# Caronositol Fertility®

D-Chiro-Inositol & Myo-Inositol 1:3.6

## *A NATURAL COMPREHENSIVE APPROACH FOR INFERTILE WOMEN WITH POLYCYSTIC OVARY SYNDROME*

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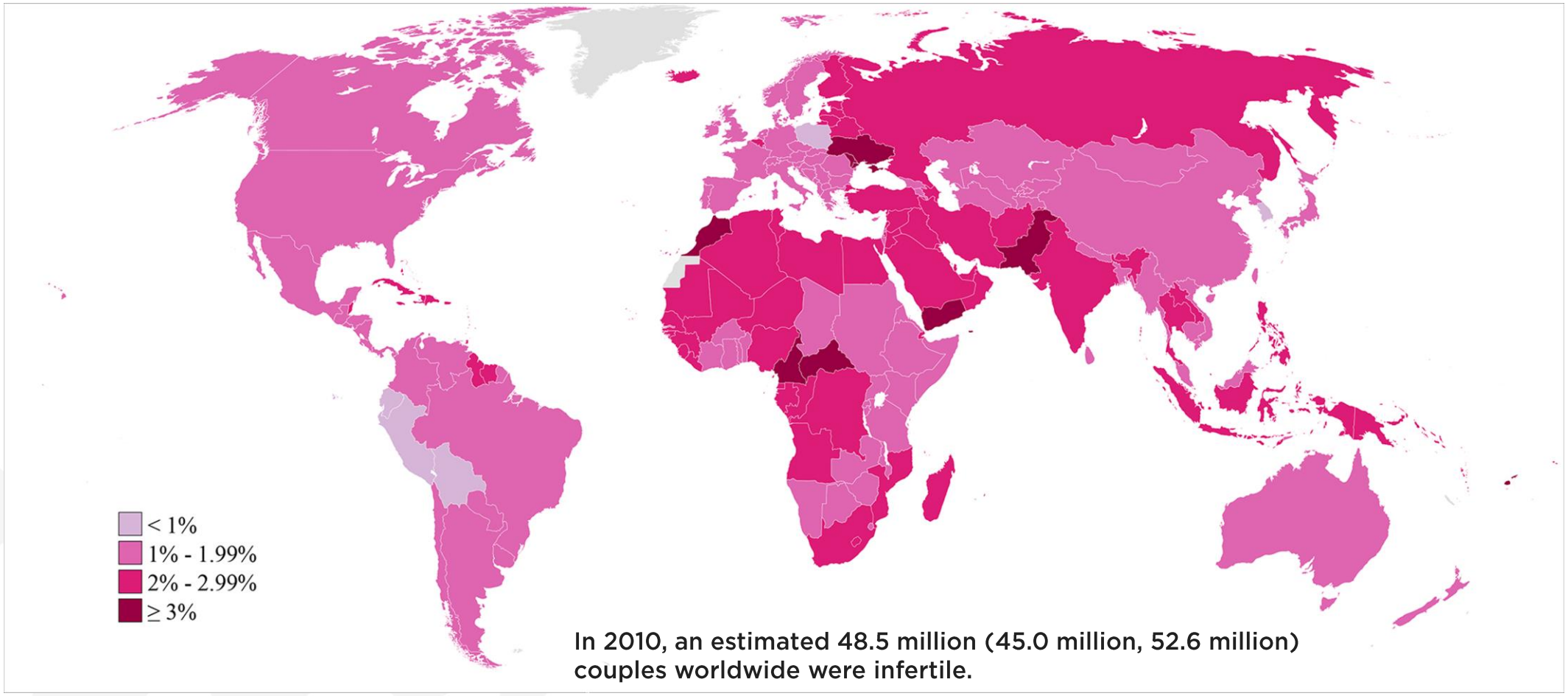
# INFERTILITY PREVALENCE

# NATIONAL, REGIONAL, AND GLOBAL TRENDS IN INFERTILITY PREVALENCE SINCE 1990: A SYSTEMATIC ANALYSIS OF 277 HEALTH SURVEYS

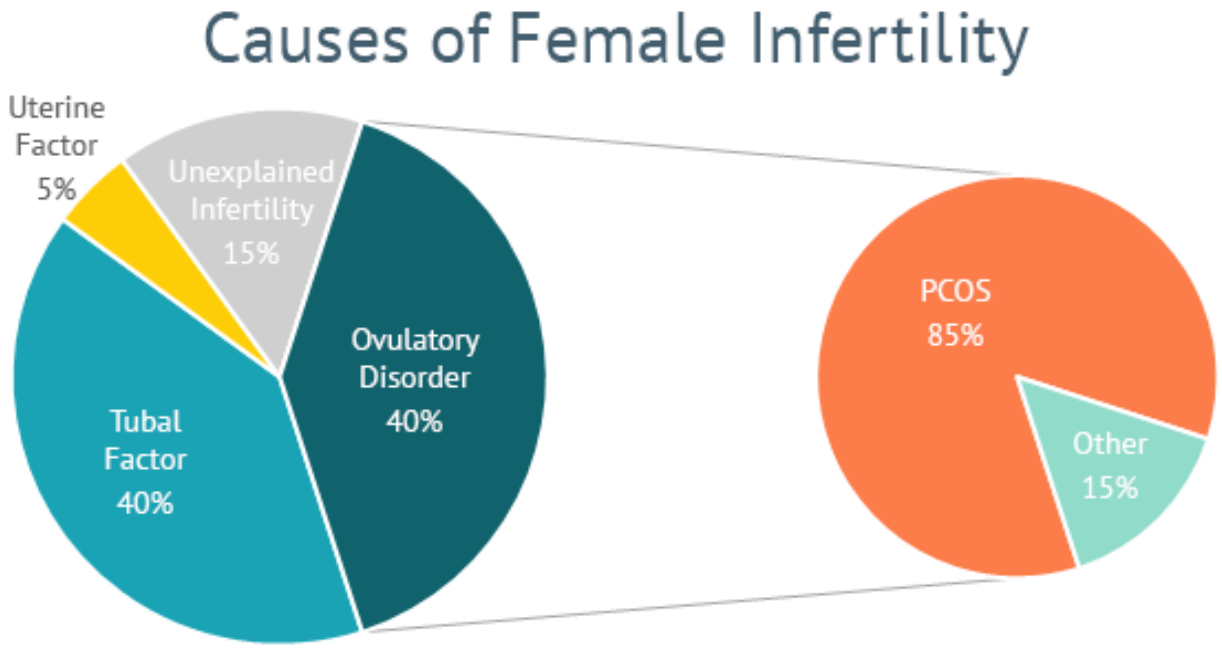



Prevalence of primary infertility among women who seek a child, in 2010.
Infertility prevalence is indexed on the female partner; age-standardized prevalence among women aged 20–44 y is shown here.

Source: WHO

# INFERTILITY CAUSES

# CAUSES OF FEMALE INFERTILITY




PCOS affects approximately 5 to 10 percent of the population, and is most prevalent in Hispanics and African Americans. Recent studies also suggest that there is a rising rate in women of Asian descent.

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Source: Dr. Celso Silva, Shady Grove Fertility Tampa Bay Medical Director. https://www.shadygrovefertility.com/blog/diagnosing-infertility/pcos-one-size-doesnt-fit-all/

# POLYCYSTIC OVARY SYNDROME

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# ¿WHAT IS POLYCYSTIC OVARY SYNDROME?

- It is a highly prevalent **endocrine-metabolic disorder**
- It is the **most common cause of anovulation** and **sterility** in women of reproductive age
- Main characteristics: **hyperandrogenism** and **chronic anovulation**

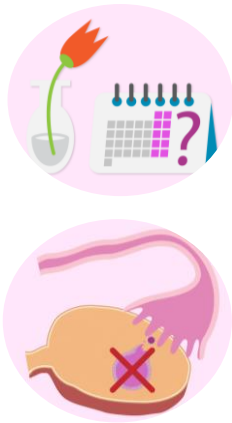
# POLYCYSTYC OVARY SYNDROME (PCOS)

**Consensus Rotterdam** of American Society for Reproductive Medicine (ASRM) – European Society for Human Reproduction and Embryology (ESHRE), for **diagnostic criteria** on PCOS:

**PCOS is characterized by two of three basic symptoms:**

- **OLIGO-OVULATION** and/or **ANOVULATION**
- **HIPERANDROGENISM**
- **POLYCYSTIC OVARY,** it is defined as the existence of 12 or more follicles (diameter between 2-9 mm) and/or ovarian volume greater than 10 mm.

# CLINICAL SYMPTOMS

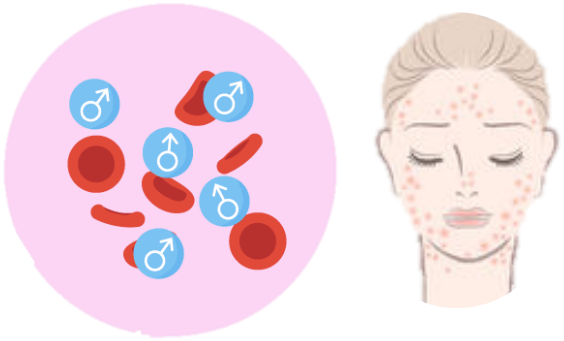


## 1 OLIGO-OVULATION and/or ANOVULATION

- **MENSTRUAL DISORDERS**: Oligomenorrhea or Amenorrhea (90% of women have chance of being diagnosed with PCOS)
- **ANOVULATION** produced by high levels of testosterone and luteinizing hormone (LH)

# CLINICAL SYMPTOMS

## 2 HIPERANDROGENISM



- **SKIN DISORDERS:**
  - **Hirsutism 70% of women with PCOS) : is produced by high levels of testosterone**
  - **Acne**
  - **Acanthosis nigricans**
  - **Alopecia**

# CLINICAL SYMPTOMS

## 3 POLYCYSTIC OVARY AND OVARY SIZE

- DISCOMFORT AND ABUNDANT BLEEDING

# CARONOSITOL FERTILITY

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# Caronositol Fertility®

*D-Chiro-Inositol & Myo-Inositol 1:3.6*

Caronositol Fertility® is the perfect combination of MYO-INOSITOL and D-CHIROINOSITOL for women with fertility problems associated to Polycystic Ovary Syndrome.

It has a clinical study, which evidences its effectiveness and the clinic's patent.

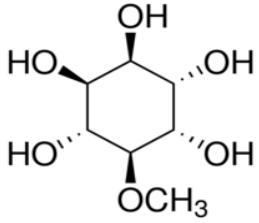
# INGREDIENT'S ORIGIN

# NATURAL ORIGIN
## (D-CHIRO-INOSITOL & MYO-INOSITOL)

DCI is obtained from the fruit of the Carob Bean Tree by the following process:

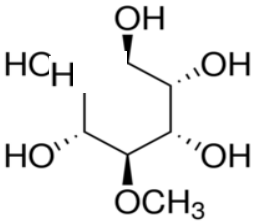
PATENT NUMBER
EP015002231

PHYSICAL PROCESS
EXTRACTION




D-PINITOL

ACID
HYDROLISIS




D-CHIRO-
INOSITOL

The origin of MYO is natural, it is obtained from the Corn's Phytin through a process that includes purification.

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# MECHANISM OF ACTION

# EFFECTS OF DCI


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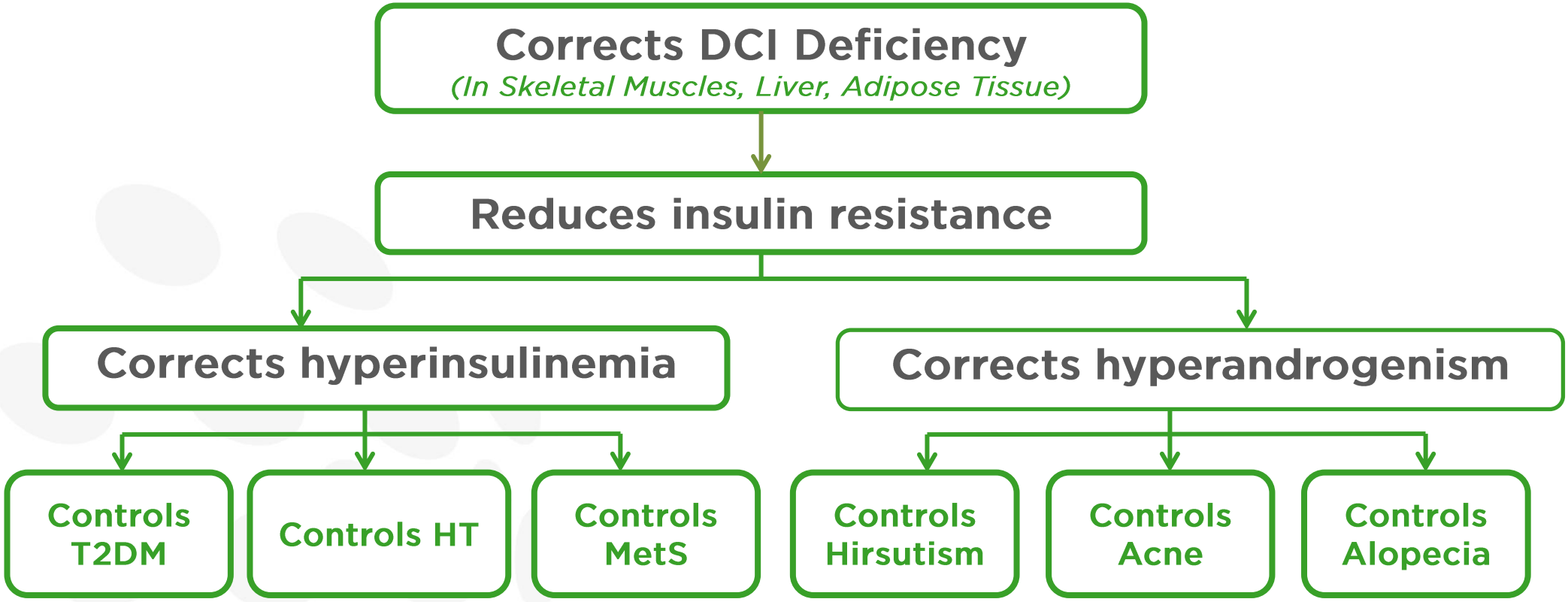
# EFFECTS OF DCI

## (D-CHIRO-INOSITOL)



# EFFECTS OF DCI

- **Oligovulation and/or anovulation**

Administration of DCI increases progesterone levels by 35% versus placebo

- **Oxidative stress in follicular fluid**

DCI reduces oxidative stress

- **Reduce levels of lutenizing hormone (LH)**

Reduces LH hormone levels by 55% and improve the FSH/LH ration by 44%

- **Androgen/estrogen imbalance**

Reducing the levels of LH, DCI helps to regulate the androgen/estrogen imbalance

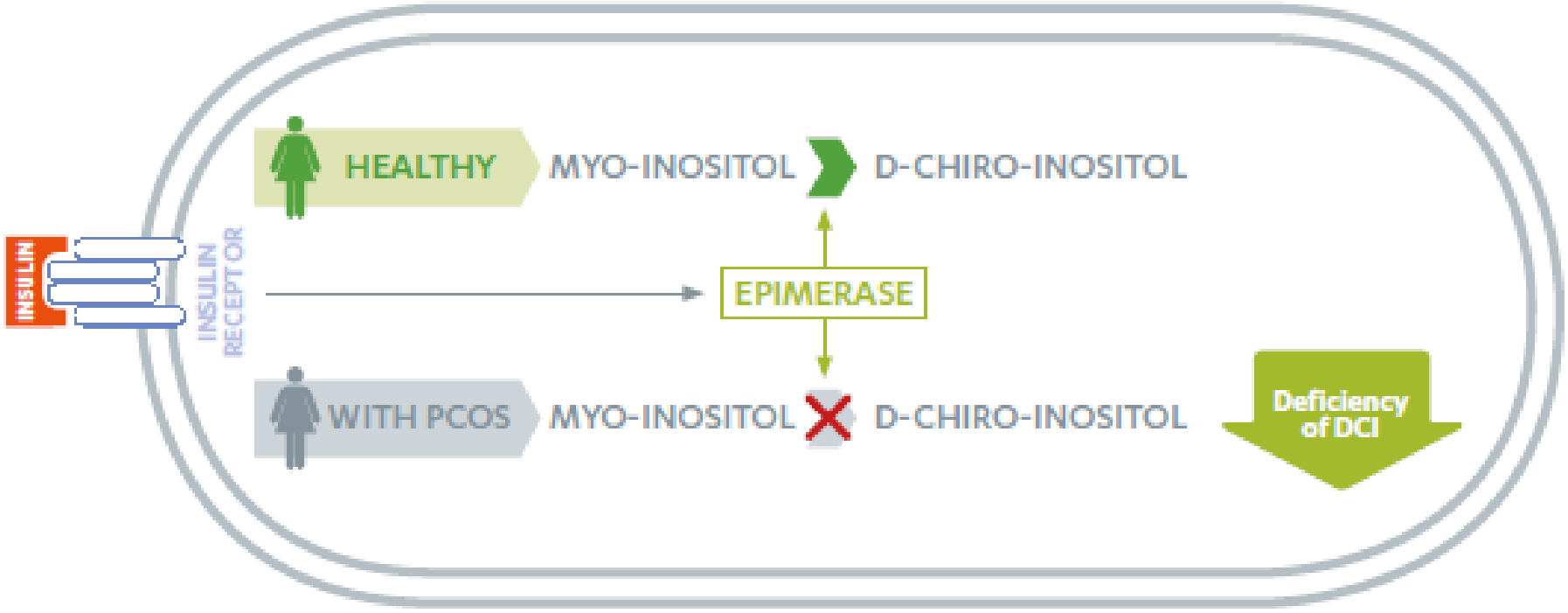
# EFFECTS OF MYO-INOSITOL (MYO)

- Myoinositol is the most abundant inositol in the human body and is the precursor to DCI
- Myoinositol is present in human follicular fluid, at high concentrations, having a positive role in follicular maturation, resulting in a good product for ovulation induction in women suffering PCOS.
- Myoinositol improves the quality of oocytes and promotes meiotic progression of germinal vesicles from oocytes with improved intracellular calcium balance
- Myoinositol is more effective than metformin restoring normal ovulation and pregnancy outcome favoring.

# MECHANISM OF ACTION CARONOSITOL FERTILITY

## (GENERAL TISSUES)

- DCI is synthesized through an epimerase that converts MYO into DCI.
- A decrease in the action of this epimerase is related with lower values of DCI and, as a result, promotes resistance to insulin and leads to different metabolic complications.



# MECHANISM OF ACTION CARONOSITOL FERTILITY

## (GENERAL TISSUES)

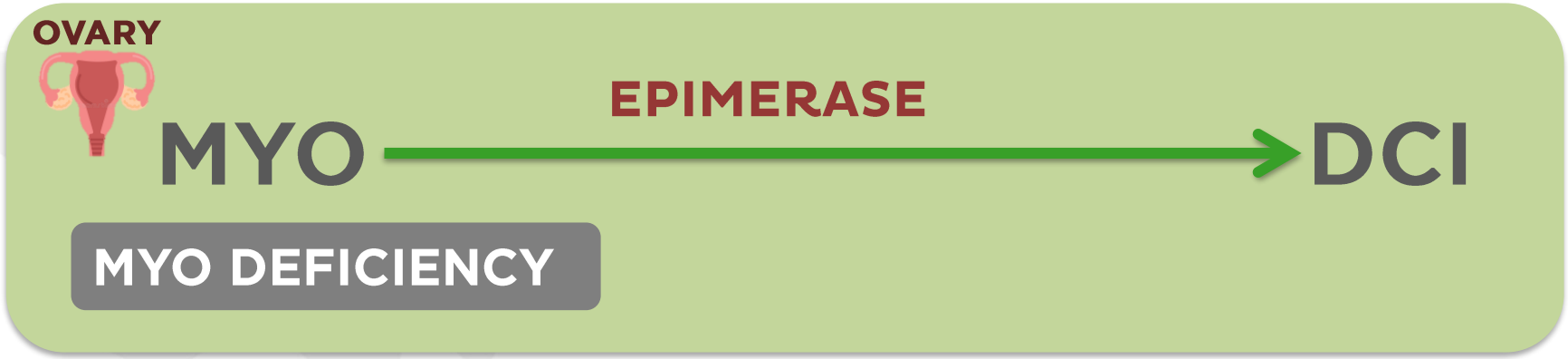

**Sistemic defiency** of DCI due to a :

- ↓ **Epimerase activity**
- ↑ **Urinary loss of DCI**

**As consequence, level of DCI in tissues can decrease importantly**

# MECHANISM OF ACTION CARONOSITOL FERTILITY (OVARY)

The situation is different in the ovary: deficiency of MYO




**Use of combination of MYO and DCI is recomended for PCOS treatment**

# RATIO 40:1 AND FERTILITY

Fertility studies in PCOS are done with MYO / DCI combination in the ratio 40: 1

Experts point out that the important thing is not the physiological ratio but

**to provide the amount of each inositol needed to restore optimal concentrations in each tissue**

# ABSOLUTE CONCENTRATION OF MYO AND DCI

Biosynthesis of MYO occurs endogenously , primarily in the kidney with a rate approaching **4g/day**

## Conversion rate:

## 7-9%


**The absolute concentrations of either MYO or DCI is more important than physiological ratio**

# CONCLUSION

The dosage of administration of each inositol should be one that is able to reestablish an adequate tissue content of the inositols derivatives to exert their physiological effects improving the functional deficiencies associated with PCOS

# CLINICAL STUDY

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# New clinical study

# by

BIOSEARCH LIFE

## RATIO

## DCI:MYO 1:3.6

## Caronositol

## Fertility®

# CLINICAL STUDY

## Comparison of the effect of a combination MI:DCI with low DCI proportion (40:1) vs. the combination with higher DCI proportion Caronositol Fertility® (1:3.6) on oocyte quality and pregnancy rates in women suffering Polycystic ovary syndrome

Mendoza et al. Manuscript under submission

**57 Women**

**Low-DCI Group: 24 volunteers receive low DCI doses (ratio 40:1)**

**High- DCI Group: 28 volunteers receive high DCI doses Caronositol Fertility® (ratio 1:3.6)**

Clinical study: ramdomized, controlled and double blind
Dosage ~ 1100mg MIO/ 300mg DCI (gelatin capsules)

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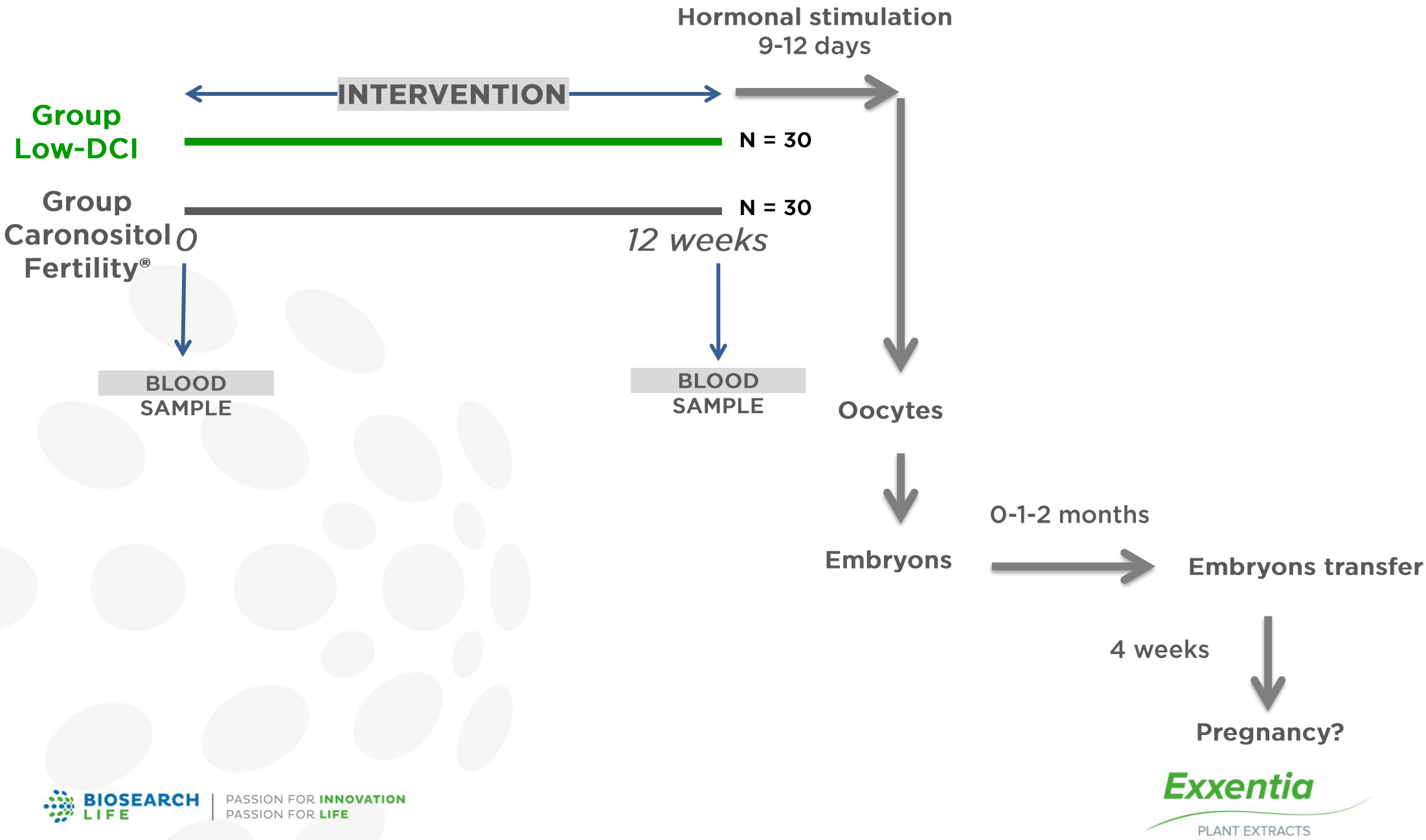
# STUDY DESIGN

| INCLUSION CRITERIA | EXCLUSION CRITERIA |
|---|---|
| **Women >30 years old** | *Advanced stage of endometriosis (III or IV)* |
| **Diagnosis of PCOS according to Rotterdam criteria with intention of IVF treatment** | *Diseases affecting the hormonal response or that may interfere with treatment* |
| **Body Mass Index(BMI)** | |

| RESULTS |
|---|
| **Fertility rate** |
| **Number of embryos** |
| **Glucose** |
| **Insulin** |
| **Testosterone** |
| **Number of oocytes** |

# STUDY DESIGN

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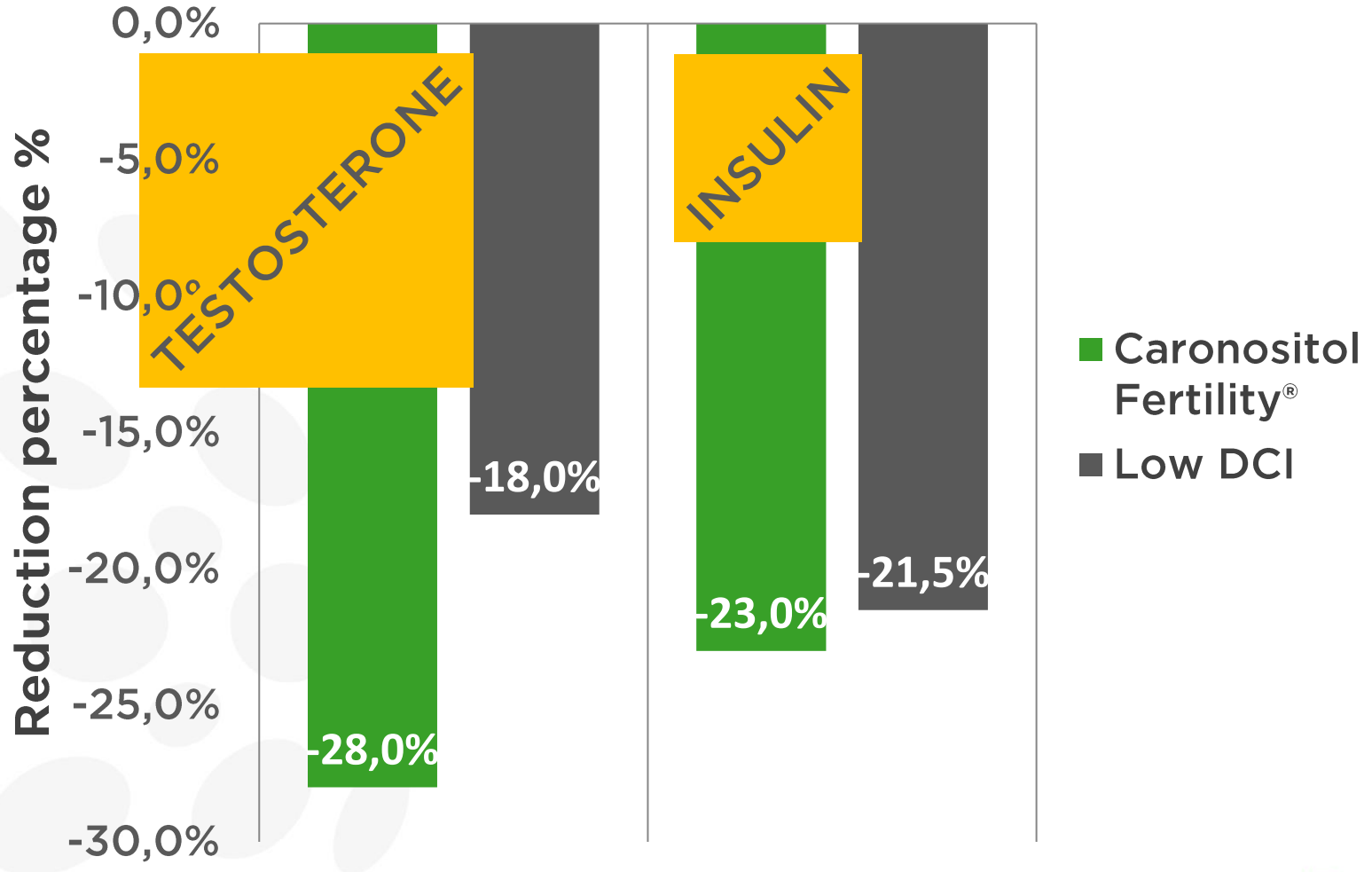
# RESULTS

## Similar levels of testosterone and insulin in both groups

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# RESULTS

## No significant differences between groups

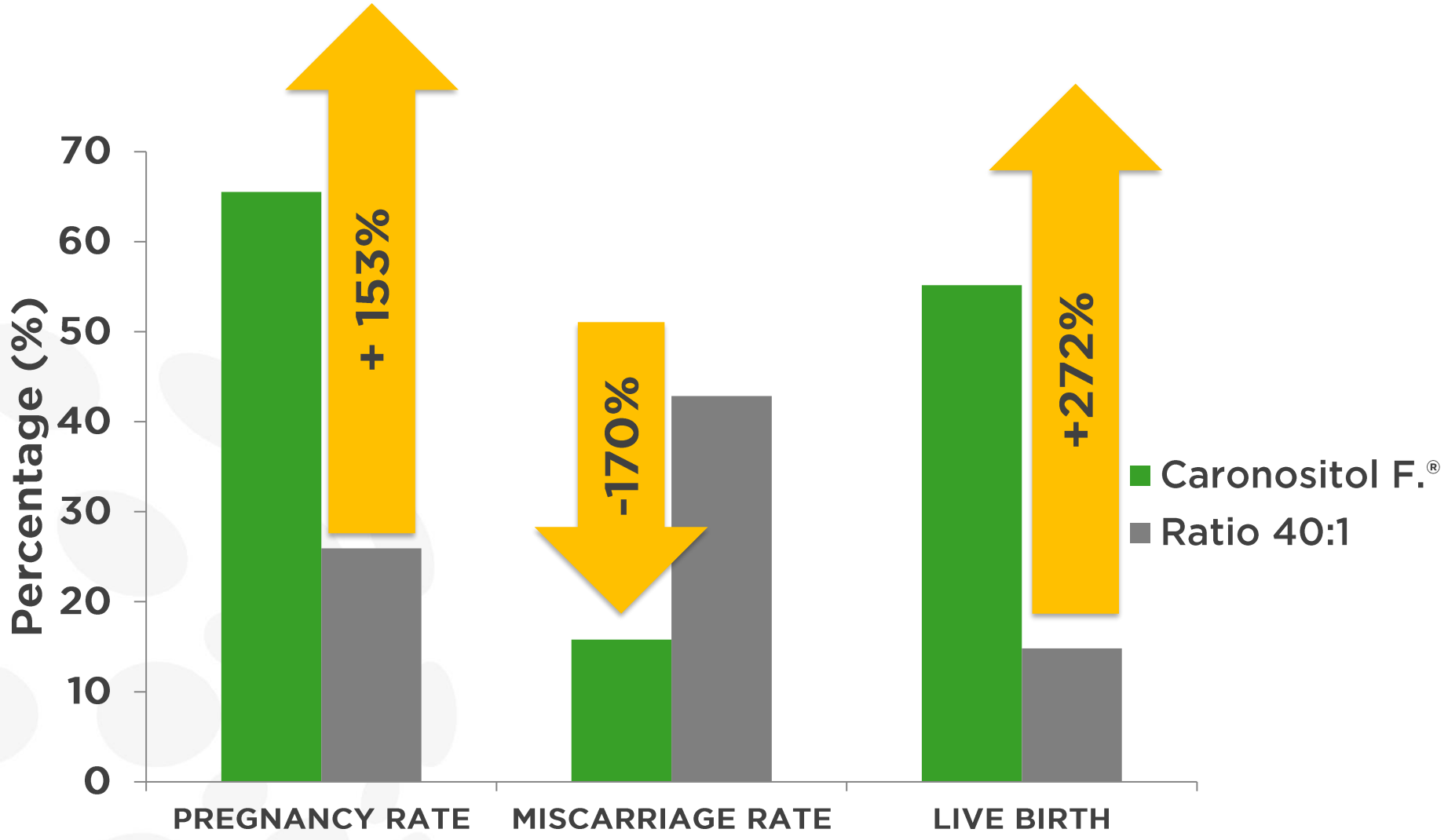
| | Low-DCI | Caronositol Fertility® | p-value |
|---|---|---|---|
| Days of stimulation (days) | 10.38 ± 0.86 | 10.46 ± 1.4 | 0.850 |
| Oocytes (number) | 13.80 ± 6.7 | 13.46 ± 5.1 | 0.850 |
| Oocytes MII (number) | 10.80 ± 7.4 | 10.46 ± 4.5 | 0.848 |
| Total embryos (number) | 7.35 ± 6.6 | 6.88 ± 3.9 | 0.767 |
| Embryos type I | 4.05 ± 5.7 | 3.08 ± 3.6 | 0.481 |

# RESULTS

| | Caronositol Fertility® SG (%) | LOW DCI CG (%) | p-value |
|---|---|---|---|
| PREGNANCY RATE | 19/29 (65.52) | 7/27 (25,93) | p<0.05 |
| MISCARRIAGE RATE | 3/19 (15.8) | 3/7 (42.86) | NS |
| LIVE-BIRTH RATE | 17/29* (55.17) | 4/27 (14.81) | p<0.05 |

* Twin pregnancy

# RESULTS

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# CONCLUSION

The study shows that the increase in **DCI DOSE AT 300MG / DAY IN COMBINATION WITH 1100MG MYO / DAY SIGNIFICANTLY IMPROVES THE PREGNANCY RATE IN WOMEN SUFFERING PCOS** compared to the effect of the combination of 27mg DCI and 1100 mg MYO

# CONCLUSION

The study demonstrates:

- The **importance of the absolute concentrations of either MYO or DCI** more than the physiological ratio
- **The suggested current dosage (40:1) is not enough to get the maximum benefit** to the use of inositols **for improvement of fertility in women suffering PCOS**
- Caronositol Fertility® **improves the fertility in women suffering PCOS.**

# PATENT

# PATENT

- Patent application based on a **new method to increase the rate of embryonic implantation in polycystic ovary syndrome** and for the **treatment of symptoms** of the syndrome:

  ***Method for increasing embryo implantation rate in a female subject suffering polycystic ovary syndrome.***

- The ratio between 1:1 to 9:1 is protected by Biosearch Life.

- EP17382791.6

# PRODUCT

Caronositol Fertility®
D-Chiro-Inositol & Myo-Inositol 1:3.6

# FINISHED PRODUCT

| | |
|---|---|
| COMPOSITION | Natural D-chiro-inositol (mínimum 95%) purified from carob pod by a patented process and Myo-inositol from phytin's corn |
| APPEARANCE | White crystalline powder |
| FERTILITY DOSAGE | 1400 mg of Caronositol Fertility® in one or more intakes |
| PACKAGING FINISHED PRODUCT | 30 Sachets |
| SHELF LIFE | 48 months from the manufacturing date |
| SAFETY & QUALITY | Studies have not reported any side effects<br>Microbiology tests according to the European Pharmacopea |

Caronositol Fertility®

*D-Chiro-Inositol & Myo-Inositol 1:3.6*

# MANY THANKS

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