VITAZAN PROFESSIONAL

OvaPress™

Optimize ovarian function with *myo*-inositol/D-*chiro*-inositol 40:1 ratio

Inositol plays a pivotal role in reproductive physiology. It acts as a direct messenger of insulin and improves glucose uptake in various reproductive tissues.[1] It is also involved in follicle maturation with menstrual cycle progression and processes of embryogenesis, such as neural tube closure.[2,3]

A meta-analysis of randomized trials investigated inositol treatment of anovulation in women with PCOS.[4] This study included 10 randomized controlled trials including a total of 362 women taking inositol (257 on *myo*-inositol, 105 on D-*chiro*-inositol), 60 on metformin, and 179 on placebo. Treatment with inositol significantly improved ovulation rate (RR 2.3; 95% CI 1.1–4.7; $I^2 = 75\%$) compared to placebo. Inositol was also associated with increased frequency of menstrual cycles (RR 6.8; 95% CI 2.8–16.6; $I^2 = 0\%$) compared with placebo.

A meta-analysis of randomized controlled trials investigated the effects of *myo*-inositol (MI) alone or in combination with D-*chiro*-inositol (DCI) on the endocrine and metabolic abnormalities of women with PCOS.[5] The 9 randomized controlled trials, that included 247 inositol cases and 249 controls, found a significant decrease in fasting insulin ($p = 0.009$) and homeostasis model assessment (HOMA) index ($p = 0.041$) after MI supplementation. The study also found a slight trend toward a reduction of testosterone concentration by MI compared to controls ($p = 0.099$). Treatment with MI for up to 16 weeks had no significant effect on SHBG levels compared to controls ($p = 0.958$), while MI supplementation up to 24 weeks revealed a significant increase in SHBG levels compared to other treatments ($p = 0.026$).

The effect of MI compared to metformin on hormonal and glycolipid profiles in women with polycystic ovary syndrome has been the subject of several studies. A systematic review and updated meta-analysis of randomized control trials included a total of 9 studies involving a total of 612 PCOS patients, of which 306 were treated with MI and 306 were treated with metformin.[6] Compared to metformin, MI was more effective in lowering triglycerides levels ($p = 0.0001$) and avoiding side effects ($p < 0.00001$). No significant differences between MI and metformin were found with respect to indicators related to body fat, glycolipid metabolism, and glucose metabolism (particularly HOMA-IR and FINS).

MI as a pretreatment for non-PCOS women undergoing IVF cycles has also been studied.[7] In a randomized, controlled study involving 100 non-PCOS patients undergoing IVF, the addition of 4 g/d MI to the control treatment of 150 IU/d FSH and 400 mcg folate resulted in a significantly lower exogenous FSH amount to reach follicular maturation.[8] A prospective controlled observation trial investigated the 3-month pretreatment with 4 g/d MI and 400 mcg/d folate or folate alone in 76 non-PCOS poor responders during IVF.[9] Treatment with MI resulted in an increased number of oocytes recovered in MII ($p = 0.01$) and of the gonadotropin Ovarian Sensitivity Index ($p < 0.05$), suggesting an MI role in improving ovarian response to gonadotropins.

Different authors have examined the benefits of administering different MI/DCI combinations. An "expert" opinion on inositols in treating polycystic ovary syndrome and non–insulin-dependent diabetes mellitus highlights that the MI/DCI physiological ratio is 40:1 in plasma and 100:1 in the ovary, and that MI, alone or with DCI, in the 40:1 physiological ratio has been proven to be effective in the treatment of PCOS and type 2 diabetes.[10]

A clinical study compared different MI-to-DCI ratios.[11] In this study, 56 PCOS patients were treated with *myo*-inositol/D-*chiro*-inositol formulations: DCI alone, 1:3.5, 2.5:1, 5:1, 20:1, 40:1, and 80:1. Each received 2 g of inositols twice per day for 3 months. The authors concluded that the 40:1 MI/DCI ratio was the best for PCOS therapy aimed at restoring ovulation and normalizing important parameters in those patients. Those improvements include return of menses, restoration of ovulation as shown by better rise in progesterone levels, decrease in LH levels, increased SHBG and E2 levels, decreased free testosterone and HOMA, and decreased basal and postprandial insulin levels. The 40:1 ratio achieved the best improvements, followed by the 20:1 and 80:1 ratios.

L-Carnitine, Chromium, 5-MTHF, and Vitamin B_{12}

A systematic review included 6 articles to evaluate the potential roles of carnitine in patients with PCOS.[12] Two observational studies showed serum carnitine levels had an inverse relationship with glycemic status, body mass index, and waist circumference. Four clinical trials examining the effect of carnitine supplementation in patients with PCOS revealed improved weight loss, glycemic status, oxidative stress, follicles, and size of ovarian cells; no significant effects were reported on sex hormones and lipid profile.

Two randomized, double-blind, placebo-controlled studies examined the effect of a 12-week supplementation of 200 mcg/d of chromium picolinate plus 1000 mg/d of carnitine or placebo in 54 overweight and obese women with PCOS.[13,14] Participants who received carnitine plus chromium supplements had significantly lower total testosterone ($p = 0.002$), and hirsutism ($p = 0.02$) compared to placebo. In addition, carnitine and chromium cosupplementation decreased weight, BMI, fasting plasma glucose, insulin resistance, triglycerides, and total and LDL cholesterol, and elevated insulin sensitivity. Cosupplementation resulted in lower hs-CRP and malondialdehyde levels, and higher total antioxidant capacity levels. Moreover, supplementation upregulated gene expression of IL-6 and TNF-α compared to placebo.

Folic acid has an established role in the prevention of neural tube defects.[15] A retrospective study investigating women undergoing assisted reproductive technology associated 5-methyltetrahydrofolate and vitamin B_{12} supplementation with possible improvement of embryo development and improved pregnancy outcomes.[16] In this study, 111 women received 5-MTHF and vitamin B_{12}, and 158 women received only folic acid. The 5-MTHF-plus-vitamin B_{12} group had a higher percentage of clinical pregnancy and live birth in comparison to the folic-acid group ($p = 0.01$ and $p = 0.02$, respectively). The 5-MTHF-plus-vitamin B_{12} group's mean number of metaphase II (MII) oocytes and 2PN Fertilization Rate (FR) were higher in comparison to the folic-acid group ($p = 0.04$ and $p = 0.05$, respectively).

Each scoop contains:

40:1 inositol blend:
- Inositol (*myo*-inositol) . . . . . 1,000 mg
- D-*chiro*-Inositol . . . . . 25 mg

Acetyl-L-carnitine hydrochloride. . . . . 125 mg
Providing 106.25 mg of acetyl-L-carnitine
Vitamin B12 (methylcobalamin). . . . . 500 mcg
Chromium (from chromium picolinate) . . . . 400 mcg
Folate
(from calcium L-5-methyltetrahydrofolate) . 400 mcg

Directions of use: **Adults:** Take 1 scoop twice daily or as directed by your health-care practitioner. Please consult your health-care practitioner for use greater than 1 month.

Cautions and warnings: Consult a health-care practitioner prior to use if you have a liver disease, kidney disease, diabetes, and/or seizure disorder.

Contraindications: Do not use this product if you are pregnant or breast-feeding.

Known adverse reactions: May cause digestive upset.

Key Benefits from the Case Series

- Improvement in cycle regularity
- Improvement in dysmenorrhea related to PCOS

Table 1: Case Studies in Naturopathic Practice on OvaPress™

Sex, Age, Compliance	Side effects	Total duration	Presenting concerns	Notes
F, 29, 100%	No	1 month	Possible PCOS, very long cycles, breakthrough bleeding, possible fibroid	Cycles went from every 8 weeks to every 6 weeks
F, 40, 100%	No	6 month	Cystadenoma, PMDD, fibroid, dysmenorrhea, and menorrhagia	No pain at ovulation, much better mood postovulation
F, 28, 100%	No	5 months	PCOS, 2–6 periods per year	Cycles went from every 12–18 weeks to 7 weeks, and now 5 weeks. Improvement in dysmenorrhea.
F, 29, 75%, trouble remembering to take twice daily	None	3 months	Anovulation, menorrhagia, acne, spotting	Folic acid (singular) helped stop breakthrough bleeding and spotting. OvaPress, had two regular cycles and improvement in acne. No more spotting.

References

1 Bashiri, Z., N. Sheibak, F. Amjadi, and Z. Zandieh. "The role of *myo*-inositol supplement in assisted reproductive techniques." *Human Fertility* (2022-06-22): 1–17. Online ahead of print.

2 Gambioli, R., G. Forte, G. Buzzaccarini, V. Unfer, and A.S. Laganà. "*myo*-Inositol as a key supporter of fertility and physiological gestation." *Pharmaceuticals,* Vol. 14, No. 6 (2021): 504.

3 Greene, N.D.E., K.-Y. Leung, V. Gay, K. Burren, K. Mills, L.S. Chitty, and A.J. Coop. "Inositol for the prevention of neural tube defects: A pilot randomised controlled trial." *The British Journal of Nutrition,* Vol. 115, No. 6 (2016): 974–983.

4 Pundir, J., D. Psaroudakis, P. Savnur, P. Bhide, L. Sabatini, H. Teede, A. Coomarasamy, and S. Thangaratinam. "Inositol treatment of anovulation in women with polycystic ovary syndrome: A meta-analysis of randomised trials." *BJOG,* Vol. 125, No. 3 (2018): 299–308.

5 Unfer, V., F. Facchinetti, B. Orrù, B. Giordani, and J. Nestler. "*myo*-Inositol effects in women with PCOS: A meta-analysis of randomized controlled trials." *Endocrine Connections,* Vol. 6, No. 8 (2017): 647–658.

6 Zhang, J.-Q., C. Xing, and B. He. "Short period-administration of *myo*-inositol and metformin on hormonal and glycolipid profiles in patients with polycystic ovary syndrome: A systematic review and updated meta-analysis of randomized controlled trials." *European Review for Medical and Pharmacological Sciences,* Vol. 26, No. 6 (2022): 1792–1802.

7 Laganà, A.S., A. Vitagliano, M. Noventa, G. Ambrosini, and R. D'Anna. "*myo*-Inositol supplementation reduces the amount of gonadotropins and length of ovarian stimulation in women undergoing IVF: A systematic review and meta-analysis of randomized controlled trials." *Archives of Gynecology and Obstetrics,* Vol. 298, No. 4 (2018): 675–684.

8 Lisi, F., P. Carfagna, M.M. Oliva, R. Rago, R. Lisi, R. Poverini, C. Manna, et al. "Pretreatment with *myo*-inositol in non polycystic ovary syndrome patients undergoing multiple follicular stimulation for IVF: A pilot study." *Reproductive Biology and Endocrinology,* Vol. 10 (2012): 52.

9 Caprio, F., M.D. D'Eufemia, C. Trotta, M.R. Campitiello, R. Ianniello, D. Mele, and N. Colacurci. "*myo*-Inositol therapy for poor-responders during IVF: A prospective controlled observational trial." *Journal of Ovarian Research,* Vol. 8 (2015): 37.

10 Facchinetti, F., M. Appetecchia, C. Aragona, A. Bevilacqua, M.S. Bezerra Espinola, et al. "Experts' opinion on inositols in treating polycystic ovary syndrome and non–insulin dependent diabetes mellitus: A further help for human reproduction and beyond." *Expert Opinion on Drug Metabolism & Toxicology,* Vol. 16, No. 3 (2020): 255–274.

11 Nordio, M., S. Basciani, and E. Camajani. "The 40:1 *myo*-inositol/D-*chiro*-inositol plasma ratio is able to restore ovulation in PCOS patients: Comparison with other ratios." *European Review for Medical and Pharmacological Sciences,* Vol. 23, No. 12 (2019): 5512–5521.

12 Maleki, V., H. Jafari-Vayghan, A. Kashani, F. Moradi, M. Vajdi, S. Kheirouri, and M. Alizadeh. "Potential roles of carnitine in patients with polycystic ovary syndrome: A systematic review." *Gynecological Endocrinology,* Vol. 35, No. 6 (2019): 463–469.

13 Jamilian, M., F. Foroozanfard, E. Kavossian, E. Aghadavod, E. Amirani, M. Mahdavinia, A. Mafi, and A. Asemi. "Carnitine and chromium co-supplementation affects mental health, hormonal, inflammatory, genetic, and oxidative stress parameters in women with polycystic ovary syndrome." *Journal of Psychosomatic Obstetrics and Gynaecology* (2019): 1–9. Online ahead of print.

14 Jamilian, M., F. Foroozanfard, E. Kavossian, M. Kia, E. Aghadavod, E. Amirani, and Z. Asemi. "Effects of chromium and carnitine co-supplementation on body weight and metabolic profiles in overweight and obese women with polycystic ovary syndrome: A randomized, double-blind, placebo-controlled trial." *Biological Trace Element Research,* Vol. 193, No. 2 (2020): 334–341.

15 Ferrazzi, E., G. Tiso, and D. Di Martino. "Folic acid versus 5-methyl tetrahydrofolate supplementation in pregnancy." *European Journal of Obstetrics, Gynecology, and Reproductive Biology,* Vol. 253 (2020): 312–319.

16 Cirillo, M., R. Fucci, S. Rubini, M.E. Coccia, and C. Fatini. "5-Methyltetrahydrofolate and vitamin B_{12} supplementation is associated with clinical pregnancy and live birth in women undergoing assisted reproductive technology." *International Journal of Environmental Research and Public Health,* Vol. 18, No. 23 (2021): 12280.

VITAZAN
PROFESSIONAL

NDMAPS™
Naturopathic Doctor Medical Advancement Panel Solutions

Improved patient outcomes through the collaboration of Vitazan Professional and expert naturopathic advisors

Formulated – Reviewed - Validated

Contact Us

info@vitazan.com
www.vitazan.com