



Effects of black cohosh(승마) and cynanchum(백수오) on menopausal symptoms and cardiovascular system

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Global incidence of VMS

Table 1 Prevalence of hot flushes according to geographic area⁹

<i>Geographic area</i>	<i>Number of women</i>	<i>Age (years)</i>	<i>% experiencing hot flushes</i>
Europe ¹⁰	4200	45-60	74
North America ¹¹	3302	42-52	<i>Symptoms in the last 2 weeks:</i> Hispanic: 49 African-American: 46-45 Caucasian: 37 Japanese-American: 34 Chinese-American: 29
Latin America ¹²	409	40-59	68.9
Asia ¹³	1028	40-65	63.1

Archer et al. Climacteric.2011

Menopausal symptoms: related to

- **Quality of Life (QoL)**
 - sleep disturbance, impairment of daytime activity
- **Cardiovascular events**
 - worsening of biochemical risk factors for atherosclerosis & CVD^{1,2}
- **Insulin resistance**
 - hot flushes: associated with higher HOMA index³

¹Caqnacci et al., Climacteric 2012, ²Lambrinooudaki et al., Climacteric 2012
³Thurston et al. J Clin Endocrinol Metab.2012

Non-hormonal treatment for VMS

TABLE 1
Nonhormonal Agents Used as Therapy for Hot Flashes

Prescription	Nonprescription
Belladonna/ergotamine tartrate/ phenobarbital combination (Bellergal,* Bellamine)	Black cohosh
Clonidine (Catapres)	Dong quai
Fluoxetine (Prozac)	Evening primrose oil
Gabapentin (Neurontin)	Ginseng
Mirtazapine (Remeron)	Melatonin
Paroxetine (Paxil)	Red clover isoflavones
Trazodone (Desyrel)	Soy isoflavones
Venlafaxine (Effexor)	Vitamin E
	Wild yam

*—Bellergal is no longer available commercially in the United States.

Dana et al. Am Family Physician 2006



BLACK COHOSH

- **Cimicifuga ramosa**

Native Americans used black cohosh

- Traditionally used remedies

: sore throat

inducing lactation

diuretics

gynecological disorders

- menstrual cramps and menopausal symptoms



- **Extracts of black cohosh**

- Roots and rhizomes are the basis for the extraction
(not the flowers)

: extracted using alcohols

: triterpene glycosides and phenolic acids

: no isoflavones or estrogenic action

- **Serotonergic activity**

: partial agonist at the 5HT1A and opiate receptors

: affinity to dopamine D2 receptor

Borrelli et al. Pharmacol Res 2008

RCTs on Black cohosh : menopausal symptoms

Reference	Sample size	Experimental treatment	Control treatments (dosage)	LT	Main clinical outcome measures	Comments
Stoll [33]	75 German women (BC = 26, CE = 29 and P = 20)	Two tablets twice daily (8 mg extract/day)	Placebo	3 months	Kupperman menopausal index, Hamilton anxiety scale, proliferation status of vaginal epithelium	Lack of oestrogen effects (dropout 6.2%)
Wuttke [48,73]	62 Czech women (BC = 20, CE = 22 and P = 20)	40 mg/day (CR BNO 1055) ^b	CE (0.625 mg/day) CE (0.6 mg/day)	3 months	Menopause rating scale, bone density, endometrial thickness, vaginal cytology	2-week run-in period. Small sample size because of participants dropped out. Use of intention-to-treat population.
Osmer [53]	286 German women (BC = 45 and P = 141)	40 mg/day	Placebo Placebo	3 months	Menopause rating scale, adverse events	1-4 weeks wash-out phase before study entry. Use of intention-to-treat population.
Frei-Kleiner [54]	122 Swiss women (BC = 70 and P = 35)	6.5 mg dried extract (corresponding to 42 mg crude drug) ^b	Placebo	3 months	Score for hot flashes, Kupperman menopausal index, menopause rating scale, adverse events	2-week run-in period. Use of intention-to-treat population (dropout 9%)
Newton [56,77]	323 American women (BC = 73, MP = 73, MPS = 74,	160 mg/day ^a (corresponding to 5 mg of triterpene glycosides)	Multibotanical preparation Multibotanical preparation + soy CE + MPA	12 months	Frequency and intensity of vasomotor symptoms (using a self-report Vasomotor Symptom Diary), Vasomotor Scale of	2-week run-in period. Use of intention-to-treat population. 16 participants were

Efficacy of black cohosh in reducing climacteric symptoms is not fully conclusive

Borrelli et al. Maturitas 2010

Black cohosh (*Cimicifuga* spp.) for menopausal symptoms (Review)

Leach MJ, Moore V



- 16 RCTs, 2,027 peri- or post-menopausal women
- Oral monopreparations of black cohosh
: median dose 40 mg/d, mean duration 23 weeks
- Outcomes: VMS, vulvovaginal atrophy, menopause symptom score, adverse effects

Leach et al. Cochrane DB 2012



Black cohosh

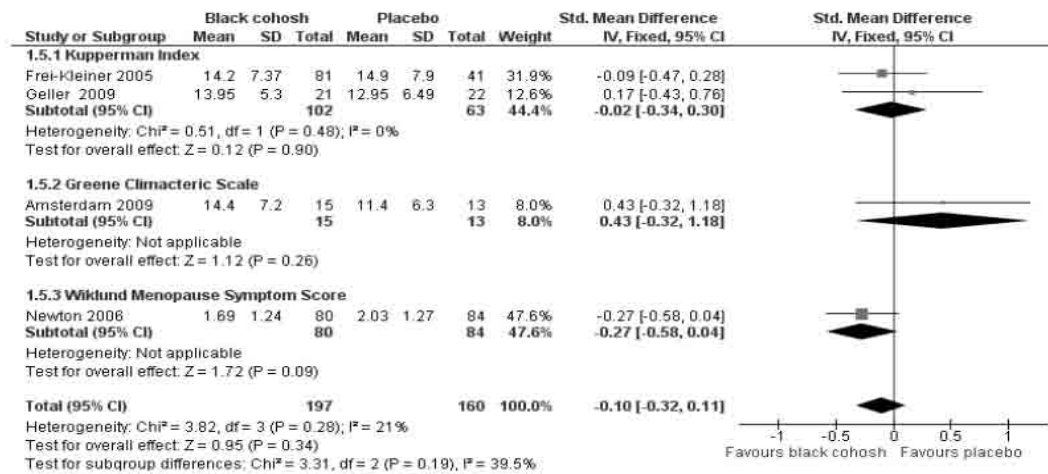
Hot flush : compared with placebo

- **VMS frequency, intensity, and night sweats**
: no significant difference between two groups
- **Menopausal symptom score & adverse effects**
: no difference

Mathew et al. Cochrane DB 2013

Black cohosh

Figure 5. Forest plot of comparison: **I Black cohosh versus placebo, outcome: 1.5 Menopausal Symptom Score.**



Mathew et al. Cochrane DB 2013

Black cohosh

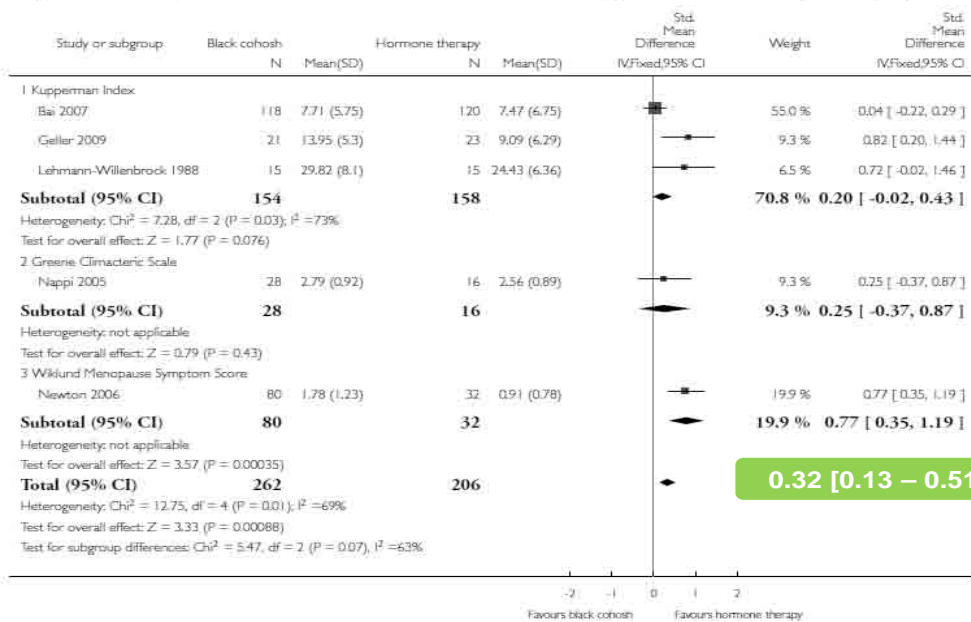
Hot flush : compared with hormone therapy

- **VMS frequency, intensity**
: Favorable effects in HT
- **Menopausal symptom score**
: HT 0.32 95% CI 0.13 – 0.51

Mathew et al. Cochrane DB 2013

Black cohosh

Analysis 2.5. Comparison 2 Black cohosh versus hormone therapy, Outcome 5 Menopausal Symptom Score.



Leach et al. Cochrane DB 2013



Black cohosh

CARDIOVASCULAR EFFECTS : IN VITRO STUDIES

- **Isolated rat aorta**
: Black cohosh extract – vasorelaxant effects via endothelium-dependent, and –independent mechanisms

Kim et al. J Ethnopharmacol 2011

- Plasminogen activator system in vascular smooth muscle cells
: BcEx stimulated plasminogen activator inhibitor and inhibit free tissue plasminogen activator (tPA)
→ might have negative influence on fibrinolysis

Lee et al. Maturitas 2013

Black cohosh

EFFECTS ON LIPID & GLUCOSE

- Double blind RCT, 351 peri & post-menopausal women
- (i) Black cohosh (160mg/d), (ii) multibotanical including black cohosh (200 mg/d), (iii) multibotanical + soy (iv) 0.625 mg EE
- 3 mo f/up

HT: LDL↓, TG↑

Adjusted mean change (3 months—baseline) in laboratory values (and 95% confidence intervals): Herbal Alternatives for Menopause Study (HALT)

	Placebo (n = 73)	Black cohosh (n = 71)	Multibotanical (n = 68)	Multibotanical + soy (n = 71)	P-Value herbs ^a	Hormone therapy (n = 27)	P-Value hormone therap ^b
Serum lipids							
Cholesterol (mg/dL)	-5.2 (-10.2, -.2)	-4.2 (-8.8, 1.6)	-10.1 (-15.4, -4.9)	-3.9 (-8.8, 1.1)	.27	-9.5 (-18.1, -.9)	.37
LDL (mg/dL)	-3.2 (-7.4, 1.0)	-3.7 (-8.0, .4)	-7.3 (-11.7, -3.0)	-3.0 (-7.1, 1.1)	.45	-12.0 (-19.1, -4.8)	.02
HDL (mg/dL)	-.4 (-1.9, 1.0)	-1.2 (-2.6, .3)	-1.9 (-3.4, -.4)	-.7 (-2.1, .8)	.51	1.8 (-.7, 4.3)	.98
Triglycerides (mg/dL)	-7.4 (-17.0, -2.1)	3.2 (-6.3, 12.7)	-2.4 (-12.3, 7.5)	-2.5 (-11.9, 6.8)	.71	7.8 (-8.5, 24.2)	.03
Glucose metabolism							
Glucose (mg/dL)	.3 (-2.6, 3.2)	2.5 (-.4, 5.4)	.4 (-2.7, 3.4)	2.1 (.7, 5.0)	.48	1.0 (-4.0, 6.0)	.20
Insulin (μIU/mL)	1.5 (-.9, 3.9)	.1 (-2.2, 2.5)	.5 (-1.9, 3.0)	.4 (-1.9, 2.8)	.48	5.4 (-1.3, 9.5)	.50
Coagulation factors							
Fibrinogen (mg/dL)	-4.6 (-14.6, 5.4)	-11.8 (-21.7, .9)	7.0 (-3.3, 17.3)	-14.1 (-24.0, -4.3)	.02 ^c	-28.9 (-46.2, -11.5)	.09

Spangler et al. Maturitas 2007

Black cohosh

SAFETY

Table 1 Non-hormonal medicines have a modest and variable efficacy on vasomotor symptoms (VMS). Acknowledgement of adverse effects and of drug interactions permits the choice of the best option in the individual case

Treatment	Efficacy on VMS	Cardiovascular caution	Breast caution	Endometrial caution	Hepatotoxicity	Hepatic metabolism	Renal excretion
Clonidine	poor	√	—	—	no reports found	√	√
Gabapentin	moderate	√	—	—	√ ^{**}	—	√
SSRIs	modest	√	√ [#]	—	—	√	√
Paroxetine	moderate	√	√ [#]	—	√	√	√
Venlafaxine	moderate	√	—	—	√	√	√
Desvenlafaxine	moderate	√	—	—	?	—	√
Phytoestrogens	poor-modest	?	√ [#]	√	?	√	√
Black cohosh	poor-modest	?	?	—	√	√	?

- No effect on cellular morphology in nipple aspiration
- Black cohosh
 - : not increase the incidence of breast cancer in mouse model, but increase pre-existing metastasis
 - : mild inhibition of CYP2D6

Ruhlen et al., Nutr Cancer 2007, Davis et al., Cancer Res 2008, Villaseca. Climacteric 2012

Black cohosh

SAFETY AFTER BREAST CANCER

- **2006 Canadian Consensus Conference on Menopause**
estrogen-dependant tumours, including ER-positive breast cancer: contraindication for use of black cohosh

Canadian consensus conference on Menopause 2006



- **NIH 2004 workshop**
in women treated for breast cancer only standard care screening for recurrence and metastases need take place with black cohosh use

NIH. Workshop on the safety of black cohosh in clinical studies; 2004. http://nccam.nih.gov/news/events/blackcohosh/blackcohosh_mtnsum.pdf. Roberts. Maturitas 2010



Cynanchum Wilfordii

- 백수오 (白首烏)- 중국
Cynanchum bungei Decne
: 진시황의 불로초
자양, 강장, 탈모/탈색예방
중국에서 인삼, 구기자와 함께 3대 명약
- 백하수오 (白何首烏) - 우리나라
Cynanchum wilfordii
: 약제효과는 백수오와 거의 유사
산지 중국 산둥 지역 - 파종 시에도 발아율이 높고 강인

Major ingredient of Cynanchum

- **EstroG-100**
: Compounds of 3 herbes
Cynanchum wilfordii, Phlomis umbrosa (sok-dan),
Angelica gigas (dong quai)

: New Dietary Ingredient (NDI) approved from FDA (US
and Canada), KFDA



Herbal Pause™ with EstroG-100™ - 60 Vcaps®

NATURAL MENOPAUSE RELIEF

Find a Store for this Product

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- Item#: 3377
 Manufacturer SKU: 733739033772
- Patented Herbal Extract Blend
 - Free of Phytoestrogens & Soy
 - A Dietary Supplement
 - Vegetarian Formula



Supplement Facts

Serving Size:	2 Vcaps®	
Servings Per Container:	30	
	Amount Per Serving	% Daily Value*
EstroG-100™ (a proprietary blend of extracts of <i>Phiomis umbrosa</i> , <i>Cynanchum wilfordii</i> and <i>Angelica gigas Nakai</i>)	514 mg	*

* Percent Daily Values are based on 2,000 calorie diet.
 † Daily Value not established.

**Does dong quai have estrogenic effects in postmenopausal women?
 A double-blind, placebo-controlled trial**

Janie D. Hirata, M.D.* Rebecca Small, M.A.§
 Lillian M. Swiersz, M.D.† Bruce Ettinger, M.D.||
 Bonnie Zell, M.D.‡

- 71 PM women randomized to dong quai or placebo
- Kupperman index

Table 2 Outcomes of Treatment With Dong Quai or Placebo for Menopausal Symptoms

Outcome	Baseline	6 weeks	12 weeks	24 weeks
Kupperman index				
Placebo	21.8 (7.5)	14.2 (6.4)*	15.0 (6.2)*	15.2 (8.9)*
Dong quai	19.0 (8.4)	11.3 (7.2)*	12.6 (6.6)*	12.2 (5.2)*
Vasomotor episodes (/wk)				
Placebo	33.2 (26.4)	33.8 (28.5)	29.3 (26.2)	26.9 (28.8)
Dong quai	47.3 (39.9)	35.4 (21.3)	34.9 (23.3)	30.7 (21.7)

Dong quai does not produce estrogen-like responses in vasomotor symptoms or in the Kupperman index

Hirata et al. Fertil & Steril 1997



Anti-menopausal Effect of the Newly-Developed Phytoestrogen, FGF271, *in Vitro* and *in Vivo*

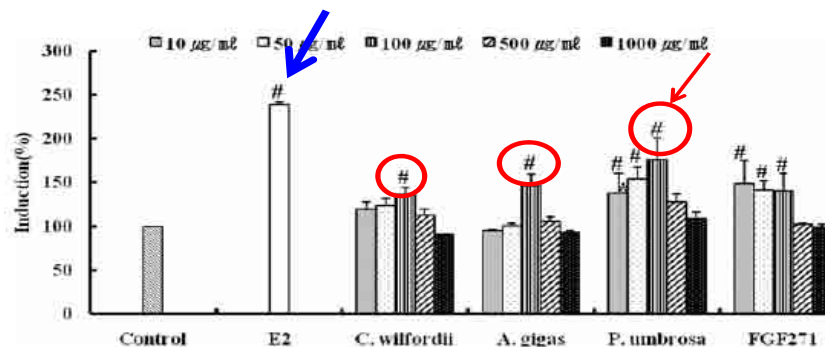
Nam-Jin Lee¹, Geun-Soo Kim¹, Bo-Yeon Kwak², Kwon-Taek Yi², Jae-Kyung Lee², Yu-Ri Jeong¹, Chun Mei Lin¹, Jae Soo Kim² and Jong-Koo Kang^{1,*}

¹College of Veterinary Medicine and Research Institute of Veterinary Medicine, Chungbuk National University, Cheongju, Korea
²Herbal Hormone Research Institute, Naturalink Tech Co., Ltd., Seoul, Korea

- **FGF271**: mixture extract of 3 herbs (Cynanchum wilfordii, Angelica gigas, Phlomis umbrosa)
Soylife (40% isoflavone): control
- Estrogenic activity of chemicals in Ishikawa & SaOS-2 cell-lines
- Body weight, BMD, uterus weight in ovariectomized (OVX) rat vs. sham control

Lee et al. Lab Anim Res 2008

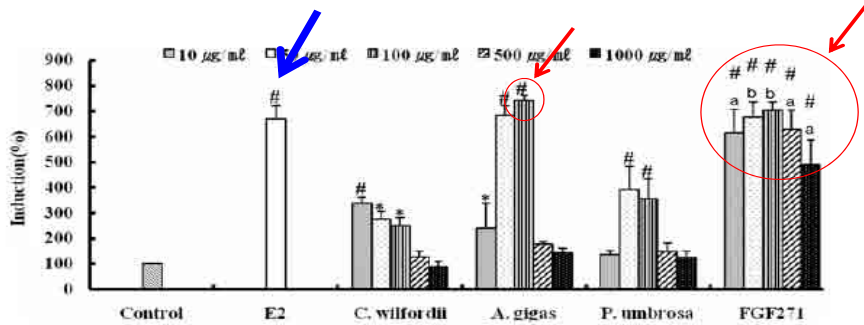
Estrogen-specific ALP (Ishikawa cells)



- **Peak estrogen specific ALP at dose of 100 µg/ml**
: Phlomis (속단) > Angelica (당귀) > Cynanchum (백수오)
- FGF271: similar effect with each component
less than 17β-estradiol

Lee et al. Lab Anim Res 2008

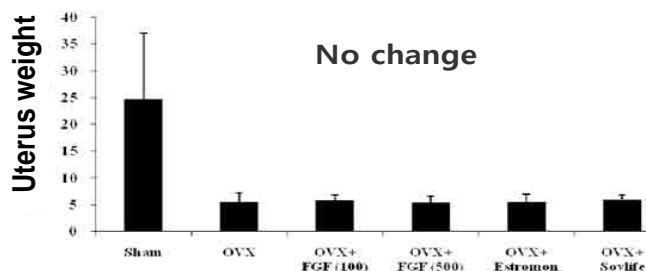
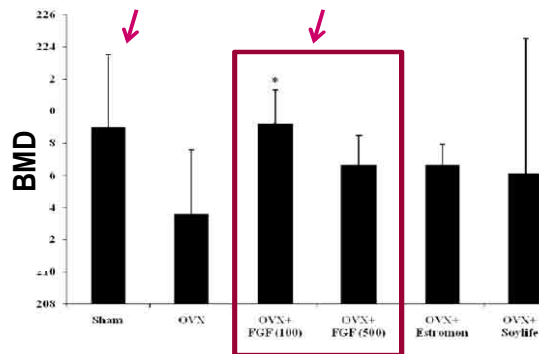
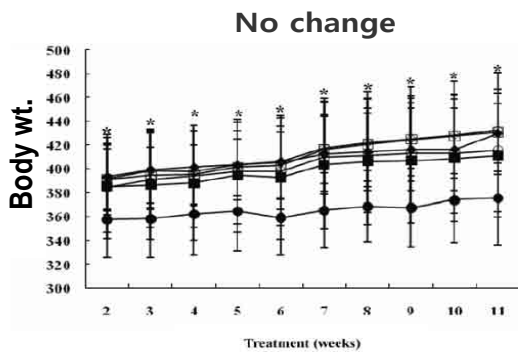
Estrogen-specific ALP (SaOS2 cells)



- **Estrogen specific ALP induction**
: Angelica (당귀) > Phlomis (속단) > Cynanchum (백수오)
- **FGF271 significantly induced ALP activity**
→ SaOS2 cells is sensitive to estrogen or chemicals
복합추출물이 estrogenic activity를 높임

Lee et al. Lab Anim Res 2008

IN VIVO: OVX rats model



Lee et al. Lab Anim Res 2008



Cynanchum wilfordii ameliorates hypertension and endothelial dysfunction in rats fed with high fat/cholesterol diets.

4. Choi DH, Lee YJ, Kim JS, Kang DG, Lee HS.
Immunopharmacol Immunotoxicol. 2012 Feb;34(1):4-11. doi: 10.3109/08923973.2011.569889.
PMID: 22176675 [PubMed - indexed for MEDLINE]
[Related citations](#)

Improved endothelial dysfunction by Cynanchum wilfordii in apolipoprotein E(-/-) mice fed a high fat/cholesterol diet.

5. Choi DH, Lee YJ, Oh HC, Cui YL, Kim JS, Kang DG, Lee HS.
J Med Food. 2012 Feb;15(2):169-79. doi: 10.1089/jmf.2010.1222. Epub 2011 Nov 14.
PMID: 22082065 [PubMed - indexed for MEDLINE] Free PMC Article
[Related citations](#)

✓ The effect of herbal extract (EstroG-100) on pre-, peri- and post-menopausal women: a randomized double-blind, placebo-controlled study.

7. Chang A, Kwak BY, Yi K, Kim JS.
Phytother Res. 2012 Apr;26(4):510-6. doi: 10.1002/ptr.3597. Epub 2011 Sep 2.
PMID: 21887807 [PubMed - indexed for MEDLINE]

Wilfoside K1N isolated from Cynanchum wilfordii inhibits angiogenesis and tumor cell invasion.

11. Kim MS, Baek JH, Park JA, Hwang BY, Kim SE, Lee JJ, Kim KW.
Int J Oncol. 2005 Jun;26(6):1533-9.
PMID: 15870866 [PubMed - indexed for MEDLINE]
[Related citations](#)

The Effect of Herbal Extract (EstroG-100) on Pre-, Peri- and Post-Menopausal Women: A Randomized Double-blind, Placebo-controlled Study

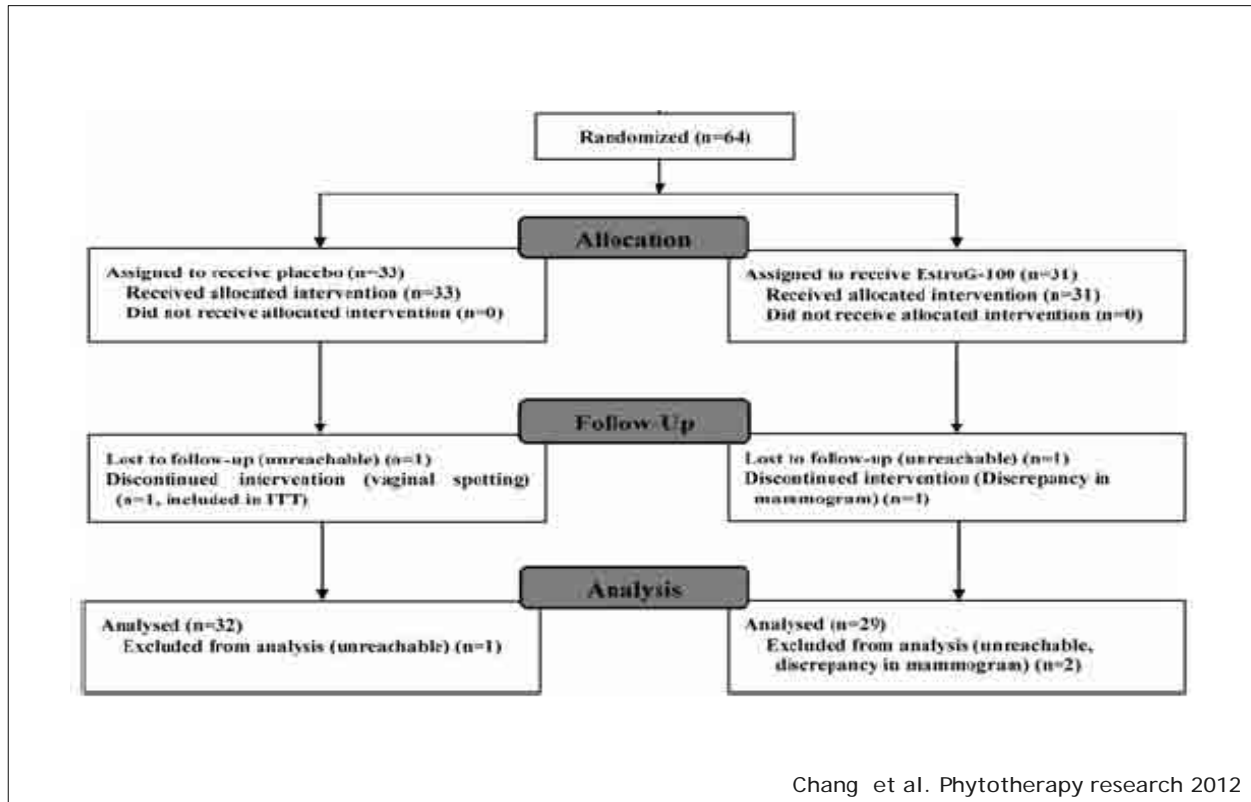
Albert Chang,^{1,2*} Bo-Yeon Kwak,³ Kwontaek Yi³ and Jae Soo Kim³

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³Herbal Hormone Research Institute, Naturalendo Tech Co., Ltd, 414 Daerung Post Tower 1, 212-8 Guro-dong, Guro-gu, Seoul 152-790, Korea

- Double blinded, placebo-controlled RCT
- **EstroG-100 powder:** extracts of Cynanchum wilfordii, Angelica gigas, Phlomis ubrosa
→ 257.05 mg (32.5:32.5:35)
- White and African American PM women
: EstroG-100 (n=31) and Placebo (n=33)
- Assessment: Kupperman score



Cynanchum wilfordii

Table 2. Mean change in scores of the each individual question of the Kupperman menopause index and vaginal dryness

	EstroG-100			Placebo		
	Week 0 (baseline)	Week 6	Week 12	Week 0 (baseline)	Week 6	Week 12
Hot flush or cold sweat (= vasomotor)	2.24 ± 0.69	1.03 ± 0.82 ^{abc}	0.79 ± 0.73 ^{abc}	2.22 ± 0.66	1.78 ± 0.75 ^c	2.06 ± 0.76
Numbness and tingling (= paresthesia)	1.31 ± 0.85	0.59 ± 0.78 ^{cd}	0.55 ± 0.74 ^{cd}	1.41 ± 0.91	1.13 ± 0.94 ^e	1.09 ± 0.96 ^c
Trouble sleeping (= insomnia)	2.28 ± 0.84	1.28 ± 0.96 ^{abcd}	0.97 ± 0.82 ^{abc}	2.03 ± 0.86	1.63 ± 1.01 ^e	1.63 ± 0.87 ^e
Nervousness	1.72 ± 0.88	0.76 ± 0.69 ^{abc}	0.66 ± 0.67 ^{abc}	1.56 ± 0.84	1.22 ± 0.83	1.34 ± 0.75
Feeling blue or depressed (= melancholia)	1.93 ± 0.88	1.03 ± 0.68 ^{abc}	0.83 ± 0.71 ^{abc}	1.59 ± 0.95	1.31 ± 0.93	1.31 ± 0.74
Dizzy spells (= vertigo)	0.97 ± 0.82	0.21 ± 0.49 ^{abc}	0.21 ± 0.41 ^{abc}	0.75 ± 0.72	0.72 ± 0.77	0.59 ± 0.80
Tired feelings (= fatigue)	2.21 ± 0.77	0.90 ± 0.77 ^{abc}	0.72 ± 0.70 ^{abc}	2.00 ± 0.88	1.69 ± 0.90 ^e	1.59 ± 0.80 ^e
Rheumatic pain (= arthralgia and myalgia)	1.59 ± 1.02	0.79 ± 0.94 ^{acd}	0.55 ± 0.78 ^{cd}	1.84 ± 0.95	1.63 ± 0.83	1.47 ± 0.88
Headaches	1.34 ± 1.04	0.69 ± 0.76 ^c	0.66 ± 0.77 ^c	1.53 ± 0.95	1.13 ± 0.91 ^e	0.84 ± 0.72 ^c
Pounding of the heart (= palpitation)	1.00 ± 0.96	0.48 ± 0.69 ^e	0.55 ± 0.63 ^e	1.31 ± 0.93	0.91 ± 0.82 ^c	0.75 ± 0.84 ^c
Sensation of crawling on the skin (= formication)	0.83 ± 0.85	0.14 ± 0.44 ^{cd}	0.28 ± 0.45 ^c	1.25 ± 1.05	0.88 ± 1.01 ^c	0.72 ± 0.96 ^c
Vaginal dryness	1.45 ± 1.02	0.72 ± 0.88 ^{abc}	0.59 ± 0.87 ^{cd}	1.75 ± 1.11	1.50 ± 1.11 ^e	1.28 ± 1.02 ^e

● **EstroG-100 use for 12 wks**

: significantly reduced KMI and vaginal dryness
 serum E2 - not increased by EstroG-100



Cynanchum wilfordii

Hypertension & endothelial dysfunction : animal study

- To test an effect of extracted Cynanchum W. (ECW) on endothelial dysfunction in rats fed with high fat/cholesterol diets
- ECW I / ECW II
: HFCD + 100 mg/kg/d
: HFCD + 200 mg/kg/d

Table 1. Effects of ECW on body weight, insulin, and blood glucose levels in rats fed with HFCD.

Group	Body weight (mg)	Insulin (mg/mL)	Glucose (mg/dl)
Control	507.9 ± 13.9	0.54 ± 0.08	95.2 ± 9.8
HFCD	550.9 ± 11.6*	1.36 ± 0.28*	97.2 ± 3.0
Fluvastatin	551.3 ± 11.5	0.64 ± 0.17 [#]	104.6 ± 2.8
ECW I	514.0 ± 8.9 [#]	0.33 ± 0.04 ^{##}	89.0 ± 4.5
ECW II	494.3 ± 13.2 ^{##}	0.52 ± 0.09 ^{##}	93.4 ± 4.2

Body weight expressed the mean of absolute weight of rats. Control, regular diet; HFCD, high fat/cholesterol diets; fluvastatin, HFCD + 3 mg/kg/day of fluvastatin; ECW-I, HFCD + 100 mg/kg/day of ECW; ECW-II, HFCD + 200 mg/kg/day of ECW. Values are expressed as mean ± SE (n=8); *p < 0.05, vs. control; [#]p < 0.05, ^{##}p < 0.05, vs. HFCD.

Choi et al., Immunopharmacol Immunotoxicol 2012

Cynanchum wilfordii

Table 2. Effects of ECW on lipid profiles in rats fed with HFCD.

Group	LDL (mg/dl)	T-Chol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)
Control	41.0 ± 2.3	87.3 ± 5.3	87.0 ± 7.6	19.8 ± 1.9
HFCD	120.8 ± 10.0**	132.0 ± 2.8*	60.3 ± 11.0	20.5 ± 0.9
Fluvastatin	107.1 ± 15.3	107.0 ± 8.6 [#]	33.8 ± 4.5 ^{##}	25.0 ± 3.7 [#]
ECW I	82.3 ± 10.4 [#]	128.3 ± 7.1	25.0 ± 2.2 ^{##}	25.5 ± 2.9 [#]
ECW II	93.2 ± 9.32 [#] ↓	120.3 ± 11.2	25.0 ± 2.1 ^{##} ↓	40.3 ± 4.8 ^{##}

LDL, low-density lipoprotein; T-Chol, total cholesterol; HDL, high-density lipoprotein. Values are expressed as mean ± SE (n=10); *p < 0.05, **p < 0.01, vs. control; [#]p < 0.05, ^{##}p < 0.01, vs. HFCD alone.

- ECW (extracted Cynanchum wilfordii) reduced LDL cholesterol and TG in HFCD-induced state
- ECW significantly recovered the diet-induced decrease in vasorelaxation to acetylcholine, high-dose ECW apparently increased vasorelaxation response to sodium nitroprusside in rats fed with HFCD

Choi et al., Immunopharmacol Immunotoxicol 2012

Wilfoside K1N isolated from *Cynanchum wilfordii* inhibits angiogenesis and tumor cell invasion

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Pages: 1533-1539

Abstract:

Wilfoside K1N is a polyoxypregnane glycoside isolated from *Cynanchum wilfordii* (Asclepiadaceae). Polyoxypregnane glycosides are associated with cellular immunity and anti-tumor activity, and increase the cytotoxicity of many anti-cancer drugs showing multidrug resistant activity on tumor cells. In the present study, we investigated the anti-angiogenic and anti-invasive activities of wilfoside K1N. In in vivo Matrigel plug assay using C57BL/6 mice, wilfoside K1N strongly inhibited basic fibroblast growth factor-induced microvessel formation. Exposure of wilfoside K1N to human umbilical vein endothelial cells (HUVEC) suppressed in vitro tube formation at a concentration not affecting cell viability. Moreover, wilfoside K1N significantly reduced the proliferation of HUVEC and calf pulmonary artery endothelial cells. In addition, wilfoside K1N decreased in vitro invasion of HT1080 human fibrosarcoma cells, and the inhibition might be through down-regulation of activity as well as quantity of matrix metalloproteinase-9. Therefore, our present study suggests that wilfoside K1N may have a potential to have strong anti-angiogenic and anti-invasive activities both in vitro and in vivo.

Kim et al. Int J oncology 2005

Cynanchum wilfordii

SAFETY: EstroG-100

- EstroG-100 did not increase uterus weight in OVX rats

Lee et al. Lab Anim Res 2008, Kim et al., Kor J Food 2008

- Biochemical and metabolic markers (liver enzyme, renal function, lipid profile): not changed
- No adverse reaction such as vaginal bleeding.

Chang et al., Phytotherapy res 2012



SUMMARY

- **Black cohosh**

- : Not consistent or weak evidence for effect on reducing vasomotor symptoms
- : Potential beneficial effect on cardiovascular system from a small number of *in vitro* studies
- : Generally considered to be safe, but long-term systemic or gynecological effects are needed to be more studied

SUMMARY

- **Cynanchum wilfordii**

- : One RCT described significant effects on menopausal symptoms without increase of systemic E2 level
- : Potential benefit on lipid profile or vascular endothelial function
- : Overall systemic or gynecologic safety, effects on bone health - evidence is lacking