

LITERATURE REVIEW

Long et al. found evidence for the effective use of some herbal preparations in the treatment of osteoarthritis in twelve trials and two systemic reviews [13]. There are several lines of weak evidence for mild to moderate relief of symptoms using Reumalex (a herbal medicine containing Pulv white willow bark, Pulv Guaiacum Resin BHP, Pulv Black Cohosh BPH, Pulv Ext Sarsaparilla and Pulv Ext Poplar Bark), willow bark extract, stinging nettle leaf (*Urtica dioica*) and the Ayurvedic herbal preparation Articulin-F (*Withania somnifera* root, *Boswellia serrata* oleo-gum resin, *Curcuma longa* rhizome and zinc). There is promising evidence for devil's claw (*Harpagophytum procumbens*) and avocado/soybean unsaponifiables and moderately strong evidence for Phytodolor (a fixed herbal formulation containing extract of *Populus tremula*, *Fraxinus excelsior* and *Solidago virgaurea*) and capsaicin cream for the relief of OA symptoms. However, the plants used in these herbal preparations do not include any plant in DJW [10]. The ingredients of DJW preparation are as follows:

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| 1. Radix Angelicae Pubescentis | 2. Radix Gentianae Macrophyllae |
| 3. Herba Asari | 4. Cortex Eucommiae |
| 5. Radix Achyranthis Bidentatae | 6. Radix Angelicae Sinensis |
| 7. Radix Paeoniae Alba | 8. Radix Codonopsis |
| 9. Radix Glycyrrhizae | 10. Herba Taxilli |
| 11. Radix Rehmanniae Preparata | 12. Rhizoma Chuanxiong |
| 13. Poria | 14. Cortex Cinnamomi |
| 15. Radix Ledebouriellae | |

This preparation has not yet been studied in clinical trial. Some plants in this preparation are indicated to relief joint pain in traditional and folk use reports. Some have analgesic and/or anti-inflammatory effects in scientific researches but some have other pharmacological effects.

The overall functions and indications including pharmacological effects of all plants in this preparation are described below.

Radix Angelicae Pubescentis

Botanical name: *Angelica pubescens* Maxim.

Family: Apiaceae

Chinese name: Duhuo

Common name: Double teeth Pubescen Angelica root

Part used and method for pharmaceutical preparations:

The roots are dug in spring or autumn and then baked and cut into slices after the fibrous parts have been removed [11].

Constituents: Osthol, columbianetin, bergapten, isoimperatorin, meranxin hydrate, nodakenetin, marmesinin, columbianine, xanthotoxin, anpubesol, angelol, thymol, angelitriol, eremophilene, humulene, nerolidiol, α -phelladrene [14], columbianadin, psoralen, umbelliferone, caffeic acid, isoferulic acid, β -sitosterol, 2-hydroxy-4-methyl acetophenone [15].

Function: To relief rheumatic conditions and pain [16].

Indications: Rheumatic arthritis with pain in the lower back and knees [16].

Pharmacological effects:

1. Reduce adjuvant-induced inflammatory pain and hyperalgesia in rats [17-18].
2. Reduce inflammation in carrageenan and formalin-induced rat paw edema and reduce pain in acetic acid-induced writhing response (from methanol, chloroform and ethylacetate extracts), formalin-induced pain (from osthole, bergapten, columbianadin, columbianetin acetate, xanthotoxin, umbelliferone and caffeic acid) and thermal-induced pain (from methanol, water, chloroform and ethylacetate extracts) in mice [15,18].

2. Radix Gentianae Macrophyllae

Botanical name: *Gentiana macrophylla* Pall.

Family: Gentianaceae

Chinese name: Qinjiao

Common name: Large leaf Gentian root, Large leaf Gentiana

Part used and method for pharmaceutical preparations:

The roots are dug in spring or autumn. After the fibrous root bark has been removed, the roots are cleaned, dried in the sun and cut into slices [11].

Constituents: Gentianine, gentianidine, gentianol, gentiopicroside, α -amyrin, swertiamarin, montanic acid, methyl montanate, roburic acid, β -sitosterol, sweroside, gentialutene, isogentialutene, gentiatibetene [14].

Function: To relief rheumatic conditions [19] and relief inflammation and pain [20].

Indications: Rheumatic arthritis and severe joint pain [19-20].

3. Herba Asari

Botanical name: *Asarum heterotropoides* Fr. var. *mandshuricum* (Maxim.) Kitag., *Asarum sieboldii* Miq. var. *seoulense* Nakai or *Asarum sieboldii* Miq.

Family: Aristolochiaceae

Chinese name: Xixin

Common name: Asarum, Manchurian Wildginger

Part used and method for pharmaceutical preparations:

The entire plant is gathered in summer and dried in the shade [11].

Constituents: Pinen, camphene, myrcene, 1,8-cineol, p-cymene, borneol, asaricin, asarone, kakuol [14].

Function: To relief pain [21].

Indications: Rheumatic arthralgia [21].

4. Cortex Eucommiae

Botanical name: *Eucommia ulmoides* Oliv.

Family: Eucommiaceae

Chinese name: Duzhong

Common name: Eucommia bark

Part used and method for pharmaceutical preparations:

The bark is gathered in summer and autumn. The rough bark is removed and discarded, and then the smooth bark is dried in the sun [11].

Constituents: Pinoresinol-di-O- β -D-glucopyranoside, medioresinol-di-O- β -D-glucopyranoside, medioresinol-4-O- β -D-glucopyranoside, liriidenoate, guaiacyl glycerol, cycloolivil, geniposide, geniposidic acid, ulmoside, eucommiol, ulmoprenol, eucommioside, aucubin, kaempferol, dulcitol, β -sitosterol, betulin, betulic acid, ursolic acid [14].

Function:

1. To strengthen the tendons and bones and to tonify the liver and the kidney [22].
2. To reduce blood pressure [23].

Indications: Deficiency condition of the kidney marked by lumbago and lack of strength, hypertension [22], backache and osteoporosis [23].

5. Radix Achyranthis Bidentatae

Botanical name: *Achyranthes bidentata* Bl.

Family: Amaranthaceae

Chinese name: Niuxi

Common name: Two toothed Achyranthes root

Part used and method for pharmaceutical preparations:

The roots are dug in winter, dried and cut into slices [11].

Constituents: Oleanolic acid- α -L-rhamnopyranosyl- β -D-galactopyranoside, emodin, physcion, betaine, fructan, peptide-polysaccharide, ecdysterone, inokosterone, rubrosterone [14].

Function:

1. To replenish the liver and the kidney, to strengthen the tendons and bones [24].
2. To relieve pain and inflammation in mucosal tissue [25].

Indications: Soreness of the lumbar and knee joints with weakness in the legs [24].

6. Radix Angelicae Sinensis

Botanical name: *Angelica sinensis* (Oliv.) Diels

Family: Apiaceae

Chinese name: Danggui

Common name: Chinese Angelica

Part used and method for pharmaceutical preparations:

The roots are dug in late autumn. After the fibrous roots have been removed, the roots are laced, or smoked with sulfur and cut into slices [11].

Constituents: Camphoric acid, myristic acid, ligustilide, myrcene, acoradiene, verbenone, cadinene, isoacoradiene, angelic acid, alloocimene, β -bisabolene, β -selinene, safrole, eucarvon, bergamotene, copaene, α -pinene, carvacrol, *p*-cresol, guaiacol, vanillin, isoeugenol, sphingomyelin, phosphatidylserine, angelicide, phosphatidylinositol, phosphatidylcholine, ligustilide dimer, vanillic acid, ferulic acid, brefeldin A, β -sitosterol, stigmasterol, daucosterol, nicotinic acid, succinic acid [14].

Function: To enrich blood, activate blood circulation and relief pain [26-27].

Indications: Rheumatic arthralgia [26].

Pharmacological effects:

1. Reduce carrageenan-induced prostaglandin E₂ production in rats [27].
2. Reduce inflammation in carrageenan-induced rat paw edema and reduce pain in acetic acid-induced writhing response in mice (from ferulic acid) [28], (from water extract) [18].
3. Reduce tremor in parkinsonian patients [29].

7. Radix Paeoniae Alba

Botanical name: *Paeonia lactiflora* Pall., *Paeonia albiflora* Pall.

Family: Ranunculaceae

Chinese name: Baishao

Common name: White Peony root

Part used and method for pharmaceutical preparations:

The roots are dug in summer. The fibrous roots are cleaned and their bark is removed. The roots are then soaked in hot boiled water and dried in the sun. They are soaked again before being cut into slices [11].

Constituents: Paeonoflorin, oxypaeoniflorin, benzoylpaeoniflorin, albiflorin, paeoniflorigenone, lactiflorin, 1S,5R- β -pinen-10-yl- β -vicianoside, daucosterol, benzoic acid, β -sitosterol, paeonilactone, catechin [14].

Function:

1. To relief pain [30-31]
2. To reduce blood pressure [31].

Indications:

1. Costal and abdominal pain, spasmodic pain of the limbs [30].
2. Arthralgia [31].

Pharmacological effects:

1. Reduce tremor in parkinsonsonian patients [29].
2. Inhibit acetic acid-induced writhing response in mice (from paeoniflorin) [32].
3. Suppress adjuvant arthritis in rats [18].

8. Radix Codonopsis Pilosulae

Botanical name: *Codonopsis pilosular* (Franch.) Nannf., *Codonopsis pilosular* Nannf. var. *modesta* (Nannf.) L.T. Shen or *Codonopsis tangshen* Oliv.

Family: Campanulaceae

Chinese name: Dangshen

Common name: Tangshen, Pilose asiabell root

Part used and method for pharmaceutical preparations:

The roots are dug in spring or autumn. They are dried in the sun and cut into pieces [11].

- Constituents:** Fructose, inulin, syringin, n-hexyl- β -D-glucopyranoside, choline, ethyl- α -D-fructofuranoside, tangshenoside I, perlolyrine, n-butylallophanate, pyroglutamic acid N-fructoside, nicotinic acid, 5-hydroxy-2-pyridine methanol, taraxerol, friedelin, α -spinasterol, stigmast-7-en-3 β -ol, stigmasterol, stigmast-7-ene-3-one, stigmasta-5,22-dien-3-one, syringaldehyde, vanillic acid, 2-furan carboxylic acid, a-tractylenolide, 5-hydroxymethyl-2-furaldehyde, methyl palmitate, palmitic acid, α -pinene, nona-2,4-dienal, borne-ol, δ -guaiene, α -curcumene [14].
- Function:** To reinforce vital energy (qi) and invigorate the function of the spleen and the lung [33-34].
- Indications:** Weakness of the spleen and the lung manifested by shortness of breath, cough, palpitation, anorexia, loose stools; diabetes caused by internal heat [33-34].
- Pharmacological effects:**
- Increase immunity in mice (from water extract), protect gastric ulcer in mice (from water, n-butanol extracts, decoction and polysaccharides) and rescue the blood pressure of rabbits with hemorrhagic shock [34].

9. Radix Glycyrrhizae

- Botanical name:** *Glycyrrhiza uralensis* Fisch, *Glycyrrhiza inflata* Bat. or *Glycyrrhiza glabra* L.
- Family:** Papilionaceae
- Chinese name:** Gancào
- Common name:** Licorice root
- Part used and method for pharmaceutical preparations:**

The rhizomes are dug in spring or autumn. After the fibrous roots and bark have been removed, the rhizomes are cut into slices and dried in the sun [11].

Constituents: Glycyrrhizin, glycyrrhizic acid, 18 β -glycyrrhetic acid, glucuronic acid, uralsaponin, licorice saponin, liquiritin, liquiritigenin, isoliquiritin, vicianin II, isoliquiritigenin, neoliquiritin, ononin, neoisoliquiritin, licoricidin, apioliquiritin, apioisoliquiritin, glycyrol, isoglycyrol, neoglycyrol, glycoumarin, licocoumarone, licopyranocoumarin, liconeolignan, β -sitosterol, glucanGBW, licurazid, 18 α -hydroxy glycyrrhetic acid, 24-hydroxy-11-deoxyglycyrrhetic acid, glycyrrhetol, 21 α -hydroxy isoglabrolide, liquoric acid, glabrolide, deoxyglabrolide, isoglabrolide, liquiritoside, liquiritogenin, isoliquiritoside, isoliquiritigenin, licoflavone A, licochaleone, herniarin, umbelliferone, ferulic acid, asparamide, mannite, glycyrrhnic acid, licochalcone [14], 18 β -glycyrrhetic acid [35].

Function:

1. To reinforce the function of the spleen and replenish vital energy (qi) [36].
2. To reduce spasmodic pain [36].

Indications:

1. Weakness of the spleen and stomach marked by lassitude and weakness [36].
2. Spasmodic pain in the epigastrium, abdomen and limbs [36].

Pharmacological effects:

1. Reduce inflammation in carrageenan-induced edema in mice (from glycyrrhizic acid) [32], (from 18 β -glycyrrhetic acid) [35], and cotton pellet granuloma formation in mice (from glycyrrhizic acid) [32].
2. Reduce prostaglandin E₂ level in mice [37].

10. Herba Taxilli

Botanical name: *Taxillus chinensis* (DC.) Danser
Family: Loranthaceae
Chinese name: Sangjisheng
Common name: Chinese Taxillus herb, Mulberry mistletoe

Part used and method for pharmaceutical preparations:

The foliated stems and branches are gathered, cut into pieces and dried in the sun [11].

- Constituents:** Rhamnazin, 3'-methyl eriodictyol, viscumneose, β -amyranol, lupeol, oleanolic acid, betulinic acid, β -sitosterol, daucosterol, meso-inositol, quercetin, avicularin, quercetin-3-arabinoside [14].
- Function:** To replenish the liver and kidney, to strengthen the tendons and bones and to relieve rheumatic conditions [38].
- Indications:** Rheumatic or rheumatoid arthralgia with aching and weakness of the loins and knees [38].

11. Radix Rehmanniae Preparata

- Botanical name:** *Rehmannia glutinosa* Libosch.
- Chinese name:** Shudihuang
- Common name:** Prepared Rehmannia root
- Part used and method for pharmaceutical preparations:**
The roots are prepared with wine, amomum fruit and tangerine peel. The prepared roots are then steamed and dried in the sun several times until they become black, soft and sticky, then they are cut into slices [11].
- Constituents:** Rhemaionoside, rehmapicroside, rehmaglutin, acteoside, jiocerebroside, glutinoside, catalpol, leonuride, melittoside, rehmannioside, dihydrocomin, purpleaside, aucubin, geniposide, 8-epiloganic acid, 6-O-E-feruloylajugol, 6-O-Z-feruloylajugol, 6-O-p-coumaroylajugol, 6-O-vanilloylajugol, jioglutoside, verbascose, D-mannitol, glucosamide, rehmannan, rehmannia glutinosa polysaccharide, β -sitosterol, palmitic acid, succinic acid, daucine [14].
- Function:** To nourish and replenish blood, reinforce the essence of life and marrow [39-40].
- Indications:** Aching and weakness of loins and knees [39-40].

12. Rhizoma Chuanxiong

- Botanical name:** *Ligusticum chuanxiong* Hort.
- Family:** Apiaceae
- Chinese name:** Chuanxiong

Common name: Szechwan lovage rhizome, Ligusticum

Part used and method for pharmaceutical preparations:

The rhizomes are dug in late May. The fibrous roots are soaked and cut into slices [11].

Constituents: Chuanxiongzone, perlyrine, ligustilide, wallichilide, 3-butylidenephthalide, butylphthalide, (3S)-3-butyl-4-hydroxyphthalide, (3S)-chuanxiongol, enidilide, neoenedilide, senkyunolide, (E)-senkyunolide E, 2-methoxy-4-(3-methoxy-1-propenyl) phenol, 2-(1-oxopentyl) benzoic acid methyl ester, 5-hydroxymethyl-6-endo-3'-methoxy-1'-hydroxyphenyl-8-oxabicyclo (3.2.1)-oct-3-en-2-one, 4-hydroxy-3-methoxystyrene, 4-hydroxy benzoic acid, vanillic acid, chrysophanol, sedanonic acid, L-isoleucyl-L-valine anhydride, L-valyl-L-valineanhydride, uracyl, trimethylamine, choline, palmitic acid, vanillin, 1-acetyl- β -carboline, spathulenol [14], tetramethylpyrazine (TMP) [41].

Function:

1. To promote the flow of blood and vital energy (qi), dispel wind and relief pain [42].
2. To increase blood circulation [43].
3. To relief pain and inflammation [43].

Indications: Rheumatic arthralgia, swelling and pain due to traumatic injury [42-43].

Pharmacological effects:

1. Reduce inflammation in carrageenan-induced rat paw edema and analgesic effect in acetic acid-induced writhing response in mice (from TMP) [29].
2. Improve brain microcirculation through inhibiting thrombus formation and platelet aggregation as well as blood viscosity [44].
3. Reduce blood pressure in rats (from TMP) [45].
4. Block the entry of extracellular calcium through calcium channels and inhibit the release of intracellular stored calcium in the vascular smooth muscle cells (from TMP) [45].

13. Poria

Botanical name: *Poria cocos* (Schw.) Wolf

Family: Polyporaceae

Chinese name: Fuling

Common name: Indian bread, Poria

Part used and method for pharmaceutical preparations:

The fungus is gathered, cut into pieces and dried in the shade [11].

Constituents: Pachymic acid, 3 β -p-hydroxybenzoyldehydrotumulosic acid [46], pachyman, pachymaran, β -D-glucan H₁₁, tumulosic acid, trametenolic acid, eburicoic acid, poricoic acid [14],

Function:

1. To cause diuresis, to invigorate the spleen function and to calm the mind [47].
2. To warm the lower back and knees [48].

Indications: Edema with oliguria; restlessness and insomnia [47].

Pharmacological effects:

1. Induce diuresis in rabbits (from ethanol extract) and prevent peptic ulcer in rats and mice (from water extract) [48].
2. Enhance immunological action in mice (from pachyman) [48].
3. Reduce inflammation in phospholipase A₂-induced mouse paw edema [49], tetradecanoyl phorbol acetate (TPA) and arachidonic acid (AA)-induced ear inflammation in mice [46,50] and carrageenan-induced edema in mice (from 3 β -p-hydroxybenzoyldehydrotumulosic acid and pachymic acid) [46].
4. Inhibit phospholipase A₂ (from hydroalcoholic extract, dehydrotumulosic acid and pachymic acid) [51].

14. Cortex Cinnamomi

Botanical name: *Cinnamomum cassia* Presl

Family: Lauraceae

Chinese name: Rougui

Common name: Cassia bark, cinnamon bark

Part used and method for pharmaceutical preparations:

The bark is cut in the period of great heat and peeled off the beginning of autumn. It is dried in the shade and cut into slices [11].

Constituents: Cinnamaldehyde, cinnamyl acetate, ethyl cinnamate, benzylbenzoate, benzaldehyde, coumarin, β -cadinene, calamenene, β -elemene, protocathechuic acid, trans-cinnamic acid, 3'-O-methyl-(L)-epicatechin, (L)-epicatechin-3-O- β -D-glucoside, cinnamtannin, procyanidin, cinnzeylanine, cinnzeylanol, cinn cassiol, lyoniresinol-3 α -O- β -D-glucopyranoside, cinnamic aldehyde-cyclic glycerol-1,3-acetal, cassioside, cinamoside, cinnaman [14], cinnamic aldehyde [52].

Function: To dispel cold and relief pain and to activate blood circulation [53].

Indications: Coldness and pain in the loins and knees [53].

Pharmacological effects:

1. Reduce inflammation in carrageenan-induced mouse paw edema, arachidonic acid-induced ear edema in mice and cotton pellet-induced granuloma in rats (from 70% methanol extract) [54].
2. Inhibit arachidonic acid release and TXB₂ formation from human platelets (from cinnamic aldehyde) [52].

15. Radix Ledebouriellae

Botanical name: *Ledebouriellae divaricatae*

Family: Apiaceae

Chinese name: Fangfeng

Common name: Ledebouriella root

Part used and method for pharmaceutical preparations:

The roots are dug in spring and autumn, dried in the sun, soaked in water and cut into pieces [11].

Constituents: Ledebouriellol, hamaudol, 3'-O-acetylhamoudol, saposhnikoran, 5-O-methylvisamminol, cimifugin, bergapten, psoralen, imperatorin, phellopterin, xanthotoxin, anomalin, scopoletin, marmesin, falcarinol, panaxynol, falacarindiol, (8E)-heptadeca-1, 8-dien-4,6-diy-3,10-diol, octanal, β -bisabolene [14].

Function: To relief rheumatic pain [55].

Indications: Rheumatic conditions [55], arthralgia, ostalgia [56].

Pharmacological effects: Suppress adjuvant arthritis in rats [18].