

Women's Health Research Update NFH/NCNM Lunch-Learn May 2016

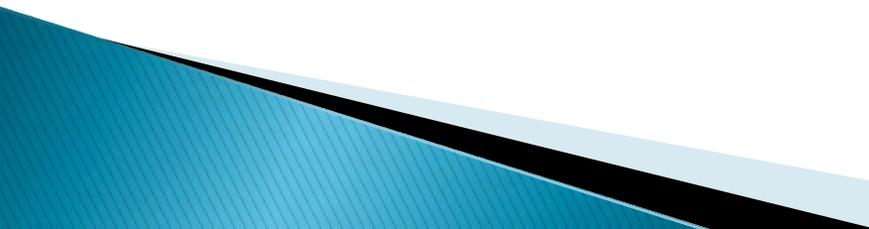
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Nutritional Fundamentals for Health



...Bridging the gap between evidence-based medicine and nutraceuticals

Disclosures

- ▶ Co-Owner; Director Research and Education for Vitonica
 - ▶ Scientific Advisory Boards
 - Nordic Naturals
 - Gaia Professional Solutions
 - Integrative Therapeutics
 - Natural Health International
 - Nutritional Fundamentals for Health
 - Pharmaca Integrative Pharmacies
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Ginger

- ▶ Acute migraines
- ▶ Chronic migraines
- ▶ Acute dysmenorrhea
- ▶ Menorrhagia
- ▶ Nausea of pregnancy
- ▶ General nausea
- ▶ Nausea of chemo



Ginger for Common Migraine

- ▶ DBRCT; compared ginger to sumatriptan, in the treatment of common migraine. One ginger capsule of 250 mg upon onset of headache or 50 mg of sumatriptan. The overall study duration was one month.
- ▶ Both sumatriptan and ginger powder decreased the mean severity of common migraine attacks within 2 hours of use. Both the sumatriptan and ginger significantly provided pain relief and no significant differences were achieved.
- ▶ *Maghbooli M, Golipour F, Esfandabadi A, Yousefi M. Comparison between the efficacy of ginger and sumatriptan in the ablative treatment of the common migraine. Phytotherapy Res 2014;28:412-415.*

Ginger and Dysmenorrhea

- ▶ N=150 reproductive aged women with primary dysmenorrhea were divided into three groups, in a double-blind clinical trial. Group 1) ginger rhizome capsules, 250 mg four times a day for three days starting day one of their menses. Group 2) 250 mg mefenamic acid capsules, four times daily days one through three. Group 3) 400 mg ibuprofen capsules four times daily again, days one through three of the menses.
- ▶ Severity of dysmenorrhea decreased in all groups and no differences were found between the groups in pain severity, pain relief or satisfaction.
- ▶ More women in the ginger group became completely pain free, vs the mefenamic acid and ibuprofen groups. The rate of satisfaction from the treatments was 20/50 women in the mefenamic acid group, 22/50 women in the ibuprofen group and 21/50 women in the ginger group.

J Alternative and Complementary Med 2009; 15(2):129–

Ginger and Dysmenorrhea

- 105 Iranian women; moderate-to-severe primary dysmenorrhea
- Ginger capsules were given in one of two methods: 1) 500 mg ginger capsules or placebo 3x/daily starting 2 days before the beginning of menses and continued through day 3 of menses. 2) 500 mg ginger capsules or placebo 3x/daily on days 1,2 and 3 of menses.
- The severity of pain was significantly reduced in the ginger group compared to the placebo group for both dosing methods with better results in the first dosing method.
- A 1.4 to 2.0 point reduction in severity was seen with ginger and with the first dosing method, ginger significantly reduced the duration of pain compared with placebo. There was a 4.6 ± 10.6 hour decrease in the duration of pain versus a 2.3 ± 18.2 hour increase in duration in the placebo group. The second ginger dosing method was not significant in pain duration between ginger and placebo.

BMC Complement Altern Med. July 10, 2012;12(1):92

Ginger: Dysmenorrhea

2015 Systematic Review–Meta–analysis

- ▶ 7 RCT: a significant effect of ginger in reducing the pain visual analog scale (PVAS) in women having primary dysmenorrhea. In total, these randomized controlled trials showed significant efficacy for primary dysmenorrhea at doses of 750–2000 mg per day during the first 3–4 days of the menstrual cycle.
- ▶ Pain Medicine 2015;16:2243–2255.

Ginger: Acute Menorrhagia

- ▶ RCT: Ginger capsules 250 mg of dried ginger; 1 capsule tid or placebo starting from the day before menstrual bleeding until the third day of the menstrual period for a total of four consecutive days for the three months of menstrual cycles.

- ▶ Results:

Ginger group decreased in mean hemorrhage by 46.6% and the placebo group by 2.1 %.

Three girls had adverse events in each group:
ginger= 1 heart burn, 1 abdominal pain, 1 diarrhea;
placebo= 1 abdominal pain, 2 flatulence.

Phytotherapy Research 2015;29:114-

N-acetyl cysteine

- ▶ PCOS (anovulation, fertility, hyperandrogenism, insulin resistance)
- ▶ Infertility (anovulation)
- ▶ Breast density
- ▶ COPD
- ▶ BV– intravaginal; consider oral

N-Acetyl-cysteine improves insulin sensitivity in PCOS

- ▶ n=6 lean and 31 obese women ages 19–33 vs control group
- ▶ NAC 1.8 gm/day; 3 gm/day if obese
- ▶ Results: Significant reduction in testosterone, FAI, insulin; increased peripheral insulin sensitivity; hepatic insulin extraction unchanged.

Fertility and Sterility 2002;77(6):1128–

N-Acetylcysteine vs Metformin

- ▶ N=100 with PCOS
- ▶ mean age of 23 years
- ▶ BMI of 23.5; hirsutism and irregular menses
- ▶ TX: metformin 500 mg TID or NAC 600 mg tid for 24 weeks
- ▶ Results:

Both groups : a small decrease in BMI, hirsutism score, IR and a decrease in serum testosterone.

Percentage with regular menses increased in the metformin group from 17% to 47% ;NAC group from 29% to 53%.

NAC significantly decreased both TC and LDL
metformin significantly decreased only TC

Eur J ObGYN Reprod Biol 2011; 159:127-

NAC vs Metformin 2015

- ▶ A) NAC 600 mg tid B) metformin 500 mg tid for 24 weeks
- ▶ FBS, insulin, lipid profile and HOMA (Homeostasis model assessment) index were measured and were compared.
- ▶ Results: After treatment, NAC improved BMI, AUB, FBS and fasting insulin and lipid profile more than metformin.

N-acetyl Cysteine

Endometriosis

- ▶ 92 women participated in the study with 47 women receiving NAC, 600 mg three times daily, for three consecutive days a week over three months. 45 women received no treatment.
- ▶ NAC treated patient cyst mean diameter slightly reduced (-1.5 mm) vs. a significant increase (+6.6 mm) in untreated patients. NAC treatment: more cysts reduced and fewer cysts increased in size.
- ▶ 24 NAC patients (vs. 1 patient within control) cancelled scheduled laparoscopy due to cyst decrease or disappearance and/or relevant pain reduction (21 cases).
- ▶ The NAC treatment group resulted in 8 pregnancies with only 6 pregnancies resulting in the controls.
- ▶ The study concluded that NAC represents a “simple effective treatment for endometriosis, without side effects, and a suitable approach for women desiring pregnancy”.

Comparison of myo-inositol and D-chiro-inositol in PCOS women

- ▶ N=50; two groups; 25 =4 gm of myo-inositol plus 400 mcg of folic acid daily vs 25 =1 gm of D-chiro-inositol plus 400 mcg/folic acid per day x6mo
 - ▶ Both the inositol isofroms are effective in improving the ovarian function and metabolism of women with PCOS
 - ▶ Myo-inositol showed the greater impact on the metabolic profile
 - ▶ D-chiro-inositol affected more positively the hyperandrogenism measurements.
 - ▶ Regularization of menstrual cycles = not statistically significant.
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- ▶ *Pizzo A, Lagana A, Barbara O. Comparison between effects of myo-inositol and D-chiro-inositol on ovarian function and metabolic factors in women with PCOS. Gynecological Endocrinology 2014; 30(3): 205-208*

PCOS

General Sample Treatment Plan

- High protein/low carb diet for 60 days, then modified Mediterranean diet; Flax seeds, ground- 1-2 tbsp/day
- Soy powder 30 gm protein/30-90 mg isoflavones
- Frequent aerobic exercise 5x/week; strength train twice/week
- Myoinositol 4 gm/day vs d-chiro-inositol 1 gm/day
- NAC 500-600 mg tid or Metformin 1-2 gm/day

Plus one or more of the following:

- Fish oils 4gm/day (ratio 1.49:1 EPA/DHA)
- Fenugreek 25 gm/day
- Chromium 1,000 mcg/day
- Vitamin D 5,000 iu/day
- Calcium 1200 mg/day
- Nettles root 400 mg/day
- Green tea extract 1-2 caps per day
- Spearmint tea 1 cup bid
- Maitake 3 caps tid
- Consider PGX powder or granules
- Black cohosh 40 mg/day, days 2, for 10 days
- Cyclic OMP 100-200 mg bid x 12 days/month

PCOS Specific Sample Tx Plan

▶ Infertility

- IR diet; therapeutic foods
- 6 hours/week aerobic exercise;
strength train biw
- NAC 600 mg tid or Metformin 500 mg
1 – 3 /day or
- Black cohosh 40mg/day; day 2 x 10
days
- Maitake Extract 3 caps tid

PCOS

Sample Tx Plan

▶ Hirsutism

- IR diet; therapeutic foods; aerobic exercise 6 hours/week; strength train biw
- licorice; (7.6% glycyrrhizic acid= 0.25 gm glycyrrhizic acid per day) 3.5 gm/day for 2 months
- d-chiro inositol 1 gm/day
- Spearmint tea 1 cup bid
- Saw palmetto
85-95% sterols 160 mg bid
- Fish oil 4 gm/day
- NAC 600 mg tid

Endometriosis: Possible Pathogenesis

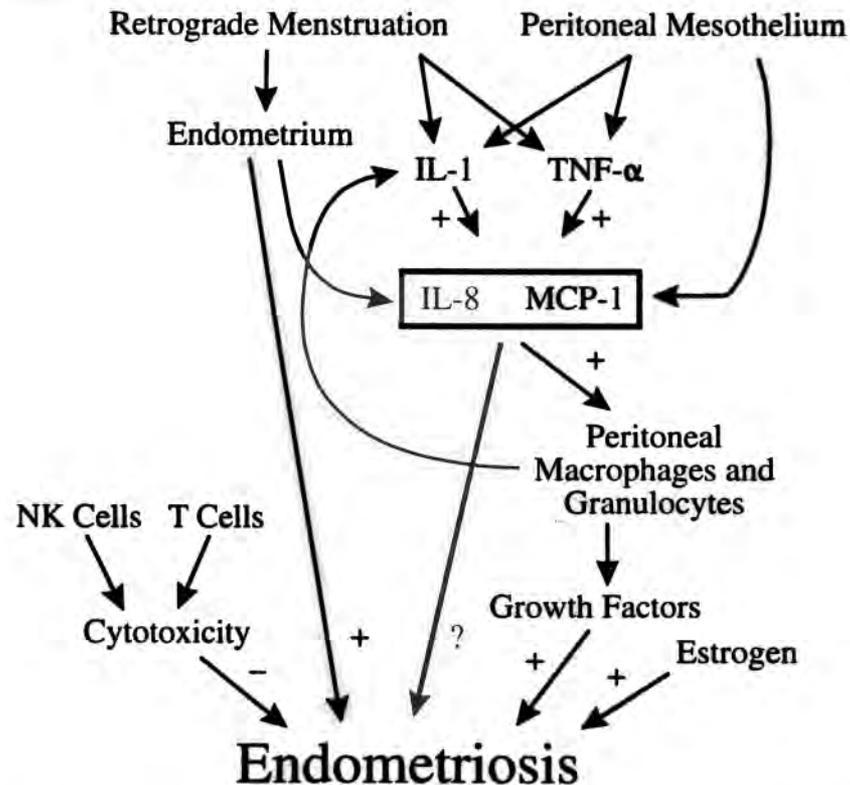


Figure 1. Factors involved in the pathogenesis of endometriosis.

ALTERNATIVE MANAGEMENT

▶ General considerations

- Immune modulation
 - Reduce inflammation
 - Decrease influence of estrogen
 - Enhance Liver function; detoxification
 - Pain relief; symptom relief
 - Psychosocial influences and consequences
 - Prevent progression of disease
 - Decrease oxidative damage
 - Inhibition of growth factors
 - Anti-angiogenesis agents
- 

Endometriosis

Chronic Sample Tx Plan

- Diet:
 - Garlic, onions, curries, Cold water fish, fruits, veggies, nuts/seeds
 - Decrease saturated fats, sugar, salt, caffeine
- EPA 1,080 mg/DHA 720 mg
- Anti-oxidant combinations= robust dosing
- NAC 600 mg tid
- Melatonin 10 mg h.s./day
- Pycnogenol 30 mg bid
- Turmeric 1,000 mg bid
- OMP 200 mg daily, days 15-26
- Consider/ MPA cyclic; OCPs/Nuvaring/contraceptive patch

Acute Dysmenorrhea

Sample Treatment Plan

▶ Acute Pain:

- Niacin 100 mg every 2–3 hours
- B 6 100 mg + Mg 100 mg every 2 hours during pain (x 6 mo.)
- Tincture
 - Valerian 2 oz + Crampbark 2 oz + wild yam 2 oz + Ginger 2 oz
 - 1 tsp. every 3 hours
- Ginger caps 250 mg qid
- (Combination product 2 caps every 2–4 hours)
- Relaxation techniques; Heat

Trametes versicolor





Trametes and GYN cancers

- ▶ Pts with stage III uterine and cervical cancers given PSK 3-6 g/d with RT showed increased survival and increased sensitivity to RT
- ▶ Cervical cancer pts receiving RT and PSK showed increase of clearance of cancer of 36% v. 11% in controls
- ▶ Regression of LSIL lesions with 3 g/d was 72.5% v. 47.5% in controls.
- ▶ Clearance of high-risk HSV strains was 91.5 % v. 8.5% in controls
 - Powell, M. *Medicinal mushrooms: a clinical guide*. East Sussex Mycology Press.2

Coriolus versicolor– HPV

- ▶ Study #1 (2009–2010)
- ▶ Population: 100 women aged 16–50, infected with low and high–risk HPV subtypes
- ▶ Intervention: Six months of Coriolus 500mg daily
- ▶ Comparison: Surgical intervention + six months of Coriolus 2 (500 mg) tablets TID.
- ▶ Outcome: Cervical cytology exams and HPV subtyping determined status. Colposcopy was performed in 53 pts and 51% of them were subjected to biopsy. The results showed that 64 (88%) out of 73 patients on Coriolus alone and 25 (93%) out of 27 patients on combined treatment were HPV–negative after 6 months.
- ▶ Statistics: None mentioned.
- ▶ Notes: 11 out of 100 of combined HPV subtypes were still infected at the end of the trial. Of the high–risk subtypes still present at the end of the trial, HPV 16 was most resistant.

Clinical Journal of Mycology. 2012;3:2–3.

Coriolus versicolor– HPV

- ▶ Study #2 (2010–2012)
- ▶ Population: 200 participants, infected with low and high–risk HPV subtypes
- ▶ Intervention: Six months of Coriolus 2 (500 mg) tablets TID.
- ▶ Comparison: None. Pre and post prospective cohort.
- ▶ Outcome: 95% of the patients reverted to HPV–negative status. HPV subtype 16 was again most resistant. HPV–positive patients of combined HPV subtypes without histological changes reverted to HPV–negative status in 3 months. Coriolus was taken by the women's partners in about 70% of the couples. 90% of these couples reverted to HPV–negative status after 6 months

- ▶ Conclusions made by authors: In patients with mild dysplasia (CIN I), Coriolus supplementation can help the body clear the infection. In cases with severe dysplasia (CIN II and CIN III), Coriolus supplementation can strengthen the immune system and reduce the risk of relapse.

Clinical Journal of Mycology. 2012;3:2–

Lavender Oil for Anxiety



Lavender Oil vs Paroxetine (Paxil)

- ▶ RDBPCT: two doses of oral lavender essential oil in comparison to a selective serotonin reuptake inhibitor, paroxetine, n=616 with GAD with Hamilton Anxiety Scale (HAMA) score of >17 points
- ▶ 80 or 160 mg dose lavender oil, paroxetine 20 mg, or placebo for 10 weeks
- ▶ **Key findings:** After 4 weeks of the study and at other study time points, the intake of 160 mg/day of lavender oil resulted in a significantly greater change in the HAMA score compared to placebo ($P < 0.01$). After 6 weeks and beyond, those taking 80 mg/day of lavender essential oil had a significantly greater change in the HAMA scores compared to placebo ($P=0.02$). At week 6 the HAMA score in those taking paroxetine approached significance ($P=0.06$) but they were not significantly better than placebo after that point.
- ▶ The primary efficacy endpoint was the HAMA total score reduction between baseline and treatment end. The HAMA total score decreased by 14.1 ± 9.3 points for Silexan 160 mg/d, 12.8 ± 8.7 points for Silexan 80 mg/d, 11.3 ± 8.0 points for paroxetine, and 9.5 ± 9.0 points for placebo
- ▶ Significantly more patients in the 160 mg/d lavender group showed an improvement in the HAMA score of 50% or more compared to the placebo group (60.3% vs. 37.8%). This was also observed in the 80 mg/d group (51.9% vs. 37.8%). The HAMA score was < 10 in significantly more of those patients taking the lavender product compared to the placebo (46.3% vs. 29.6%).
- ▶ All three treatment groups, the 80 mg/day, 160 mg/day and the paroxetine contained a greater percentage of patients who were "much/very much improved" or had a "moderate/marked" therapeutic effect as compared to the placebo group.

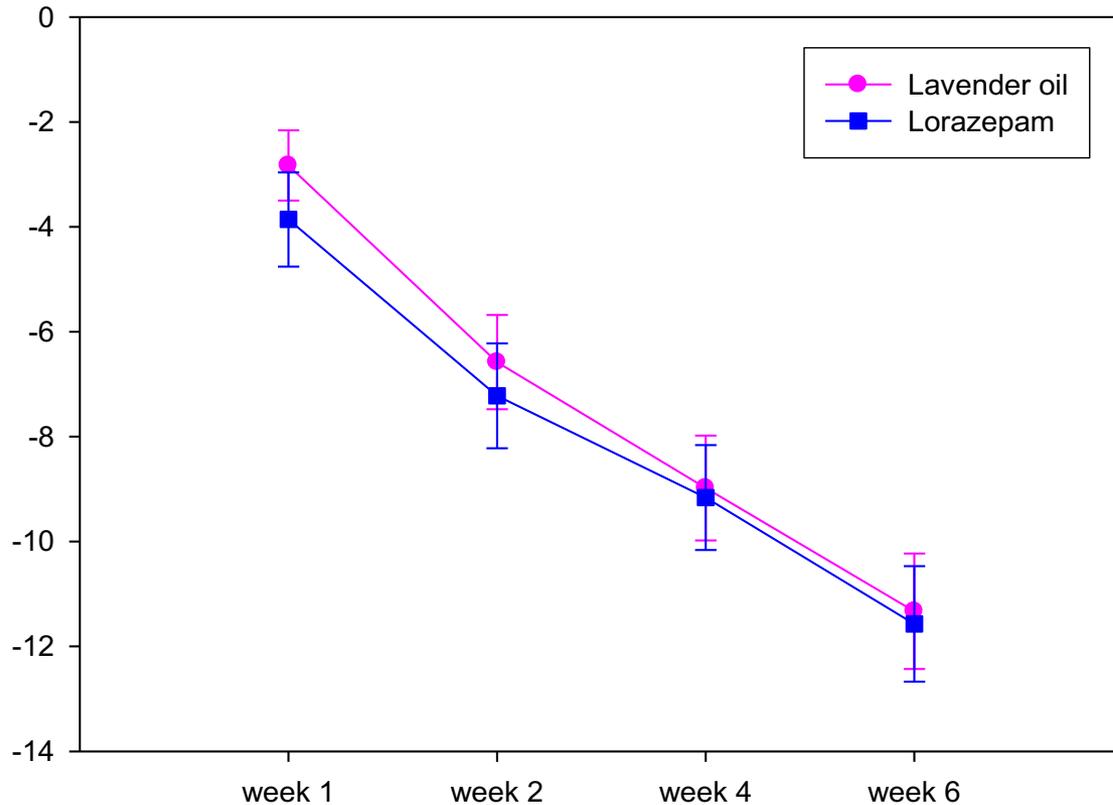
Kasper S, Gastpar M, Muller WE, Volz HP, Moller HJ, Schlafke S, Dienel A. *Int J Neuropsychopharmacol.* January 23, 2014:1-11

Lavender Oil extract in patients with Generalized Anxiety Disorder (GAD)

- ▶ Multi-center, randomized, double-blind clinical trial in comparison to lorazepam (Ativan)
- ▶ N = 77, 6 weeks treatment; 80 mg daily
- ▶ Results
 - **Therapeutic equivalence of WS[®] 1265 and lorazepam**
 - Anxiolytic efficacy (HAMA reduction by 11 points)
 - “Somatic anxiety” and “psychic anxiety decreased similarly in both groups
- Woelk H, Schälke S. A multi-center, double-blind, randomised study of the Lavender oil preparation Silexan in comparison to Lorazepam for generalized anxiety disorder. *Phytomedicine* 2010;17:94–99.

WS[®] 1265 improves anxiety

Mean change in HAM-A total score from baseline during the active treatment period



Lavender Oil improves anxiety compared to lorazepam and placebo

- ▶ Review of 3 RDBCTs of Silexan vs.:
 - placebo (10 wks) in subsyndromal anxiety
 - lorazepam (6 wks) in GAD
 - placebo (10 wks) in restlessness and agitation
- ▶ Total n=280
- ▶ Patients showed average HAMA total score decreases by between 10.4 +/-7.1 and 12.0 +/-7.2 at week 6 and by between 11.8+/-7.7 and 16.0+/- 8.3 at week 10
- ▶ In GAD silexan and lorazepam showed comparable HAMA total score reductions
- ▶ Kasper S, Gastpar M, Müller WE, et al. Efficacy and safety of silexan, a new, orally administered lavender oil preparation, in subthreshold anxiety disorder – evidence from clinical trials. *Wien Med Wochenschr* (2010) 160/21–22: 547–556

Lavender

Comparisons to other Meds/Herbs

- ▶ Lavender has been compared to benzodiazepines, paroxetine, imipramine, Kava
 - ▶ In a 6-week study, Kava was found to produce a mean reduction of the HAMA score of 10 points, whereas the mean reduction of that score from lavender (WS[®] 1265) has ranged from 11.3 points (6-week study) to 16 points (10-week study)
 - ▶ Pharmaceutical anxiolytics (primarily benzodiazepines) typically produce HAMA reductions in the range of 11 to 15.3, suggesting comparable to superior efficacy of WS[®] 1265 without the attendant side effects.
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Lavender- Anxiety

- ▶ 97 healthy subjects in RDBPCT
- ▶ Orally administered lavender capsules (100 mL and 200 mL)
- ▶ The authors concluded that lavender has anxiolytic effects in humans under conditions of low anxiety, but were unable to draw conclusions about high anxiety or clinical anxiety disorders.

Hum Psychopharmacol. 2009 Jun;24(4):319-30.

Lavender– Anxiety/Depression

- ▶ The HAMA total score decreased by 10.8 points for lavender and 8.4 points for placebo. The Total score decreased were 9.2 points for lavender and 6.1 points for placebo.
- ▶ Compared to the placebo, the men and women in the lavender group had a better over–all clinical outcome and showed more significant improvements in their daily living skills and health related quality of life.

European Neuropsychopharmacology
2016;26:331–340.

Lavender oil- MOA

- ▶ Potentiates expression of GABA-A receptors in cell culture
 - ▶ Has shown spasmolytic activity on guinea pig ileum
 - ▶ linalool, a main active ingredient of lavender oil, has been shown in animals to inhibit glutamate binding in the brain
 - ▶ linalool has also inhibited acetylcholine release and influenced ionic conductance in neurons
 - ▶ linalyl acetate is described to exert a relaxing effect.
 - ▶ Lavender oil has reduced dose-dependently spontaneous motility and caffeine-induced hyperactivity of mice.
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Lavender Oil for Anxiety: other studies

- ▶ Bielski RJ, Bose A, Chang CC. *Ann Clin Psychiatry*. 2005 Apr-Jun;17(2):65-9.
- ▶ Allgulander C, Hartford J, Russell J, Ball S, Erickson J, Raskin J, Rynn M. *Curr Med Res Opin*. 2007 Jun;23(6):1245-52.
- ▶ European Directorate for the Quality of Medicines and Healthcare (2005) Lavender oil. In: *European Pharmacopoeia 5.0*, p1894. Strasbourg, European Directorate for the Quality of Medicines & HealthCare.
- ▶ Schuwald AM, Nöldner M, Wilmes T, et al. *PLoS One*. 2013 Apr 29;8(4):e59998
- ▶ Doroshenko O, Rokitta D, Zadoyan G, Klement S, Schläfke S, Diemel A, Gramatté T, Lück H, Fuhr U. *Drug Metab Dispos*. 2013 May;41(5):987-93.

Dr. Tori Hudson Resources

- ▶ Women's Encyclopedia of Natural Medicine, 2008, second edition
- ▶ www.drtorihudson.com
- ▶ www.awomanstime.com
- ▶ www.instituteofwomenshealth.com
- ▶ www.naturopathicresidency.org
- ▶ Monthly columns:
 - Emerson Ecologics
 - Townsend Letter for Doctors