***Review***

**Chinese single herbs and active ingredients for postmenopausal osteoporosis: From preclinical evidence to action mechanism**

Jing Lin1,2, Jun Zhu3, Yan Wang1,4, Na Zhang1,4, Hans-Jürgen Gober4, Xuemin Qiu1,2, Dajin Li1,2, Ling Wang1,3,\*

1. Laboratory for Reproductive Immunology, Hospital & Institute of Obstetrics and Gynecology, Shanghai Medical College, Fudan University, Shanghai, China;
2. Shanghai Key Laboratory of Female Reproductive Endocrine-related Diseases, Shanghai, China;
3. Department of Obstetrics and Gynecology, Wenling People’s Hospital, Wenzhou Medical University, Zhejiang, China;
4. Department of Pharmacy, Kepler University Clinic, Neuromed Campus, Linz, Austria.

**Abbreviated Names:**

LinJ, ZhuJ, Wang Y, Zhang N, GoberH, Qiu X, Li D, Wang L

**Corresponding author:**

Dr. Ling Wang, Laboratory for Reproductive Immunology, Hospital & Institute of Obstetrics and Gynecology, Fudan University Shanghai Medical College, 413 Zhaozhou Road, Shanghai 200011, China.

E-mail: xxxxxx; Tel: xxxxxx; Fax: xxxxxx

**Conflict of Interest:** xxxxxx

**Abstract**

Postmenopausal osteoporosis is a systemic metabolic skeletal disease generally ascribable to a dearth of estrogen. Whether traditional Chinese medicine is effective in management of postmenopausal osteoporosis remains unclear. This article reviews the experimental evidence of both in vitro and in vivo preclinical studies with the theme of the application of Chinese single herbs and active ingredients in postmenopausal osteoporosis……

***Keywords***: Traditional Chinese medicine (TCM), single herbs, active ingredients, postmenopausal osteoporosis, bone morphogenetic protein (BMP), estrogen receptor (ER)

**1.** **Introduction**

Postmenopausal osteoporosis is a systemic metabolic skeletal disease characterized by structural deterioration and high fragility of bone tissue, generally ascribable to a dearth of estrogen. Osteoporosis affects 200 million women worldwide, and the probability of women over 50 affected by an osteoporotic fracture has been estimated to approach one third (*1*)……

Therapeutic agents currently used for osteoporosis include menopausal hormone therapy (MHT), bisphosphonates, calcitonin, selective estrogen receptor modulators (SERMs), parathyroid hormone (PTH) analogs, and so on. However……

In recent years, a growing interest has risen in the treatment of postmenopausal osteoporosis with traditional Chinese medicine (TCM). Compared with Western medicine, TCM has fewer adverse events with long-term use, for which extensive experience has been accumulated over thousands of years (*7-11*)……

Therefore, an understanding of Chinese single herbs and active ingredients for postmenopausal osteoporosis is needed by physicians and other health care providers. This review provides evidence for use of……

**2. Single herbs commonly used in postmenopausal osteoporosis**

2.1. *Herba Epimedium*

Epimedium brevicornum Maxim is a centuriesold traditional herb. Derived from the dried leaf of Epimedium brevicornum Maxim, Herba Epimedium (known as YinYangHuo in Chinese) is a popular Chinese traditional herb with a broad range of indications, especially for fatigue, sexual dysfunction, rheumatic diseases, and osteoporosis……

2.1.1. *Clinical trials*

To determine the therapeutic effect of Herba Epimedium and to provide clear evidence for clinical practice, Wang *et al.* identified 37 clinical trials using Herba Epimedium in co-prescription with other TCM herbs as anti-osteoporotic drugs……

2.1.2. *In vivo findings*

*In vivo* studies found that Herba Epimedium extract and its bioactive components could prevent ovariectomized (OVX) induced bone loss in rats, as evidenced by……

2.2. *Rhizoma Drynariae*

The traditional Chinese herb Rhizoma Drynariae (GuSui-Bu) is commonly used to manage musculoskeletal traumatic disorders of orthopedics with satisfactory results, as it tonifies the kidney……

2.3*. Salvia miltiorrhiza*

Salvia miltiorrhiza, known as Danshen in Chinese, is one of the best-known Chinese traditional herbs whose root has been clinically exploited in treating postmenopausal syndrome……

**3. Active ingredients commonly used in postmenopausal osteoporosis**

As forms of Chinese herbal medicine, active ingredients of Chinese medicine are isolated from single herbs or traditional herbal formulas and prepared using modern advanced pharmaceutical technology, such as icariin from Herba Epimedium……

3.1. *Saikosaponins*

Radix Bupleuri, made from dried roots of Bupleurum scorzonerifolium Willd, is commonly used in the prescriptions of traditional Chinese medicine……

3.2. *Linarin Flos*

Chrysanthemi Indici, one of the most important drugs in traditional Chinese medicine, possesses biological properties such as antioxidative, antibacterial……

3.3. *Echinacoside*

Echinacoside is one of the major constituents of Herba Cistanches, a famous traditional Chinese medicine. As a natural polyphenolic compound, echinacoside possesses effective antiinflammatory……

3.4. *Sweroside*

Fructus Corni has wide application in the clinic with a long history, of which Sweroside is an important constituent……

3.5. *Psoralen*

Psoralen is extracted from Psoralea corylifolia, which is one of the most commonly prescribed herbs for the treatment of bone and joint diseases……

**4. Conclusion**

In conclusion, Chinese herbal medicine substantially influences postmenopausal osteoporosis as a safer and more effective alternative. However, current clinical studies are not well funded to prove their therapeutic efficacy……

**Acknowledgements**

This work was supported by the National Natural Science Foundation of China No…….

**Reference**

1. Gallagher JC, Tella SH. Prevention and treatment of postmenopausal osteoporosis. J Steroid Biochem Mol Biol. 2014; 142:155-170. (As a sample of journal reference)
2. Darby S, Hill D, Auvinen A, *et al*. Radon in homes and risk of lung cancer: Collaborative analysis of individual data from 13 European case-control studies. BMJ. 2005; 330:223. (As a sample of journal reference with more than 15 authors)
3. Shalev AY. Post-traumatic stress disorder: diagnosis, history and life course. In: Post-traumatic Stress Disorder, Diagnosis, Management and Treatment (Nutt DJ, Davidson JR, Zohar J, eds.). Martin Dunitz, London, UK, 2000; pp. 1-15. (As a sample of book reference)
4. Ministry of Health, Labour and Welfare of Japan. Dietary reference intakes for Japanese. *http://www.mhlw.go.jp/houdou/2004/11/h1122-2a.html* (accessed June 10, 2019). (As a sample of web reference)

……

**Table 1. Single herbs commonly used in cancer treatment**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Common name | Other names | Latin name | Major active ingredients | *Ref.* |
| Radix astragali | Huang qi; Milk vetch | *Astragalus membranaceus* | Polysaccharides, saponins, and flavonoids | (*15-17*) |
| Turmeric | Jianghuang | *Curcuma longa* | Curcumin, demethoxycurcumin, and bisdemethoxycurcumin | (*18-21*) |
| Ginseng | Rensen; Panax | *Panax Ginseng* | Triterpene glycosides and ginsenosides | (*22-25*) |
| Garlic | Dasuan | *Allium sativum* | Allicin and alliin | (*26-28*) |
| Mylabris | Banmao | *Mylabris phalerata* | Cantharidin | (*29,30*) |
| Toad venom | Chansu | *Bufo bufo gargarizans* Cantor | Bufadienolides | (*12,31-33*) |

**Figure Legends**

**Figure 1. The mechanism of action of Chinese single herbs on pre-osteoblasts. (A)……; (B)……**

**Figure 2. The mechanism of action of Chinese single herbs on pre-osteoclasts.** Chinese single herbs interact with at least six pathways in pre-osteoclasts: *i*) up-regulate expression of OPG while down-regulate RANKL, *ii*) suppress MAPKs/NF-κB regulated……