THERAPEUTIC VALUES OF HERBAL MEDICINES: AN UPDATE OF SYSTEMATIC REVIEWS

Onanong Waleekhachonloet[1*], Thananan Rattanachodpanich[1], Kitiyawadee Doukprom[2], Chulaporn Limwattananon[2], Areewan Cheawchanwattana[2], Pariya Thomudtha[2],

[1] Faculty of Pharmacy, Mahasarakham University, Thailand
[2] Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand

ABSTRACT

Background: In Thailand, herbal products are mostly classified as dietary supplements by food and drug administration (FDA). The manufacturer is allowed to make a health claim but not for treatment or prevention of a specific disease. This compilation aimed to evaluate efficacy and effectiveness of the herbal medicines using prior systematic reviews of available randomized controlled trials.

Material and method: Computerized literature searches were performed on the Cochrane Library and MEDLINE databases from January 2003 to July 2009.

Results: A total of 155 reviews of therapeutic values of herbal medicines were extracted and summarized. Most evidences were considered "promising", because of methodological limitations. The three most common systematic reviews involved cardiovascular system (N=20), psychiatrics (N=17), and genitourinary tract (N=16). Fifty two reviews showed an effectiveness of herbs for various disease categories.

Conclusion: Since a number of herbal studies is continuously increasing during these recent years, gathering and synthesizing the update evidence to help making appropriate clinical decisions is warranted.

Keyword: Herbal medicines, Herbs, Systematic reviews

BACKGROUND

In several countries, herbal medicines have been widely used as an alternative to modern pharmaceutical products for treatment of illnesses. In the US, the medicinal herbs called "botanicals" are classified along with vitamins, minerals, and other health products in the "dietary supplement" category under the Dietary Supplement and Health Education Act. Under this Act[1], the manufacturer of a botanical is allow by the US Food and Drug Administration (USFDA) to make a "health" claim, i.e., the herbal product affects the structure and function of the body but not a claim of effectiveness for the prevention or treatment of specific disease. In addition, the manufacturers have to provide a disclaimer informing the user that the FDA has not evaluated the ingredient. To customers, herbal medicine has provided an opportunity to gain access to remedies that apparently provide simple solutions to their health concerns. To

physicians and other health care providers, however, the herbal medicine is not well adopted into daily practice because of the controversial issue on the efficacy and effectiveness. Results from the herbal trials often do not reach statistical significance due to a relatively small sample size as compared with the trials of conventional medicines.

Therefore, this study aimed to conduct the comprehensive compilation of systematic reviews of therapeutic value of herbal medicine for various clinical conditions.

METHODS

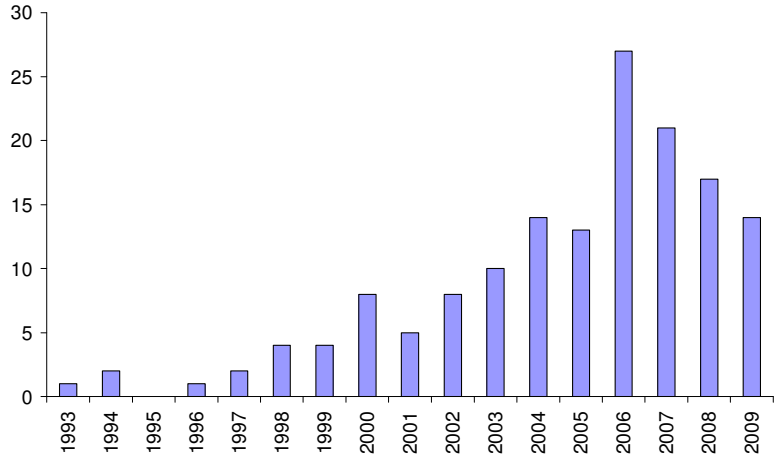
Computerized literature searches were performed on the Cochrane Library and MEDLINE databases from January 1993 to July 2009. The primary search terms included “herb” OR “herbal” OR “herbal medicine” OR “medicinal herbs”. All searches were limited to systematic reviews or meta-analyses which were published in English language. Based on these keywords, 436 reviews were obtained. The reviews were included if they reported effectiveness of single or compound herbal medicines.

According to this criterion, 151 systematic reviews were included in this article. Details of each systematic review were extracted and summarized using data collection forms. The following characteristics and data were described: primary author, types of herbal medicines, study design, number of participants, and conclusions on effectiveness. In this article, only the herbal medicines that seem to have therapeutic value based on evidence were presented.

RESULTS AND DISCUSSION

This compilation showed the trend of an increase in number of the systematic reviews of herbal medicines over time. From less than 10 reviews each year before the year 2003 to more than 20 reviews a year after the year 2006 (Figure 1).

Figure 1: Numbers of systematic reviews of herbal medicine by year until July 2009



The three most common reviews involved cardiovascular system (N=20), psychiatrics (N=17), and genitourinary tract (N=16) as shown in table 1.

For infection, it was found that Chinese herbs combined with Western medicine may improve symptoms, quality of life, and lung infiltration in SARS patients[3]. Phyllanthus marus, Phyllanthus genus, chinese herbs were effective for hepatitis B[6-7]. One review showed that Chinese herbs were as effective as interferon alfa in seroreversion of HBeAg and HBV DNA. *Pelargonium sidoides* (Umckaloabo) was found to be effective in alleviating symptoms of acute respiratory infection in adults[16]. For urinary tract infection, a systematic review showed that cranberry juice could improve symptoms of urinary tract infection significantly in women over a 12 month period[17].

For respiratory system, four systematic reviews showed that Echinacea was effective for common cold[20-23]. Echinacea decreased the odds of developing the common cold by 58% (OR=0.42; 95% CI= 0.25-0.71) and decreased duration of a cold by 1.4 days (WMD= -1.44; 95% CI= -2.24 to -0.64)[22].

For CNS diseases, two of six studies showed an effectiveness of Gingko biloba and compound Chinese herbs for dementia[37,40]. No significant differences in symptom progression were found when compared between Ginkgo extract and cholinesterase inhibitors. Meta-analyses found that the compound Chinese herbs were more effective than no treatment or placebo although the overall effect was small. No severe adverse events were reported. Insufficient evidences supported the use of Huperzine A (Chinese herb *Huperzia serrata*)[36,38] and Yizhi capsule[39] for dementia. A systematic review of claudication showed that Gingko biloba could increase pain free walking distance significantly when compared with placebo (weighted mean difference ranged from 33 to 34 meters) [41]. For alzheimer's disease, *Melissa officinalis*, *Salvia officinalis*, Yi-Gan San, BDW (Ba Wei Di Huang Wan), *Ginkgo biloba*, and Huperzine A (*Huperzia serrata*) were effective for cognitive impairment of the disease. *M. officinalis* and Yi-Gan San were also useful in agitation[42].

Findings from almost all reviews (nine of ten reviews) did not support using of herbal medicine in ischemic stroke. Various herbs including Ginkgo biloba[45], Vinpocetine[46], Mailuoning[48], Chuanxiong[50], Puerarin, Shenmai, Milk vetch, Mailuoning, *Ginkgo bilob*a, Ligustrazine, Danshen agents, Xuesetong, and *Acantho panax*[51], Dan Shen[47,52], Tongxinluo[54], were reviewed but there were insufficient evidence of an effectiveness. Only one review showed that Sanchi appears to be beneficial and safe for acute ischemic stroke but the small sample and inferior quality of studies prevented a definite conclusion[49]. For improving of recovery after stroke, Danqi Piantang Jiaonang (DJ) seem to be effective with good tolerability[56].

For psychiatric disorders, *Suo quo wan* found to be effective in clozapine induced hypersalivation[57]. The use of Ginkgo biloba extract, dang gui cheng qi tang or xiao yao san, dang gui cheng qi tang, or Rhizoma rhei palmatum (rhubarb) with antipsychotics was beneficial for Schizophrenia[59-60]. Kava[61-64] and St John's wort[67] were found to be effective for anxiety and depression respectively. However, serious adverse events including dermatological and neurological complications, and liver damage has been reported. Phytotherapies which potentially have significant use in psychiatry, and urgently require more research are *Rhodiola rosea* (roseroot) and *Crocus sativus* (saffron) for depression; *Passiflora incarnata* (passionflower), *Scutellaria lateriflora* (scullcap) and *Zizyphus jujuba* (sour date) for anxiety disorders; and *Piper methysticum* (kava) for phobic, panic and obsessive-compulsive disorders.

For genitourinary tract, evidence supported an effective of Korean red ginseng for erectile dysfunction[74], Er-xian decoction for postmenopausal symptoms[76-77],

Chinese herbs for dysmenorrhea[78-79], and Serenoa repens for benign prostate hyperplasia[82-85]. For benign prostate hyperplasia, four of seven reviews showed that Serenoa repens could improve urinary symptoms, peak flow rate, and nocturia significantly. Serenoa repens was also compared with finasteride and the result showed that Serenoa repens had similar effects but fewer adverse effects[82-85].

For gastrointestinal diseases, using of ginger for more than one gram could prevent postoperative nausea and vomiting (RR = 0.69, 95%CI 0.51-0.89 and RR=0.61, 95%CI 0.45-0.84, respectively)[88]. Four of six reviews in irritable bowel syndrome (IBS) found convincing evidence that peppermint oil (*Mentha piperita* Linnaeus) [91], soluble fibers[92] including psyllium seed, wheat bran, and corn bran, Chinese herb compounds[93] (Huatan Liqi Tiaofu decoction, Tongxie Yaofang modified and Tongxie Yaofang plus Sini San decoction, Geqin Shujiang Saocao decoction, Huanchang decoction, Congpi Lunzhi Formula, Xiangsha Liujunzi decoction, Shunji mixture, Gegan Qinlian Pellet, and Liyiting decoction) and compound of *Zataria multiflora*, curcumin from *C. longa*, *Ziziphora clinopoides*, *Ginkgo biloba*, essential oil of *Satureja khuzestanica*, glycoprotein from *Gardenia jasminoides*, ethanolic extract and nicotine from *Nicotiana tabacum*, and polysaccharide from *Rheum tanguticum*[94] can alleviate IBS significantly. Iberogast[95] and preparation STW[96] had significant effect in treatment of functional dyspepsia compared to placebo. STW5 showed no significant differences from cisapride.

For musculoskeletal system, all three reviews of rheumatoid arthritis showed that gamma linoleic acid (GLA) had significant effects in reducing pain, joint tenderness, and stiffness[99-101]. Two of three reviews in osteoarthritis showed an effectiveness of avocado-soybean unsaponifiables[102].

For various types of cancers and cancer related symptoms[107-115], only one review that included 34 RCTs of 2815 patients with non small cell lung cancer showed an additive effect of Astragalus-based Chinese herbal medicine over chemotherapy[107]. The review reported significant mortality reduction (RR = 0.58-0.67, 95%CI 0.49-0.87), improvement of tumor response (RR = 1.28-1.34, 95%CI 1.12-1.46), and Karnofsky performance status (RR = 1.28, 95%CI 1.12-1.46) [107].

For cardiovascular diseases, Hawthorn extract had significant benefit as an adjunctive therapy for chronic heart failure by improving maximum workload and pressure heart rate[123]. Salvia pellet had significant effect on reducing angina symptoms (RR =1.13) and improving electrocardiogram (RR=1.39) [117]. Two systematic reviews of hyperlipidemia showed that garlic could significantly decrease total cholesterol and triglyceride compared with placebo when used for at least on month and the effect persisted for six months[125-126]. In addition, soy[129], policosanol[131], and psyllium-enriched cereal[132] could improve blood lipid profile significantly. Horse chestnut[137], cyclo 3 fort[138-139] were effective for venous insufficiency treatment. Only one systematic review of ischemic heart disease showed an effectiveness of garlic, guggul, Arjuna in a clear manner with high quality data[122]. However, the finding was not consistent with other reviews.

There was a systematic review of heroin detoxification which included 21 RCTs, with 2,949 patients. Herbs including *Radix Ginseng* (Renshen) (8 studies), *Rhizoma Corydalis* (Yanhusuo) (7 studies), *Radix Aconiti Lateralis Preparata* (Fuzi) (5 studies), *Radix Glycyrrhizae* (Gancao), *Flos Daturae* (Yangjinhua), and *Radix Angelicae Sinensis* (Danggui) were effective and safe for heroin detoxification[145].

Table 1 Systematic reviews of herbal medicine by disease category

Disease category	Disease	Total reviews	Reviews that found effectiveness	Promising Herbs
Infection (N=16)	SARS [2,3]	2	1	Compound herbs, national herbs, Kanfeidian, Potenili, Compound Chinese herbs, Chinese traditional patient medicines[3]
	Hepatitis B/C[4-10]	7	2	Phyllanthus genus5[6], Chinese herbs[7]
	Influenza[11-13]	3	0	-
	HIV[14]	1	0	-
	Viral myocarditis[15]	1	0	-
	Acute respiratory Infection[16]	1	1	*Pelargonium sidoides* (Umckaloabo)
	Urinary tract infection[17]	1	1	Cranberries
Respiratory tract (N=11)	Asthma[18-19]	2	0	-
	Common cold[20-23]	4	4	
	Bronchitis[24-25]	2	0	-
	Sore throat[26]	1	0	-
	COPD[27]	1	0	-
	Sinusitis[28]	1	0	-
Endocrine system (N=4)	Diabetes Mellitus[29]	1	0	-
	Hyperthyroidism[30]	1	0	-
	Obesity[31-32]	2	1	Ephedra, ephedrine[31]
Cognitive (N=10)	Dementia[33-40]	8	2	Gingko biloba[37,40]
	Claudication[41]	1	1	Gingko biloba
	Alzheimer's disease (AD) [42]	1	1	*Melissa officinalis*, *Salvia officinalis*, Yi-Gan San, BDW (Ba Wei Di Huang Wan), *Ginkgo biloba*, and Huperzine A (*Huperzia serrata*)
Central nervous system(N=2)	Neuropathic pain[43]	1	0	-
	Parkinson's disease[44]	1	0	-
Cerebrovascular system (N=12)	Ischemic stroke[45-54]	10	1	Sanchi[49]
	Recovery after stroke[55-56]	2	1	Danqi Piantang Jiaonang (DJ) [56]
Psychiatrics (N=17)	Clozapine induce hypersalivation[57]	1	1	*Suo quo wan*
	Insomnia[58]	1	0	-
	Schizophrenia[59-60]	2	1	*Ginkgo biloba* extract, dang gui cheng qi tang or xiao yao san, dang gui cheng qi tang, *Rhizoma rhei palmatum*(rhubarb) [59]
	Anxiety[61-66]	6	3	Kava extract[61-64]
	Depression[67-71]	6	3	St. John's wort (Hypericum perforatum L)[67], Hypericum [69]
Genetourinary tract (N=16)	Uterine fibroids[72]	1	0	-
	Dysfunctional Uterine Bleeding (DUB)[73]	1	0	-
	Erectile dysfunction[74]	1	1	Korean red ginseng
	Pre-menstrual syndrome[75]	1	0	-
	Post-menopausal[76-77]	2	0	Er-xian decoction(EXD)[77]
	Dysmenorrhea[78-79]	2	1	Chinese herbal medicine[79]
	Ectopic pregnancy[80]	1	0	-
	Benign prostate Hyperplasia[81-87]	7	4	Serenoa repens[82-85]
Gastrointestinal (N=11)	Nausea/vomiting[88]	1	1	Ginger
	Irritable bowel syndrome[89-94]	6	4	- Peppermint oil, melatonin, clay-like materials[91] - Peppermint oil, Soluble fibre: psyllium seed, wheat bran and corn bran, Herbal formula: Tong xie yao fang, Padma Lax, STW 5 and STW 5–II[92] - Chinese herbs[93] - *Zataria multiflora*, curcumin from *C. longa*, *Ziziphora clinopoides*, *Ginkgo biloba*, essential oil of *Satureja khuzestanica*, glycoprotein from *Gardenia jasminoides*, ethanolic extract and nicotine from *Nicotiana tabacum*, and polysaccharide from *Rheum tanguticum*[94]
	Dyspepsia[95-96]	2	2	Iberogast[95], preparation STW 5 (containing e.g. Iberis, peppermint, chamomile) [96]
	Pancreatitis[97]	1	0	-
	Liver disease[98]	1	0	-

Disease category	Disease	Total reviews	Reviews that found effectiveness	Promising Herbs
Musculoskeletal (N=8)	Rheumatoid arthritis [99-101]	3	3	Gamma linoleic acid (GLA) compound
	Osteoarthritis[102-104]	3	2	Avocado-soybean unsaponifiables[102]
	Low back pain[105-106]	2	0	
Cancers	Cancers and cancer related symptoms[107-115]	9	1	Astragalus-based Chinese herbal medicine [107]
Cardiovascular system (N=20)	Acute myocardial infarction[116-121]	6	0	Salvia pellet[120], Suxiao Jiuxin[117]
	Ischemic heart disease[122]	1	0	Garlic, guggul, Arjuna
	Congestive heart failure[123-124]	2	1	Hawthorn extract[123]
	Hyperlipidemia[125-133]	9	6	Garlic[125,126], Soy[129], Soy isoflavone[130], Policosanol[131], Psyllium[132]
	Hypertension[134]	1	0	-
Vascular (N=5)	Venous insufficiency [135-139]	5	4	Horse chestnut (Aesculus hippocastanum L)[135-138], Cyclo 3 Fort[139]
Dermatological system (N=2)	Eczema[140-141]	2	0	-
Other	Macular degeneration [142]	1	0	-
	Measles[143]	1	0	-
	Liver damage[144]	1	0	-
	Withdrawal symptom of heroin detoxification[145]	1	1	CHM: *Radix Ginseng* (Renshen) (eight studies), *Rhizoma Corydalis* (Yanhusuo) (seven studies), *Radix Aconiti Lateralis Preparata* (Fuzi) (five studies), *Radix Glycyrrhizae* (Gancao), *Flos Daturae* (Yangjinhua), and *Radix Angelicae Sinensis* (Danggui)
	Nephrotic syndrome [146]	1	0	-
	Tinnitus[147]	1	0	-
	Migraine[148]	1	0	-
	Neurocognitive[149]	1	0	-
	Preeclampsia[150]	1	0	-
	Head lice[151]	1	0	-
	Chronic prostatitis[152]	1	0	-

CONCLUSIONS

Our compilation reveals that a considerable number of systematic reviews of therapeutic values of herbal medicine are available at the present. In majority of the result from the reviewers, the reviewers considered the available evidences as "promising". Only a few evidences are sufficient for clinical decisions.

One notable remark is that methodological quality of most reviewed primary studies has been criticized for limitation. What we preformed is making an implication for the therapeutic values of herbal medicines from existing systematic reviews, which might be oversimplified. Readers who want to be confirmed for the evidence for a given herb for a specific disease and clinical condition should read through the originally reviewed studies. To our knowledge, our compilation is completed up to July 2009. Most of these systematic reviews elaborated on the herbal preparations which are marketed and used in developed countries. The use of herbal medicines in the developing and transitional countries has been rarely evaluated by systematic reviews. Furthermore, health care providers may combine different herbs and adapt the prescriptions to their patients. It is likely that these traditional forms of herbal medicines will remain under researched partly due to lacks of financial incentive and partly due to methodological issues.

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