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Chinese Food Supplement Products Containing Medicinal Plants with Different Mechanisms of Antiosteoporotic Activity

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Abstract **Original Research Article**

The aim of current study is collection and comparison of content and different dosage forms of the most common manufactured Chinnese food supplement products containing antiosteoporotic medicinal plant extracts. The investigation has been made through the electronical database of medical sourses Google Scholar, PubMed, SciFinder Scholar, Science Direct, Web of Science. The following approaches in the evaluation of trade multisupplements were: 1) collection of data for manufactured supplement products, containing antiosteoporotic plant extracts; 2) estimation of the most used drug forms; 3) summariring the multipreparations; 4) describing the most common plants in combined supplements; 5) mechanisim of action of plants. The results from the evaluation show that the most spread products containing extracts from medicinal plants with antiosteoporotic effect originated from: *Astragalus mongholicus Bung* caps.*, Cimicifuga racemosa L. (*Bionorica Menopret tabl.*), Cinnamomum cassia (Cinnamon* caps.*); Cordyceps sinensis (Berk.) Sacc. (Cordyceps extract* caps.*), Drynaria fortunei Kunze ex Mett., Eclipta prostrata L. (*powder*), Epimedium brevicornum Maxim. (Yin-Yang Huo 500 mg* caps.*),* ***Erythina variegate L.*** Liquid Extract**,** ***Morinda officinalis F.C.*** (tincture)*, Psoralea corylifolia L. (*powder*), Pueraria lobate (Willd.) Ohwi* caps*., Sophora japonica L.* **(**tincture). An observational study shows different trade form preparations: tablets, capsules, powders, solutions of monocomponent and multicomponent products containing extracts from medicinal plants for osteoporosis. The most applied drug forms can be presented as follows: *Angelica* sinensis (tabl., caps.), *Cimicifuga racemosa* tabl., *Drynaria fortunei Kunze ex Mett.* (caps., tincture, powder), *Eclipta prostrata* (tincture), *Salvia* caps., *Morinda officinalis* (powder, tincture), *Pueraria lobate* caps. An important multicomponent formulation is USANA Phyto Estrin, Hormone Balance Menopause Relief caps., Gu Ling Pian, Dang Gui Bu Xue Tang, Jian Gu Er Xian Wan, Qing E Wan, Zi Shen Wan, Bu Shen Yi Jing Fang, Gu Kang Fang, Yi Shen Zhuang Gu He Ji, Wu Jia Bu Gu, Bu Shen Mi Gu Ye, Bu Shen Zhuang Gu, Er Xian Decoction, Fu Fang Lu Rong Jian Gu Jiao Nang, Gu Wei Ling Jiao Nang, Zeng Gu Wan, Jian Gu Ke Li. The most important mechanisms of antiosteoporotic action of Chinnese plants include: bone formation by: activation of osteoblast proliferation and differentiation, enhancing of osteoblast activity, increasing of bone protein osteocalcin, increasing of bone mineralization; decreasing of bone degradation by: suppression of bone resorption. blocking of osteoclastogenesis, inhibition of osteoclast activity and differentiation, reduction of reactive oxygen species.

Keywords: Osteoporosis, Chinnese food supplements, medicinal plant extracts, mechanisms of antiosteoporotic effect.

INRODUCTION

The investigation has been made through the existing electronical database of medical sourses, such as; Scopus, PubMed, Medline, Cochrane Library. The following approaches in the evaluation of trade multisupplements were: 1) estimation of the most used drug forms; 2) collection of data for supplements, containing antiosteoporotic plant extracts; 3) summariring the multipreparations; 4) describing the most common plants in supplements; 5) mechanisms of antiosteoporotic action of Chinnese plants. The study covers analysis of collected data, comprising the results for the part of distribition of different multicomponents with and estimation of the most common combinations.

I, Anteoporotic Chinnese medicinal plants and the used plant parts.

Osteoporosis is a desease, associated with oxidative stress and inflammation. The disease is characterized by increased bone fragility and low bone mass. In postmenopausal women the reduction of

estrogen leads to elevation of oxidative stress and lipid accumulation, which can promote osteoblasts apoptosis [1].

An observational study shows different trade form preparations: tablets, capsules, powders, solutions of monocomponent and multicomponent products containing extracts from mechanisms of antiosteoporotic action of Chinnese plants medicinal plants against osteoporosis. The most applied drug forms can be presented as follows: *Angelica sinensis* (tabl., caps.), *Cimicifuga racemosa* tabl., *Drynaria fortunei* (caps., tincture, powder), *Eclipta prostrata L.* (powder, tincture), *Epimedium brevicornum Maxim.* (Yin-Yang Huo caps.), *Erythina variegate L.* Liquid Extract, *Morinda officinalis F.C.* (powder, tincture), *Psoralea corylifolia L.* (powder), Pueraria lobate (Willd.) Ohwi caps., *Salvia caps., Sophora japonica L.* (tincture) [1].

The most often used antiosteoporotic Chinnese plants and the used plant parts are presented in Table 1.

Table 1: Anteoporotic Chinese plants and used plant parts

Latin Name	Chinese Name	Plant part
Acanthopanax senticosus (Rupr. et Maxim.) Harms	Ci Wu Jia	Root/Rhizome
Achyranthes bidentata Bl	Huai Niu Xi	Root
Aconitum carmichaeli Debx.	Chuanwu	Root
Actea (Cimicifuga) racemosa L.)	Sheng-Ma	Rhizome
Allium sativum L.	Jinxiang Da Suan	Bulb
Anemarrhena asphodeloides Bunge	Zhimu	Rhizome
Angelica sinensis (Oliv.) Diels	Dang Gu	Root
Astragalus membranaceus (Fisch.) Bunge var. mongholicus (Bunge) P. K. Hsiao	Běi Qí	Root
Astragalus mongholicus Bung	Huang-Qi	Root
Aucklandia lappa Decne.	Yunmuxiang	Root
Bupleurum chinense DC	Chai Hu	Rhizome
Carya cathayensis Sarg	Shān Hé Táo	Fruit
Cinamomum cassia Presl	Rou Gui	Bark
Carthamus tinctorius L.	Hong-Hua	Flower
Cistanche deserticola Y.C. Ma	Rou-Cong-Rong	Stem
Codonopsis pilosula (Franch.) Nannf.	Dăngshēn	Root
Cordyceps sinensis (Berk.) Sacc.	Dong-Cong-Xia-Cao	Plant
Curculigo orchioides Gaertn.	Xian Mao	Rhizome
Cuscuta chinensis Lam.	Tu Si Zi	Seed
Dioscorea hypoglauca Palibin	Pu-Reun-Ma	Rhizome
Dioscorea opposita Thunb.	Huai Shan	Rhizome
Dipsacus asper Wall.	Xu Duan	Root
Dipsacus japonicas Miq.	Xu-Duan	Root
Drynaria fortunei Kunze ex Mett.	Gu-Sui-Bu	Rhizome
Eclipta prostrata L.	Mo-Han-Lian	Herba
Epimedium brevicornum Maxim	Yin-Yang-Huo	Leaf
Erythina variegate L.	Hai-Tong-Pi	Bark
Eucommia ulmoides Oliv.	Du Zhong	Bark
Ferula spp.	A-Wei	Resin
Juglans regia L.	Hú táo	Seed
Ligustrum lucidum W.T. Aiton	Nu-Zhen-Zhi	Fruit
Lycium barbarum L.	Gou-Qi-zi	Fruit
Morinda officinalis F.C. How	Bā Jí Tiān	Root
Ormosia henryi Prain	Lu-Mu	Root
Paeonia suffruticosa Andrews	Mu Dan Pi	Bark
Panax ginseng C. A. Mey.	Ren Shen	Root/Rhizome
Panax notoginseng (Burkill) F. H. Chen	Sanqi	Root
Phellodendron chinense Schneid.	Huáng Bai	Bark
Pheretima aspergillum (E Perrier)	Guang-dilong	Bark
Polygonium multiflora Thunb	He Shou Wu	Root
Prunus persica (L.) Batsch (Seed) Do-in	Do-in	Seed

Psoralea corylifolia L.	Bu-Gu-Zhi	Fruit
Pueraria lobate (Willd.) Ohwi	Ge-Gen	Root
Rehmannia hueichingensis Libosch	Huai Dihuang	Root
Salvia miltiorrhiza Bunge	Dan-Shen	Root/Rhizome
Sambucus williamsii Hance	Jie-Gu-Mu	Stem
Schisandra chinensis (Turcz.) Baill.	Wǔ wèi zi	Fruit
Sophora japonica L.	Huai Hua Mi	Root
Sophora flavescens Aiton	Ku-Shen	Root
Spatholobus suberectus Dunn	Ji-xue-teng	stem
Trifolium pretense L.	Hong-Che-Hou-Cao	Twig

II. Effects of anteoporotic compounds from Chinese medicinal plants.

Anti-osteoporotic effect of medical herbs [1] is a result of their content of phytonutrients [2]. One of the most important phyto-agents, which can prevent bone healt are phytoesrogens and components of essential oils. The main mechanisms for action of these compounds of nature orign are associated wuth reduction of osteoclastogenesis, stimulation of osteoblast proliferation, activation of the biosynthesis of estrogen. The essential oils that inhibited bone breakdown included sage (monoterpenes), juniper, pine oil (alpha-pinene, beta-pinene and bornylacetate), eucalyptus and rosemary [1].

Hormone-regulating herbal supplement Macafem stimulate a woman's estrogene hormones production, which can bloch the osteoblasts apoptosis [1]. *Epimedium brevicornum Maxim* promotes the biosynthesis of estrogen by aromatase CYP19 [3]. Gushukang [4], *Panax notoginseng* [5], *Bushen Huayu* extract from herba *Epimedii (Yinyanghuo)*, rhizoma *Drynaria fortunei Kunze ex Mett. (Gusuibu)* [6], Icariside from YiGu capsule [7], radix *Dipsaci* and *Cynomorium songaricum* stimulate osteoblast proliferation and levels of Osteoprotegerin [8].

Dioscorea spongiosa inhibites osteoclast formation [2]. Gushukang [4], *Panax notoginseng* [5] and Yijung-Tang [10] and *Cimicifugae* rhizoma are inhibitors on bone resorption [9]. *Sambucus williamsii Hance*, *Sambucus sieboldiana* and *Taxus yunnanensis L.* suppress bone resorption too [2]. The anti-osteoporotic effect of Yijung-tang is mediated by inhibition of osteoclast differentiation [10]. Yijung-tang [10], *Prunus domestica L.* [13] and Viscumneoside from *Viscum coloratum Nakai* block osteoclastogenesis [14].

Catechin, Epicatechin, Gallocatechin and Epigallocatechin from dried leaves of *Camellia sinensis L.* [1], Magnolol [11] and Honokiol [12] from *Magnolia officinalis L., Prunus domestica L*. [13] and Isotaxiresinol from *Taxus yunnanensis L.* [2] stimulate osteoblasts function. 8-Prenylnaringenin from *Humulus lupulus L.* promotes osteoblastic differentiation, inhibits osteoclasts differentiation, regulates the secretion of Osteoprotegerin [1]. Linoleic acid, found in sunfflower seed oil, exerts anti-inflammatory effects in bone. Sunfflower seeds supplementation stimulates the proliferation, differentiation and mineralization of osteoblastic cells [15]. *Angelica gigas* normalizes ovarian hormone levels and has antiosteoporosis properties [16]. Licorice isoliquiritigenin suppresses osteoclastogenesis and prevents inflammatory bone loss [17]. *Cimicifuga heracleifolia* is therapeutically similar to black cohosh in relieving menopausal symptoms [18].

Plants of the genus *Cimicifuga* (*Ranunculaceae*) have been known as a dietary supplement for preventiomg of osteoporosis due to antiosteoporotic action of the presentce on plants of triterpenoid saponins, flavonoids like isoflavone formononetin and chromones [19]. *Cimicifuga racemosa L.* supplements are available as capsules, tinctures, and tea. Anti-osteoporosis activity of extract of rhizomes of *Cimicifuga heracleifolia L.* is associated with reduction of osteoclast levels and stimulaton of the function of osteoblasts [20], and inhibition of bone-resorbing mediators from deoxyactein and actein [21].

It is demonstrated that osteoblastic proliferation stimulating activity possess extracts of *Dioscorea spongiosa* [22], of *Psoralea corylifolia L.* [23] and *Cnidium monnieri L.* [24]. Extracts of *Dioscorea spongiosa* stimulate exhibite a potent inhibitory activity on osteoclastogenesis [22].

Chinese herbal medicines have been used for a long time to treat osteoporosis and *Angelica sinensis* (Dong quai); *Panax ginseng* or *Panax quinquefolius* Kanggusong capsules, Yigu capsule, Xianlinggubao capsule, Bushen Zhuanggu granule, Zhuangguqiangjin tablets and Shujinbogu tablets are the most used [25].

Recent studies have suggested that *Camellia sinensis L.* green tea polyphenols are promising agents for preventing bone loss in women by improving bone turnover rate and increasing of antioxidant capacity and a decrease of oxidative stress damage [26]. Tea polyphenols enhance osteoblastogenesis and suppress osteoclastogenesis *in vitro.* Greater bone strength vis a result from increasing bone formation and inhibition of bone resorption. These osteoprotective effects appear to be mediated through antioxidant or antiinflammatory pathways [27].

Among nutritional factors, recent observations suggest that *Prunus domestica L.* is the most effective

fruit in both preventing and reversing bone loss. Animal study indicated that dried plum prevented the ovariectomy-induced reduction in bone mineral density [28]. Due to content of large amounts of phenolic compounds and boron, dried fruits of *Prunus domestica L.* may exert positive effects on bone in postmenopausal women and may play a role in prevention of osteoporosis. It has been shown that extracts from *Prunus domestica L.* improve bone density and microstructure of bone, decrease osteoclastogenesis via down-regulation of gene expression for receptor activator of nucleus factor kB ligand and osteoprotegerin in the bone and stimulate bone formation mediated by increasing of serum markers of bone formation: insulin-like growth factor, total alkaline phosphatase, bone-specific alkaline phosphatase [29].

Isoflavones significantly reduce the number of osteoclasts, inhibit the bone resorption and enchance bone mineral density. Icariin from *Epimedium brevicornum Maxim* promotes the biosynthesis of estrogen [3]. Gushukang [4], *Panax notoginseng* saponins [5], and Icariside from YiGu capsule [7]. *Panax notoginseng* saponin [5] and Yijung-Tang [10] and triterpenoids from *Cimicifugae* rhizoma are inhibitors on bone resorption [9]. Lignans from *Sambucus williamsii Hance*, Vanillic acid from *Sambucus sieboldiana* and Isotaxiresinol from *Taxus yunnanensis* L. suppress bone resorption too [2].

Catechin, Epicatechin, Gallocatechin and Epigallocatechin from dried leaves of *Camellia sinensis* L. [1], Magnolol [11] and Honokiol [12] from *Magnolia officinalis L., Prunus domestica L.* [13] and Isotaxiresinol from *Taxus yunnanensis L.* [2] stimulate osteoblasts function. Triterpenoids from *Cimicifugae rhizoma* are inhibitors on bone resorption [9].
Antiosteoporotic compounds in Chinese medicinal plants are sumnarised in Table 2.

Table 2: Anteoporotic compounds in Chinese medicinal plants

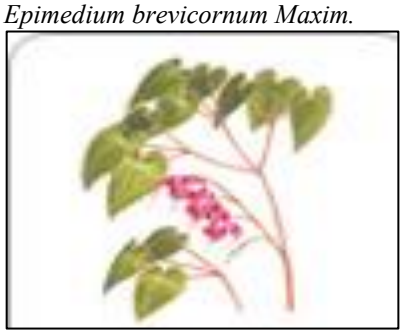
Chinese medicinal plants	**COMPOUNDS**
Actaea heracleifolia Kom.	Cimicidol-3-O-xyloside
Astragalus mongholicus Bunge	Formononetin Astragaloside
Carthamus tinctorius L.	Acacetin, Matairesinol, Tilianine
Camellia sinensis L	Catechin, Epicatechin, Gallocatechin and Epigallocatechin
Cistanche deserticola Y.C. Ma	Echinacoside
Cuscuta chinensis Lam. Seed	Quercetin, Kaempferol, Isorhamnetin, Hyperoside and Astragalin
Cordyceps sinensis (Berk.) Sacc.	Cordycepin, Cordymin
Dioscorea spp.	Diosgenin, Diospongins B and C, Syrinaresinol
Curculigo orchioides	Curculigoside
Dipsacus japonicas Miq.	Asperosaponins
Dipsacus asperoides C. Y. Cheng et T. M. Ai Root	Asperosaponins
Drynaria fortunei Kunze ex Mett.	Naringin, Sophoraflavanone G
Eclipta prostrata L.	Diosmetin, Echinocystic acid,
Epimedium brevicornum Maxim.	Epimedins, Icariin, Icariside, Maohuoside
Eucommia ulmoides	Geniposidic acid, Lignans
Juglans regia L.	Ellagic acid, flavonoids
Lycium barbarum	Zeaxanthin
Magnolia officinalis L.	Magnolol [11] and Honokiol [12]
Psoralea corylifolia L.	Bakuchiol, Bavachin, Neobavaisoflavone, Psoralen, Psoralidin, Corylin
Prunus domestica L.	Magnolol [11] and Honokiol [12]
Pueraria lobate (Willd.) Ohwi	Isoformononetin, Puerarin
Salvia miltiorrhiza MBunge	Cryptotanshinone, Tanshinones I, IIA and VI, Salvianolic acids A, B
Sambucus williamsii Hance	Ficusal, Ceplignan,Vanillic acid
Sophora japonica L.	Genistein, Sophoricoside
Sophora flavescens Aiton	Formononetin
Scutellaria baicalensis	Baicalin, Baicalein
Taxus yunnanensis L. [2]	Isotaxiresinol
Trifolium pretense L.	Formononetin
Viscum coloratum Nakai	Viscumneosides I, IX and X

III. Supplements containing anteoporotic Chinese plant extracts.
Antiosteoporotic supplements from Chinese medicinal plants are included in Table 3. and Table 4.

Table 3: Antiosteoporotic supplements from Chinese medicinal plants

Actea racemosa racemosa L.  Bionorica Menopret 5 mg tabl. Kira Menopause Relief 6.5 mg tabl. Menopause Black Cohosh 5 mg tabl. Pharma Menoherb 6.5 mg tabl.	*Actaea heracleifolia (Kom.) J.Compton*  Actaea heracleifolia (Kom.) J.Compton extr.
Drynaria fortunei Kunze ex Mett.  Bone Dense Drynaria 500 mg caps. Gu Sui Bu rhizome powder Gu Sui Bu Tincture Drynaria	*Cordyceps sinensis (Berk.) Sacc*  Cordyceps extract 5000 mg caps. Cordyceps sinensis 2400 mg tabl. Cordyceps extract 20:1 1000 mg caps. Cordyceps 750 mg caps. Cordyceps sinensis 740 mg caps. Cordyceps extract 650 mg caps. Cordyceps extract 550 mg caps. VITA1 Cordyceps Sinensis 500 mg caps. Cordyceps extract 500 mg caps. BIO-Cordyceps – 400 mg caps.
Astragalus mongholicus Bung  Astragalus Extract 500 mg tablets Astragalus 425 mg caps. Astragalus Root 470 mg caps. Astragalus, 500 mg caps. Astragalus, 550 mg caps. Astragalus Root Powder Astragalus, 2,000 mg 30 ml	*Salvia miltiorrhiza Bunge Dan-Shen*  Red Sage 500 mg caps. Salvia sclarea 450 mg caps. Garden Sage 400 mg caps. Red Sage 400 mg caps. Sage Leaf 285 mg caps Meno Plus 125 mg tabl. Root Salvia Miltiorrhiza Tincture

Table 4: Antiosteoporotic supplements from Chinese medicinal plants

Cinnamomum cassia Presl  Cinnamon Cassia Herbal Extract Caps 500mg Cinnamon 500 mg Capsules Cinnamon Cassia Essential Oil	*Psoralea corylifolia L.*  Bu Gu Zhi Liquid extract Bu Gu Zhi fruit powder Psoralea Fruit Powder
Erythina variegate L.  Hai-Tong-Pi Bark Hai Tong Pi bark Liquid Extract	*Morinda officinalis F.C. How*  Ba Ji Tian Radix Morindae powder Ba Ji Tian Tincture Morinda
Eclipta prostrata L.  *Mo Han Lian - Eclipta poder*	*Epimedium brevicornum Maxim.*  Yin-Yang Huo 500 mg caps.
Sophora japonica L.  Sophora Japonica 500 mg Extract caps. *Huai Hua Mi Root Tincture*	*Pueraria lobate (Willd.) Ohwi*  Kudzu Liquid Extract Kudzu Remedys Nutrition 1 mg caps.

IV. Multisupplements from Chinese medicinal plants.

In Table 5. and in Table 6. are presented the most applied antiosteoporotic multisupplements from Chinnese medicinal plants.

Table 5: Multisupplements from Chinese medicinal plants

Gu Ling Pian *Cuscuta chinensis* Lam.(Seeds**)** *Drynaria fortunei* (Kunze ex Mett.) J. Sm.(Rhizome)	**Dang Gui Bu Xue Tang** *Angelica sinensis* (Oliv.) Diels (Root) *Astragalus membranaceus* (Fisch.) Bunge var. *mongholicus* (Bunge) P. K. Hsiao (Root)
Jian Gu Er Xian Wan *Dipsacus asper* Wall. (Root) *Dioscorea opposita* Thunb. (Rhizome) *Panax ginseng* C. A. Mey. (Root and rhizome)	**Qing E Wan** *Eucommia ulmoides* Oliv. (Bark) *Juglans regia* L. (Seed) *Allium sativum* L. (Bulb)
Zi Shen Wan *Anemarrhena asphodeloides* Bunge (Rhizome) *Cinnamomum cassia* Presl (Bark) *Phellodendron chinense* Schneid. (Bark)	**USANA Phyto Estrin tabl.** *Angelica sinensis* (Oliv.) Diels (Root) *Cimicifuga racemosa* *Glycine max L.*
Bu Shen Yi Jing Fang *Cistanche deserticola* Y. C. Ma (Stem) *Drynaria fortunei* (Kunze ex Mett.) J. Sm. (Rhizome) *Epimedium brevicornu* Maxim. (Leaf) *Polygonium multiflora* Thunb (Root)	**Gu Kang Fang** *Angelica sinensis* (Oliv.) Diels (Root) *Cistanche deserticola* Y. C. Ma (Stem) *Salvia miltiorrhiza* Bunge (Root) *Ziziphus jujuba* Mill. (Fruit)
Yi Shen Zhuang Gu He Ji *Astragalus membranaceus* (Fisch.) Bunge var. *mongholicus* (Bunge) P. K. Hsiao (Root) *Codonopsis pilosula* (Franch.) Nannf. (Root) *Epimedium brevicornu* Maxim. (Leaf) *Paeonia suffruticosa* Andrews (Bark) *Schisandra chinensis* (Turcz.) Baill.(Fruit)	**Wu Jia Bu Gu** *Acanthopanax senticosus* (Rupr. et Maxim.) Harms (Root and rhizome) *Achyranthes bidentata* Bl. (Root) *Angelica sinensis* (Oliv.) Diels (Root) *Astragalus membranaceus* (Fisch.) var. *mongholicus* (Bunge) P. K. Hsiao (Root) *Rehmannia hueichingensis* Libosch (Root)
Hormone Balance Menopause Relief caps. Angelica sinensis L. Cimicifuga racemosa L. Trifolium pretense L. *Salvia miltiorrhiza Bunge*	**Bu Shen Mi Gu Ye** *Achyranthes bidentata Bl.(Root)* *Carya cathayensis Sarg (Fruit)* *Epimedium brevicornu Maxim.(Leaf)* *Eucommia ulmoides Oliv. (Bark)* *Rehmannia hueichingensis Libosch (Root)* *Trichosanthes kirilowii Maxim. (Root)*
Bu Shen Zhuang Gu *Angelica sinensis* (Oliv.) Diels (Root) *Achyranthes bidentata* Bl. (Root) *Carthamus tinctorius* L. (Flower) *Dipsacus asper* Wall. (Root) *Drynaria fortunei* (Kunze ex Mett.) J. Sm. (Rhizome) *Morinda officinalis* How (Root)	**Er Xian Decoction** *Anemarrhena asphodeloides* Bunge (Rhizome) *Angelica sinensis* (Oliv.) Diels (Root) *Curculigo orchioides* Gaertn. (Rhizome) *Epimedium brevicornu* Maxim. (Leaf) *Morinda officinalis* How (Root) Bā Jí Tiān *Phellodendron chinense* Schneid. (Bark)

Table 6: Multisupplements from Chinnese medicinal plants.

Fu Fang Lu Rong Jian Gu Jiao Nang *Angelica sinensis* (Oliv.) Diels (Root) *Eucommia ulmoides* Oliv. (Bark) *Panax notoginseng (Burkill)* F. H. Chen (Root) *Polygonium multiflora* Thunb (Root) *Whitmania pigra* Whitman (Root) *Wurfbainia villosa* (Lour.) Skornick. A.D. Poulsen (Root)	**Gu Wei Ling Jiao Nang** *Achyranthes bidentata* Bl. (Root) *Angelica sinensis* (Oliv.) Diels (Root) *Astragalus membranaceus* (Fisch.) var. *mongholicus* (Bunge) P. K. Hsiao (Root) *Bupleurum chinense* DC. (Rhizome) *Cinamomum cassia* Presl (Bark) *Pheretima aspergillum* (E Perrier)
Gu Song Kang Jiao Nang *Aconitum carmichaeli* Debx. (Root) Aconitum kusnezoffii Reichb. (Tuber) (Root) *Curculigo orchioides* Gaertn. (Rhizome) *Epimedium brevicornu* Maxim. (Leaf) Glycyrrhiza uralensis Fisch. (Root and rhizome)	**You Gui Wan** *Aconitum carmichaeli* Debx. (Root) *Angelica sinensis* (Oliv.) Diels (Root) *Cinnamomum cassia* Presl (Bark) *Cuscuta chinensis* Lam. (Seed**)** *Dioscorea opposita* Thunb. (Rhizome)

Phellodendron chinense Schneid. (Bark) *Morinda officinalis* How (Root)	*Eucommia ulmoides* Oliv. (Bark) *Lycium barbarum* L. (Fruit) *Rehmannia. hueichingensis* Libosch (Root)
Zeng Gu Wan *Astragalus membranaceus* (Fisch.) Bunge var. *mongholicus* (Bunge) P. K. Hsiao (Root) *Aucklandia lappa* Decne. (Root) *Dioscorea hypoglauca* Palibin (Rhizome) *Drynaria fortunei* (Kunze ex Mett.) J. Sm. (Rhizome) *Epimedium brevicornu* Maxim. (Leaf) *Panax notoginseng* (Burkill) F. H. Chen (Root) *Prunus persica* (L.) Batsch (Seed) *Salvia miltiorrhiza* Bunge (Root) *Spatholobus suberectus* Dunn (**S**tem**)**	**Jian Gu Ke Li** *Aconitum carmichaeli* Debx. (Root) *Angelica sinensis* (Oliv.) Diels (Root) *Curculigo orchioides* Gaertn. (Rhizome) *Dioscorea opposita* Thunb. (Rhizome) *Dipsacus asper* Wall. (Root) *Drynaria fortunei* (Kunze ex Mett.) J. Sm.(Rhizome) *Eucommia ulmoides* Oliv.(Bark) *Ligustrum lucidum* Ait.(Fruit) *Polygonium multiflora* Thunb (Root) *Spatholobus suberectus* Dunn (Stem) *Paeonia suffruticosa* Andrews (Bark**)**

IV. Mechanism of action of **Chinese anti-osteoporotic medicinal plants**.

Multisupplement Hormone Balance Menopause Relief caps. contsibs plants Black Cohosh, Dong Quai, Sage, Red Clover, Licorice. Increased bone resorption mediated by osteoclasts is central to pathogenesis. Under pathologic conditions cytokines nuclear factor kB and tumor-necrosis facror alpha are often increased, leading to enhanced osteoclastogenesis. *Actaea racemosa L. (Cimicifuga racemosa L., Black cohosh*) is a popular herbal supplement for the treatment of menopausal symptoms. This plant is recently shown to have the beneficial effect of preventing bone loss. It is demonstrated that isolated from *Actaea racemosa L.* triterpenoid glycoside: 25-acetylcimigenol xylopyranoside blocks *in vitro* osteoclastogenesis induced by nuclear factor - kB and attenuates tumor-necrosis factor alpha-induced bone loss *in vivo*. Black cohosh is native herb from North America and it has estrogen-like properties, which help balance the hormone levels in the body. The phytoestrogens it contains have a record of balancing hormones and thereby benefiting bone health. Black cohosh supplements are available as capsules, tinctures, and teas, and can easily be incorporated into your daily routine [30]. Licorice isoliquiritigenin suppresses osteoclastogenesis and prevents inflammatory bone loss [31].

The bone loss associated with ovarian hormone deficiency at menopause is the most common type of osteoporosis. High levels of phytoestrogenic isoflavones are associated with a low incidence of osteoporosis.

Trifolium pratense L. isoflavones may decelerate bone density reduction while increasing the bone's mineral density. *Trifolium pratense L. isoflavones are effective in bone loss* induced by estrogens deficiency. Isoflavones significantly increase bone mineral density and the bone turnover and inhibit the bone resorption due to reduce the number of osteoclasts [32]. Bushen *Huayu* extract is able to prevent the bone loss in postmenopausal women [33]. The therapeutic mechanisms are raising the bone density by *stimulation of the osteoblasts* and decreasing of the serum levels of Interleukine-6 and declining of bone resorption in postmenopausal women [34]. Components of Bushen *Huayu* extract are herba *Epimedii* (*Yinyanghuo*) and rhizoma *Drynariae* (*Gusuibu*) [33]. Traditional chinese medicine herb used in treating osteoporosis is *Epimedium sagittatum (Yin yang huo)*. The active ingredient of herba *Epimedii* Icariin may have a potential role in the prevention and treatment of osteoporosis by stimulating estrogen biosynthesis [35] and increasing the levels of a tumor-necrosis factor-related cytokine osteoprotegerin, of bone morphogenetic protein - a promoter of osteogenesis and of synthesized by active osteoblasts collagen I. Rhizoma *Drynariae* may enhance the treatment effects on osteoporosis by reducing metabolic disorder [34].

Gushukang is herbal remedy used in traditional chinese medicine for the prevention and treatment of osteoporosis. Pharmacological studies indicated that Gushukang can increase estrogen and bone density, promote bone formation and restore bone microstructure, improve bone bio-mechanical parameters and promote healing of bone fracture. inhibitie bone absorption, slowing down bone mass loss [36].

Traditional Chinese prescriptions to treat osteoporosis, such as Gu Ling Pian, Bu Shen Yi Jing Fang, Bu Shen Zhuang Gu, Zeng Gu Wan, Jian Gu Ke Li contain the rhizome *Drynaria fortunei* (Kunze) J. Sm. (*Polypodiaceae*), which effects include:

1) enhancing of bone formation by accumulation of bone matrix proteins such as type I collagen [37];
2) stimulation of osteoblast differentiation [37];
3) activatiom of bone mineralization [37];
4) suppression of osteoclastogenesis
5) inhibition of osteoclast differentiation [38].

Lycium barbarum polysaccharides have potent antioxidant effects, that protect osteoblasts from oxidative damage, thereby promoting bone health [39]. The planr inhibits osteoclastogenesis and reduce bone resorption [40].

*Morinda officinalis Ho*w from *Rubiaceae* in Chinese traditional medicine has been used for strengthening bones by increasing of bone mineral density. The plant is included in multisupplements: Bu Shen Zhuang Gu*,* Er Xian Decoction, Gu Song Kang Jiao Nang. The root extract suppresses bone resorption and an enhances bone formation. The plant contains a variety of active compounds that contribute to these effects, including morindin, geniposide, and saponins [41]. Active compounds like morindin have been shown to stimulate osteoblast proliferation and differentiation. Osteoblasts are the cells responsible for bone formation**,** and by stimulating their activity. *Morinda officinalis L. F.C. How* can contribute to bone regeneration and bone mineralization. Plant possesses anti-inflammatory and antioxidant effects, which help protect bone cells from oxidative stress and inflammation - both of which contribute to bone loss. Chronic inflammation can lead to increased osteoclast activity, and oxidative stress can damage osteoblasts, both accelerating bone loss. The anthraquinones exhibitinhibitory effects on osteoclastic bone resorption [42].

Panax ginseng C. A. Mey. is included in Jian Gu Er Xian Wan. Ginsenosides promote osteoblast differentiation [43], and inhibit osteoclast activity, stimulating bone regeneration [44]. Ginseng's antioxidant effects in protecting osteoblasts from oxidative stress, contributing to its bone-protective effects. [45].

Salvia miltiorrhiza Bunge (*Labiatae*), a traditional Chinnese medicine and exerts free radical scavenging activities. [46]. Tanshinone IIA and Salvianolic acid B reduce osteoclast differentiation [47]. and stimulate osteoblast differentiation, both of which contribute to bone formation. [48].

Dual-action anti-osteoporotic Chinese plants both stimulate bone formation (osteoblast activity) and inhibit bone resorption (osteoclast activity)**.** This dual mechanism helps restore the balance of bone remodeling. Some of these plants are *Psoralea corylifolia L.* and *Curculigo orchioides Gaertn. Psoralea corylifolia L*. increses osteogenesis and suppresses bone resorption *Curculigo orchioides Gaertn.* promotes osteoblast proliferation and suppresses osteoclastogenesis.

Some Chinese anti-osteoporotic medicinal plants exhibit a triple mechanism of action**,** meaning they act through three complementary pathways in bone metabolism as is present in Table. 7.

Table 7: Chinese anti-osteoporotic medicinal plants with a **triple mechanism of action.**

Chinese anti-osteoporotic medicinal plants	**Triple mechanism of action**
Drynaria fortunei Kunze ex Mett.	1) promotes bone formation osteogenesis 2) reduces bone resorption 3) anti-inflammatory effect
Panax ginseng C. A. Mey.	1) enhances osteoblast activity 2) suppresses osteoclasts formation 3) antioxidant protection
Salvia miltiorrhiza Bunge	1) inhibits osteoclast differentiation 2) supports osteoblast survival4 3) anti-inflammatory effect

The most important mechanisms of action of Chinnese anti-osteoporotic medicinal plants are included in Table 8**.**

Table 8: M**echanism of action of Chinese anti-osteoporotic medicinal plants**

	Mechanism	**Chinese medicinal plants**	
I.	**Promotion of bone formation**		
1.	Activation of osteoblast proliferation	*Cistanche deserticola* *Curculigo orchioides* *Eucommia ulmoides*	*Cinnamomum cassia* *Drynaria fortunei* *Psoralea corylifolia*
2.	Stimulation of osteoblast differentiation	*Cistanche deserticola* *Drynaria fortunei* *Epimedium brevicornum* *Panax notoginseng* *Pueraria lobata*	*Cuscuta chinensis* *Dipsacus asperoides* *Panax ginseng* *Salvia miltiorrhiza*
3.	Enhancing of osteoblast activity	*Epimedium brevicornum* *Glycine max*	*Eucommia ulmoides* *Pueraria lobata*
4.	Increasing of bone protein osteocalcin	*Cistanche deserticola* *Eucommia ulmoides*	*Drynaria fortunei*
5.	Promotion of osteoblast gene expression	*Drynaria fortune*	*Eucommia ulmoides*
6.	Activation of bone mineralization	*Achyranthes bidentata* *Drynaria fortunei* *Ligustrum lucidum*	*Cuscuta chinensis* *Dipsacus asper* *Psoralea corylifolia*

II.	**Decreasing of bone degradation**		
1.	Suppression of bone resorption	*Curculigo orchioides* *Panax ginseng*	*Epimedium brevicornum* *Salvia miltiorrhiza*
2.	Reduction of reactive oxygen species	*Camellia sinensis* *Panax ginseng*	*Lycium barbarum*
3.	Blocking of osteoclast formation osteoclastogenesis	*Achyranthes bidentata* *Drynaria fortunei* *Glycine max* *Psoralea corylifolia*	*Curculigo orchioides* *Epimedium brevicornum* *Salvia miltiorrhiza* *Pueraria lobata*
4.	Inhibition of osteoclast differentiation	*Drynaria fortunei* *Lycium barbarum*	*Eucommia ulmoides*
5.	Suppression of osteoclast activity and inflammatory cytokines	*Astragalus membranaceus* *Scutellaria baicalensis*	
6.	Decreasing of osteoclast differentiation	*Astragalus membranaceus* *Epimedium brevicornum* *Salvia miltiorrhiza*	*Drynaria fortunei* *Scutellaria baicalensis*

Epimedium brevicornum Maxim possesses many antiosteoporotic mechanisms. Icariin of plant enhances bone formation by [49]:

1) stimulation of osteoblast differentiation [50];
2) increasing of bone matrix production (osteocalcin and collagen) [51];
3) protection of osteoblasts from oxidative stress-induced apoptosis [52]

Icariin to reduces bone resorption by:

1) inhibitiion of osteoclast formation osteoclastogenesis [51];
2) reduction of the expression of RANKL (which stimulates osteoclasts);
3) bliocking the osteoclast formation and activity [49];
4) suppression of osteoclast differentiation [51];
5) enhancing the expression of osteoprotegrin (which inhibits osteoclasts).

Icariin has antioxidant properties, reducing reactive oxygen species and protecting osteoblasts from oxidative stress-induced apoptosis. It also modulates inflammatory pathways, including NF-κB signaling, reducing the production of pro-inflammatory cytokines (like TNF-α and IL-1β) that contribute to osteoclast formation [50].

Astragalus membranaceus (Fisch.) Bunge has been shown to increase osteoblast proliferation and differentiation, which are essential processes for bone formation**.** Astragaloside promotes osteogenic differentiation, enhancing the production of bone matrix proteins such as collagen and osteocalcin [53]. Plant inhibits osteoclastogenesis, decreases osteoclast activity and bone resorption, blocks inflammatory cytokines amd decreases osteoclast differentiation [54]. *Astragalus membranaceus (Fisch.) Bunge* contains antioxidants, such as flavonoids, which help neutralize free radicals and reduce oxidative stress, a key contributor to bone loss and osteoblast apoptosis. The anti-inflammatory effects of are primarily attributed to the modulation of cytokines, such as TNF-α and IL-6, which are typically elevated in osteoporotic conditions. By reducing these pro-inflammatory cytokines, plant prevents osteoclastogenesis and bone resorption [55].

Recent studies have indicated *that Angelica sinensis (Oliv.) Diels* also has significant benefits for bone health, especially in terms of increasing bone mineral density and inhibiting bone resorption. Plant contains Ligustilide, Ferulic acid, Angelicin which has been shown to stimulate osteoblast proliferation and differentiation, which are essential processes for bone formation. Ligustilide is a major active compound and promote osteogenic differentiation [56]. *Angelica sinensis (Oliv.) Diels*:

1) suppresses osteoclastogenesis (formation of osteoclasts;
2) upregulates osteoprotegerin, an inhibitor of osteoclast formation;
3) downregulates RANKL (a key osteoclast differentiation factor) [57];
4) reduces inflammatory cytokines like TNF-α, IL-6, and IL-1β, that promote osteoclastogenesis and bone resorption [58].

Oxidative stress is one of the main contributors to bone loss and osteoblast apoptosis. Antioxidants such as ferulic acid, reduces oxidative stress in bone cells and protect osteoblasts from oxidative damage [58].

Glycine max L. offers significant potential in the prevention and management of osteoporosis through several mechanisms of Genistein activity [59,60], that:

1) improves bone mineral density\
2) enhances bone formation
3) promotes osteoblast activity **[**59]
4) inhibits osteoclastogenesis
5) decreases osteoclast activity5
6) reduses bone resorption. [60].

CONCLUSION

An observational study shows different trade form preparations: tablets, capsules, powders, solutions of specific Chinese medicinal plants, that promote bone

health through various pharmacological mechanisms. The plants exert their dual or multi-target effects on bone formation**,** bone resorption**,** hormonal regulation, and cell protection in osteoporotic condition.

The most applied drug forms can be presented as follows: *Angelica* sinensis (tabl., caps.), *Cimicifuga racemosa* tabl., *Drynaria fortunei Kunze ex Mett.* (caps., tincture, powder), *Eclipta prostrata* (tincture), *Salvia* caps., *Morinda officinalis* (powder, tincture), *Pueraria lobate* caps.

An important multicomponent formulation are: USANA Phyto Estrin, Hormone Balance Menopause Relief caps., Gu Ling Pian, Dang Gui Bu Xue Tang, Jian Gu Er Xian Wan, Qing E Wan, Zi Shen Wan, Bu Shen Yi Jing Fang, Gu Kang Fang, Yi Shen Zhuang Gu He Ji, Wu Jia Bu Gu, Bu Shen Mi Gu Ye, Bu Shen Zhuang Gu, Er Xian Decoction, Fu Fang Lu Rong Jian Gu Jiao Nang, Gu Wei Ling Jiao Nang, Zeng Gu Wan, Jian Gu Ke Li. The most important mechanisims of action are: bone formation by: activation of osteoblast proliferation and differentiation, enhancing of osteoblast activity, increasing of bone protein osteocalcin, increasing of bone mineralization; decreasing of bone degradation by: suppression of bone resorption. blocking of osteoclastogenesis, inhibition of osteoclast activity and differentiation, reduction of reactive oxygen species.

More human clinical trials are needed to validate the effectiveness of these plants and their active compounds. Exploring combinations of these plants with conventional drugs like bisphosphonates or denosumab could provide synergistic effects for osteoporosis treatment. Further research into the molecular mechanisms of these herbs will help in identifying specific targets and interactions for osteoporosis therapy.

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Author contributions

All authors have contributed equal.

Ethical statements

- The authors declared that no clinical trials were used in the present study.
- The authors declared that no experiments on humans or human tissues were performed for the present study.
- The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.
- The authors declared that no experiments on animals were performed for the present study.
- The authors declared that no commercially available immortalized human and animal cell lines were used in the present study

Data availability

All of the data that support the findings of this study are available in the main text or Supplementary

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