

THE DIFFERENCE BETWEEN INOSITOL, MYO-INOSITOL AND D-CHIRO INOSITOL

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Introduction

The history of inositol is a fascinating and somewhat complex story. **It is also an ancient story, as inositol exists since there is life on earth.** Molecule with great stability, inositol plays key functions at biological level so important as to be considered as prebiotic molecule.

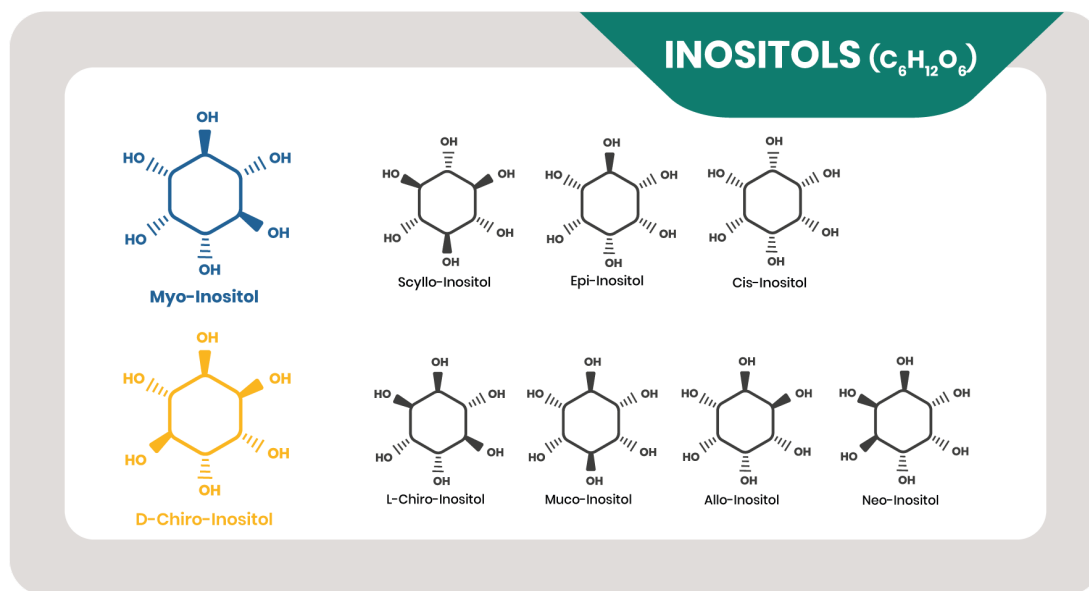
INOSITOL PLAYS KE FUNCTIONS AT BIOLOGICAL LEVEL

But what is inositol? What is it for? And, above all, what difference is there between myo-inositol and d-chiro-inositol? From the United States, to China, to Italy, **we retrace the key steps of scientists and researchers who have studied the functions, differences and therapeutic**

applications of inositols since their discovery. So let's start from **1850** when **Johanes Joseph Scherer** first **isolated inositol** from a muscle, which it takes its name from (inos = muscle in Greek).

What is inositol?

Inositol is a natural molecule found in the phospholipids of cell membranes, in the lipoproteins of the plasma and, in the form of phosphate, in the cell nucleus. When we talk about inositol, we actually refer to a group of **nine different stereoisomers**, so it would be more correct to use the plural "Inositols". Among these, however, **the term inositol is generally used to refer to the most bioavailable type, myo-inositol.**

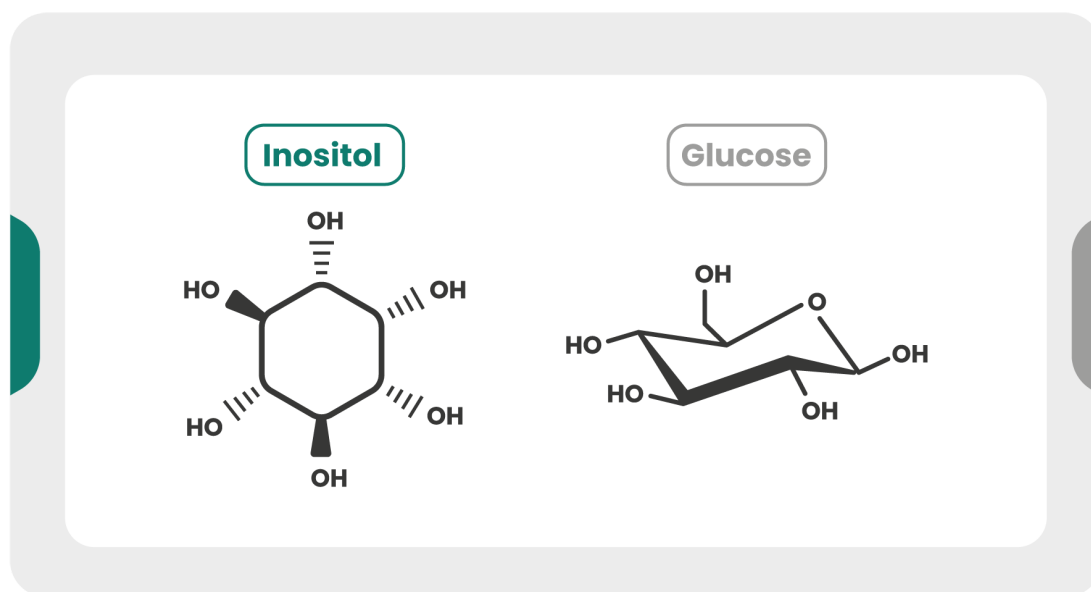


THE TERM INOSITOL IS GENERALLY USED FOR REFER TO THE MOST BIOAVAILABLE TYPE, MYO-INOSITOL

After Scherer's discovery, several researchers dedicated their time to the study of myo-inositol in organs over the following years. In **1964, Eisenberg and Bolden** discovered that the testes were rich in free myo-inositol, as well as the seminal fluid, where the concentration is almost triple that found in plasma [1].

Difference between myo-inositol and d-chiro inositol

Myo-inositol has a chemical structure similar to glucose and is involved in cell signaling. In particular, it is able to stimulate glucose uptake, promoting the decrease in blood levels.



D-chiro inositol, myo-inositol stereoisomer, is also involved in insulin signaling: both, as inositolophosphoglycans, are "second messengers of

insulin". However, although their biological functions are often confused, **it is good to remember that they play different roles.**

MYO AND D-CHIRO INOSITOL, AS INOSITOLPHOSPHOLIPIDS, ARE BOTH "SECOND MESSENGERS" OF THE INSULIN, BUT THEY CARRY OUT DIFFERENT FUNCTIONS.

It was the scientist **Larner in 1988** who intuited that **myo-inositol and d-chiro inositol were part of two different insulin chemical mediators.** Although very similar, the functions of the two isomers are different. In fact, myo is involved in the transporters activation and the use of glucose, while d-chiro is involved in the glycogen synthesis and storage.

MYO-INOSITOL IS INVOLVED IN THE TRANSPORTERS ACTIVATION AND THE USE OF GLUCOSE, WHILE D-CHIRO IS MAINLY INVOLVED IN THE GLYCOGEN SYNTHESIS AND STORAGE.

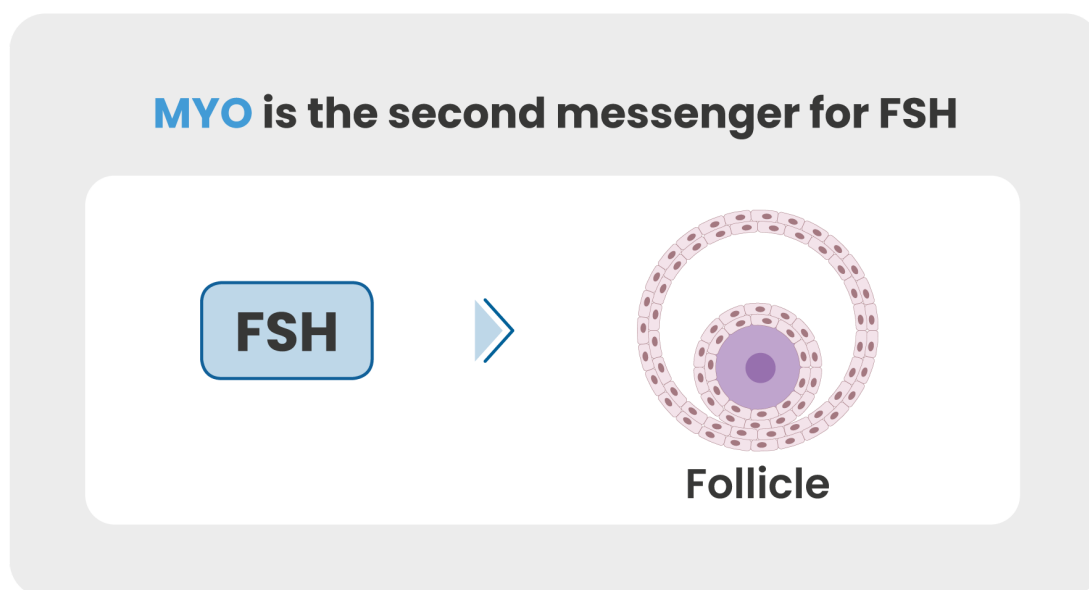
The differences between the two molecules were in-depth studied **in the attempt to find a therapeutic response to a syndrome known as PCOS or polycystic ovary syndrome.**

Myo and D-Chiro in PCOS

As anticipated, it was Larner **in the late 1980s** who first supposed that myo-inositol and d-chiro-inositol were

part of two different insulin chemical mediators. In the same years, in the gynecological field, **PCOS (polycystic ovary syndrome)** started to be correlated to the insulin resistance and hyperinsulinemia. It was shown that the ovary has insulin receptors and that the androgens production depends on them. At ovarian level, myo and d-chiro inositol play different roles:

- **myo-inositol** mediates **glucose uptake** and **FSH signal** (follicle stimulating hormone).



- **d-chiro-inositol** is involved in the insulin-dependent synthesis of androgens and promotes glucose storage.

In the ovaries of a healthy woman, 99% of the inositol intracellular pool is made up of Myo-inositol, while the remaining part is made up of D-chiro-inositol. **Another important difference between myo and d-chiro is the respective presence and distribution in the tissues.** In

fact, each tissues regulates the production of the two inositols myo and d-chiro in such a way to always have a specific ratio [2].

MYO AND D-CHIRO INOSITOL HAVE A DIFFERENT DISTRIBUTION IN THE TISSUES

In **PCOS women**, we observe a **myo deficiency at ovarian level** causing an impairment of the FSH signal. Research has also showed how d-chiro is synthesized from myo-inositol. In other words, **a small amount of myo-inositol is converted into d-chiro inositol** by an **enzyme** called **epimerase** which in turn is stimulated by insulin.

Therapeutic uses of myo-inositol

In **1992 Prof. Chiu**, a researcher at the University of Hong Kong, **was one of the first to demonstrate the efficacy of the myo-inositol treatment in women seeking pregnancy**, strengthening the correlation between the presence of myo-inositol and fertility. Today, myo-inositol represents a safe and effective therapy that finds therapeutic application for various ailments and pathologies:

- In **PCOS**, the administration of myo-inositol resulted in the remission of symptoms and the reduction of male hormones secretion; but also the regulation of cholesterol levels, a more efficient breakdown of fats with a consequent decrease in appetite and weight. (Also read: Myo-inositol and polycystic ovary syndrome)

- As regard **male infertility**, inositol has improved, according to several studies, motility and sperm count, while it improves the oocyte and embryonic quality in women.
- Again, myo-inositol induces an increase in the sensitivity of the serotonin receptor, also known as the good mood hormone, **with benefits on anxiety disorders**.
- The benefits of inositol have been also investigated as regard the diabetes and the **prevention of metabolic syndrome**.

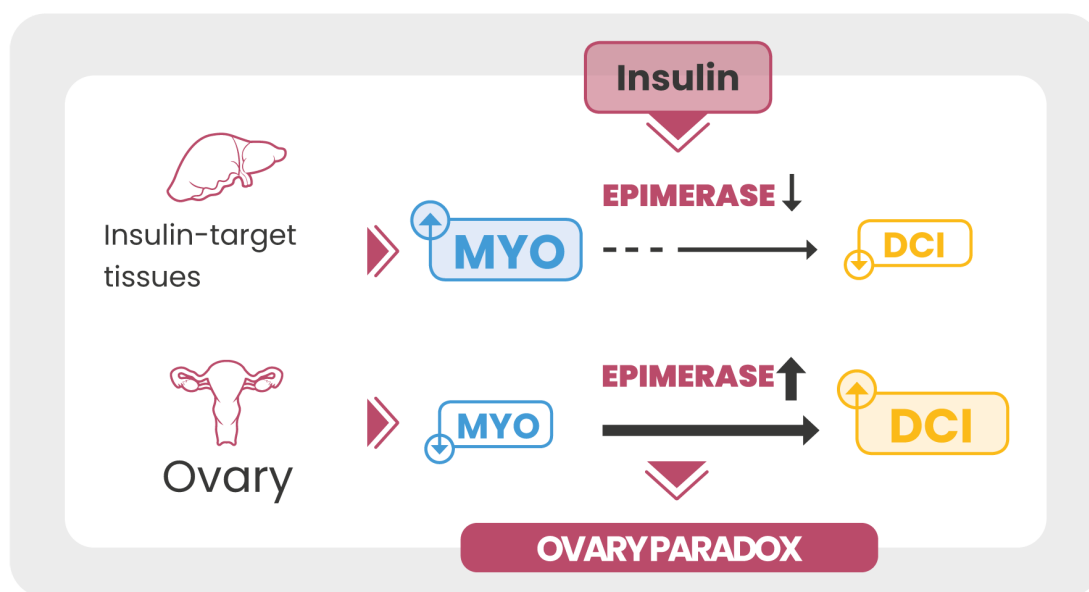
D-chiro-inositol

The use of D-chiro-inositol alone to treat **PCOS** women dates back to the late 1990s by a group of American researchers. In a well-known study, **Nestler** reported innovative results on the use of d-chiro-inositol for the treatment of PCOS. He showed that with the use of 1.200 mg of D-chiro-inositol for 8 weeks, it was possible to improve insulin sensitivity, ovarian function, reduce androgens and triglyceride levels in obese PCOS patients, and restore the menstrual cycle . **Unfortunately, these apparently surprising results were not reconfirmed in subsequent studies**. A crucial difference compared to the first clinical trials concerned precisely the dosages of D-

chiro inositol, increased to 2.400 mg. These results led to an interruption of the trials. [1]

THE FIRST POSITIVE RESULTS ON D-CHIRO INOSITOL WERE NOT RECONFIRMED IN THE FOLLOWING STUDIES, SO MUCH THAT THE RESEARCH WAS STOPPED. WHY?

As anticipated, d-chiro-inositol is partially converted by Myo through epimerase, an insulin-sensitive enzyme. Myo-inositol is instead the most abundant. But, in compromised health conditions such as PCOS, the situation changes. In fact, **in PCOS women the activity of the epimerase enzyme is increased: this induces a substantial reduction of Myo and D-chiro ratio at intraovarian level, because there is an enhanced conversion of myo to d-chiro due to the excessive levels of circulating insulin.**



This phenomenon, better known as the **ovarian paradox**, arises from an intuition, subsequently **demonstrated through experimental data**: since **the ovary is never insulin resistant** and that the activity of epimerase (mediated by insulin) was more understood in women PCOS, causing a myo-inositol deficiency and therefore a reduced oocyte quality [3].

THE INTUITION ON OVARIAN PARADOX, SUPPORTED BY CLINICAL EVIDENCE SHOWING THE EFFECTIVENESS OF MYO-INOSITOL-BASED TREATMENTS OF PCOS AND FOR FERTILITY, OFFER AN ANSWER TO THE CONTRADICTIVE RESULTS ON THERAPIES WITH HIGH DOSAGE OF D-CHIRO-INOSITOL ALONE FOR PROLONGED PERIODS.

However, the role of d-chiro in reducing insulin levels remains irrefutable.

Myo and D-chiro 40:1: a question of balance

Starting from the intuition on the ovarian paradox, and the different roles that myo and d-chiro play, a group of Italian scientists focused the attention on the importance of **a correct myo and D-chiro inositol supplementation**, taking into account the need **to restore the impairment by restoring the correct myo/d-chiro ratio at ovarian level too.**

But the question is: which is the optimal dosage to take advantage of the d-chiro-inositol efficacy without compromising the ovarian functionality?

To answer this question, we try to summarize some fundamental assumptions, reaffirmed in a review published recently in one of the most authoritative endocrinology journals in the world, Cell Press [4]. 1) **The myo/d-chiro-inositol ratio is specific tissue.** 2) In healthy women, Myo and D-chiro physiological ratio in the follicular fluid is 100:1, namely a myo-inositol abundance and only a small part of d-chiro inositol [5]. 3) In **PCOS** women, **at ovarian level, this ratio is dramatically altered** to the detriment of myo-inositol, while there is an excess of d-chiro inositol, due to the high epimerase activity and hyperinsulinemia [3]. 4) **Myo deficiency at ovarian level in PCOS women compromises the FSH signal**, the key hormone for follicles maturation, resulting in a **reduced oocyte quality**, anovulation and subfertility. Therefore, Myo-inositol plays a crucial role in FSH signaling, oocyte maturation and embryonic development [4]. 5) Unlike myo-inositol, **the role played by d-chiro-inositol at ovarian level remains controversial**, with a worsening of the oocyte quality and ovarian response when **high doses of d-chiro inositol for prolonged periods are used** [6].

Conclusions

Finally, considering the specific Myo and D-chiro-inositol ratio (remember the 100:1 ratio in the ovary) and the different physiological roles of the two inositols, the combined oral therapy of Myo and D-chiro inositol in the 40:1 ratio (the physiological plasma ratio) has been proposed as an alternative and effective treatment for PCOS women [4].

Sources

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