The Effectiveness of Natural Products for Women’s Health

8th Annual NHRI Scientific Symposium
“Evidence-based natural solutions to symptoms of perimenopause and menopause”
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Objectives

• select research in botanical and nutrient treatments for common symptoms of menopause.
• Symptom specific non-Rx options
• Dosing guidelines/adverse events
Fundamental Goals of Intervention

• Symptom relief
  - with minimal impact on increasing risks of other diseases
• Disease Prevention and Treatment
• Opportunity for changes in life
• Education about health
Categories of Treatment Intervention

- Diet, Exercise, stress management
- Nutritional supplements
- Botanical medicines
- Compounded Bio-Identical HT
- Pharmaceutical Co. BHT
- Non bio-identical hormones
- Other medications
Perimenopause/Menopause Symptoms

- Decline in fertility
- Irregular uterine bleed
- Vasomotor symptoms
- Insomnia
- Urogenital changes
- Vulvovaginal changes
- Incontinence
- Urinary tract infection
Perimenopause and Menopause Symptoms

- Mood swings, depression, anxiety
- Concentration and memory
- Sexual Function
- Weight gain, headache, palpitations, joint pain,
- Skin, eyes, hair, teeth, oral health
- Fatigue
- Oddities: burning mouth, frozen shoulder, voice impairment
Black Cohosh
(Cimicifuga racemosa)
Clinical Research

Over 100 published scientific papers and presentations on the efficacy and safety of standardized black cohosh extract.
Black Cohosh
Breast Cancer Safety
Safety Studies

Design:
• *In vitro*, MCF-7 cell culture model to determine estrogen-agonist and -antagonist activity of commercially available herbal menopause preparations

Findings:
• Isopropanolic black cohosh extract had *no effect* on estrogen-sensitive cells *in vitro*.
• Results suggest safety for women with a history of breast cancer.

Safety Studies

Design:
- Six-week, *in vivo* investigation of isopropanolic black cohosh extract ability to stimulate estrogen-receptor positive cells in an animal model

Findings:
- No estrogen stimulating effects were found.
- Prolactin, follicle-stimulating hormone, and luteinizing hormone levels were unchanged.

Black Cohosh associated with breast cancer risk reduction

- Black cohosh use was associated with a 61 percent reduction in the risk of breast cancer with an odds ratio of 0.39, 95% CI: 0.22-0.70. The breast protective effect was similar for a specific black cohosh preparation, Remifemin, odds ratio 0.47, 95%, CI: 0.27-0.82.

*Int. J. Cancer 2007; 120:1523-1528.*
Black Cohosh
Liver Safety
New NIH Expert Panel
2008

- Analysis of case reports, adverse event reports, animal data, historical use, regulatory status.
- 30 non-duplicate reports
- All reports of liver damage were assigned possible causality, none were probably or certain causality. Clinical and animal data did not reveal unfavorable information.
- NEW: should be labeled to include a cautionary statement.
Black Cohosh Drug Interactions

In vitro study:
- Black cohosh extracts increased the cytotoxicity of doxorubicin and docetaxel
- Decreased the cytotoxicity of cisplatin
- No effect on radiation or analog cyclophosphamide

Black Cohosh Dose and Safety

- Dosages: 20-40 mg St. Extract bid
- Contraindications
  - None known
  - Avoid during pregnancy and lactation
- Cautions: liver disease
- Adverse Effects
  - Occasional gastrointestinal discomfort
  - Overdose may cause vertigo, headache, nausea, vomiting, impaired vision, impaired circulation
- Drug Interactions
  - Caution if hepatotoxic drugs
  - Avoid if Cisplatin
  - Ok with tamoxifen or raloxifene

Black Cohosh

• Summary:
  - the most studied plant for menopause sx
  - does not have estrogenic action
  - Does not contain phytoestrogens
  - Safe in breast cancer patients
  - Mechanism unclear
  - Good safety profile
Ginseng and Menopause

- 384 menopausal women randomized to receive either 2 caps of Ginsana (S.E.) or placebo for 16 weeks.
- Results: Only the PGWB (psychological general well-being index (P<0.01) and its scale of depression, well being and health showed statistically significant improvement.

Ginseng-VMI, CVD

- 72 postmenopausal women; red ginseng given was 3 gm per day
- Kupperman index for the red ginseng group significantly reduced from 18.93 to 13.32 compared with the placebo from 15.21 to 15.10. The Menopause Rating Scale score dropped significantly from 12.45 to 8.32 in the ginseng group compared with 10.23 to 9.26 in the placebo group. The hot flash score also reduced significantly.
- Red ginseng also elicited a significant decrease in total cholesterol from 138.11 to 108.82, drop in LDL; no changes in HDL cholesterol or C-reactive protein.
- Carotid intima-media thickness was significantly reduced in the red ginseng group.

Menopause 2012;19(4):461-466
Ginseng Safety Issues

• For both species, occasional cases of insomnia or agitation have been reported. This is more likely to occur if consumed with caffeine. Persons with hypertension should use ginseng cautiously.

• Asian ginseng is contraindicated during pregnancy or lactation. It may also cause some women to experience menstrual abnormalities, including breast tenderness.

• For both species, caution should be observed with diabetic patients taking oral hypoglycemics or insulin. There are some reports that Asian ginseng may interfere with the actions of warfarin.
Ginseng

• Drug interactions
  - Probable and mild
    increases effect of alcohol, caffeine
  - Probable and moderate
    hypoglycemic drugs = theoretical enhancement of blood sugar lowering

  - Unlikely
    might decrease platelet aggregation = Warfarin
Hops and Menopause

RCT, 67 menopausal women were given either a placebo or a 100 mcg or 250 mcg standardized hops extract for 12 weeks. At 6 weeks, the 100 mcg dose was significantly superior to placebo, but not after 12 weeks. There was a more rapid decrease in menopause symptoms scored for both doses of hop extract, especially the hot flush score.

Hops and Menopausal Symptoms

- 36 menopausal women; RCT; placebo or hop extract x 8 weeks; switched to the opposite group for another 8 weeks.
- After 8 weeks: both groups= significant and actually higher average reductions in the placebo group.
- After 16 weeks: only hops extract in the second 8 weeks had a reduction in all outcome measures whereas the placebo group in the second 8 weeks had an increase for all outcome measures.
- Although the overall treatment efficacy of the hops treatment compared with the placebo did not show a significant effect, the time specific uses did indicate significant reductions in the KI and the VAS for the hops group, and a marginal reduction in symptoms for the MRS after 16 weeks.

Kava and Menopause

RCTs

• Kava extract vs placebo x 12 wks.
  Significant improvement in KI, ASI and daily symptom diary w/kava.
  
    Warnecke. Zeitschrift Phytotherapie 1990;11

• Kava extract vs placebo x 8 wks.
  Significant improvement in KI and HAMA at wks 1,4,8. DSI reduced
  with kava at wks 4 and 8.
  
    Warnecke. Fortschr Med 1991;4

• Anxiety in menopause: Kava with and wo/ HRT
  100 mg Kava or placebo x 6 months. Women with HRT and kava
  showed the greatest reduction in HAMA.
  
    De Leo. Minerva Ginecol 2000;52
Kava and anxiety in Perimenopausal Women

- Calcium 1 gm plus Kava 100 mg vs Calcium 1 gm plus Kava 200 mg vs Calcium
- Rapid decline within 1 month - anxiety
- Slower and less significant-depression and climacteric symptoms

Cagnacci et al. Maturitas 2003;44: 103-109
Kava Extract
Safety Update

• Side effects: GI upset, skin rash, and sebaceous reaction following long-term ingestion
  Large amounts of traditional preparations have resulted in drowsiness and impaired reaction time.
• Kava should not be used with anxiolytics, antidepressants, or neuroleptics.
• Kava may potentiate the CNS effects of alcohol.
• Recommended dose:
  45 to 7- mg kavalactones tid
  up to 210 kavalactones per day
Kava Extract
Hepatotoxicity

- Reports from late 2001 have indicated that kava may be associated with liver damage.
- Until additional information clarifies the extent of the risk involved, it is strongly recommended that all individuals consult their physician before taking kava. In addition, based on the available information, it seems that people with liver disease and those taking medications that have the potential to damage the liver should not take kava.

_BMJ_ 2001;322:139.
Kudzu
Pueraria mirifica

• RDBPCT
• 20, 30 or 50 mg of Pueraria mirifica in capsules or placebo, daily, for 24 weeks.
• The average vaginal dryness symptom in the treatment group decreased after 12 weeks and the maturation index increased after 24 weeks.

Kudzu

• N=52
• 25 mg dose vs 50 mg dose
• Both dosages were similarly effective
• A statistically significant decrease in climacteric scores was observed in both groups

Maca-GO and Postmenopausal women

2 months:
- Non significant decrease in FSH and increase in E2
- Significant increase in LH and increase in Progesterone
- No change in estradiol
Symptom relief: nervous, reduced day VMI, increased libido

8 months:
- Decreased FSH
  - Increase LH
  - Increased Progesterone
  - Increased Estradiol

Maca-GO and Perimenopause

MACA-GO results:
- reduction in body weight, blood pressure
- increased in HDL, iron
- 74%-87% of women had a reduction in
- reduced VMI, insomnia, nervousness, depression and heart palpitations

dose: 1 gm bid

Maca: effects on anxiety, depression, sexual dysfunction

- RCT: 14 postmenopausal women; 3.5 gm of powdered Maca (Lepidium meyenii) vs placebo for 6 weeks.
- The Greene Climacteric Scale revealed a significant reduction in psychological symptoms including anxiety, depression and sexual dysfunction after Maca consumption compared with baseline and placebo.

Lepidium (Maca) and sexual dysfunction

• Systematic review: clinical evidence for or against the efficacy of Maca for sexual dysfunction.
• Two of these trials suggested a positive effect of Maca on sexual dysfunction or libido in menopausal women or adult men.
• One other RCT did not show effect of Maca in cyclists.
• Fourth study: assessed the effects of Maca in men with erectile dysfunction and did show significant effects.
• While the evidence is limited, there does appear to be some effectiveness of maca in improving sexual function.

RED CLOVER

- Red Clover isoflavone extract
- 40 mg vs. 160 mg isoflavones vs. placebo
- 37 postmenopausal women; 12 weeks; clinical trial

EVALUATION:
- Vasomotor symptoms
- FSH, SHBG, vaginal pH, MI, HDL
- Urinary isoflavones

RESULTS:
- No difference in flushing
- Small increase HDL

Knight, etal. Climacteric 1999;2:79-84
RED CLOVER

- Red Clover isoflavone extract
- 40 mg vs. placebo
- 51 postmenopausal women
- 12 weeks

EVALUATION:
- Symptom diary
- FSH, E2, SHBG, LFTs, Urinary isoflavone
- MI, transvaginal US

RESULTS:
- No significant difference in hot flushing
- (small at 4 and 8 weeks)

RED CLOVER

• N=30; Postmenopausal
• 40 mg daily red clover isoflavone extract for 16 weeks

EVALUATION:
  – Symptom diary
  – FSH

RESULTS:
  – 50% reduction in frequency vs. 20% placebo
  – Also 47% reduction in severity

Jeri A. Female Patient 2002;27:35-37
RED CLOVER

• Postmenopausal women n=23
• 40 mg Red Clover extract for 2 months – 3 months

EVALUATION:
  – Menopause symptom record
  – FSH, SHBG, Lipids, glucose
  – US, estradiol, CMP, CBC

RESULTS:
• 56% reduction in hot flush frequency
• 43% reduction in hot flush severity
• 52 % reduction in severity of night sweats
• .4 mm increase in endometrial thickness
• No significant changes in metabolic markers

Nachtigall, et al. 9th annual world congress on menopause
1999;17-21
Red Clover and Hot Flashes

- 30 postmenopausal women
- 80 mg red clover isoflavones or placebo daily for 12 weeks.
- 44% decrease in hot flashes in the red clover group.
- Green Climacteric Scale: 13% decrease with red clover and no change in placebo

Red Clover and Hot Flashes (ICE Study)

• Red clover isoflavones no more effective than placebo in reducing incidence of hot flashes

• Promensil 82 mg/day isoflavones vs Rimostil 57 mg/day vs placebo

Tice et al, JAMA 2003;290
Red Clover and hot flashes

- RDBCT
- Black cohosh vs red clover vs placebo vs CEE/MPA
- Reductions in number of vasomotor symptoms =
  - black cohosh 24%
  - Red clover 57%
  - Placebo 63%
  - CEE/MPA 94%

Red Clover

- 109 postmenopausal women; 2 capsules daily of a red clover extract totaling 80 mg of isoflavones, or a placebo, for 3 months.
- Hospital Anxiety and Depression Scale (HADS) and the Zung’s Self Rating Depression Scale (SDS).

- After taking the red clover extract, women had a significant in both of the rating scales, with a 75% reduction for anxiety and 78.3% reduction for depression using the HADS tool, and an 80.6% reduction in the total SDS score. After taking the placebo pills, the HADS and SDS scores only reduced by an average of 21.7%.

Maturitas 2010;65:258-261
Pycnogenol

- In a double-blind study, Taiwanese peri-menopausal women, aged 45-55, were given either placebo or 100 mg of Pycnogenol twice daily for 6 months.
- 155 women received the Pycnogenol and seventy-five the placebo. The Women’s Health Questionnaire with 36-items was used to evaluate the climacteric symptoms at baseline, and at 1,3 and 6 months.
- BP decreased similarly in both groups. HDL increased and LDL decreased significantly from baseline with Pycnogenol, but no significant differences were seen in HDL between the two groups. However, LDL was more significantly reduced in the Pycnogenol group.
- Perimenopause symptoms of depression, vasomotor symptoms, memory, anxiety, sexual function, sleep all improved significantly (P< 0.001) with Pycnogenol as soon as one month after starting the treatment, in both severity and frequency. Most symptoms also improved with placebo, but not significantly.

Acta Obstetricia et Gynecologica. 2007;86:978-985
Sibiric Rhubarb (Rheum rhaponticum)

- RCT; 109 perimenopausal women with climacteric complaints.
- Tx: st. ext. ERr 731, from the roots of Rheum rhaponticum, also known as Sibiric Rhubarb. One tablet (250 mg), containing 4 mg of dry extract was given to women (n=54) or placebo given to the other group (n=55) for 12 weeks.
- Menopause Rating Scale II (MRS II). After 12 weeks, the MRS II total score and each MRS II symptom significantly decreased in the rhubarb extract group compared to the placebo group. (P < 0.0001). The overall menopause QOL score was also significantly better in the treatment group compared with placebo. No adverse events were observed.

Sibiric Rhubarb (Rheum rhaponticum)

- A standardized extract, ERr 731
- Observational study: three hundred sixty-three menopausal women with menopausal symptoms were given 1 tablet of ERr 731, containing 4 mg, for 6 months.
- The Menopause Rating Scale; 252 women completed the study.
- Significant decrease of the total MRS score from an average of 14.7 points at baseline to 6.9 points at the end of the six months (P < .0001). This was a decrease of 7.8 points.
- Most pronounced improvement, in first 3 months of treatment/most symptomatic at baseline = > 18 points.
- Hot flashes, irritability, sleep problems, depressive mood, and physical/mental exhaustion.

Sibiric Rhubarb (Rheum rhaponticum)

- RCT; n=109 perimenopausal women
- ERr 731; 1 tablet, 4 mg dry extract x 12 wks
- HAMA: from 27.5 points to 9.4 points
- MRS: anxiety decreased 2.2 points in tx group vs 0.3 in placebo
- Wellbeing: improved in tx group but not placebo
- WHQ: 22 point increase in tx group and decreased 7.6 points in placebo

Kaszkin-Bettag M Menopause 2007;14(2):270-283
SJW in Menopause

• One non placebo controlled, drug monitoring study was conducted in women with menopause symptoms and found that 900 mg of St. Johns wort for 12 weeks significantly improved psychological and psychosomatic symptoms as well as a feeling of sexual well-being.

Black Cohosh and SJW

Average Menopause Rating Scale score decreased 50% in the treatment group/19.6% in the placebo group. The Hamilton Depression Rating Scale score decreased 41.8% in the treatment group/12.7% in the placebo group. In both the general menopause rating scale and in the depression scale, the St. John’s wort + black cohosh group was significantly superior to the placebo group.

Black Cohosh/St John’s wort

- Prospective, controlled open-label observational study
- N=6141 women at 1287 outpatient gyn clinics in Germany
- Dose: Remifemin 20 mg tablet bid
  - Remifemin plus: 3.75 mg iCR extract and 70 mg SJW (from 245 mg to 350 mg)
Results: Combination product > black cohosh only for mood symptoms

Briese V, et al. Maturitas 2007;57:405-414
SJW/Black cohosh

- Peri or postmenopausal Korean women
- Mean Kupperman index scores at 4 and 12 weeks were significantly lower in the treatment group ($P \leq 0.002$).
- Average decrease in the Kupperman Index was 20 points in the treatment group and only 8.2 points in the placebo group.
- Vaginal dryness and low libido did not improve
- Average hot flash scores were significantly lower in the black cohosh/St. Johns wort group.

Hypericum P. and Menopause

- 50 women received 20 drops three times daily of St. John’s wort extract (Hyperin) that contained hypericin 0.2 mg/mL and 50 women received a placebo of distilled water. The study duration was two months.

- In women taking St. John’s wort, the frequency began to decline during the 1st and 2nd months, but showed more improvement during the 2nd month. Women who used St. John’s wort showed more improvement in hot flash frequency than placebo. The decline in duration of hot flashes was statistically significant at week 8 and the decline was much more evident in the St. John’s wort group. The severity of hot flashes was relieved in the St. John’s wort group during the 2 months of treatment and was more significant in the second month. Women in the placebo group did not show any significant decrease in severity of hot flashes during the 1st month, but they did have some improvement during the 2nd month, but not as great as those women in the St. John’s wort group.

Vitex and SJW

- Vitex was a component of the multibotanical formula in the HALT study, and in the Cancelleiri study
- Recent menopause related study: Vitex with SJW
- RCT 16 week trial of late perimenopausal or postmenopausal women who reported hot flushes and other menopause symptoms, the herbal combination showed no significant difference from that of placebo.

Multi-botanical Formula

- Burdock root, Wild yam
- Motherwort, Dong quai, Licorice root

100% had reduction in symptoms
(67% showed reduction with placebo)
71% had reduction in total number of sx.
(17% showed reduction with placebo)

Hudson T, et al. JNM;1997;7(1):73-77
3 Combination Korean Herbs

- Cynanchum wilfordii + Phlomis umbrosa + Angelica gigas
- RDBPCT; n=64; 12 weeks
- KMI significantly reduced

Phytotherapy Research 2011; Wiley online library
Valerian

- Postmenopausal women - aged 50 to 60 years
- 530 mg of concentrated valerian extract twice per day vs placebo twice per day, for 4 weeks.
- Overall, 30% of the women taking valerian and 4% taking placebo reported an improvement in their sleep quality

Omega-3 f.a. and Hot Flashes

- ethyl-eicosapentaenoic acid (E-EPA) omega-3 fatty acid or placebo for 8 weeks. The E-EPA supplementation was one capsule three times per day (350 mg of EPA/50 mg of DHA). baseline level of hot flashes = average of 2.8 per day.
- After 8 weeks, the hot flash frequency decreased in the E-EPA group by a mean of 1.58 per day and only 0.50 per day in the placebo group.
- Significant reduction of 55% in hot flash frequency in the E-EPA group vs 25% decrease in the placebo group.
- Greater responder rate in the E-EPA group compared with the placebo group of 58.5% vs 34.4%.
- No differences in hot flash severity and no differences were noted in the quality of life scores between the two groups.

EFAs- Hot flashes (and depression)

• 20 perimenopausal/menopausal women
• 2 gm/day (1 gm= 840 mg EE and 375 mg DHA for 8 weeks
• Number of hot flashes per day improved significantly from baseline-day and night
• Significant decrease in MADRS scores- response rate – 70%; >50% decrease and remission rate of 45%

Freeman et al. Menopause 2011;18(3):279
Menopause Symptoms

*Integrative Clinical Solutions*

Tori Hudson, N.D.
Clinical Professor, NCNM/Bastyr/SCNM
Medical Director, A Woman’s Time
Program Director, IWHIM
Director Education/Research, Vitanica
Hot Flashes

• Mild to Moderate
  - Black cohosh extract 40-80 mg bid
  - Combination product ((Dong quai, licorice, burdock, motherwort, wild yam) 2 tid
  - Maca-GO Extract  2 bid
  - Pycnogenol  100 mg bid
  - Sibiric Rhubarb (ERr731)  250 mg/day

• Severe
  May need Hormone Therapy
  or, lower dose HT + botanicals/neutraceuticals
Anxiety + Hot flashes

• Mild to Moderate
  - Kava, 70 mg kavalactones tid
  - Maca- st. extract 2 1,000 mg bid+
    Kava 70 mg kavalactones tid
  - Black Cohosh 40 mg st extract bid +
    kava 70 mg kavalactones tid

consider :Black cohosh or Maca or combo
product + GABA, L-theanine, passion flower)
Anxiety

• GABA
• L-theanine
• Inositol
• Hops, skullcap, valerian, lavender, kava
Lavender Oil extract in patients with Generalized Anxiety Disorder (GAD)

- Indication: Generalized Anxiety Disorder
- Design: Multi-center, randomized, double-blind clinical trial in comparison to lorazepam
- N = 77, 6 weeks treatment; 80 mg daily
- Results
  - Therapeutic equivalence of WS® 1265 and lorazepam
  - Anxiolytic efficacy (HAMA reduction by 11 points)
  - Improvement in quality of life (SF-36)

WS® 1265 improves anxiety

Mean change in HAM-A total score from baseline during the active treatment period
Lavender Oil improves anxiety and quality of life

- Randomized, double-blind, placebo-controlled, multi-center study.
- N=221, 10 weeks treatment
- Results
  - Anxiolytic efficacy (HAM-A): clear effects after 2 weeks of treatment
  - Improvement of sleep disturbances: clear effects after 4 to 6 weeks
  - Indication: Anxiety disorder
  - Improvement in Quality of life

Anxiety and Palpitations

**Anxiety**
- *Kava*
- Lemon balm
- Valerian
- Skullcap
- Hops
- *Lavender*

**Palpitations**
- Hawthorne
- Motherwort
Depression

• Mild - Moderate
  1. Black cohosh 40 mg bid
     +++
     SJW .3% hypericin 300 mg bid-tid
  2. Maca-GO Extract 1,000 mg bid
     +++
     SJW .3% hypericin 300 mg bid-tid
Depression

• Moderate Hormone Therapy
  
  +++
  
  SJW 300 mg .3% hypericin tid
  SAMe  400 mg/day
  L-tyrosine, phenylalanine, tryptophan
Perimenopause/PMS

- Hot flashes/mood changes + cyclic classic PMS symptoms
- Black cohosh/SJW
  - +++
- PMS herbal formula (B6, Ca, Vitex, SJW, Mg, Ginkgo, GLA)
Insomnia

- Mild-Moderate
  1 of the following:
  Women’s Phase II
  Black cohosh
  Maca-GO
  +++
  Valerian 2 caps before bed
  Consider L-tryptophan 1,000 mg/1500 mg h.s.
    5 HTP 200 mg h.s.
    Melatonin 1-10 mg h.s.
Melatonin

• Dosing
  likely safe= 5 mg/day
  possibly safe= up to 40 mg/day for short periods
  likely unsafe= pregnancy preparation, pregnancy

• Adult dosing
  Delayed sleep syndrome: 5 mg, 5 hours h.s.
  Insomnia elderly: 30-120 minutes h.s. 0.1mg to 0.3 mg
  insomnia of unknown origin: 1-5 mg h.s.
  jet lag: day of travel close to target bedtime at destination and then every 24 hours for several days; 0.1 mg-5 mg
L-Tryptophan: improves sleep latency; obstructive sleep apnea; PMDD- decreases mood swings, tension, irritability; depression; SAD; smoking cessation

500 mg- 2,500mg before bed; take w/CHO

5 HTP: decreases time required to fall asleep and decreases number of awakenings; increases REM sleep and deep sleep of other stages

100-300 mg per day; take w/CHO

Wyatt; Biology of Psychiatry 1972
Guilleminault. Elcetoencephalogr Clin Neurophysiol 1973
5-hydroxytryptophan (5-HTP)

- Decreases the time required to get to sleep
- Decreases night time awakenings

Wyatt; Biology of Psychiatry 1972
Guilleminalut. Elcectoencephalogr Clin Neurophysiol 1973

- Increases REM sleep and deep sleep of other stages
Summary
Botanica/Neutraceutical Options

• Benefits
  - Especially effective for mild-moderate symptoms
  - Can be used in combination with HT - able to then use lower doses of HT
  - Good safety profile; low adverse events

• Risks
  short list of known drug interactions
  short history of concomitant OTC and Rx use
Dr. Tori Hudson Resources

• Women’s Encyclopedia of Natural Medicine, 2008, second edition
• www.drtorihudson.com
• www.awomanstime.com
• www.instituteofwomenshealth.com