The Promise for PCOS game-changers: myo-inositol supplementation

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Greetings

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- Founder and director of Continental center for women's healthcare (Smouha, Alexandria and Sheikh Zayed, Cairo, Egypt).
- Co-Founder and treasurer of Middle Eastern Society for Adolescent and Pediatric Gynecology (MESPAG).

- PCOS is a public health concern and optimal management is not achieved.
- Nature gifted us with great solutions to our problems.
- A better future for PCOS cases is here.
- The future is `myo-inositol`.

myo-inositol: Not experimental any more

- Inositol is a sugar made in the body and found in foods
- `myo-inositol` and D-chiro-inositol are the most common forms found in supplements.
- `myo-inositol` is naturally present in both animal and plant cells (as a free form or in phospholipids)

- Backbone for numerous secondary messaging signaling
- Essential for proper glucose metabolism.
- Directly involved in cell growth and in reproduction physiology.

- During a physiological menstrual cycle, signals from the hypothalamus–pituitary–gonadal (HPG) axis promote the progression of folliculogenesis through the stimuli of FSH and LH.
- Inositol cascade is primarily involved in the signaling of insulin and gonadotropins.
- In 2018 ESHRE guidelines, it was considered experimental in PCOS management.[1]
- In 2023 ESHRE guidelines, `myo-inositol` became an evidence-based recommendation.[2]

ESHRE 2018

Inositol			
EBR		Inositol (in any form) should currently be considered an experimental therapy in PCOS, with emerging evidence on efficacy highlighting the need for further research.	* ⊕○○○

ESHRE 2023

4.7#		Inositol	
4.7.1	EBR	Inositol (in any form) could be considered in women with PCOS based on individual preferences and values, noting limited harm, potential for improvement in metabolic measures, yet with limited clinical benefits including in ovulation, hirsutism or weight.	❖❖❖ ⊕○○○
4.7.2	EBR	Metformin should be considered over inositol for hirsutism and central adiposity, noting that metformin has more gastrointestinal side-effects than inositol.	❖❖❖ ⊕○○○

- All living cells contain `myo-inositol` phospholipids in their membranes
- Human diet from either animal and plant sources contain `myo-inositol`.
- Now let's **play and guess** which is a good source of `myo-inositol`

- Look for seeds and fresh fruits/vegetables
- Leafy vegetables are poor in `myo-inositol`

Get to Know myo-inositol

- Was once considered to belong to the vitamin B family
- Even if you don't know its values, your body can't ignore it.
  - **de novo synthesis** from D-glucose
- Good **absorption and availability**
  - Nearly 99.8% of ingested amount is absorbed.
  - Normally, the circulating fasting plasma `myo-inositol` concentration = **30 µM**.

myo-inositol and Diabetes

- Disturbed Inositol metabolism is associated with **insulin-resistance**.
  - `myo-inositol` supplementation → insulin-mimetic effects in DM and PCOS models.
- Low concentration predicts long-term DM **microvascular complications**.
  - In DM complicated kidney, sciatic nerve, retina and lens, depletion of intracellular `myo-inositol` is documented human subjects.[3]

Magical Spell for PCOS

Associated with improvement in:

1. Hyperinsulinemia.
2. Metabolic parameters.
3. Hyperandrogenism.
4. Ovarian function.
5. Ovulation induction.
6. Oocyte quality.
7. Embryo quality

- `myo-inositol` supplementation seems to be a simple, safe and effective first-line treatment for women with PCOS.[3]
- Main **mechanism of action**:[3]
  - Improving **insulin sensitivity** of target tissues,
  - Refreshing the reproductive axis, and
  - Better hormonal functions (reduction of clinical and biochemical hyperandrogenism and of dislipidemia).

More PCOS magic with myo-inositol

- Improved insulin peripheral **sensitivity** and insulinemia.[3]
- Leaner **anthropometric** measurments (after 16 weeks or more of treatment).[3]

- **Hormonal parameters:**[3]
  - ↓ LH, FSH,and testosterone circulating levels, and
  - ↑ SHBG, estrogens and progesterone circulating levels
  - Restore spontaneous ovarian activity
  - ↑ Fertility

- **Cardiovascular parameters:**[3]
  - ↓ systolic and diastolic blood pressure,
  - ↓ plasma triglycerides,
  - ↑ HDL cholesterol,
  - ↓ LDL and total cholesterol concentrations.

- A meta analysis revealed that effects of `myo-inositol` supplementation trespassed achieving conception.[4]
- Interestingly, `myo-inositol` proved to be a significant supporter of physiological gestation as well fertility
- `myo-inositol` supplementation was associated with successful ovulation and restoration of regular cycles.

- Additionally, significantly lower odds of GDM was seen in patients who received `myo-inositol`.

- Encouraging data from clinical trails of `myo-inositol` have been consistently published
  - Reviews of published studies available since 2012.
- A 2014 **review** provided level Ia evidence of significant improvements in hormonal and reproductive aspects of PCOS cases.[5]

- **Not only abundance, but balance**
  - In PCOS cases, an imbalance between Inositol isomers (mainly myo- and chiro-inositol) leads to a reduction in insulin and FSH signaling.[6]
  - A myo- to chiro-inositol ratio of **40:1** is thought to be physiological for most tissues

Superior ART outcomes with `myo-inositol`

- Pre-treatment of `myo-inositol` is a very new method that was evaluated in multiple small studies to manage poor ovarian response in assisted reproduction.
- Increasing evidence indicates that inositols play a vital role, namely in **oocyte and spermatozoa development**.[6]

- Via both petentiated **signaling** and appropriate **glucose** for growth maturation.[7]
  - In the ovary, `myo-inositol` mediates the granulosa response to FSH stimuli.[7]
- It also plays a crucial role in determining oocyte maturation.[7]
  - Adequate `myo-inositol` (in PCOS cases) = proper glucose available for growing oocytes.[6]

Supplementation with `myo-inositol` during ART

- In both PCOS and non-PCOS women, with `myo-inositol` supplementation during ART:
  - Lower amount of **gonadotropins** required
  - Better **oocyte quality and maturation**
  - Healthier **embryo development**, and
  - Significantly higher rate of **successful pregnancies**.

But what about Metformin?

- Recent studies further empower `myo-inositol` as a competitive insulin sensitizer.
- Direct comparative studies vs. Metformin were conducted

myo-inositol vs. Metformin in PCOS

- A **RCT** reported that while improvements in anthropometric measurements were noted with both `myo-inositol` and metformin, the magnitude of improvement was **comparable** between the two treatments.(8)
- A 2023 **meta-analysis** concluded that both are **equally beneficial** in improving metabolic and hormonal parameters.(9)
- **In ART:** A 2022 study reported that `myo-inositol` was associated with significantly **better outcomes** in PCOS women receiving **antagonist cycles**.(10)

- **`myo-inositol`** was reportedly **safer** than Metformin.
- Adverse events were 5 times more common with Metformin compared to `myo-inositol`.(11)
  - With Metformin: abdominal pain, lactic acidosis, and generalized weakness.
  - With `myo-inositol`: nausea, mild diarrhea, and menorrhagia.

Haven't she heard about `myo-inositol`?

Coenzyme Q10

- Coenzyme Q10 (CoQ), is an endogenous lipophilic quinone.
- CoQ10 supplementation was linked to:
  - Greater response to **ovulation induction**.
  - Decreased odds of fetal **aneuploidy**.
  - Lower cycle **cancellation rate**.
  - Higher odds of a **clinical pregnancy**.

Even in women older than 35 years, CoQ10 is associated with:[12]

- Larger **quantity** and better **quality** of oocytes.
- Optimized oxidative metabolism of **follicular fluid**.
- Boosted **mitochondrial function** of oocytes.
- Better odds of a successful pregnancy.


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UN WOMEN

Methylfolate

- myo-inositol is not the only supplement with growing supporting evidence in PCOS.
- Methylfolate is now believed to be a superior approach to folic acid supplementation.
- Supplementation with methylfolate is as effective as treatment with folic acid.
- However, unlike folic acid, methylfolate is an active compound and doesn't need enzymatic transformation.

- This is why methylfolate is not affected by functional polymorphisms in Methylenetetrahydrofolate reductase (MTHFR) gene.
- MTHFR gene mutation can cause infertility and/or recurrent pregnancy loss if methylfolate is not supplemented.

- Recently developed drug compounds now include both myo-inositol and methylfolate supplementation with required doses.


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Take Home Message

It’s `myo-inositol`, sweet and discreet,

Found in beans, fruits, and whole grains you eat.

It whispers to cells, “Let insulin in,”

And helps ovaries get back to their spin.

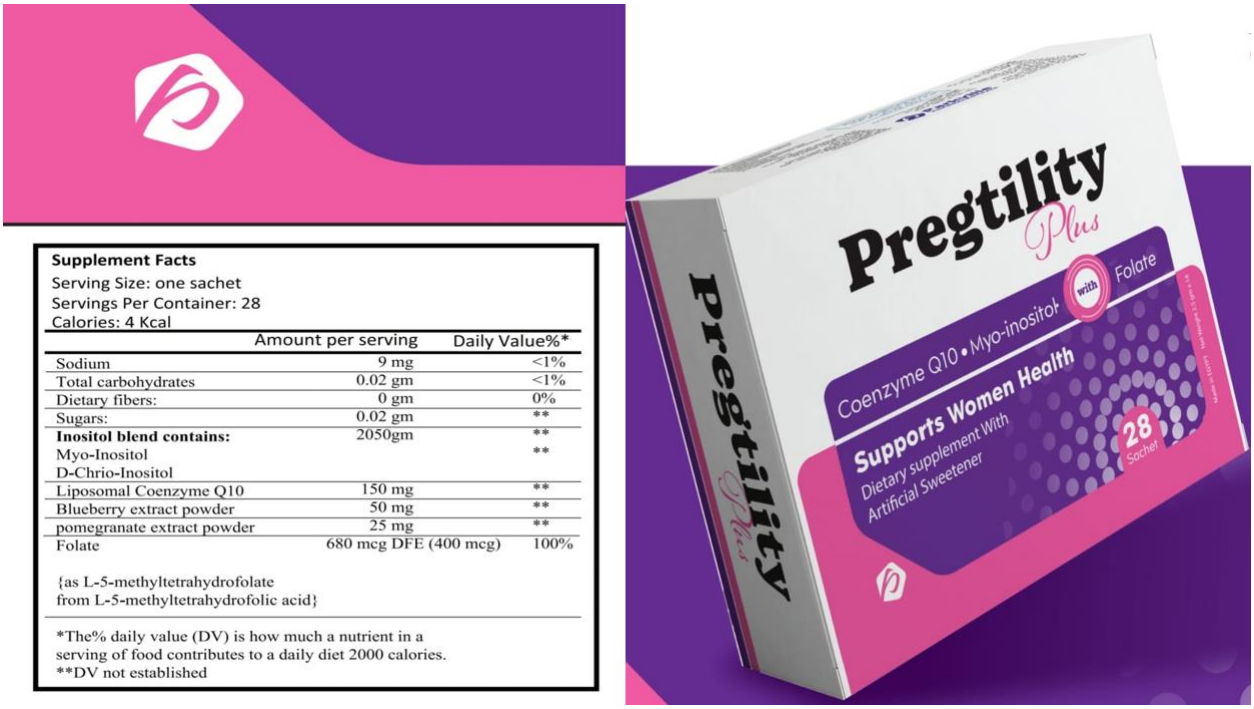
No medals, no thanks, not even a clap—

Just hiding in food like a watchful champ.

It helps with the sugar, the cycles, the skin—

But no one says, “Hey! That’s what helped me win!”

On the Shelf



Supplement Facts

Serving Size: one sachet
Servings Per Container: 28
Calories: 4 Kcal

	Amount per serving	Daily Value%*
Sodium	9 mg	<1%
Total carbohydrates	0.02 gm	<1%
Dietary fibers:	0 gm	0%
Sugars:	0.02 gm	**
Inositol blend contains:	2050gm	**
Myo-Inositol		**
D-Chrio-Inositol		
Liposomal Coenzyme Q10	150 mg	**
Blueberry extract powder	50 mg	**
pomegranate extract powder	25 mg	**
Folate	680 mcg DFE (400 mcg)	100%
{as L-5-methyltetrahydrofolate from L-5-methyltetrahydrofolic acid}		

*The% daily value (DV) is how much a nutrient in a serving of food contributes to a daily diet 2000 calories.
**DV not established

Bloom Ville
iron
Capsules

28mg to grow and glow

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THE STORY BEHIND INNOVA3 CO-ENZYME Q10 XTEND

INNOVA3 CO-ENZYME 10 XTEND is the most advanced formulation for CO-ENZYME 10 existing in the market. To give a better understanding of INNOVA3 CO-ENZYME Q10 XTEND, we will explain the exact design, features, and properties of our molecule.

CO-ENZYME Q10 XTEND

We have developed thermostable and UV resistant Co-Enzyme Q10 moelcule, that gives maximum stability to overcome the theromdegredable drawback of CO-Enzyme Q10. Such formulation is named under **"CO-ENZYME Q10 XTEND"**

We have designed the Co-Enzyme on the molecule level as well as on the carrier level.

Such technology combination gives our molecule a superiority over conventional Co-Enzyme in every aspect of pharmacokinetics, bioavailability, cell targeting, and efficacy.

MICELLE DEVELOPMENT

After developing the main thermostable molecule, we combined the molecule into micelle for target organ delivery. That is the **DRONECELL Technology**, that makes the molecule ready for specific mitcochondrial uptake without efflux

LipoSEL CARRIER

Next step, started by incorporating the CO-Enzyme Xtend Micelle into Self Emysifying Liposomal carriers (LIPOSEL), to improve the bioavailability and overcome the solubiloty issue thorught GIT Portal Blood Circulation

LipoLYM CARRIER

Another types of liposomal carriers are developed to improve absorbtion throught lymphatic route using LIPOPHILIC Carriers (LIPOLYM)

QR code for slides and references

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