Clinical Studies on Chaste Tree (*Vitex agnus castus* L.)

Corpus Luteum Irregularities/Hyperprolactinemia

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Merz *et al*., 1996	Hyperprolactinemia	O, PC, Cm (intra-individual comparison) n=20 healthy men	14-day treatment period for each phase with 7-day wash-out phase between phases	Phase 1: placebo Phase 2: One capsule 3x/day (120 mg/day) Phase 3: Two capsules 3x/day (240 mg/day) Phase 4: Four capsules 3x/day (480 mg/day)	Bionorica BNO1095 capsules containing 20 mg BP1095E1 extract [6–12:1 extract (spissum) (70% ethanol)] equivalent to 40 mg crude drug	Pharmacological data were obtained on the influence of 14-day vitex treatment on Thyroxin Releasing Hormone (TRH)-stimulated prolactin release compared to placebo. Significant increase (p=0.003) in prolactin levels in men receiving the lowest dose (120 mg per day), but slight reduction in prolactin level in those receiving higher dose. There were no significant dose-dependent changes in the 24-hour serum prolactin profile.
Milewicz *et al*., 1993	Luteal phase defects due to hyperprolactinemia	R, DB, PC n=37 women with luteal phase defects due to latent hyperprolactinemia (ages 19–42 years old)	3 months	1 capsule vitex extract/day or 1 capsule placebo/evening	Strotan® soft-gel capsule containing 20 mg vitex fruit aqueous, alcoholic, dry native extract	After 3 months, vitex group experienced significant reduction in symptoms compared to placebo group. Significant reduction in prolactin release in response to TRH stimulation compared to placebo (p<0.0001). Mid-luteal progesterone levels, low at baseline, were normal after 3 months in vitex group. Luteal phase normalization and luteal progesterone synthesis normalization were seen in vitex group with no observable changes in these parameters in placebo group. No side effects were noted.
Propping *et al*., 1991	Corpus luteum insufficiency, menstrual disorders, and PMS	O, MC, U n=1,592 women with corpus luteum insufficiency; including 418 with hypermenorrhea; 355 with polymenorrhea; 202 with secondary amenorrhea,186 with dysmenorrea; 175 with PMS, anovulation; 145 experiencing sterility; 66 with menorrhagia; 32 with disturbed menstruation (average age 32.9 years)	16 years (average treatment period, 6 months)	43 drops tincture/day	Agnolyt® vitex fruit tincture (Each 100 ml of aqueous-alcoholic solution contains 9 ml of 1:5 tincture)	In 90% of cases, physician's clinical observation assessment was good or satisfactory, with 33% of patients free of complaints and a positive response to treatment in 51% noted. Patients experienced relief at about 8–9 weeks after beginning treatment. Out of 145 patients who were trying to conceive during treatment period, 56 became pregnant. Adverse effects, including nausea, skin rashes, headaches, and dyspepsia, were reported by 2.4% of patients.
Propping and Katzorke, 1987	Corpus luteum insufficiency	O, U n=18 infertile normoprolactinemic women (24–39 years old)	3 months	40 drops tincture/day	Agnolyt® vitex fruit tincture	Treatment was deemed successful in 13 of 18 patients (outcome was assessed by normalization of the mid-luteal progesterone level and by correction of pre-existing short menstrual cycle). 2 women became pregnant, and 11 patients had significantly improved serum progesterone values. There was a trend towards normalization of progesterone levels in 4 cases. These findings are indicative of corpus luteal function enhancement.

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Menstrual Cycle Irregularities

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Bubenzer, 1993	Oligo-menorrhea, corpus luteum insufficiency, poly-menorrhea	O, U n=120 women with hormone imbalance syndromes	6 months		Strotan® soft-gel capsule containing 20 mg vitex fruit aqueous, alcoholic, dry native extract	Of the subjects, 63% had normalized cycle (most had extended follicular phase), and those with disturbed temperatures during their cycles normalized. Patients with very low progesterone benefited particularly. 29% became pregnant.
Loch *et al.*, 1991	Menstrual irregularity	O, U n=2,447 women with a variety of menstrual disorders	9 years (average treat-ment period, 5 months)	42 drops tinc-ture/day	Agnolyt® vitex fruit tincture	Both patients and physicians noted improvement of symptoms. Of the patients, 90% demonstrated very good, good, or satisfactory results; 2.3% experienced minor side effects.
Loch and Kaiser, 1990	Secondary amenorrhea	P, O, U n=15 female out-patients with secondary amenorrhea (17–29 years old)	6 1/2 months	40 drops tinc-ture/day with some liquid in mornings apart from meals	Agnolyt® vitex fruit tincture	In 10 of 15 patients, the onset of menstruation was observed at about 6 months of treatment. Hormone values for progesterone and LH increased, while FSH decreased slightly or did not change. Authors concluded that Agnolyt® can be recommended for long-term treatment of secondary amenorrhea.
Bleier, 1959	Oligo-menorrhea, polymenor-rhea, menor-rhagia	O n=126 women (35 with oligomenor-rhea, 33 with poly-menor-rhea, 58 with menorrhagia)	2–3 months	15 drops, 3x/day with water 1/2 hour before meals	Agnolyt® vitex fruit tincture	In 58 patients with menorrhagia, a statistically significant shortening of bleeding period was achieved. In 33 patients with polymenorrhea, duration between periods lengthened (on average, from 20 days to 26 days). In 33 cases of oligomenorrhea, the average cycle was shortened from 39 to 31 days. Fourteen patients became pregnant.
Probst and Roth, 1954	Secondary amenorrhea, oligohy-pomenorrhea, cystic granular hyperplasia of endometrium, anovulatory cycle	O, Cm, U n=82 women (57 in vitex group; 25 in group combining vitex with estrogen)	5–24 months	15 drops vitex tincture, 3x/day vs. 1 tablet ethenyl estradiol, 3x/day with same vitex dosage	Alyt® vitex fruit tincture, same as Agnolyt® tincture of aqueous-alcoholic solution	Of women in vitex group 87.7% showed normalization of bleeding in menstrual cycle compared to 52% in the vitex/estradiol combination group. Of those women in vitex group, 100% were diagnosed with anovulatory cycle, 50% with secondary amenorrhea and 44% with oligo-hypomenorrhea experienced a distinct increase in the basal temperature curve. Only 16% of the women in the combination therapy group observed an increase in basal temperature. The authors concluded that vitex was particularly indicated in patients with deficient cor-pus luteum function.

Premenstrual Syndrome (PMS)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Schellenberg, 2001	PMS	R, DB, PC, PG n=170 women aver-age menstrual cycle = 28 days; average duration of menses = 4.5 days (average age 36 years)	3 menstrual cycles	One, 20 mg tablet/day	PreMens® (Ze440) extract tablets 40 mg (20 mg native dry extract, 20 mg lactose as excipient)	Improvement in vitex group in the main efficacy vari-ables from baseline to end of third cycle in women's self assessment and physician's assessment of irritability, mood change, anger, headache, breast fullness, and other menstrual symptoms including bloating ($p<0.001$). Over half of women had 50% or greater improvement of symptoms. 4 women in vitex group and 3 in placebo group reported mild adverse events, none which caused discontinuation. Authors conclude that vitex fruit is a safe and effective treatment for relief of symptoms of PMS.
Loch *et al.*, 2000	PMS	OL, MC n=1,634 women with PMS; data from 857 gynecologists (mean age 35.8 years)	3 menstrual cycles	One, 20 mg capsule, 2x/day	Femicur® capsules containing 1.6–3.0 mg dried extract [6.7–12.5:1] corresponding to 20 mg drug	93% reported PMS symptoms lessened or disappeared after vitex treatment over 3 menstrual cycles. Changes from baseline were recorded on questionnaires by physicians before treatment and after 3 cycles. Significant decrease of all symptoms. Of the patients, 42% reported that they no longer suffered from PMS; 51% showed a decrease in symptoms.

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Premenstrual Syndrome (PMS) (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Berger *et al*, 2000	PMS	P, MC n=43	8 menstrual cycles; including 2 baseline, 3 treatment, and 3 post-treatment	One, 20 mg tablet/day in the morning	PreMens® Ze440 tablet containing 20 mg vitex fruit, hydro-alcoholic, native dry extract, 6.0–12.0:1 (*w/w*)	Significant score reduction (42.5%) using the MMDQ (Moos Menstrual Distress Questionnaire) as the main effect parameter ($p<0.001$). Symptoms gradually returned after cessation of treatment. However, a difference from baseline remained (20%; $p<0.001$) up to 3 cycles thereafter.
Berger *et al.*, 1999	Late luteal phase dysphoric disorder (PMS III –R)	C, E, MC n=132 women, 65 on oral contraceptives and 67 not on oral contraceptives (19–30 years old)	6 months (3 cycles followed by 3-month observation period)	One, 20 mg tablet/day in morning	PreMens® Ze440 tablet containing 20 mg vitex fruit, hydro-alcoholic, native dry extract, 6.0–12.0:1 (*w/w*)	Using Visual Analog Scale (VAS), the only marginal differences were observed between the contraceptive and non-contraceptive groups during the medication period and post-medication period. All clinically relevant reduction in VAS scores of approximately 60% of all patients was reached. Of all patients, 90% believed that vitex helped and 75% said they would use vitex in the future. A good use-risk ratio was determined for both groups. Clinically relevant score-values of PMS declined during the 3 cycle therapy and rose again thereafter.
Lauritzen *et al.*, 1997	PMS	MC, C,R, Cm n=105 women with PMS; Agnolyt® group n=46, pyridoxine group n=59 after exclusion (18–45 years old)	3 months	Vitex group: 1 capsule Agnolyt®/day plus 1 capsule placebo/day. B6 group: 1 placebo capsule, 2x/day, on days 1–15; 1 B6 capsule, 2x/day, on days 16–35 of menstrual cycle.	Agnolyt® capsules containing 3.5–4.2 mg vitex fruit, dry native extract, 9.58–11.5:1 (*w/w*) vs. B6 capsules containing 100 mg pyridoxine HCL	Agnolyt® was superior to pyridoxine. On the premenstrual tension syndrome (PMTS) scale, vitex group had reduction in score points from 15.2 to 5.1 vs. 11.9 to 5.1 in B6 group. Of patients in vitex group, 77.1% vs. 60.6% of patients in B6 group showed improvement on Clinical Global Impression (CGI) scale. No serious adverse events were noted. Side effects included gastrointestinal complaints (equally distributed between both groups), skin reactions (two patients in vitex group), and transitory headache (one patient in vitex group).
Turner and Mills, 1993	PMS	R, DB, PC n=217 women (105 in vitex group, 112 in placebo group) with PMS (physiological symptoms)	3 months	600 mg, 3x/day vs. soya-based placebo	Vitex capsules (brand not stated)	Vitex was statistically more effective than placebo only in alleviating jitters and restlessness; there was no statistical significant difference for other PMS symptoms including impaired concentration, fluid retention, or pain.
Dittmar and Böhnert, 1992	PMS	O, MC, U n=1,542 women with PMS (13–62 years old)	166 days average treatment duration	40 drops/day in morning	Agnolyt® vitex fruit tincture	Of patients, 33% reported total relief of symptoms, 57% reported partial relief, 4% reported no improvement. On 5% no data were obtained, and 2% terminated treatment because of side effects. Physicians observed a positive response (good or very good) to treatment in 92% of patients.
Coeugniet *et al.*, 1986	PMS	O, U n=36 women with PMS	3 months	40 drops/day	Agnolyt® vitex fruit tincture	After 3 months, physical and psychological alterations experienced during luteal phase of cycle were significantly reduced ($p<0.5$), including reduction in headaches, breast tenderness, bloating, fatigue, appetite, sweet cravings, nervousness, restlessness, anxiety, irritability, lack of concentration, depression, mood swings, and aggressiveness. Interval of luteal phase normalized from average of 5.4 days to 11.4 days and a diphasic cycle was established.

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Other

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Giss and Rothenburg, 1968	Acne vulgaris, acne indurate, acne conglobata, acne follicularis	C, Cm n=161 patients with acne (30% male; 70% female)	1–2 years (minimum 3-month treatment period)	20 drops tincture, 2x/day (morning and evening) for 4–6 weeks; then 15 drops daily for 1–2 years.	Agnolyt® vitex fruit tincture vs. standard acne therapy	118 patients received Agnolyt®, and 43 received standard acne therapy. Over 2 years, a statistically significant improvement of acne conditions was reported in the mostly female vitex group compared to placebo.

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