g 60 [39] 51/F Grey hair SWP Oral, 1-2 g 60 [41] 53/F Grey hair SWP NA 240 [41] 54/F Grey hair HSW Oral, 2 × 6 g 180 [41] 54/F Grey hair HSW Oral, 2 × 6 g 180 [41] 54/F Grey hair HSW Oral, 3 × 6 g 60 [44] 34/M NA HSW Oral, 3 × 6 g 10 [44] 34/M Health care R. HSW SIW, NA 5 [45] 46/M Health care R. HSW SIW, NA 5 [47] 51/M Grey hair	Cao et al. [33]	28/M	Grey hair	P. HSW	NA, 10 pieces	06	42	Recovery	NA
38/M Hair loss HSW Decoction, 4 g 90 [37] 47/F Hair loss Yishen wufa Oral, 3 × 10 ml 20 [37] 50/F Health care HSW tea Oral, 1-2 g 60 [38] 57/M Health care HSW tea Oral, 1-2 g 20 [39] 51/F Grey hair SWW Oral, 1-2 g 20 [41] 54/F Grey hair HSW Oral, 1-2 g 20 [41] 54/F Grey hair HSW Oral, 1-2 g 20 [41] 34/F Grey hair HSW Oral, 1-2 g 60 [44] 34/M NA HSW Oral, NA 15 [44] 34/M Health care R. HSW Oral, NA 10 [44] 34/M Health care R. HSW SIW, NA 5 [44] 34/M Health care R. HSW SIW, NA 10 [45] 46/M Health care R. HSW SIW, NA<	Liu et al. [34]	26/M	Hair loss	Yangxue shengfa	Oral, 2×4 capsules	09	30	Recovery	NA
(37] 47/F Hair loss Yishen wufa Oral, 3×10 ml 20 (37] 50/F Hair loss SWW Oral, 1-2 g 60 (38] 46/F Health care HSW tea Oral, 1-2 g 60 (39] 51/F Grey hair SWW Oral, 1-2 g 20 (39] 51/F Grey hair SWW Oral, 1-2 g 20 (41] 53/F NA SWP Oral, 2× 6 g 180 (41] 54/F Grey hair HSW OAR, 2× 10 g 60 [44] 34/M NA HSW OAR, NA 120 [44] 34/M Health care R. HSW SIW, NA 20 11. [45] 46/M Health care R. HSW SIW, NA 30 12. [44] 34/M Hair loss R. HSW SIW, NA 30 12. [45] 36/M Hair loss R. HSW Decoction, 30 g Once a week (3w) 12. [48] 35/M Thinning hair	Yan [35]	28/M	Hair loss	MSH	Decoction, 4 g	06	28	Recovery	NA
50/F Hair loss SWW Oral, NA 7 46/F Health care HSW tea Oral, 1-2 g 60 57/M Health care HSW tea Oral, 1-2 g 20 51/F Grey hair SWP Oral, 1-2 g 20 53/F Grey hair HSW Oral, 1-2 g 20 34/F Grey hair HSW Oral, NA 15 34/M HSW OAP, NA 15 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 30 36/M Hair loss R. HSW SIW, NA 30 36/M Grey hair HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3× 6 tablets 40 66/M Grey hair SWP Oral	Wu and Niu [36]	47/F	Hair loss	Yishen wufa	Oral, 3×10 ml	20	14	Recovery	NA
46/F Health care HSW tea Oral, 1-2g 60 57/M Health care HSW tea Oral, 1-2g 20 51/F Grey hair SWP Oral, 2 × 6g 180 53/F NA SWP NA 240 54/F Grey hair HSW Oral, NA 15 31/F Constipation HSW Oral, NA 15 38/F Grey hair HSW OAP, NA 120 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 5 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, 3 × 6 tablets 40 54/M Hair loss SWP Oral, 3 × 6 tablets 40	Liu et al. [37]	50/F	Hair loss	SWW	Oral, NA	7	25	Recovery	NA
57/M Health care HSW tea Oral, 1-2 g 20 51/F Grey hair SWW Oral, 2 × 6 g 180 53/F NA SWP NA 240 54/F Grey hair HSW OAB, 2 × 10 g 60 31/F Grey hair HSW OAB, NA 15 38/F Grey hair HSW OAB, NA 120 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 5 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 54/M Hair loss SWP Oral, NA NA 54/M Hair loss SWP Oral, NA NA 54/M Hair loss SWP Oral, NA NA 54/M Hair loss SWP Oral,	Chan at al [38]	46/F	Health care	HSW tea	Oral, 1-2 g	09	25	Recovery	NA
51/F Grey hair SWW Oral, 2 × 6g 180 53/F NA SWP NA 240 54/F Grey hair HSW OAP, 2 × 10g 60 31/F Constipation HSW Oral, NA 15 38/F Grey hair HSW OAP, NA 120 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 5 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW Decoction, 30 g Once a week (3w) 38/M Grey hair HSW Decoction, 30 g Once a week (3w) 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 54/M Hair loss SWP Oral, 3 × 6 tablets 30	Cileii et al. [30]	57/M	Health care	HSW tea	Oral, 1-2 g	20	15	Recovery	NA
53/F NAA SWP NA 240 54/F Grey hair HSW OAP, 2 × 10 g 60 31/F Constipation HSW OAP, NA 15 38/F Grey hair HSW OAP, NA 120 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 5 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW SIW, NA 5 38/M Grey hair HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, 3 × 6 tablets 40 54/M Hair loss SWP Oral, 3 × 6 tablets 40	Yun et al. [39]	51/F	Grey hair	SWW	Oral, 2×6 g	180	18	Recovery	NA
54/F Grey hair HSW OAP, 2 × 10g 60 31/F Constipation HSW Oral, NA 15 38/F Grey hair HSW OAP, NA 120 34/M NA HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 5 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, 3 × 6 tablets 40 54/M Hair loss SWP Oral, 3 × 6 tablets 40	Furukawa et al. [40]	53/F	NA	SWP	NA	240	09	Recovery	NA
31/F Constipation HSW Oral, NA 15 38/F Grey hair HSW OAP, NA 120 34/M NA HSW HSW tea (liquor), NA 30 (4) 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW SIW, NA 5 38/M Grey hair HSW Decoction, 30 g Once a week (3w) 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 54/M Hair loss SWP Oral, 3 × 6 tablets 30	Yan et al. [41]	54/F	Grey hair	HSW	OAP, $2 \times 10 \mathrm{g}$	09	35	Recovery	NA
38/F Grey hair HSW OAP, NA 120 34/M NA HSW HSW tea (liquor), NA 30 (4) 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 5 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 56/M Grey hair SWP Oral, 3 × 6 tablets 30	He [42]	31/F	Constipation	HSW	Oral, NA	15	10	Recovery	NA
34/M NA HSW HSW tea (liquor), NA 30 (4) 34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 10 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 26/M Grey hair SWP Oral, 3 × 6 tablets 30	Chen [43]	38/F	Grey hair	HSW	OAP, NA	120	63	Recovery	NA
34/M Health care R. HSW SIW, NA 20 46/M Health care R. HSW SIW, NA 10 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW SIW, NA 30 38/M Grey hair HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 26/M Grey hair SWP Oral, 3 × 6 tablets 30	Cho et al. [44]	34/M	NA	HSM	HSW tea (liquor), NA	30 (4)	34	improved	NA
46/M Health care R. HSW SIW, NA 10 49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW SIW, NA 30 38/M Grey hair HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 26/M Grey hair SWP Oral, 3 × 6 tablets 30		34/M	Health care	R. HSW	SIW, NA	20	20	Recovery	NA
49/F Health care R. HSW SIW, NA 5 36/M Hair loss R. HSW SIW, NA 30 38/M Grey hair HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 26/M Grey hair SWP Oral, 3 × 6 tablets 30	Wang et al. [45]	46/M	Health care	R. HSW	SIW, NA	10	27	Recovery	NA
36/M Hair loss R. HSW SIW, NA 30 38/M Grey hair HSW Decoction, 30 g Once a week (3w) 51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 26/M Grey hair SWP Oral, 3 × 6 tablets 30		49/F	Health care	R. HSW	SIW, NA	5	27	Recovery	NA
38/MGrey hairHSWDecoction, 30 gOnce a week (3w)51/MSequelae of strokeHSWDecoction, 15 g1535/MThinning hairNuHairOral, NANA54/MHair lossSWPOral, 3 × 6 tablets4026/MGrey hairSWPOral, 3 × 6 tablets30	Zhu [46]	36/M	Hair loss	R. HSW	SIW, NA	30	30	Recovery	NA
51/M Sequelae of stroke HSW Decoction, 15 g 15 35/M Thinning hair NuHair Oral, NA NA 54/M Hair loss SWP Oral, 3 × 6 tablets 40 26/M Grey hair SWP Oral, 3 × 6 tablets 30	Vong ond I : [47]	38/M	Grey hair	HSW	Decoction, 30 g	Once a week (3w)	NA	Recovery	NA
$35/M$ Thinning hair NuHair Oral, NA NaHair loss SWP Oral, 3×6 tablets 40 $26/M$ Grey hair SWP Oral, 3×6 tablets 30	1411g ana 121 [47]	51/M	Sequelae of stroke	HSW	Decoction, 15 g	15	NA	Recovery	NA
$54/M$ Hair loss SWP Oral, 3×6 tablets 40 $26/M$ Grey hair SWP Oral, 3×6 tablets 30	Laird et al. [48]	35/M	Thinning hair	NuHair	Oral, NA	NA	120	Recovery	NA
$26/M$ Grey hair SWP Oral, 3×6 tablets	Vana and Dong [40]	54/M	Hair loss	SWP	Oral, 3×6 tablets	40	17	Recovery	NA
	Tang and Long (T)	26/M	Grey hair	SWP	Oral, 3×6 tablets	30	59	Recovery	Yes

TABLE 1: Continued.

Fin and Yi [50] 3.2 F Interfilling P HSW Decortion, NA B Untreated Recovery Yes Zhao [31] 3.2 F Interfilling F HSW Oral, 3.× 6 tablets 40 90 Recovery Yes Lif(22) 5.5 M Deziness, timultus HSW Oral, 2.× 6 tablets 50 0 Recovery Yes Cirt(ans et al. [35] 38/M Grey hair HSW Oral, 2.× 6 tablets 50 0 Recovery NA Panis et al. [55] 3.6 M Grey hair P HSW Oral, 3 tablets 120 30 Recovery NS Chen et al. [56] 5.f NA Chord hair SWP Oral, 3 tablets 120 30 Recovery NS Chen et al. [56] 3.6 M Crev plant PRA NA Recovery NS Achen (4) 5.0 F Crev plant RNP NA A Choccinon, 30g 0 Recovery NS Achen (4) 4.6 F Crev plant SWP	Reference	Age/gender	Reasons for medication	HSW type	Administration and dosage	Duration of intake, day	Hospitalization, day	Outcome Rechallenge?	echallenge?
17/M Grey hair SWW Oral, 3 × 6 tablets 40 90 Recovery 55/M Dizziness, tinnitus HSW Oral, 2 tablets 30 8 Covery 38/M Hair loss Shen-Min Oral, 2 tablets 56 6 Recovery 35/M Grey hair HSW Oral, 2 tablets 56 6 Recovery 35/M Grey hair HSW Oral, 3 × 5 tablets 120 30 Recovery 35/M Grey hair HSW Oral, 3 × 5 tablets 120 30 Recovery 36/J Grey hair HSW Oral, 12 0 30 Recovery 36/J Grey hair HSW Oral, 12 4 0 Recovery 36/J Grey hair HSW Decoction, 100g 10 18 Recovery 46/M Hstrown Decoction, 100g MA 0 18 Recovery 45/M Grey hair HSW Decoction, 100g MA 10 Recovery	Fu and Yu [50]	32/F	Infertility	P. HSW	Decoction, NA	18	Untreated	Recovery	NA
65/M Dizziness, timitus HSW STW, 30-50 ml 20 30 Recovery 33 28/M Grey hair Shen-Min Oral, 2 tablets 56 6 Recovery 34 Grey hair Shen-Min Oral, 2 tablets 56 6 Recovery 35/M Grey hair P. HSW Oral, 3 tablets 120 30 Recovery 5/F Oral SWP Oral, 3 x 5 tablets and 2 x 4 capsules 60 18 Recovery 58 Z8/M Hair loss SWP + Yangue shengfa Oral, 3 x 5 tablets and 2 x 4 capsules 60 18 Recovery 58 Z8/M Hair loss R. HSW Decoction, 10g NA Recovery 45/F Grey hair R. HSW Decoction, 10g NA Recovery 46/F Hair loss R. HSW Decoction, 10g NA Recovery 45/M Grey hair HSW onlineant Oral, 10A NA Recovery 45/F Grey hair SWP Oral, 10A	Zhao [51]	17/M	Grey hair	SWW	Oral, 3×6 tablets	40	06	Recovery	Yes
38/M Grey bair SWP Oral, 3 × 6 tablets 30 20 Recovery 4.2/F Grey hair Shen-Min Oral, 2 tablets 56 6 Recovery 4.2/F Grey hair HSWW Decoction, 30 g 45 50 Recovery 5.7/F Oral, and SWP Oral, 1 ablets 120 30 Recovery 5.7/F Grey hair HSWP Oral, 1 ablets 20 40 8ccovery 5.1/F Grey hair HSWP Oral, 1 AD 30 NA Recovery 4.6/M Grey hair R. HSW Decoction, 10 g 30 NA Recovery 4.6/M Grey hair HSW Decoction, 10 g 30 NA Recovery 1.5/F Grey hair HSW Decoction, 15 g 30 NA Recovery 6/F Grey hair SWP Liuwei Dihaang Wan Oral, NA 7 30 Recovery 17/M Grey hair SWP Oral, 3 × 6 tablets and 2 × 4	[63]	65/M	Dizziness, tinnitus	MSH	SIW, 30–50 ml	20	30	Recovery	Yes
53] 28/F Hair loss Shen-Min Oral, 2 tablets 56 6 Recovery 42/F Grey hair PHSW OcAP, 10g 90 30 Recovery 5/F NA SWP Decortion, 30g 45 50 Recovery 5/F NA SWP Chronic prostatitis SWP + Yangxue shengfa Oral, 3x5 tablets 20 40 Recovery 59/F Hair loss SWP + Yangxue shengfa Oral, RD 30 Recovery 59/F Hair loss R. HSW Decoction, 10g NA Recovery 45/M Chronic prostatitis SWP Decoction, 10g NA Recovery 15/F Grey hair, hair loss R. HSW Decoction, 10g NA NA Recovery 15/F Grey hair HSW Decoction, 10g NA NA Recovery 15/F Grey hair SWP Oral, NA Oral, NA NA Recovery 20/F Nocrey hair SWP Oral, NA	L1 [52]	38/M	Grey hair	SWP	Oral, 3×6 tablets	30	20	Recovery	NA
42/F Gev Phair HSW OAP, 10 g 90 30 Recovery 5/F Grey hair PHSW Decoction, 30 g 45 50 Recovery 5/F Grey hair PHSW Oral, 3x5 tablets 20 40 Recovery 58/F Grey hair loss SWP + Amgxue shengfa Oral, 8D 0 18 Recovery 59/F Grey hair loss SWP + Amgxue shengfa Oral, 8D 0 18 Recovery 45/M Grey hair, bair loss R. HSW Decoction, 100 g 0 18 Recovery 15/F Grey hair SWP Decoction, 100 g 0 30 Recovery 15/F Grey hair SWP Oral, 10A 0 30 Recovery 15/F Grey hair SWP Oral, 10A 0 30 Recovery 15/F Grey hair HSW Oral, 10A 0 30 Recovery 15/F Grey hair SWP Oral, 10A 0 30	Cárdenas et al. [53]	28/F	Hair loss	Shen-Min	Oral, 2 tablets	26	9	Recovery	NA
35/M Grey hair P HSW Decoction, 3 og 45 50 Recovery 2/F NA SWP Oral, 3 tablets 120 30 Recovery 36/F Grey hair HSW Oral, 3.5 tablets and 2.4 capsules 60 18 Recovery 59/F Grey hair loss SWP + Yangue shengfa Oral, RD 30 NA Recovery 46/F Hair loss R HSW Decoction, ISB 30 NA Recovery 46/F Grey hair SWP Decoction, ISB 30 NA Recovery 15/F Grey hair SWP Oral, NA 90 90 90 Recovery 20/F Constipation HSW Decoction, ISB 30 Recovery 90 90 Recovery 20/F Coral, bair SWP Oral, NA Oral, NA 30 Recovery 20/F Coral, bair SWP Oral, NA 90 90 90 Recovery 20/F Corey hair	Han [54]	42/F	Grey hair	HSW	OAP, 10 g	06	30	Recovery	Yes
5/F NA SWP Oral, 3 tablets 120 30 Recovery 5/F Grey hair HSW Oral, RD 20 40 Recovery 5/F Hair loss SWP + Yangxue shengfa Oral, RD 30 NA Recovery 5/F Hair loss R. HSW Decoction, NA 6 30 Recovery 45/M Grey hair, lar loss R. HSW Decoction, ISQ 30 Recovery 15/F Grey hair SWP Decoction, ISQ 30 Recovery 18/F Grey hair HSW Oral, NA 90 90 8covery 18/F Grey hair HSW Oral, NA 7 30 Recovery 17/M Grey hair SWP Oral, NA 6 14 30 Recovery 46/F Grey hair SWP Oral, NA 6 14 30 Recovery 58/F Dizziness HSW Oral, RD Oral, RD 14 29 Recovery	Yang [55]	35/M	Grey hair	P. HSW	Decoction, 30 g	45	50	Recovery	NA
86] GAP, MA OAP, NA 20 40 Recovery 88] 28/M Hair loss SWP + Yangxue shengfa Oral, RD 60 18 Recovery 59/M Chronic prostatitis SWP Oral, RD 60 18 Recovery 46/F Hair loss R. HSW Decoction, 100 g 0 10 Recovery 45/M Grey hair, hair loss R. HSW Decoction, 100 g NA Recovery 15/F Grey hair SWP Decoction, 100 g NA Recovery 66/F Constipation HSW Decoction, 100 g 30 Recovery 20/F Neurasthenia SWP + Liuwei Diluang Wan Oral, NA 7 30 Recovery 20/F Neurasthenia SWP Oral, NA 6 30 Recovery 17/M Grey hair SWP Oral, NA 6 NA Recovery 49/M Hypertension HSW Oral, 10 ml 5 9 Recovery	Panis et al. [56]	5/F	NA	SWP	Oral, 3 tablets	120	30	Recovery	Yes
of Ling [58] 28/M Hair loss SWP + Yangxue shengfa Oral, 3 × 5 tablets and 2 × 4 capsules 60 18 Recovery 50 78/M Chronic prostatitis SWP Oral, RD Oral, RD 30 NA Recovery 50 45/M Grey hair R. HSW Decoction, 16 g 30 NA Recovery 51 15/F Grey hair R. HSW Decoction, 16 g 30 Recovery 61 15/F Grey hair SWP Decoction, 16 g 30 Recovery 61 15/F Grey hair SWP Oral, NA 7 30 Recovery 41 20/F Neurasthernia SWP + Liuwei Diluang Wan Oral, NA 14 29 Recovery 45 Grey hair SWP Oral, NA A A Recovery 67 36/F Grey hair SWP Oral, RA NA Recovery 67 36/F Grey hair SWP Oral, 3 × 5 tablets 30 Recove	Chen et al. [57]	20/F	Grey hair	HSW	OAP, NA	20	40	Recovery	NA
tet al. [59] 78/M Chronic prostatitis SWP Oral, RD 30 NA Recovery 90] 45/F Hair loss R. HSW Decoction, NA 6 30 Recovery 80] 45/F Hair loss R. HSW Decoction, 100g NA 30 Recovery 81] 15/F Grey hair HSW Oral, NA 7 30 Recovery 41 20/F Constipation HSW ontment Oral, NA 7 30 Recovery 41 20/F Constipation HSW ontment Oral, NA 14 30 Recovery 45 Gery hair SWP Oral, NA 14 30 Recovery 55 Grey hair HSW Oral, NA 6 NA Recovery (67] 38/F Grey hair HSW Oral, NA 6 NA Recovery (68] 38/F Dizziness HSW Oral, NA 3 Recovery (68]	Huo and Ling [58]	28/M	Hair loss	SWP + Yangxue shengfa	Oral, 3×5 tablets and 2×4 capsules	09	18	Recovery	Yes
50] 46/F Hair loss R.HSW Decoction, 100g NA 30 Recovery 51] 45/M Grey hair, hair loss R.HSW Decoction, 100g NA Recovery 51] 15/F Grey hair, hair loss R.HSW Decoction, 15g 30 NA Recovery 65/F Constipation HSW ointment Oral, NA 7 30 Recovery 41 20/F Neurasthenia SWP + Liuwei Dihuang Wan Oral, NA 14 20 Recovery 43 17/M Grey hair SWP Oral, NA 14 30 Recovery 45/F Grey hair SWP Oral, NA 6 NA Recovery (67] 38/F Dizziness HSW Oral, NA 6 NA Recovery (67] 38/F Dizziness HSW Oral, S. 6 tablets 7 15 Recovery (67] 49/M Hypertension SWP Oral, 3. 5 tablets 20 NA Recove	Mazzanti et al. [59]	78/M	Chronic prostatitis	SWP	Oral, RD	30	NA	Recovery	NA
901 45/M Grey hair, hair loss R. HSW Decoction, 10 g NA Recovery 61] 15/F Grey hair HSW Decoction, 15 g 30 NA Recovery 61] 15/F Grey hair SWP Oral, NA 7 30 Recovery 63] 6/F Constipation HSW ointment Oral, NA 7 30 Recovery 4] 20/F Neurasthenia SWP - Liuwei Diluang Wan Oral, NA 14 29 Recovery 55 17/M Grey hair SWP Oral, NA 6 NA Recovery 67] 38/F Grey hair SWP Oral, NA 6 NA Recovery 67] 38/F Dizziness HSW Oral, SA 6 tablets 30 6 Recovery 67] 46/M Hypertension HSW Oral, 3 × 6 tablets 30 Recovery 67] 56/M Grey hair SWP Oral, 3 × 5 tablets 20 6 <t< td=""><td>[00]</td><td>46/F</td><td>Hair loss</td><td>R. HSW</td><td>Decoction, NA</td><td>9</td><td>30</td><td>Recovery</td><td>Yes</td></t<>	[00]	46/F	Hair loss	R. HSW	Decoction, NA	9	30	Recovery	Yes
51] 15/F Grey hair HSW Decoction, 15 g 30 NA Recovery 61] 18/F Grey hair SWP Oral, NA 7 90 90 Recovery 63] 66/F Constipation HSW ointment Oral, NA 7 30 Recovery 4] 20/F Neurasthenia SWP + Liuwei Dihuang Wan Oral, 3 × 6 tablets and 2 × 9 3 10 Recovery 55 40/F Grey hair SWP Oral, RD 14 30 Recovery 16/S 46/F Grey hair HSW Oral, RD 6 NA Recovery 16/S 49/M Hypertension HSW Oral, 3 × 6 tablets 30 6 Recovery 4 Abou [69] 26/M Grey hair SWP Oral, 3 × 6 tablets 30 Recovery 4 Z 30/M Grey hair SWP Oral, 3 × 6 tablets 30 8 Recovery 5 Z 40/M Hypertension SWP Oral, 3 ×	SIIAO [00]	45/M	Grey hair, hair loss	R. HSW	Decoction, 100 g	NA	30	Recovery	Yes
d Li [62] 18/F Grey hair SWP Oral, NA 7 30 Recovery 65] 66/F Constipation HSW ointment Oral, NA 7 30 Recovery 41 20/F Neurasthenia SWP + Liuwei Dihuang Wan Oral, NA 14 29 Recovery 55] 17/M Grey hair SWP Oral, NA 6 NA Recovery 667 46/F Grey hair HSW Oral, NA 6 NA Recovery 1681 49/M Hypertension HSW Decoction, 30 g 7 15 Recovery 1681 49/M Hypertension HSW Oral, SA 6 NA Recovery 4 About [69] 26/M Grey hair SWP Oral, 3×6 tablets 20 6 Recovery 17/M Grey hair HSW Oral, 3×5 tablets 2 94 Recovery 17/Z 28/F Oral, MA NA SWP Oral, 10 ml 15	Leng [61]	15/F	Grey hair	HSW	Decoction, 15 g	30	NA	Recovery	NA
63] 66/F Constipation HSW ointment Oral, NA 7 30 Recovery 4] 20/F Neurasthenia SWP + Liuwei Dihuang Wan Oral, NA 14 29 Recovery 55] 17/M Grey hair SWP Oral, NA 14 29 Recovery 67] 46/F Grey hair SWP Oral, NA 6 NA Recovery 67] 38/F Grey hair HSW Decoction, 30g 7 15 Recovery (68] 49/M Hypertension HSW Oral, 15g 10 8 Recovery 45/M Hypertension SWP Oral, 3 × 5 tablets 20 60 Recovery 45/M Grey hair SWP Oral, 10 ml 15 15 Recovery 7 36/F NA SWP Oral, 10 ml 15 15 Recovery 17/M Grey hair SWP Oral, 10 ml 15 15 Recovery 17/M	Dai and Li [62]	18/F	Grey hair	SWP	Oral, NA	06	06	Recovery	NA
4] 20/F Neurasthenia SWP + Liuwei Dihuang Wan Oral, NA 3 10 Recovery 55] 17/M Grey hair SWP Oral, NA 14 29 Recovery 67] 46/F Grey hair SWP Oral, NA 6 NA Recovery 67] 38/F Grey hair HSW Decortion, 30 g 7 15 Recovery 68] 49/M Hypertension HSW Decortion, 30 g 7 15 Recovery 6A A9/M Hypertension SWP Oral, 3 × 5 tablets 20 60 Recovery 6A Ab/M Grey hair SWP Oral, 10 ml 15 15 Recovery 7A 36/F NA SWP Oral, 10 ml 15 15 Recovery 7A 36/F NA SWP Oral, NA NA NA Recovery 7A 19/F Grey hair SWP Oral, NA NA NA NA	Yuan [63]	66/F	Constipation	HSW ointment	Oral, NA	7	30	Recovery	Yes
55] 17/M Grey hair SWP Oral, NA 14 29 Recovery 67] 46/F Grey hair SWP Oral, RD 14 30 Recovery 67] 38/F Grey hair HSW Oral, NA 6 NA Recovery (68] 49/M Hypertension HSW Decoction, 30 g 7 15 Recovery (68] 49/M Hypertension HSW Oral, 15 g 10 20 Recovery d Zhou [69] 26/M Grey hair SWP Oral, 3 × 5 tablets 20 60 Recovery 7 36/F NA SWP Oral, 10 ml 15 15 Recovery 17/M Grey hair SWP Oral, 10 ml 15 15 Recovery 17/M Grey hair SWP Oral, 10 ml 15 16 Recovery 12/In 19/F Grey hair SWP Oral, 10 ml NA NA Recovery 12/In<	Sun [64]	20/F	Neurasthenia	SWP + Liuwei Dihuang Wan	Oral, 3×6 tablets and 2×9 g	3	10	Recovery	Yes
al. [66] 46/F Grey hair SWP Oral, RD 14 30 Recovery [67] 38/F Grey hair HSW Oral, NA 6 NA Recovery [68] 49/M Hypertension HSW Decoction, 30 g 7 15 Recovery class 49/M Hypertension HSW Oral, 15 g 10 20 Recovery d Zhou [69] 26/M Grey hair SWP Oral, 3 × 5 tablets 20 60 Recovery [72] 36/F NA SWP Oral, 10 ml 15 15 Recovery [72] 36/F NA SWP Oral, 10 ml 15 15 Recovery [72] 28/M Grey hair SWP Oral, 10 ml 15 15 Recovery [72] 28/M Grey hair SWP Oral, 10 ml 10 60 Recovery [74] 19/F Grey hair SWP Oral, 10 ml NA NA R	Yang [65]	17/M	Grey hair	SWP	Oral, NA	14	29	Recovery	Yes
[67] 38/F Grey hair HSW Oral, NA 6 NA Recovery : [68] 58/F Dizziness HSW Decoction, 30 g 7 15 Recovery : [68] 49/M Hypertension HSW Oral, 3 × 6 tablets 30 20 Recovery d Zhou [69] 26/M Grey hair SWP Oral, 3 × 5 tablets 20 60 Recovery [72] 36/F NA SWP Oral, 10 ml 15 Recovery [72] 36/F NA SWP Oral, 10 ml 15 Recovery [72] 36/F Grey hair SWP Oral, 3 × 5 tablets 10 60 Recovery [72] 28/M Grey hair SWP Oral, 3 × 5 tablets NA NA Recovery [73] 27/F Grey hair SWP Oral, NA NA NA Recovery [75] 31, F Dizziness SWP Oral, RA NA Recovery	Park et al. [66]	46/F	Grey hair	SWP	Oral, RD	14	30	Recovery	NA
[68] 58/F Dizziness HSW Decoction, 30 g 7 15 Recovery d Zhou [69] 49/M Hypertension HSW Oral, 3 × 6 tablets 10 20 Recovery d Zhou [69] 26/M Grey hair SWP Oral, 3 × 5 tablets 20 60 Recovery [72] 36/F NA SWP Oral, 10 ml 15 Recovery [72] 36/F NA SWP Oral, 10 ml 15 Recovery [72] 28/M Grey hair SWP Oral, 3 × 5 tablets 10 60 Recovery 1 Zhen [74] 19/F Grey hair SWP Oral, NA NA Recovery 1 Zhen [74] 27/F Grey hair SWP Oral, RD Several weeks 21 Recovery	Sheng [67]	38/F	Grey hair	HSW	Oral, NA	9	NA	Recovery	Yes
CLOS 49/M Hypertension HSW SIW, 15 g 10 20 Recovery d Zhou [69] 26/M Grey hair SWP Oral, 3 × 5 tablets 20 60 Recovery 17/M Grey hair SWP Oral, 3 × 5 tablets 2 94 Recovery [72] 36/F NA SWP Oral, 10 ml 15 Recovery [72] 28/M Grey hair SWP Oral, 3 × 5 tablets 10 60 Recovery 1 Zhen [74] 19/F Grey hair SWP Oral, NA NA Recovery 1 Zhen [74] 27/F Grey hair SWP Oral, NA NA NA Recovery 31, F Dizziness SWP Oral, RD Several weeks 21 Recovery	[07] [07]	58/F	Dizziness	HSW	Decoction, 30 g	7	15	Recovery	Yes
d Zhou [69] 26/M Grey hair SWP Oral, 3 × 6 tablets 30 59 Recovery 17/M Grey hair SWP Oral, 3 × 5 tablets 2 94 Recovery 17/M Grey hair HSW Decoction, 50 g 2 94 Recovery 17/I Grey hair SWP Oral, 10 ml 15 Recovery 18/A Grey hair SWP Oral, NA NA 30 Recovery 1 Zhen [74] 27/F Grey hair SWP Oral, NA NA NA Recovery 21/F Dizziness SWP Oral, RD Several weeks 21 Recovery	LI et al. [00]	49/M	Hypertension	HSW	SIW, 15 g	10	20	Recovery	Yes
17/M Grey hair SWP Oral, 3 × 5 tablets 20 60 Recovery 30/M Grey hair HSW Decoction, 50 g 2 94 Recovery [72] 36/F NA SWP Oral, 10 ml 15 15 Recovery 8] 28/M Grey hair SWP Oral, NA NA 30 Recovery 1 Zhen [74] 27/F Grey hair SWP Oral, NA NA Recovery al. [75] 31, F Dizziness SWP Oral, RD Several weeks 21 Recovery	Fan and Zhou [69]	26/M	Grey hair	SWP	Oral, 3×6 tablets	30	59	Recovery	Yes
30/M Grey hair HSW Decoction, 50 g 2 94 Recovery 36/F NA SWP Oral, 10 ml 15 15 Recovery 28/M Grey hair SWP Oral, 10 ml 10 60 Recovery 19/F Grey hair SWP Oral, NA NA 30 Recovery 27/F Grey hair SWP Oral, NA NA Recovery 31, F Dizziness SWP Oral, RD Several weeks 21 Recovery	Li [70]	17/M	Grey hair	SWP	Oral, 3×5 tablets	20	09	Recovery	Yes
36/F NA SWP Oral, 10 ml 15 15 Recovery 28/M Grey hair SWP Oral, 3 × 5 tablets 10 60 Recovery 19/F Grey hair SWP Oral, NA NA 30 Recovery 27/F Grey hair SWP Oral, NA NA Recovery 31, F Dizziness SWP Oral, RD Several weeks 21 Recovery	Ye [71]	30/M	Grey hair	HSW	Decoction, 50 g	2	94	Recovery	Yes
28/MGrey hairSWPOral, 3 × 5 tablets1060Recovery19/FGrey hairSWPOral, NANA30Recovery27/FGrey hairSWPOral, NANARecovery31, FDizzinessSWPOral, RDSeveral weeks21Recovery	Zhang [72]	$36/\mathrm{F}$	NA	SWP	Oral, 10 ml	15	15	Recovery	Yes
19/FGrey hairSWPOral, NANA30Recovery27/FGrey hairSWPOral, NANARecovery31, FDizzinessSWPOral, RDSeveral weeks21Recovery	Niu [73]	28/M	Grey hair	SWP	Oral, 3×5 tablets	10	09	Recovery	Yes
27/FGrey hairSWPOral, NANANARecovery31, FDizzinessSWPOral, RDSeveral weeks21Recovery	Us and 7han [74]	19/F	Grey hair	SWP	Oral, NA	NA	30	Recovery	Yes
31, F Dizziness SWP Oral, RD Several weeks 21 Recovery	rie allu zileli [/4]	27/F	Grey hair	SWP	Oral, NA	NA	NA	Recovery	Yes
	But et al. [75]	31, F	Dizziness	SWP	Oral, RD	Several weeks	21	Recovery	Yes

SWP: Shou-Wu-Pian; SWW: Shou-Wu-Wan; OAP: oral administration of powder; SIW: soaked in water to drink; P. HSW: processed HSW; R. HSW: raw HSW; HSW: unclear whether it was processed; RD: recommended dosages; NA: not available.

TABLE 2: Characteristics of included case series.

Reference	Number of cases	Gender (F/M)	Age (a)	Duration of intake, day	Type of liver injury (number)	Outcome
Dong et al. [76]	18	5/13	18-63	1–120	H (18)	18 recoveries
Lian et al. [77]	52	22/30	22-69	5-120	H (30); C (9); M (13)	52 recoveries
Zhang et al. [78]	13	11/2	35-66	4-15	H (6); C (4); M (3)	12 recoveries; 1 LT
Zhang et al. [79]	36	13/23	24-73	NA	H (21); C (2); M (13)	33 recoveries; 1 cirrhosis; 2 deaths
Ding [80]	65	45/20	34-71	7-90	NA	64 recoveries; 1 death
Guo [81]	15	8/7	18-57	7–56	H (8); C (3); M (4)	15 recoveries
Xie et al. [82]	10	3/7	46.1 ± 10.2	30-105	H (5); C (4); M (1);	9 recoveries; 1 death
Song [83]	26	12/14	38-71	9-93	NA	26 recoveries
Wang [84]	20	7/13	34-67	NA	NA	20 recoveries
Jung et al. [85]	25	7/18	24-65	1–180	H (18); M (7)	23 recoveries; 1 LT; 1 death
Chen et al. [86]	12	5/7	20-70	15-90	H (4); C (4); M (4)	12 recoveries
Liu and Li [87]	7	5/2	31-64	60-180	NA	7 recoveries
Liu [88]	9	3/6	34-68	NA	NA	9 recoveries
Xu et al. [89]	40	24/16	45.2	9-168	H (22); C (8); M (10)	38 recoveries; 2 deaths
Yang et al. [90]	13	8/5	32-68	7-30	NA	13 recoveries
Zhou and Qiu [91]] 11	5/6	34-58	NA	NA	11 recoveries
Zhang et al. [92]	6	3/3	24-50	$4-24 \mathrm{w}$	NA	6 recoveries

NA: not available; H: hepatocellular; C: cholestatic; M: mixed; LT: liver transplantation.

TABLE 3: Use reasons of case reports.

Disease originally treated	Patients (number)
Gray hair, hair loss	43 (59.7%)
Health care	8 (11.1%)
Dizziness	3 (4.2%)
Vitiligo	2 (2.8%)
Constipation	2 (2.8%)
Others ^a	8 (11.1%)
Unknown	6 (8.3%)
Total	72 (100%)

^aIncluding infertility, hypertension, allergic rhinitis, hyperlipidemia, cerebral infarction sequelae, chronic nephritis and neurasthenia, and chronic prostatitis.

[77, 79, 86, 88, 91]. The reasons for medication of 72 cases of case reports are shown in Table 3.

3.4. Dosage Forms and Usage. In case series, there is insufficient information on HSW forms and usage of each patient, but it is worth noting that, in two case series, the ratio of processed HSW to raw HSW is 5:13 and 25:11, respectively [76, 79]. The HSW forms of case reports are shown in Table 4; in terms of usage, all involved Chinese patent medicines are of oral formulation; the types of HSW decoction pieces used included tea, liquor, powder, and decoction.

3.5. Dose and Duration of Taking HSW. In case series, there is insufficient information on dose and duration of taking HSW of each patient, but some articles indicate that the majority of patients take Chinese patent medicine in accordance with the instructions. For the 28 cases who consumed Chinese

TABLE 4: The classification of the drug of case reports.

Dosage forms	Patients (number)
Chinese patent medicine	
Shou-Wu-Pian	17 (23.61%)
Shou-Wu-Wan	4 (5.56%)
Yishen wufa	2 (2.78%)
Others ^b	5 (6.94%)
Decoction pieces	
R. HSW	13 (18.06%)
P. HSW	10 (13.89%)
Unknown	21 (29.17%)
Total	72 (100%)

^bIncluding Huolisu Koufuye, Jing-Wu-Pian, NuHair, Shen-Min, and Yangxue shengfa capsules.

patent medicines in case reports, 17 (17/28, 60.7%) cases are in accordance with the recommended dosage and the remaining are unknown. Of the 44 cases who used HSW decoction pieces, 19 cases (19/44, 43.2%) did not report the daily dose; the other 25 cases' daily dose ranged from 1 to 100 g with a median of 15 g; when the daily dose was \leq 12 g (11/25), the median of duration is 30 d, but if the daily dose is >12 g (14/25), the median of duration is 60 d. For all the patients of case reports, the duration from starting to take HSW to the onset of symptoms ranged from 1 to 240 days, with a median of 30 days (Table 5).

3.6. Clinical Manifestations and Outcome. According to case reports and case series, most of the patients had been hospitalized with jaundice, fatigue, anorexia, and yellow or tawny

TABLE 5: The duration of taking HSW of case reports.

Duration (day)	Patients (number)
<10	10 (13.89%)
10-30	27 (37.50%)
31–60	19 (26.39%)
>60	12 (16.67%)
Unknown	4 (5.56%)
Total	72 (100%)

TABLE 6: The length of hospitalization of case reports.

Hospitalization (d)	Patients (number)
<15	8 (11.1%)
15-30	37 (51.4%)
31–60	14 (19.4%)
>60	5 (6.9%)
Unknown	8 (11.1%)
Total	72 (100%)

urine. A handful of patients were found with abdominal distension, abdominal pain, diarrhea, rash, pruritus, and other symptoms. After admission examination, a few cases were found with epigastrium tenderness, first percussion over the liver, hepatomegaly or splenomegaly, and even ascites [77, 86, 89]. Nine case series reported liver damage types of 221 patients, including 132 (132/221, 59.7%) cases of hepatocytes type, 34 (34/221, 15.4%) cases of cholestatic type, and 55 (55/221, 24.9%) cases of mixed type.

In addition to two (2/450, 0.4%) cases who received liver transplantation [78, 85] and seven (7/450, 1.6%) who died [79, 80, 82, 85, 89], the remaining 441 (441/450, 98%) cases recovered or had liver function improvement after discontinuing HSW products and conservative care. In case reports, the length of 64 patients' hospitalization ranged from 6 to 120 d, with a median of 29.5 (Table 6). The case series that reported the average length of hospitalization was about four weeks [79, 81, 83, 84, 89, 91, 92].

3.7. Recurrence and Family History. In case reports, 23 (23/72, 31.9%) cases were reported with liver damage associated with HSW for many times, and 3 (3/72, 4.2%) cases had family history of HSW induced hepatitis [61, 67, 71]. In case series, seven articles reported 53 (53/138, 38.4%) cases with liver damage related to HSW many times [77, 82–84, 91, 92].

4. Discussion

Based on the above information we know that HSW associated with liver injury can occur at any age group and with no gender orientation. The main reason for using HSW is that patients suffer from gray hair and hair loss; this may be associated with those patients who are more likely to use HSW products, but whether patients suffering from gray hair or hair loss are prone to occurrence of liver damage associated with HSW remains to be further studied.

Although many studies suggest that processing could reduce the toxicity of HSW [15, 93], all HSW products may lead to liver damage regardless of herbal processing. In the *Chinese Pharmacopoeia* (2010), predetermined daily dose of raw HSW is 3–6 g and of processed HSW is 6–12 g [2]. Although only 25 cases of case reports have the HSW dosage information, 14 cases exceed maximum dosages (12 g/d). The results show that, when daily dose is less than 12 g, from the beginning of consuming HSW to the occurrence of liver damage, the median time is 60 days, while when daily dose is more than 12 g the median time is 30 days; this suggested that HSW associated with liver damage has a "dose-time-toxicity" relationship; animal experiments also had proved it [93].

Because more than 30% of patients in case reports and cases series were reported liver damage occurred many times which was induced by HSW, and a few cases have a family history of liver damage induced by HSW; these suggested that HSW associated with liver damage may be related to personal body factors of patients.

The mechanism of HSW induced liver damage is still unclear and mainly toxic substances are also an uncertainty [15, 94]; even few animal experiments did not find hepatotoxicity of HSW [95, 96]. Some studies suggested that the adverse reactions of traditional Chinese medicine are closely related to patient self-medication, arbitrarily increase in the dose, or long-term use [97–99]; this systematic review and some papers included in it also have the same standpoint.

HSW can cause different degrees of liver injury, even need of liver transplantation (2/450), and death (6/450). However, most HSW induced liver injuries are reversible; after withdrawal of HSW products and corresponding treatments, the vast majority of patients can recover liver function.

Because HSW induced liver injury is not a specific diagnostic method and some cases included in this review also take other drugs or herbal medicines, so considering the doctors experience, medical technology, and other limiting factors may not show all liver injury is caused by HSW.

5. Conclusion

Many cases of liver damage associated with HSW had been reported worldwide; HSW has liver toxicity and may cause different degrees of liver damage. The liver damage in most patients is reversible, after discontinuation of HSW products, and active treatment can restore liver function, but there are also a small number of patients with liver failure and even death. We suggest that patients should take HSW products under the guidance of a physician or pharmacist and avoid using them for long-term or in high-dose. If fatigue, anorexia, nausea, yellowing of skin and sclera, yellow urine, and other symptoms appear after medication, patients should be alerted to the occurrence of liver damage and promptly stop the medicine and treatment.

Conflict of Interests

The authors declare that they have no financial conflict of interests.

Authors' Contribution

Xiang Lei and Jing Chen contributed equally to this work. Hongcai Shang and Guihua Tian contributed equally to this work.

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