



## Hormonal Effects of Essential Oils

**In general, there is relatively little known about the hormonal effects of essential oils, and the information is contradictory and conclusions uncertain.**

J Pharm Pharmacol. 2002 Nov;54(11):1521-8.

### **Assessment of estrogenic activity in some common essential oil constituents.**

#### **Abstract**

Estrogenic responses have not only been associated with endocrine function, but also with cognitive function. Several studies have indicated that estrogen replacement therapy has favourable effects on cognition, and may have potential in the prevention and treatment of Alzheimer's disease. Thus, ligands for the estrogen receptor, that have a better efficacy and adverse-effect profile than drugs currently available, require investigation. This study was undertaken to investigate the potential estrogenic activity of a number of essential oil constituents. Initially, estrogenic activity was determined by a sensitive and specific bioassay using recombinant yeast cells expressing the human estrogen receptor. At high concentrations, estrogenic activity was detected for citral (geranial and neral), geraniol, nerol and trans-anethole, while eugenol showed anti-estrogenic activity. Molecular graphics studies were undertaken to identify the possible mechanisms for the interaction of geranial, neral, geraniol, nerol and eugenol with the ligand-binding domain of the estrogen alpha-receptor, using the computer program HyperChem. Citral, geraniol, nerol and eugenol were also able to displace [(3)H]17beta-estradiol from isolated alpha- and beta-human estrogen receptors, but none of these compounds showed estrogenic or anti-estrogenic activity in the estrogen-responsive human cell line Ishikawa Var I at levels below their cytotoxic concentrations, and none showed activity in a yeast screen for androgenic and anti-androgenic activity. The potential in-vivo estrogenic effects of citral and geraniol were examined in ovariectomized mice, but neither compound showed any ability to stimulate the characteristic estrogenic responses of uterine hypertrophy or acute increase in uterine vascular permeability. **These results show that very high concentrations of some commonly used essential oil constituents appear to have the**

potential to interact with estrogen receptors, although the biological significance of this is uncertain.

## **Anti-androgen**

### **A famous study from a few years ago:**

J Pediatr Endocrinol Metab. 2016 Jan;29(1):103-7. doi: 10.1515/jpem-2015-0248.

#### **Prepubertal gynecomastia and chronic lavender exposure: report of three cases.**

##### **Abstract**

##### **INTRODUCTION:**

Prepubertal gynecomastia is a rare condition characterized by the growth of breast tissue in males as a consequence of early exposure to sexual hormones. When this condition is present, pathological sources of testosterone/estrogen production, such as adrenal or gonadal tumors must be searched for. A few reports have described an association between gynecomastia and substances that produce stimulation of the estrogen receptor, such as lavender and tea tree oil.

##### **METHODS:**

Here we describe the cases of three boys who presented with prepubertal gynecomastia and were chronically exposed to lavender. Two of these boys were exposed to a cologne, named agua de violetas, used by Hispanic communities in the US, and in their countries of origin.

##### **RESULTS:**

We studied a sample of the cologne used by one of the patients. Analysis of the chemical composition of the agua de violetas cologne was performed using high-performance liquid chromatography as well as off-line mass spectrometric detection. All these, combined with the physical appearance and the smell, determined that the cologne had lavender as an ingredient.

##### **CONCLUSION:**

Exposure to estrogenic substances, such as lavender, should be explored in children presenting with prepubertal gynecomastia/thelarche.

### **One of many rebuttals to this study:**

Tony Larkman2015 Sep 14 4:38 p.m.

It is disappointing that the authors didn't include or at least refer to the following two articles in this paper: 1. Politano VT et al (2013), *Uterotrophic Assay of Percutaneous Lavender Oil in Immature Female Rats*; International Journal of Toxicology; 32(2): 123-9 (<http://www.ncbi.nlm.nih.gov/pubmed/23358464>) 2. Carson CF et al. (2014), *Lack of*

evidence that essential oils affect puberty; Reproductive Toxicology; 44:50-1  
(<http://www.ncbi.nlm.nih.gov/pubmed/24556344>)

The first paper largely exonerates lavender oil through the 'gold standard' uterotrophic assay while the second hypothesizes a mechanism that may be causal in incidences of both gynecomastia and premature thelarche as well as the 'in vitro' findings of Henley et al (2007) where they in fact used polystyrene in their test system and not glass. Based on these it is not impossible to conceive that other endocrine disruptors may have been inadvertently present in the material tested.

A further, as yet untested, hypothesis for these manifestations is the high incidence of adulteration in essential oils. The incidence of adulteration in TTO is remarkably high as reported in Wong YF et al. (2014) *Enantiomeric distribution of selected terpenes for authenticity assessment of Australian Melaleuca alternifolia oil*; Industrial Crops & Products; 67: 475-83

(<http://ijt.sagepub.com/content/early/2013/01/24/1091581812472209>) where more than 50% of 43 commercial samples tested failed to comply with the proposed chiral ratios. Of 15 commercially sourced samples in the European Union 73% of these showed significant differences in chiral abundances while TTO from both North America and Asia also displayed similar results where  $\geq 50\%$  of the tested samples did not match the expected results. In material of Chinese origin the incidence rises to 100%. An extraordinary range of compounds never found in pure TTO has been coincidentally detected so it has been further hypothesized that this, along with the likelihood that the material used is heavily oxidized, may be significant source of problems such as allergic contact dermatitis attributed to the use of TTO as well as conditions related to endocrine disruption.

It is disappointing for the tea tree oil industry as a whole that TTO continues to be mentioned as a potential endocrine disruptor without a more balanced view being presented when there are clear indications available in the literature that the original proposal by Henley et al in 2007 may be flawed. The fact that TTO was not present at all in any of the material tested is also disappointing as TTO can in no way be implicated yet its mention continues to promulgate the link and implicate TTO unfairly.

### **The study referred to:**

Int J Toxicol. 2013 Mar-Apr;32(2):123-9. doi: 10.1177/1091581812472209. Epub 2013 Jan 28.

### **Uterotrophic assay of percutaneous lavender oil in immature female rats.**

#### **Abstract**

The estrogenic potential of lavender oil was evaluated in a percutaneous uterotrophic bioassay in immature female rats. Four groups of 10 immature female rats each were

randomly selected on postpartum day (PPD) 16. During the 3-day treatment period (PPDs 19-21), the immature rats were separated from the dams, caged in groups of 5 in a litter box for 6 hours, and administered the vehicle control article (corn oil) or lavender oil at 20 or 100 mg/kg per day. All dosages were administered as a 5 mL/kg volume in a Hilltop Chamber (25 mm diameter; absorbent material removed) placed on the shaved back of each immature rat, and secured with micropore tape and Vetrap. A positive control group was gavaged twice daily with 2.5 µg/kg per day of 17α-ethinyl estradiol. Daily observations included viability, clinical signs, body weights, and body weight gains. All rats were euthanized 24 hours after the third and final treatment, the uteri and ovaries were removed, and the paired ovaries and wet and blotted uterine weights were recorded. No unscheduled deaths occurred. No skin reactions were observed. Both dosages of lavender oil significantly reduced body weight gains after the third day of treatment, but terminal body weights and mean absolute and relative uterine weights did not differ significantly from vehicle control values. Positive controls showed significant increases in body weight and increased mean absolute and relative uterine weights as expected. **Based on these data, lavender oil, at dosages of 20 or 100 mg/kg, was not active in the rat uterotrophic assay and gave no evidence of estrogenic activity.**

**This article shows that lavender and tea tree do have some anti-androgen effects, but it is positive if used for the right condition. In this case it is used externally for excess hair growth.**

J Endocrinol Invest. 2013 Jan;36(1):50-4. doi: 10.3275/8766. Epub 2012 Nov 26.

**Possible efficacy of Lavender and Tea tree oils in the treatment of young women affected by mild idiopathic hirsutism.**

**Abstract**

**BACKGROUND:**

Hirsutism is defined as the presence of excessive terminal hair in androgen-dependent areas of a woman's body. Regarding this it has been suggested that Lavender and Tea tree oils may have antiandrogenic activities.

**AIM:**

To evaluate therapy based on Lavender and Tea tree oils in women suffering from mild idiopathic hirsutism (IH).

**SUBJECTS AND METHODS:**

A prospective, open-label, placebo- controlled, randomized study was performed: women affected by mild IH were randomly assigned to receive oil spray containing Lavender and Tea tree oils (group T) (no. = 12) or placebo (group P) (no. = 12) twice a day for 3 months in areas affected by hirsutism. Evaluation of hirsutism was carried out at baseline and after 3 months by Ferriman-Gallwey score and by measuring hair

diameter taken from some body areas. A hematological and hormonal evaluation was carried out at baseline and after 3 months.

#### **RESULTS:**

No significant variations were found in any of the hormones studied in groups T and P between baseline and after 3 months. A statistically significant decrease of hirsutism total score and of hair diameter was found in group T, while no statistically significant difference in these two parameters was observed in group P; in group T percentual reduction of hair diameter was significantly greater than in group P.

#### **CONCLUSIONS:**

Lavender and Tea tree oils applied locally on skin could be effective in reducing mild IH; this treatment could represent a safe, economic and practical instrument in the cure of this disease.

**This study shows that lavender taken internally does not interfere with hormonal contraception.**

Drugs R D. 2014 Dec;14(4):265-72. doi: 10.1007/s40268-014-0065-5.

**No interacting influence of lavender oil preparation silexan on oral contraception using an ethinyl estradiol/levonorgestrel combination.**

#### **Abstract**

##### **PURPOSE:**

Silexan is an oral Lavender oil preparation with proven anxiolytic efficacy. Given the high prevalence of anxiety and restlessness in younger women, oral contraceptives and Silexan will likely be co-administered.

##### **METHODS:**

A double-blind, randomised, 2-period crossover study was performed to investigate the effects of Silexan on the pharmacokinetics and pharmacodynamics of Microgynon®), a combination oral contraceptive containing ethinyl estradiol 0.03 mg (EE) and levonorgestrel 0.15 mg (LNG) in healthy, fertile, adult females. During 2 consecutive cycles of 28 days, oral contraception was given for 21 days combined with 1 × 160 mg/day Silexan or placebo. Plasma concentration-time profiles of EE and LNG were obtained on day 18 ± 1 up to 24 h after dosing. The primary outcome measure was the area under the concentration-time curve over a dosing interval of  $\tau = 24$  h ( $AUC_{\tau}$ ) for EE and LNG plasma levels. An interaction with Silexan was formally excluded if the 90 % confidence interval for the  $AUC_{\tau}$  ratio during co-administration with Silexan or placebo was included within the range of 0.80-1.25. Secondary outcomes included EE and LNG peak concentration ( $C_{max}$ ) and time to  $C_{max}$  ( $t_{max}$ ), follicle size, endometrial thickness, the Hoogland score, and serum levels of estradiol, progesterone, and sex hormone-binding globulin.

**RESULTS:**

A total of 24 women (mean age 27.3 years; mean body mass index 22.2 kg/m<sup>2</sup>) participated. The confidence intervals for the EE and LNG AUC<sub>T</sub> and C max ratios fell within the pre-specified limits, indicating no interaction (point estimates [Silexan/placebo] AUC<sub>T</sub> EE 0.97, LNG 0.94; C max EE 0.99, LNG 0.96). For LNG, t max was slightly delayed. No secondary outcome indicated any impairment of contraceptive efficacy.

**CONCLUSIONS:**

Co-administration of Silexan did not affect the efficacy of a combination oral contraceptive containing EE and LNG and was well tolerated.

**Spearmint and peppermint teas are implicated in anti-androgen effects; this may or may not be relevant in aromatherapy.**

Urology. 2004 Aug;64(2):394-8.

**Effects of peppermint teas on plasma testosterone, follicle-stimulating hormone, and luteinizing hormone levels and testicular tissue in rats.**

**Abstract****OBJECTIVES:**

To justify the effects of *Mentha piperita* labiatae and *Mentha spicata* labiatae herbal teas on plasma total testosterone, luteinizing hormone, and follicle-stimulating hormone levels and testicular histologic features. **We performed this study because of major complaints in our area from men about the adverse effects of these herbs on male reproductive function.**

**METHODS:**

The experimental study included 48 male Wistar albino rats (body weight 200 to 250 g). The rats were randomized into four groups of 12 rats each. The control group was given commercial drinking water, and the experimental groups were given 20 g/L *M. piperita* tea, 20 g/L *M. spicata* tea, or 40 g/L *M. spicata* tea.

**RESULTS:**

The follicle-stimulating hormone and luteinizing hormone levels had increased and total testosterone levels had decreased in the experimental groups compared with the control group; the differences were statistically significant. Also, the Johnsen testicular biopsy scores were significantly different statistically between the experimental groups and the control group. Although the mean seminiferous tubular diameter of the experimental groups was relatively greater than in the control group, the difference was not statistically significant. The only effects of *M. piperita* on testicular tissue was segmental maturation arrest in the seminiferous tubules; however, the effects of *M.*

spicata extended from maturation arrest to diffuse germ cell aplasia in relation to the dose.

### **CONCLUSIONS:**

Despite the beneficial effects of *M. piperita* and *M. spicata* in digestion, we should also be aware of the toxic effects when the herbs are not used in the recommended fashion or at the recommended dose.

## **Fennel and anise oils are potentially estrogenic**

J Ethnopharmacol. 1980 Dec;2(4):337-44.

### **Fennel and anise as estrogenic agents.**

#### **Abstract**

Fennel, *Foeniculum vulgare*, and anise, *Pimpinella anisum*, are plants which have been used as estrogenic agents for millennia. Specifically, they have been reputed to increase milk secretion, promote menstruation, facilitate birth, alleviate the symptoms of the male climacteric, and increase libido. In the 1930s, some interest was shown in these plants in the development of synthetic estrogens. The main constituent of the essential oils of fennel and anise, anethole, has been considered to be the active estrogenic agent. However, further research suggests that the actual pharmacologically active agents are polymers of anethole, such as dianethole and photoanethole.

**We know thuja oil as toxic because of its thujone compounds, which are known to induce seizures. Here we see that it can treat PCOS.**

J Ethnopharmacol. 2015 Jun 20;168:25-30. doi: 10.1016/j.jep.2015.03.029. Epub 2015 Mar 27.

### **Thuja occidentalis L. and its active compound, $\alpha$ -thujone: Promising effects in the treatment of polycystic ovary syndrome without inducing osteoporosis.**

#### **Abstract**

#### **ETHNOPHARMACOLOGICAL RELEVANCE:**

*Thuja occidentalis* L. (Cupressaceae) has been used in folk medicine for the treatment of rheumatism, amenorrhea, cystitis, and uterine carcinomas, and as an abortifacient and contraceptive.

#### **AIM OF THE STUDY:**

The present study aimed to determine whether *T. occidentalis* oil and  $\alpha$ -thujone could be beneficial in the treatment of polycystic ovary syndrome (PCOS).



### **MATERIALS AND METHODS:**

T. occidentalis oil and  $\alpha$ -thujone were administered to rats with letrozole-induced PCOS for 21 days. At the end of 21 days, the rats were sacrificed and blood samples were taken by cardiac puncture. The levels of serum gonadotropins, steroids, blood lipid, leptin, and glucose and the values of antioxidant parameters were measured.

### **RESULTS:**

The results demonstrated that estradiol and progesterone levels significantly increased, while luteinizing hormone (LH) and testosterone levels decreased in the T. occidentalis- and  $\alpha$ -thujone-administered groups. The plasma low-density lipoprotein-cholesterol (LDL-C), leptin, and glucose concentrations were also significantly decreased in the T. occidentalis and  $\alpha$ -thujone groups when compared to the control group.

Histopathological findings demonstrated that the T. occidentalis and  $\alpha$ -thujone groups displayed good healing. According to the phytochemical analyses, 25 compounds were identified in the T. occidentalis oil. The main constituents of the oil were the monoterpene ketones  $\alpha$ - and  $\beta$ -thujone, fenchone, and sabinene, as well as the diterpenes beyerene and rimuene.

### **CONCLUSION:**

T. occidentalis essential oil and its active component,  $\alpha$ -thujone, can be used for the treatment of PCOS without inducing osteoporosis.

**Reproductive damage can happen from common adulterants and contaminants in oils.**

J Agric Food Chem. 2001 Aug;49(8):3705-8.

### **Production process contamination of citrus essential oils by plastic materials.**

#### **Abstract**

Twelve samples of plastic materials employed in the industrial extraction of citrus essential oils were analyzed for the presence of phosphorated plasticizers, chloroparaffins, and phthalate esters. The samples tested were found to release these contaminants into the essential oils during the production process. Contamination tests were carried out using dichloromethane and uncontaminated samples of citrus essential oils as extractants. The extracts were analyzed by HRGC/FPD, ECD, and MS. Only one sample of plastic material was found to release triaryl phosphates, 5 samples released chloroparaffins, 6 released diisobutyl phthalate, and 8 released bis(2-ethylhexyl) phthalate. Significantly larger quantities of contaminants were released by new plastic parts than by used plastic parts.

Daru. 2014 Nov 28;22:78. doi: 10.1186/s40199-014-0078-1.



## **Presence of phthalate derivatives in the essential oils of a medicinal plant *Achillea tenuifolia*.**

### **Abstract**

#### ***BACKGROUND:***

Phthalate, esters of phthalic acid, are mainly applied as plasticizers and cause several human health and environment hazards. The essential oils of *Achillea* species have attracted a great concern, since several biological activities have been reported from varieties of these medicinal species. On the other side, due to the problems regarding the waste disposal in developing countries, phthalate derivatives can easily release from waste disposal to the water and soil resulting in probable absorption and accumulation by medicinal and dietary plants. As a matter of fact, although the toxicity of phthalate derivatives in human is well-known, food crops and medicinal plants have been exposing to phthalates that can be detected in their extracts and essential oils. *Achillea tenuifolia* (Compositae) is one of these herbaceous plants with traditional applications which widely growing in Iran.

#### ***FINDING:***

The plant root was subjected to hydro-distillation for 4 h using Clevenger type apparatus to obtain its essential oil before and after acid treatment. Both of the hydro-distilled essential oils were analysed by GC-MS method resulted in recognition of their constituent. Phthalate contamination as (1, 2-benzenedicarboxylic acid, bis (2-methylpropyl) ester (5.4%) and phthalic acid (4.5%), were identified in the first and second extracted oils, respectively.

#### ***CONCLUSION:***

As a warning, due to the potential role of phthalates to cause reproductive toxicity, disturb of endocrine system and causing cancers, medicinal plants have to be considered through quality control for detection of these compounds.