

# Research Progress on Iridoid Glycosides and Pharmacological Effects of Zuogui Wan

Kaixia Xu, Yafei Guo, Yingli Wang and Qianjin Feng\*

Shanxi University of Chinese Medicine, China

\*Corresponding author: Qianjin Feng, Shanxi University of Chinese Medicine, Jinzhong 030619, China



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## ABSTRACT

Zuogui Wan (ZGW) has been used as a typical recipe for tonifying kidney essence in Traditional Chinese Medicine (TCM). The iridoid glycosides active ingredient are the important material basis for efficacy.

**Keywords:** Zuogui Wan; Iridoid Glycosides; Pharmacological Effect

**Abbreviations:** ZGW: Zuogui Wan; TCM: Traditional Chinese Medicine; ZGWRS: ZGW Contained Rat Serum; BGP: Bone Gla-Protein; IOP: Intraocular Pressure; LDP: Density Lipoprotein

## Mini Review

The formula of Zuogui Wan (ZGW) is from a traditional Chinese medicine (TCM) book titled "Jingyue Quanshu". It has been used as a classic recipe for tonifying TCM kidney, such as diabetic nephropathy, for hundreds of years. ZGW consists of *Rehmannia glutinosa* (Shu Di Huang), *Cuscuta chinensis* (Tu Si Zi), *Cornus officinalis* (Shan Zhu Yu), *Lycium barbarum* (Gou Qi Zi), *Dioscorea oppositifolia* (Shan Yao), and *Cyathula officinalis* (Chuan Niu Xi), etc. As a valuable TCM, ZGW has also been used to treat osteoporosis and type 2 diabetic nephropathy. Ju et al. reported that ZGW could prevent and treat osteoporosis [1]. In addition, ZGW can significantly increase Gla-containing protein content and reduce calcitonin content in osteoporosis rats without ovaries. The composition of TCM is remarkably complicated, especially after entering in the body. The therapeutic effect of TCM is attributed to the synergistic effects of its multiple components. Serum pharmacology has been introduced to the study on therapeutic material basis of TCM [2,3].

The results indicate that the active components in the ZGW contained rat serum (ZGWRS) prepared by administering rats with ZGW can significantly influence the forming of osteocalcin and the secretion of bone Gla-protein (BGP) by Gegenbaur cells in vitro and improve hyperplasia and the differentiation of Gegenbaur cells most

likely by estrogenic effects to adjust ERK/Smads signal channels [4-6]. In addition, ZGWRS can inhibit the apoptosis of thymocytes induced by corticosterone, possibly by regulating the ratio of Bcl-2 to Bax [7]. ZGWRS with complicated chemical composition and multiple-target features can exert a systematic influence on rats.

## Chemical Compositions and Pharmacological Effects

Morroneiside, loganin, sweroside, loganic acid and 8-epiloganic acid are the bioactive herbal ingredients isolated from *Cornus officinalis* (Shan Zhu Yu) that is a major herb component of ZGW. Morroneiside and loganin are the compounds from *Cornus officinalis* (Shan Zhu Yu). It has been reported that morroneiside and loganin can improve the morphological changes of rat mesangial cells and regulate their growth by reducing oxidative stress, which provides a molecular mechanism for the use of morroneiside and loganin in the early stages of diabetic nephropathy [8]. In addition, loganin can significantly inhibit the expression of fibronectin and IL-6 that are harmful to the mesangial cells in kidney [9]. Sweroside can attenuate and inhibit apoptosis and has a direct osteogenic effect on the proliferation and differentiation of human MG-63 cells and rat osteoblasts in vitro [10]. *Cornus officinalis* (Shan Zhu Yu) has been safely used for the treatment of osteoporosis in postmenopausal women or elderly men in Asia with a long history. Sweroside is one of the main bioactive herbal ingredients in ZGW.

Loganic acid is an active iridoid in *Cornus officinalis* (Shan Zhu Yu) and is a major polar compound of ZGW. A single dose of 0.7% loganic acid extract in vehiculum containing 0.15% sodium hyaluronate administered directly into the conjunctival sac of animal model (New Zealand rabbits) can decrease 15 % intraocular pressure (IOP) in 60 min in average. Loganic acid itself can decrease IOP ~23%, indicating its potential application in ocular hypertension therapy [11]. Coumaric acid, a hydroxyl derivative of cinnamic acid, is a bioactive herbal ingredient from *Lycium barbarum* (Gou Qi Zi). It can reduce the peroxidation of low density lipoprotein (LDL) and has shown biological functions including anti-mutagenesis, anti-genotoxicity, anti-microbial, and antioxidant activities. Coumaric acid can also inhibit cellular melanogenesis and plays important roles in immune regulation. In addition, coumaric acid can capture peroxide substance and reduce the incidence of vascular atherosclerosis. [12]. Kaempferol-3-glucuronide is a bioactive herbal ingredient from *Cuscuta chinensis* (Tu Si Zi). Kaempferols can be efficiently absorbed by human body, even at low oral doses. Kaempferol-3-glucuronide is its major metabolite found in plasma and urine [13]. Studies have shown that dietary kaempferol can reduce the risk of chronic diseases, especially cancers. Kaempferol may augment antioxidant in body to against free radicals, preventing the development of cancer [14]. 5-Hydroxymethyl-2-furfural glucuronide and dihydro-5-hydroxymethyl-2-furfural glucuronide are bioactive herbal ingredients from *Rehmannia glutinosa* (Shu Di Huang). They can be hydrolyzed to 5-hydroxymethyl-2-furfural in vivo and have almost same functions. 5-(hydroxymethyl)-2-furfural (5-HMF) has many biological functions, such as antioxidant activity, inhibiting sickling of red blood cells, and hypoxic injury [15,16].

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## Competing interests

The authors declare that they have no competing interests.

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