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The Potential Effects and Use of Chinese Herbal Medicine Pine Pollen (*Pinus pollen*): A Bibliometric Analysis of Pharmacological and Clinical Studies

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Abstract

The objectives of this study are to conduct a comprehensive literature search and bibliometric analysis to identify the breadth and volume of pharmacological and clinical studies on pine pollen (*Pinus pollen*) and to identify the potential effects and the use of pine pollen. Three Chinese electronic databases and two English electronic databases were searched for pharmacological and clinical studies on pine pollen. Data were extracted and analyzed and included publication year, authors, study type, pharmacological research topics or clinical diseases/conditions, usage and type of preparation, authors' conclusions, and adverse effects. Of 239 publications identified, 180 were pharmacological studies, 37 were clinical trials, and 22 were reviews. Numbers of publications increased particularly from 2004 onward. The top 10 most frequent topics in pharmacological studies were immune regulation, antisenility, antioxidation, liver protection, inhibiting prostate hyperplasia, inhibiting tumor cell proliferation, lowering blood glucose, lowering blood lipids, antifatigue, and improving intestinal function. The top 10 most frequent clinical diseases treated or where pine pollen was used as an adjuvant were bedsores, diaper dermatitis, hyperlipidemia, oral mucositis, eczema, hyperplasia of prostate, hypertension, prostatitis, type 2 diabetes mellitus, and radiodermatitis. Eight trials reported no adverse events associated with pine pollen, one reported mild gastrointestinal reactions, but symptoms

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Conflicts of interest

There are no conflicts of interest.

disappeared without special management. There have been an increasing number of publications on pine pollen during the past 20 years. Pharmacological studies have shown many potential benefits, and clinical studies have indicated some positive effects when it is either used as a single herb or as an adjuvant to treat disease. Its use as a topical agent, especially for skin diseases, was notable.

Keywords

Bibliometric analysis; Chinese herbal medicine; pine pollen; *Pinus pollen*; skin disease

Introduction

Pine pollen (*Pinus pollen*) is a Chinese herbal medicine, also known as “Songhuafen” or “Songhuang,” being first recorded in the Tang Dynasty’s *Xin Xiu Ben Cao*; it has been used in medicinal products and as a healthy food for thousands of years.[1] Pine pollen is a dry, fine, bright, or light yellow color powder. It is mainly derived from *Pinus massoniana* Lamb., from *Pinus tabuliformis* Carriere, or from other plants of the same species. Pine pollens have a reputation of being a “natural micronutrient storeroom” and are rich in many kinds of body-demanding amino acids, minerals, vitamins, enzymes, and flavonoids.[2,3] *Shen Nong’s Herbal Classic* recorded that this herb could increase urination, promote blood circulation, and disperse cold or hot evil in the heart and abdomen, and if administered over a long time, it could “lighten the body,” replenish *qi*, and prolong life span. Shizhen Li, an outstanding traditional Chinese medicine practitioner in the Ming Dynasty, recorded in the *Compendium of Materia Medica* that pine pollen lias the characteristics of sweet in flavor, warm in property, and nontoxic; it can nourish the heart and lung, replenish *qi*, disperse wind, and stop bleeding. Some pharmacological studies have reported that pine pollen has various functions such as regulating immunity,[4] protecting the liver,[5,6] antitumor,[7] antioxidation, anti-inflammatory,[8,9] antiaging,[1,10] antifatigue,[11] lowering blood lipids,[12] and lowering blood glucose.[13]

This work aimed to conduct a comprehensive literature search and bibliometric analysis to identity the breadth and volume of pharmacological and clinical studies on pine pollen and to identity its use and potential effects.

Methods

The literature was systematically searched and analyzed using a bibliometric approach. This approach does not involve a research protocol requiring approval by an institutional review board.

Bibliometric analysis is a quantitative method used to analyze the literature and reveal overall issues, directions, and potential advantages of the topic from various aspects and perspectives. The data can be utilized to inform a pilot study for a randomized controlled trial (RCT).

Sources and search strategies

Five databases were searched including PubMed, EMBASE, China National Knowledge Infrastructure, Chongqing China Science and Technology Journal Database, and Wanfang Database, from their inception to October 2018. To identify relevant publications, only “Pine Pollen,” “Song Hua,” and “Song Huang” were used as search terms and without applying any other search restrictions.Note Express 3.0.4.6732 software (Beijing Ai Qin Hai Le Tech Co., Ltd., Beijing, China) was employed to manage the retrieved literature. Two authors (SBL and NL) independently screened and retrieved the literature based on the inclusion/exclusion criteria. If there was any uncertainty or discrepancy, a third author (JPL) adjudicated.

Inclusion criteria

Inclusion criteria were pharmacological or clinical studies on pine pollen with no restriction on the study type and the studies which were designed to investigate the function or effect of pine pollen. Only Chinese or English language articles were included due to resource limitations.

Data extraction

Two authors (SBL and NL) developed a structured data extraction form, and the following data were extracted: (1) publication information, including study ID, first author of the article, year of publication, study design, and language; (2) pharmacological research topics investigated based on Pharmacology (8^{th} ed.)[14] or diseases investigated according to the International Statistical Classification of Diseases and Related Health Problems 10^{th} Revision (ICD-10) (http://apps.who.int/classifications/icd10/browse/2010/en); (3) usage and preparations of pine pollen; (4) conclusions, classified as effective, ineffective, or unclear. “Effective” was defined as whether the study achieved its objective and statistically favored pine pollen; “ineffective” – The study did not achieve its objective or was not significant for pine pollen; “unclear” – The author did not provide a clear conclusion; (5) adverse events or adverse effects in clinical studies.

Five authors (SBL, NL, FLB, BYL, and YPZ) performed data extraction. All were trained in the standard and skills of data extraction. Extracted data were verified by SBL. Any discrepancies were discussed with a third author.

Data analysis

Data were managed using Microsoft Excel 2010 (14.0.6024.1000). Counts, percentages, and frequencies were used as indicators, and each indicator was analyzed and described.

Results

General description of included studies

Figure 1 gives the flowchart of the literature searches and study selection. A total of 3540 articles were identified, and initial screening excluded 3301 papers for various reasons. Finally, 239 publications were included in this bibliometric analysis. Of these, 96.23% (n = 230) were published in Chinese and 3.77% (n = 9) were in English. Of the 239 publications,

180 (75.31%) were pharmacological studies, followed by 37 (15.48%) clinical studies and 22 (9.21%) reviews.

Year of publication

Figure 2 shows the trends in the publication by year. Very few publications on pine pollen were found before 2003. The earliest clinical study literature identified was published in 1966 and was related to pine pollen used for infant diaper dermatitis.[15]

Between 2004 and 2008, the number of published articles on the effects of pine pollen showed a significant growth. Between 2008 and 2016, the number of publications was variable, but the overall trend was relatively stable and the number of publications tended to increase each year, with a maximum of 22 publications in 2010. The trend appeared to decline in 2017–2018, but note that this did not cover a full year of publications.

Key authors and author group

According to Price's law,[16,17] key author's definition refers to the author who publishes the number N of articles ($N = 0.749[n_{max}]^{1/2}$, where "n_{max}" is the number of papers published by the most productive author in a subject area) or more papers in a subject area. If all key authors have published a total of 50% or more of the total number of papers in this subject area, they constitute the "key author group" for the subject area. The key author group can play a guiding role in the subject area and constantly drive the research in that subject area to a new level.

In this bibliometric analysis, we counted the first authors of all the included articles and their respective number of publications about pine pollen and its effects. After calculation, the authors who published two or more papers were designated the key authors in this subject area. The results of this study showed that there were 31 key authors publishing a total of 79 articles, accounting for 33.05% (79/239) of all the papers included. The percentage is far from the requirements of Price's key author group. Therefore, there was no key author group in the field of pine pollen research.

Pharmacological studies

Analysis of all 180 pharmacological studies appeared to show that pine pollen had a positive effect. Based on Pharmacology (8^{th} ed)[14] edited by pharmacologist Baofeng Yang, the number of articles on pharmacology was counted. A total of 20 research topics were addressed. The results showed that the literature on pine pollen and the regulation of immunity was the most commonly mentioned (36/180, 20.00%), followed by the literature on antiaging (25/180, 13.89%). The top 10 frequent topics on the use of pine pollen in the published literature from different pharmacological studies are shown in Table 1.

Clinical studies

The 37 clinical studies included were all published in Chinese and included 15 RCTs, 14 case series, six controlled clinical trials (CCTs), and two case reports. Table 2 provides data on the characteristics of included 37 trials.[18–54]

All clinical studies showed positive effects from pine pollen used alone or as adjuvant therapy. Fom RCTs,[22,23,37,38] three CCTs,[33,34,37] and one case series[39] (7/37, 18.92%) reported no adverse events attributed to pine pollen during treatment. One RCT,[26] which combined pine pollen with metformin for the treatment of type 2 diabetes, reported that the adverse events in the pine pollen group were mild gastrointestinal reactions (e.g., bloating, diarrhea, and loss of appetite), but symptoms disappeared without special intervention. No adverse events were reported by any other studies.

Based on ICD-10 (http://apps.who.int/classifications/icd10/browse/2010/en), the clinical studies tested a total of 17 diseases. The results showed that the studies on the use of pine pollen, either alone or as adjuvant therapy, were most common for bedsores (6/37, 16.22%), followed by diaper dermatitis (5/37, 13.51%). The top 10 indications based on the number of published clinical studies on different diseases are shown in Table 3.

Usage and preparations of pine pollen in clinical studies

Of the 37 clinical studies, 21 studies (21/37, 56.76%) reported pine pollen was used alone, while the remaining studies (16/37, 43.24%) reported pine pollen used in combination with other therapies including conventional medications, herbal medications, and other therapies.

More than half of clinical studies (22/37, 59.46%) reported pine pollen used as a topical agent, while other studies (21/37, 40.54%) reported oral use of pine pollen. It is worth noting that the topical use of pine pollen to treat skin problems was the most common application, e.g., bedsores, diaper dermatitis, and eczema.

Discussion

Main findings

The developing trend in research topics can be reported by analyzing the statistics of the number of documents and their temporal changes.[55] The results of this study suggest that the number of published articles on the effects of pine pollen is generally on the rise. This suggests that the research interest on the effects of pine pollen is increasing.

The key author group can play a guiding role in the subject area and drive the research in the subject area to a new level by creating interest to attract other researchers. Their research is authoritative and instructive. The establishment of a key author group not only means the stability of a research team but also means the maturity of a research field. The lack of stability of the research team indicates that the choice of research topics is random and discrete, and it is impossible to form a unified goal.[56–58] The results of this study showed that there were 36 key authors working on the effects of pine pollen, but they were insufficient to quality as a Price’s key author group.

This suggests that the current research on the effects of pine pollen is not yet mature and does not reflect a stable research field, suggesting the lack of research personnel in the field. Therefore, the establishment of research teams in this subject area could be accelerated.

The pharmacological studies suggested that pine pollen had multiple functions, such as immune regulation, antiaging, antioxidation, liver protection, inhibiting tumor cell proliferation, inhibiting prostate hyperplasia, antifatigue, lowering blood glucose, lowering blood lipids, and improving intestinal function. However, the quality of the included pharmacological studies was not evaluated. Therefore, the credibility of the currently available evidence needs to be further confirmed.

According to the statistics on the clinical studies analyzed, pine pollen was used alone (as a monotherapy) or in combination with other interventions (as an adjuvant therapy) for a wide range of diseases (e.g., bedsores, diaper dermatitis, hyperlipidemia, oral mucositis, eczema, hyperplasia of prostate, hypertension, prostatitis, type 2 diabetes mellitus, and radiodermatitis). More than half of clinical studies have reported that pine pollen was used as a topical agent for skin diseases, suggesting that pine pollen may have great potential in the treatment of skin diseases. Among all the included clinical studies on pine pollen, the potential beneficial effects of pine pollen were demonstrated. For clinical studies that reported adverse events, no events were related to pine pollen. However, the number of clinical trials with high levels of evidence (RCTs) is small, which may suggest that the firm evidence regarding the effects and safety of pine pollen could not be concluded.

Although experimental research is the key to achieving further development in clinical practice,[59] the clinical study is the best way to test the value of basic experimental research. Whether pine pollen is truly effective and safe in its clinical application must be confirmed by clinical studies. To demonstrate its effects and safety, more high-quality clinical trials may be needed.

Significance of this study

As a Chinese herbal medicine, pine pollen has a long history of application in China, and its resources are very rich. The results of this study can not only provide a certain reference for the future pharmacological research of pine pollen but also provide ideas for its clinical application. In particular, the analysis of previous clinical studies about pine pollen found that more than half of clinical studies have reported that pine pollen was used as a topical agent for skin diseases, suggesting that pine pollen may have great potential for the treatment of skin diseases.

Strengths and limitations

As a quantitative statistical analysis method of analyzing the literature, bibliometric analysis is based on the amount of the literature. This can reveal the overall layout, development, direction, and disciplines and potential advantages of the subject from many aspects and perspectives. This method has been widely used in various disciplines.[60] This bibliometric study conducted a multifaceted and multilevel analysis of the research of pine pollen for the first time, revealing the research hotspots and future directions to determine its benefit.

The language and database restriction for literature searching is a potential limitation. Due to resource constraints, other databases such as AMED and Web of Science were not searched; therefore, some publications may have been missed. Limiting publication language to

Chinese and English may have omitted publications in other languages such as Korean and Japanese.

Conclusion

There have been an increasing number of publications on pine pollen during the past 20 years. Pharmacological studies have shown many potential benefits, and clinical studies have indicated some positive effects when either used as a single herb or as an adjuvant to treat disease. Its use as a topical agent, especially for skin diseases, was notable.

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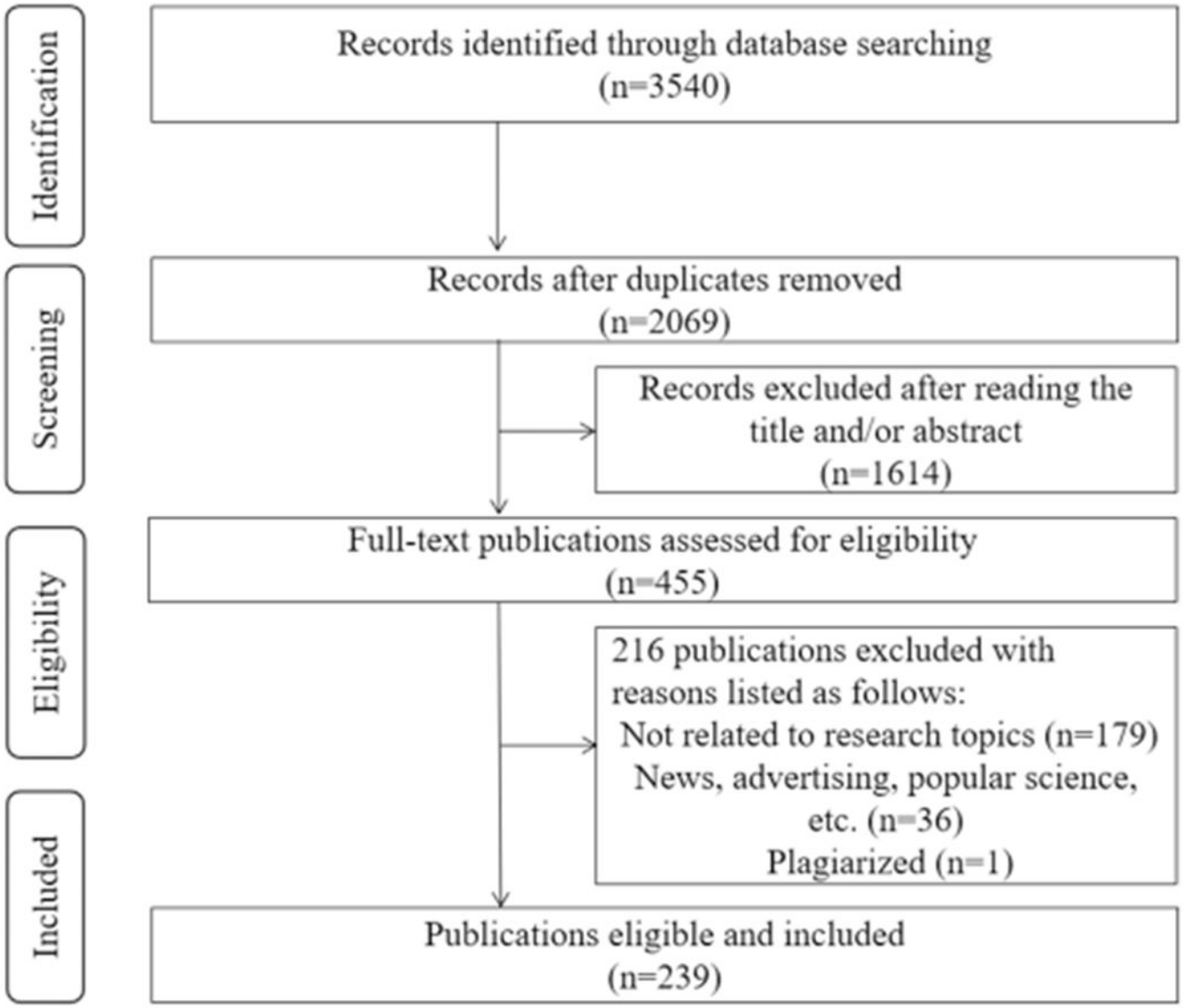

Figure 1:
The flowchart of study searching and selection

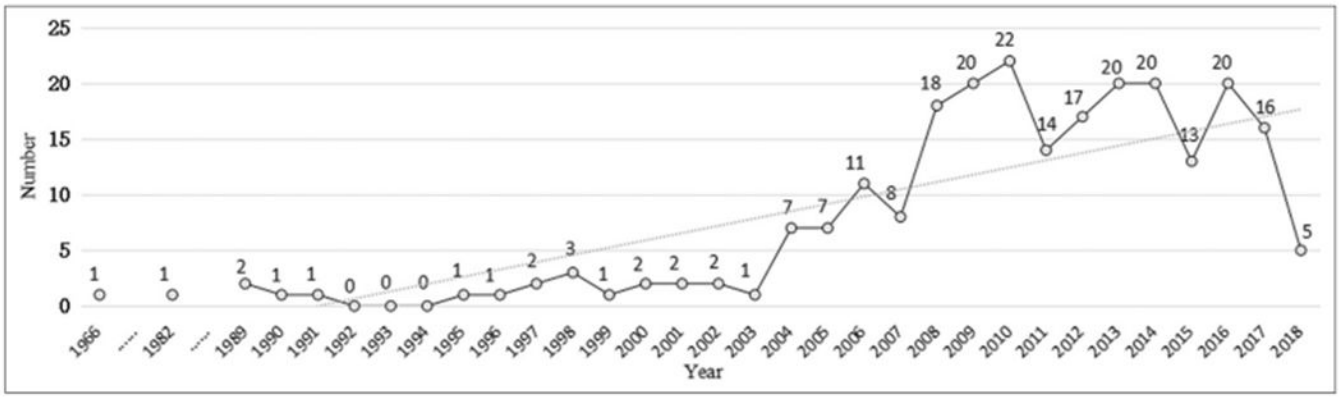

Figure 2:
Trends in the year of publications on pine pollen

Table 1:

The top 10 most frequent research topics being studied on pine pollen' pharmacology

Rank	Study topics	*n* (%)
1	Immune regulation	36 (20.0)
2	Antiaging	25 (13.89)
3	Antioxidation	20 (11.11)
4	Liver protection	16 (8.89)
5	Inhibiting tumor cell proliferation	15 (8.33)
6	Inhibiting prostate hyperplasia	12 (6.67)
7	Antifatigue	8 (4.45)
8	Lowering blood glucose	7 (3.89)
9	Lowering blood lipids	6 (3.33)
10	Improving intestinal function	6 (3.33)
Total (top 10 topics)		151 (83.89)
Percentage=(*n*/180)%		

Table 2:

Characteristics of the included 37 clinical studies

Study ID	Study type	Diseases	Sample size		Ages		Intervention		Treatment sessions	Outcome measurements	Adverse events
			E	*C*	*E*	*C*	*E*	*C*			
Ba *et al.*, 2016[18]	RCT	Bedsores	23	23	45-69 years	45-69 years	Pine pollen, topical; sensitive antibiotics, oral or intravenous	0.5% iodophor, topical; sensitive antibiotics, oral or intravenous	7 days	Effective rate	Not reported
Li, 2013[19]	RCT	Bedsores	28	28	46-84 years	46-83 years	Pine pollen, topical; Long Zhu ointment, topical	Moisture-exposed bum ointment, topical	4 weeks	PUSH tool; wound healing time	Not reported
Zhang *et al.*, 1997[20]	RCT	Bedsores	33	30	20-85 years	18-81 years	Pine pollen, topical; silver sulfadiazine, topical	Sterile Vaseline, topical	Not reported	Wound healing time; wound healing time index	Not reported
Cai, 2014[21]	RCT	Diaper dermatitis	30	30	Not reported	Not reported	Pine pollen, topical; iodophor, topical	Iodophor, topical	Not reported	Effective rate; wound healing time	Not reported
Chen and Zhang, 2013[22]	RCT	Diaper dermatitis; eczema	100	100	Not reported	Not reported	Pine pollen, topical	Talcum powder, topical	3 months	Effective rate; adverse events	None
Ouyang *et al.*, 2013[23]	RCT	Eczema	50	50	7-45 days	7-45 days	Pine pollen, topical	Erythromycin Ointment, topical	10 days	Effective rate; adverse events	None
Huang *et al.*, 2013[24]	RCT	Hyperlipidemia	50	50	≧40 years	≧40 years	Antibang capsules (the main ingredient is pine pollen), oral	Placebo, oral	Not reported	Effective rate; blood lipid level (TG, HDL-C and TC)	Not reported
Wang and Qian, 2009[25]	RCT	Hypertension	54	53	50.20±6.33 years	48.89±4.36 years	Pine pollen, oral	Placebo, oral	Not reported	Effective rate; blood pressure changes; blood lipid level	Not reported
Fang *et al.*, 2014[26]	RCT	Type 2 diabetes mellitus	35	30	30-72 years	32-70 years	Pine pollen, oral; Metformin, oral	Metformin, oral	12 weeks	FBG; PBG; HbAlc; insulin level; HOMA-IR; HOMA-β; adverse events	Yes
Fang *et al.*, 2011[27]	RCT	Type 2 diabetes mellitus	30	30	≧18 years	≧18 years	Pine pollen capsules, oral	Conventional western medicine, oral	8 weeks	Effective rate; blood sugar levels; HbAlc; adverse events	None
Gong and Li, 2012[28]	RCT	Hyperplasia of prostate	123	83	50-82 years	53-81 years	Pine pollen combined with Ruanji Tongbi prescription, oral	Finasteride, oral	3 months	Effective rate; adverse events	None
Lu *et al.*, 2014[29]	RCT	Oral mucositis	40	40	Not reported	Not reported	Pine pollen combined with sesame oil, topical	Compound gargle solution chlorhexidine gluconate, topical	5 days	Effective rate	Not reported

Study ID	Study type	Diseases	Sample size		Ages		Intervention		Treatment sessions	Outcome measurements	Adverse events
			E	*C*	*E*	*C*	*E*	*C*			
Liu, 2013[30]	RCT	Oral mucositis	188	184	42.0±3.0 years	42.0±3.0 years	Pine pollen, topical; pine pollen tablet, oral	Metronidazole, Prednisone acetate, Vitamin B2, topical; metronidazole, Vitamin B2, oral	6 months	Effective rate	Not reported
Gu *et al.*, 2012[31]	RCT	Oral mucositis	45	45	28-71 years	28-71 years	Pine pollen, topical; honey, topical; oxygen blowing	Compound gargle solution chlorhexidine gluconate, topical	5 days	Effective rate; wound healing time	Not reported
Liao and Zhai, 2013[32]	RCT	Radiodermatitis	40	40	27-68 years	27-68 years	Pine pollen, topical	Moisture exposed burn ointment, topical	2 weeks	Wound healing time	Not reported
Du *et al.*, 2008[33]	CCT	Hyperlipidemia	50	50	56.30±5.63 years	56.18±5.92 years	Pine pollen supercritical CO_2 extract soft capsule, oral	Placebo, oral	30 days	Effective rate; adverse events	None
Fan, 2006[34]	CCT	Hyperlipidemia	50	50	18-68 years	18-65 years	Pine pollen, oral	Blank	45 days	Effective rate; TC; TG; hemogram; liver and kidney function; adverse events	None
Hu and Zhu, 2007[35]	CCT	Hypertension	54	53	50.20±6.33 years	48.89±4.36 years	Pine pollen capsule, oral	Placebo, oral	6 weeks	Effective rate; blood pressure level; blood lipid level; symptom change	Not reported
Zhang *et al.*, 2018[36]	CCT	Adverse effect of chemotherapy	31	31	55.41±2.47 years	54.26±2.45 years	Pine pollen, oral	Placebo, oral	5 days	Adverse events (the number in the experimental group was significantly lower than that in the control group); quality of life	Yes
Wen *et al.*, 2016[37]	CCT	Constipation	56	57	53.8 years	52.9 years	Pine pollen tablet, oral	Placebo, oral	10 days	Stool frequency; stool consistency; adverse events	None
Yang, 2012[38]	CCT	Disorders of skin	23	23	67-94 years	67-94 years	Pine pollen, topical; baby wipes, topical	Zinc oxide ointment, topical	Not reported	Effective rate	Not reported
Jin and Zheng, 2000[39]	Case series	Diaper dermatitis	72		0-3 years		Pine pollen combined with talcum powder, topical		3 days	Effective rate; adverse events	None
Zhu, 1989[40]	Case series	Diaper dermatitis	87		≧1 years		Pine pollen, topical		Not reported	Effective rate	Not reported
Hong, 1966[41]	Case series	Diaper dermatitis	15		Not reported		Pine pollen, topical		6-7 days	Degree of satisfaction	Not reported

Study ID	Study type	Diseases	Sample size		Ages		Intervention		Treatment sessions	Outcome measurements	Adverse events
			E	*C*	*E*	*C*	*E*	*C*			
Jiao, 2008[42]	Case series	Bedsores	34		48-87 years		Pine pollen combined with sesame oil, topical; sensitive antibiotics, oral or intravenous; high protein and high vitamin diet		7 days	Effective rate; adverse events	None
Zhou, 2003[43]	Case series	Bedsores	30		65-92 years		Pine pollen, topical		4-6 weeks	Effective rate	Not reported
Liu, 2014[44]	Case series	Prostatitis	68		25-60 years		Pine pollen tablet combined with terazosin tablet, oral		6 weeks	NIH-CPSI scores; EPS-WBC	Not reported
Wang, 2006[45]	Case series	Prostatitis; Hyperplasia of prostate	50		45-95 years		Pine pollen combined with Ba Zheng San prescription, oral		Not reported	Effective rate	Not reported
Bai, 2010[46]	Case series	Hyperplasia of prostate	53		<50 years: 6 patients; 50-78 years: 47 patients		Pine pollen combined with Saren Garidi (Mongolian medicine), oral		10 days	Effective rate	Not reported
Huang, 1998[47]	Case series	Hyperlipidemia	32		30-50 years		Pine pollen tablet, oral		4 months	Effective rate	Not reported
Liu *et al.*, 2008[48]	Case series	Eczema	48		7-66 years		Pine pollen, topical (chronic eczema: oral and topical)		10 days	Effective rate	Not reported
An and Wang 2013[49]	Case series	Senility	100		50-83 years		Pine pollen capsule, oral; physical therapy		2 months	Effective rate; TC; TG; HDL-C; Apo AI; Apo B; HYP; Ca2+	Not reported
Zhang *et al.*, 2009[50]	Case series	Localized edema	36		35-68 years		Pine pollen, topical; ultraviolet ray irradiation		3-5 days	The degree of healing	Not reported
Xiao, 1982[51]	Case series	Chronic ulcer of skin	100		≦68 years		Pine pollen, topical		10-30 days	Effective rate; wound healing time	Not reported
Zhang *et al.*, 2001[52]	Case series	Radio dermatitis	8		Not reported		Pine pollen combined with Aloe Vera, topical		4-21 days	Wound healing time	Not reported
Guo *et al.*, 2010[53]	Case report	Bedsores	1		72 years		Pine pollen, topical		6 days	Cured	Not reported
Zhang, 1997[54]	Case report	Chicken pox	1		12 years		Pine pollen, topical		2 days	Cured	Not reported

E: Experimental group, C: Control group, TG: Triglyceride, TC: Serum total cholesterol, HDL-C: High-density lipoprotein cholesterol, HbAlc: Glycated hemoglobin, FBG: Fasting blood-glucose, PBG: Postprandial blood glucose, HOMA-IR: Homeostasis model assessment-insulin resistance; HOMA-β: Homeostasis model assessment-β, NIH-CPSI: National Institute of Health-Chronic Prostatitis Symptoms Index, EPS-WBC: Expressed prostatic secretions-white blood cells; Apo AI: Apolipoprotein AI, Apo B: Apolipoprotein B, HYP: Hydroxyproline, RCT: Randomized controlled trial, CCT: Controlled clinical trial, PUSH: Pressure ulcer scale for healing

Table 3:

The top 10 most frequent diseases being treated with pine pollen alone or as an adjuvant therapy

Rank	Disease	ICD-10 codes	Type and quantity of research				Total (%)
			RCTs	CCTs	Case series	Case reports	
1	Bedsores	L89	3	0	2	1	6 (16.22)
2	Diaper dermatitis	L22	2	0	3	0	5 (13.51)
3	Hyperlipidemia	E78	1	2	1	0	4 (10.81)
4	Oral mucositis	K12	3	0	0	0	3 (8.11)
5	Eczema	L20	2	0	1	0	3 (8.11)
6	Hyperplasia of prostate	N40	1	0	2	0	3 (8.11)
7	Hypertension	I10	1	1	0	0	2 (5.41)
8	Prostatitis	N41	0	0	2	0	2 (5.41)
9	Type 2 diabetes mellitus	E11	2	0	0	0	2 (5.41)
10	Radiodermatitis	L58	0	1	1	0	2 (5.41)

Percentage=(*n*/37)%: Chen and Zhang, 2013[22] studied diaper dermatitis and eczema in the same study; Wang, 2006[45] studied prostatitis and hyperplasia of prostate in the same study. ICD-10: International classification of diseases 10th revision, RCTs: Randomized controlled trials, CCTs: Controlled clinical trials