

# INTEGRATORE ALIMENTARE A BASE DI VITAMINE, INOSITOLO, BETAINA, RESVERATROLO, COENZIMA Q10 E SELENIO

CON EDULCORANTE SENZA GLUTINE E SENZA LATTOSIO

> Disponibile in confezione da 30 e da 20 bustine 3,5 g l'una  $\ominus$

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# RIFERTOSAN DONNA Il nuovo integratore per la fertilità femminile

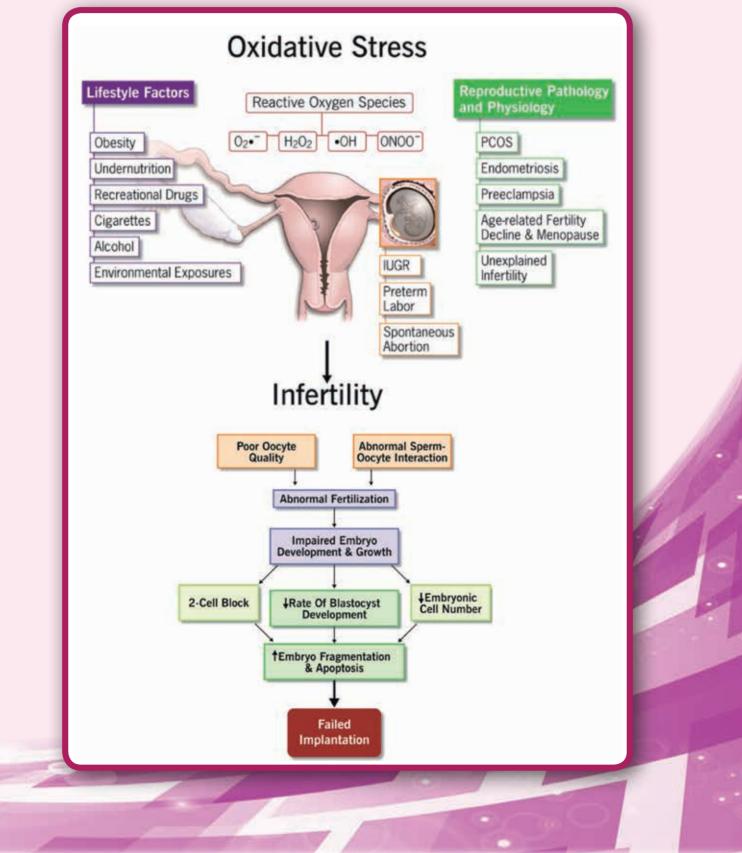
- In un unico prodotto tutti i principi attivi alle massime concentrazioni consentite per un'azione combinata a molteplici livelli
- Per una corretta ottimizzazione della fertilità femminile sia in vivo che in vitro

# RIFERTOSAN DONNA IN UN SOLO PRODOTTO LA POSSIBILITÀ DI UN INTERVENTO MULTISTEPS SULLA INFERTILITÀ FEMMINILE

- Azione antiossidante
- Somministrazione di acido folico attivo
- Protezione completa dall'iperomocistinemia
- Massima efficacia nella sindrome dell'ovaio policistico
- Azione di contrasto dell'aging ovocitario



# È SCIENTIFICAMENTE DIMOSTRATO CHE I RADICALI LIBERI SONO IN GRADO DI DIMINUIRE LA FERTILITÀ FEMMINILE A VARI LIVELLI



Hum Reprod Update. 2008 Jul-Aug;14(4):345-57. doi: 10.1093/humupd/dmn011. Epub 2008 Jun 4.

## Oxidative stress and antioxidants: exposure and impact on female fertility.

#### Ruder EH1 Hartman TJBlumberg JGoldman MB

Reproductive failure is a significant public health concern. Although relatively little is known about factors affecting fertility and early pregnancy loss, a growing body of literature suggests that environmental and lifestyle factors play an important role. There is sufficient evidence to hypothesize that diet, particularly its constituent antioxidants, and oxidative stress (OS) may influence the timing and maintenance of a viable pregnancy. We hypothesize that conditions leading to OS in the female affect time-to-pregnancy and early pregnancy loss.

#### **METHODS:**

We review the epidemiology of female infertility related to antioxidant defenses and oxidation and examine potential sources of OS from the ovarian germ cell through the stages of human pregnancy and pregnancy complications related to infertility. Articles were identified through a search of the PubMed database.

#### **RESULTS:**

Female OS is a likely mediator of conception and threshold levels for OS exist, dependent on anatomic location and stage of preconception.

#### **CONCLUSIONS:**

Prospective pregnancy studies with dietary assessment and collection of biological samples prior to conception with endpoints of time-to-pregnancy and early pregnancy loss are needed.

<u>Reprod Biol Endocrinol</u>. 2012 Jun 29;10:49. doi: 10.1186/1477-7827-10-49.

The effects of oxidative stress on female reproduction: a review.

Agarwal A1, Aponte-Mellado A, Premkumar BJ, Shaman A, Gupta S.

ABSTRACT: Oxidative stress (OS), a state characterized by an imbalance between pro-oxidant molecules including reactive oxygen and nitrogen species, and antioxidant defenses, has been identified to play a key role in the pathogenesis of subfertility in both males and females. The adverse effects of OS on sperm quality and functions have been well documented. In females, on the other hand, the impact of OS on oocytes and reproductive functions remains unclear. This imbalance between pro-oxidants and antioxidants can lead to a number of reproductive diseases such as endometriosis, polycystic ovary syndrome (PCOS), and unexplained infertility.

Pregnancy complications such as spontaneous

abortion, recurrent pregnancy loss, and preeclampsia, can also develop in response to OS. Studies have shown that extremes of body weight and lifestyle factors such as cigarette smoking, alcohol use, and recreational drug use can promote excess free radical production, which could affect fertility. Exposures to environmental pollutants are of increasing concern, as they too have been found to trigger oxidative states, possibly contributing to female infertility. This article will review the currently available literature on the roles of reactive species and OS in both normal and abnormal reproductive physiological processes. Antioxidant supplementation may be effective in controlling the production of ROS and continues to be explored as a potential strategy to overcome reproductive disorders associated with infertility. However, investigations conducted to date have been through animal or in vitro studies, which have produced largely conflicting results. The impact of OS on assisted reproductive techniques (ART) will be addressed, in addition to the possible benefits of antioxidant supplementation of ART culture media to increase the likelihood for ART success. Future randomized controlled clinical trials on humans are necessary to elucidate the precise mechanisms through which OS affects female reproductive abilities, and will facilitate further explorations of the possible benefits of antioxidants to treat infertility.

#### <u>Curr Opin Obstet Gynecol</u>. 2009 Jun;21(3):219-22. Impact of oxidative stress on female fertility.

Ruder EH1, Hartman TJ, Goldman MB.

**RECENT FINDINGS:** Oxidative stress is associated with decreased female fertility in animal and in-vitro models, but no studies to date have directly assessed the relationship in women. Exposures associated with oxidative stress and with evidence to influence the timing and maintenance of a viable pregnancy include pregnancy complications (e.g. preeclampsia), extremes of body weight, alcohol, tobacco, and caffeine intake. Intake of antioxidant nutrients, including use of multivitamins, impacts the generation of reactive oxygen species and may play a beneficial role in female fertility.

**SUMMARY:** Infertility is a significant public health problem and diagnosis and treatment are stressful, invasive, and costly. The role of oxidative stress in female fertility is an understudied and compelling area for investigation. Identifying modifiable factors to decrease oxidative stress in the gynecologic environment may be an inexpensive and noninvasive therapy for increasing fertility.

# E CHE UNA ADEGUATA TERAPIA ANTIOSSIDANTE È IN GRADO DI MIGLIORARE LA FERTILITÀ FEMMINILE

<u>Fertil Steril.</u> 2014 Mar;101(3):759-66. doi: 10.1016/j. fertnstert.2013.11.008. Epub 2013 Dec 17.

Female dietary antioxidant intake and time to pregnancy among couples treated for unexplained infertility.

#### <u>Ruder EH<sup>1</sup>, Hartman TJ<sup>2</sup>, Reindollar RH<sup>3</sup>, Goldman MB<sup>4</sup></u>.

Mean nutrient intake exceeded the estimated average requirement (EAR) for vitamins C and E. No differences in mean intake of any of the antioxidants were noted between women who delivered a liveborn infant during the study period vs. those who did not. In multivariable models, intake of β-carotene from dietary supplements was associated with shorter TTP among women with body mass index (BMI) ≥25 kg/m(2) (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.09-1.53) and women <35 y (HR 1.19, 95% CI 1.01-1.41). Intake of vitamin C from dietary supplements was associated with shorter TTP among women with BMI <25 kg/m(2) (HR 1.09, 95% CI 1.03-1.15) and women <35 y (HR 1.10, 95% CI 1.02-1.18). Intake of vitamin E from dietary supplements among women ≥35 y also was associated with shorter TTP (HR 1.07, 95% CI 1.01-1.13).

### CONCLUSION(S):

Shorter TTP was observed among women with BMI <25 kg/m(2) with increasing vitamin C, women with BMI  $\geq$ 25 kg/m(2) with increasing  $\beta$ -carotene, women <35 y with increasing  $\beta$ -carotene and vitamin C, and

Curr Opin Obstet Gynecol. 2013 Jun;25(3):173-80. doi: 10.1097/GCO.0b013e3283609138.

The effect of micronutrient supplements on female fertility.

### Buhling KJ1, Grajecki D

### **RECENT FINDINGS:**

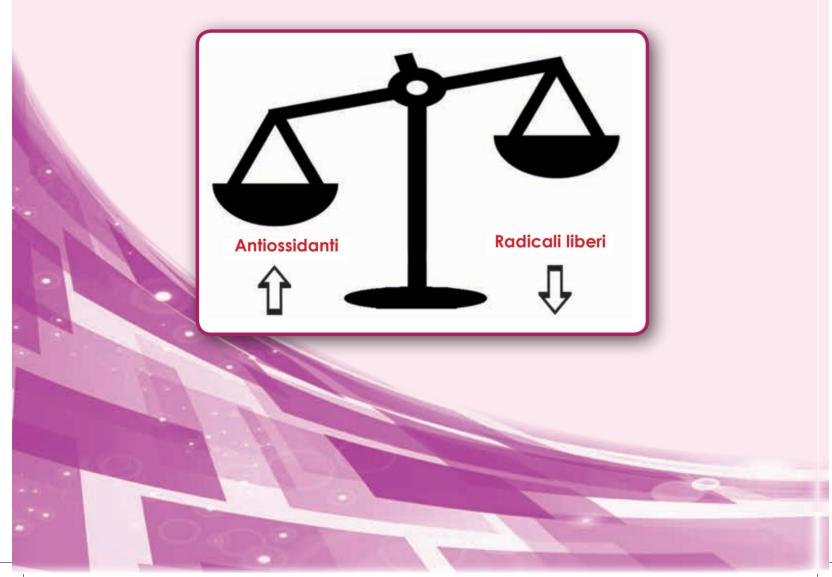
Reports of randomized trials are rare. Most studies are focused on multivitamin supplementations. For some micronutrients, a positive impact on fertility could be shown. This article reviews the available clinical studies as well as the pathophysiological background of possible effects and summarizes the potential benefits of selected micronutrients on female fertility.

#### **SUMMARY:**

Apart from lowering the malformation risk by periconceptional supplementation of folic acid, substitution with different micronutrients, particularly folic acid, vitamin B6, vitamin C, vitamin D, vitamin E, iodine, selenium, iron, and DHA might have a positive impact on infertility treatment. The multivitamin formulation should take the pathophysiology, clinical studies, and upper limits into account.

# RIFERTOSAN DONNA MOLTEPLICI PRINCIPI ATTIVI PER UNA COMPLETA AZIONE ANTIOSSIDANTE CONTRO LO STRESS OSSIDATIVO

- VITAMINA C
- VITAMINA E
- COENZIMA Q10
- SELENIO
- RESVERATROLO

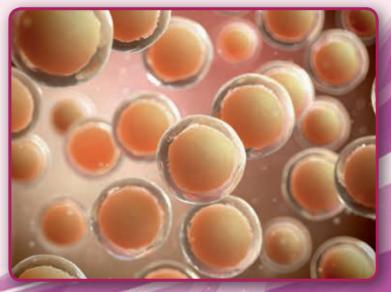


# **RIFERTOSAN DONNA** ASSUNZIONE DI ACIDO FOLICO ATTIVO

- 5-metiltetraidrofolato sotto forma di sale della glucosammina
- Supera il problema della conversione in forma attiva dell'acido folico o dei folati in caso di deficit genetici degli enzimi di conversione come nei deficit genetici del MTHFR
- Attraversa la barriera gastrica e viene assorbito in ambiente intestinale

MASSIMA EFFICACIA NELLA SINDROME DELL'OVAIO POLICISTICO MIGLIORE CONTROLLO DELLE ALTERAZIONI METABOLICHE ED ORMONALI GRAZIE ALL' AZIONE COMBINATA DI MOLTEPLICI SOSTANZE AD EFFETTO SINERGICO:

- INOSITOLO AD ALTO DOSAGGIO (4gr/die)
- VITAMINA D3
- RESVERATROLO
- COENZIMA Q10



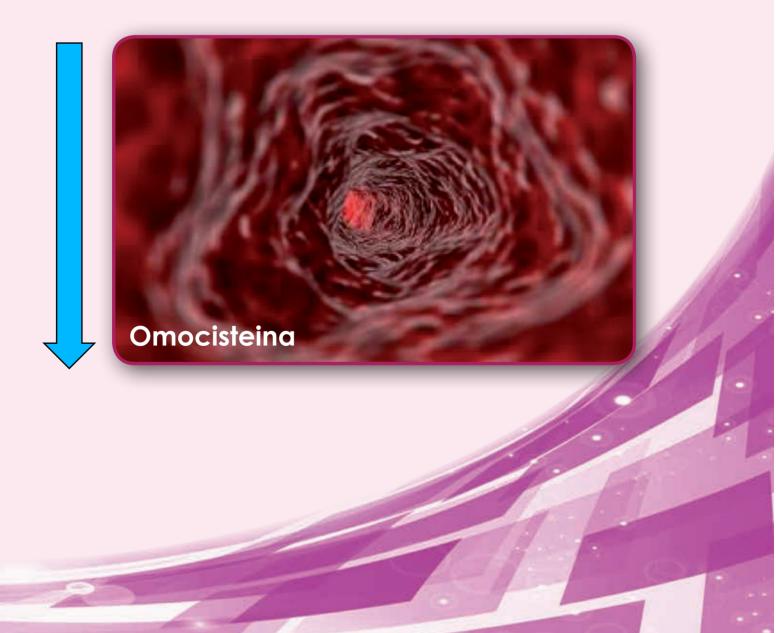
# **RIFERTOSAN DONNA** EFFICACIA NELL'ENDOMETRIOSI

- AZIONE ANTIOSSIDANTE
- COENZIMA Q10
- **RESVERATROLO AD ALTO DOSAGGIO**
- VITAMINA C



# RIFERTOSAN DONNA PERFETTO CONTROLLO DELL'OMOCISTEINA

- ACIDO FOLICO ATTIVO
- VITAMINA B6
- VITAMINA B12
- BETAINA



# **RIFERTOSAN DONNA**

È IL PRIMO INTEGRATORE LE CUI SOSTANZE POSSONO AVERE UN RUOLO FONDAMENTALE NEL CONTRIBUIRE AD UNA CORRETTA PRESERVAZIONE DELLA FERTILITÀ FEMMINILE GRAZIE ALLA PRESENZA DI ANTIOSSIDANTI, COENZIMA Q10 E RESVERATROLO



# LA VITAMINA D: UN RUOLO FONDAMENTALE NELLA FISIOLOGIA OVARICA CHE SI ESPLICA A DIVERSI LIVELLI



Fertil Steril. 2014 Aug;102(2):460-468.e3. doi: 10.1016/j.fertnstert.2014.04.046. Epub 2014 Jun 3.

Role of vitamin D in ovarian physiology and its implication in reproduction: a systematic review.

#### Irani M1, Merhi Z2.

#### **RESULT(S)**:

In human granulosa cells, VD alters AMH signaling, FSH sensitivity, and progesterone production and release, indicating a possible physiologic role for VD in ovarian follicular development and luteinization. In the serum, 25-hydroxyvitamin D (25OH-D) is positively correlated with AMH, and appropriate VD supplementation in VD-depleted women can suppress the seasonal changes that occur in serum AMH. In VD-deficient women with PCOS, VD supplementation lowers the abnormally elevated serum AMH levels, possibly indicating a mechanism by which VD improves folliculogenesis. The antiinflammatory sRAGE serum levels significantly increase in women with PCOS after VD replacement. Although follicular fluid 25OH-D correlates with IVF outcomes, there is a lack of data pertaining to the impact of VD supplementation on pregnancy rates following IVF.

#### CONCLUSION(S):

This review underscores the need for understanding the mechanistic actions of VD in ovarian physiology and the critical need for randomized trials to elucidate the impact of VD supplementation on controlled ovarian hyperstimulation/IVF outcome and ovulatory dysfunction associated with PCOS.

Curr Opin Obstet Gynecol. 2014 Jun;26(3):145-50. doi: 10.1097/GCO.00000000000065.

Vitamin D and female fertility.

Lerchbaum E1, Rabe T.

#### **RECENT FINDINGS:**

In the past year, several observational studies reported a better in-vitro fertilization outcome in women with sufficient vitamin D levels (≥30 ng/ml), which was mainly attributed to vitamin D effects on the endometrium. One randomized controlled trial found an increased endometrial thickness in women with polycystic ovary syndrome (PCOS) receiving vitamin D during intrauterine insemination cycles. Further, vitamin D supplementation had a beneficial effect on serum lipids in PCOS women. Vitamin D treatment improved endometriosis in a rat model and increased vitamin D intake was related to a decreased risk of incident endometriosis. Vitamin D was also favorably associated with primary dysmenorrhea, uterine leiomyoma, and ovarian reserve in late reproductive aged women.

#### SUMMARY:

In women undergoing in-vitro fertilization, a sufficient vitamin D level (≥30 ng/ml) should be obtained. Vitamin D supplementation might improve metabolic parameters in women with PCOS. A high vitamin D intake might be protective against endometriosis.

Arch Gynecol Obstet. 2014 Apr;289(4):865-70. doi: 10.1007/s00404-013-3055-x. Epub 2013 Oct 26.

# LA VITAMINA D HA UN RUOLO FONDAMENTALE NELL'"OUTCOME" DEI PROGRAMMI DI FECONDAZIONE ASSISTITA OMOLOGA

**<u>Reprod Biol Endocrinol</u>**, 2014 May 31;12:47. doi: 10.1186/1477-7827-12-47

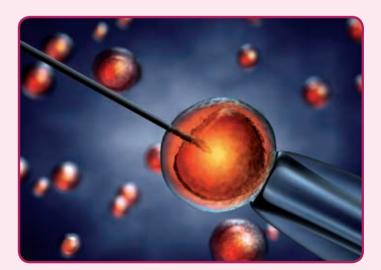
Vitamin D and assisted reproduction technologies: current concepts.

<u>Vanni VS, Vigano' P1, Somigliana E, Papaleo E, Paffoni</u> <u>A, Pagliardini L, Candiani M.</u>

#### Abstract

Accumulating evidence from animal and human studies suggests that vitamin D is involved in many functions of the human reproductive system in both genders, but no comprehensive analysis of the potential relationship between vitamin D status and Assisted Reproduction Technologies (ART) outcomes is currently available. On this basis, the purpose of this systematic review and metaanalysis was to perform an in-depth evaluation of clinical studies assessing whether vitamin D status of patients undergoing ART could be related to cycle outcome variables. This issue is of interest considering that vitamin D deficiency is easily amenable to correction and oral vitamin D supplementation is cheap and without significant side effects. Surprisingly, no studies are currently available assessing vitamin D status among male partners of couples undergoing ART, while seven studies on vitamin D status of women undergoing controlled ovarian hyperstimulation (COH) for ART were found and included in the review. Results show that vitamin D deficiency is highly prevalent among women undergoing COH,

ranging from 21% to 31% across studies conducted in Western countries and reaching 75-99% in Iranian studies. Data on vitamin D deficiency (25-hydroxyvitamin D serum levels <20 ng/ml) in relation to ART outcomes could be extracted from three studies and included in the meta-analysis, yielding a common risk ratio (RR) of 0.89 (95% CI 0.53-1.49) and showing a lower but not statistically significant likelihood of clinical pregnancy for vitamin-D-deficient women compared with vitamin-D-sufficient patients. In conclusion, there is insufficient evidence to support the routine assessment of vitamin D status to predict the clinical pregnancy rate in couples undergoing ART. The partly conflicting results of the available studies, potentially explaining the lack of statistical significance for a negative influence of vitamin D deficiency on clinical pregnancy rate, are likely secondary to confounders and insufficient sample size, and further larger cohort and randomised controlled studies are required.



# LA VITAMINA D HA UN RUOLO FONDAMENTALE NELL'"OUTCOME" DEI PROGRAMMI DI FECONDAZIONE ASSISTITA OMOLOGA

Hum Reprod. 2014 Sep;29(9):2032-40. doi: 10.1093/ humrep/deu156. Epub 2014 Jun 20.

Vitamin D deficiency and pregnancy rates in women undergoing single embryo, blastocyst stage, transfer (SET) for IVF/ICSI.

## Polyzos NP1, Anckaert E2, Guzman L3, Schiettecatte J2, Van Landuyt L4, Camus M4, Smitz J2, Tournaye H4.

All patients underwent ovarian stimulation for IVF/ICSI and Day 5 SET. Serum samples were obtained 7 days prior to embryo transfer and stored frozen at -20°C. Samples were collectively analyzed for their 25-OH vitamin D content. Vitamin D deficiency was defined as serum 25-OH vitamin D levels <20 ng/ml in accordance with the Institute of Medicine and the Endocrine Society clinical practice guidelines.

### MAIN RESULTS AND THE ROLE OF CHANCE:

Clinical pregnancy rates were significantly lower in women with vitamin D deficiency compared with those with higher vitamin D values (41 versus 54%, P = 0.015). Logistic regression analysis was performed to identify whether vitamin D deficiency is independently associated with clinical pregnancy rates after controlling for 16 potential confounding factors. According to our results vitamin D deficiency was independently associated with lower clinical pregnancy rates, odds ratios [ORs (95% confidence interval (CI) 0.61 (0.39-0.95)] for vitamin D deficiency (deficient versus non-deficient women), P = 0.030. Finally, even when restricting our analysis to women undergoing elective SET (274 patients), vitamin D deficiency was again independently associated with pregnancy rates [OR (95% CI) 0.56 (0.33-0.93), P = 0.024].

# LA VITAMINA D HA UN RUOLO FONDAMENTALE NELL'"OUTCOME" DEI PROGRAMMI DI FECONDAZIONE ASSISTITA ETEROLOGA

Fertil Steril. 2014 Feb;101(2):447-52. doi: 10.1016/j. fertnstert.2013.10.008. Epub 2013 Nov 5.

Influence of vitamin D levels on in vitro fertilization outcomes in donor-recipient cycles.

Rudick BJ1, Ingles SA2, Chung K3, Stanczyk FZ3, Paulson RJ3, Bendikson KA3.

## Abstract

#### **OBJECTIVE:**

To elucidate the role of vitamin D in reproduction by examining the relationship between recipient vitamin D levels and pregnancy rates in donorrecipient IVF cycles.

#### **RESULT(S)**:

In a diverse population of 99 recipients (53% Caucasian, 20% Asian, 16% Hispanic, 7% African American), adjusted clinical pregnancy rates were lower among vitamin D-deficient recipients than among vitamin D-replete recipients (37% vs. 78%). Live-birth rates were 31% among vitamin D-deficient recipients, compared with 59% among vitamin D-replete recipients. There were no differences in adjusted clinical pregnancy and livebirth rates among recipients who were vitamin D deficient [25(OH)D<20 ng/mL] vs. among those who were vitamin D insufficient [20 ng/mL  $\leq$  25(OH)D<30 ng/mL].

## CONCLUSION(S):

Nonreplete vitamin D status [25(OH)D<30 ng/mL] was associated with lower pregnancy rates in recipients of egg donation. Since the oocyte donorrecipient model is able to separate the impact of vitamin D on oocyte vs. endometrium, these data suggest that the effects of vitamin D may be mediated through the endometrium.



# LA VITAMINA D HA UN RUOLO FONDAMENTALE NEL TRATTAMENTO DELLA POLICISTOSI OVARICA

Clin Endocrinol (Oxf). 2012 Sep;77(3):343-50. doi: 10.1111/j.1365-2265.2012.04434.x.

Vitamin D in the actiology and management of polycystic ovary syndrome.

#### Thomson RL Spedding SBuckley JD

### Abstract

Vitamin D defi ciency is common in women with polycystic ovary syndrome (PCOS), with the 67-85% of women with PCOS having serum concentrations of 25-hydroxy vitamin D (25OHD) <20 ng/ml. Vitamin D defi ciency may exacerbate symptoms of PCOS, with observational studies showing lower 25OHD levels were associated with insulin resistance, ovulatory and menstrual irregularities, lower pregnancy success, hirsutism, hyperandrogenism, obesity and elevated cardiovascular disease risk factors. There is some, but limited, evidence for benefi cial effects of vitamin D supplementation on menstrual dysfunction and insulin resistance in women with PCOS. Vitamin D defi ciency may play a role in exacerbating PCOS, and there may be a place for vitamin D supplementation in the management of this syndrome, but current evidence is limited and additional randomized controlled trials are required to confi rm the potential benefi ts of vitamin D supplementation in this population.



# COENZIMA Q10: UN'AZIONE FONDAMENTALE PER L'ATTIVITÀ MITOCONDRIALE NELLA POLICISTOSI OVARICA E NELL'ETÀ MATERNA AVANZATA

**<u>Reprod Biomed Online</u>**. 2014 Jul;29(1):119-24. doi: 10.1016/j.rbmo.2014.03.011. Epub 2014 Mar 26.

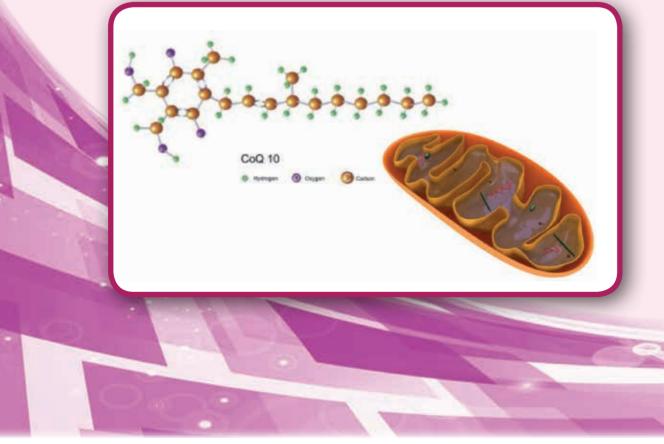
Combined coenzyme Q10 and clomiphene citrate for ovulation induction in clomiphene-citrate-resistant polycystic ovary syndrome.

## El Refaeey A1, Selem A2, Badawy A3

### Abstract

This prospective randomized controlled trial evaluated the effect of combined oral coenzyme Q10 (CoQ10) and clomiphene citrate for ovulation induction in clomiphene-citrate-resistant polycystic ovary syndrome (PCOS). A total of 101 infertile women with PCOS resistant to clomiphene citrate were randomized either to combined CoQ10 and clomiphene citrate (51 patients, 82 cycles) or to

clomiphene citrate alone (50 patients, 71 cycles). The outcome measures were number of follicles, serum oestradiol, serum progesterone, endometrial thickness and ovulation, clinical pregnancy and miscarriage rates. Numbers of follicles >14 mm and ≥18 mm were signifi cantly higher in the CoQ10 group. Endometrial thickness on the day of human chorionic gonadotrophin was signifi cantly greater in the CoQ10 group (8.82 ± 0.27 mm versus 7.03 ± 0.74 mm). Ovulation occurred in 54/82 cycles (65.9%) in the CoQ10 group and 11/71 cycles (15.5%) in the control group. Clinical pregnancy rate was significantly higher in the CoQ10 group (19/51, 37.3%) versus the control group (3/50, 6.0%). Combination of CoQ10 and clomiphene citrate in the treatment of clomiphenecitrate-resistant PCOS patients improves ovulation and clinical pregnancy rates. It is an effective and safe option and can be considered before gonadotrophin therapy or laparoscopic ovarian drilling.



Fertil Steril. 2015 Sep;104(3):724-7. doi: 10.1016/j. fertnstert.2015.05.023. Epub 2015 Jun 11.

Coenzyme Q-dependent mitochondrial respiratory chain activity in granulosa cells is reduced with aging.

### Ben-Meir A1, Yahalomi S2, Moshe B3, Shufaro Y2, Reubinoff B2, Saada A3.

### Abstract

#### **RESULT(S)**:

Complex II + III activity was 1.9 times higher in young patients compared with older patients (18.3  $\pm$  5.8 and 9.6  $\pm$  3 nmol/min/mg, respectively) whereas II and CS were not statistically significantly different. Increased II + III activity in the presence CoQ1 was observed in both groups but was statistically significantly higher in the older patients, reaching similar levels. Compared with baseline (II + III + Q/II + III), the increase was 2.47 times higher in older patients compared with young patients (6.5  $\pm$  2.0 and 2.62  $\pm$  0.83, respectively).

### CONCLUSION(S):

Coenzyme Q10-dependent MRC activity in GC reduces with aging. This reduction is diminished upon in vitro CoQ1 supplementation, indicating that CoQ10 deficit is the underlying cause for the mitochondrial dysfunction. The results show that functional CoQ10 status can be assessed by measuring complex II + III activity in GC and might provide a useful monitoring tool for future clinical studies of oral CoQ10 supplementation to older patients undergoing IVF treatment.

Aging Cell. 2015 Oct;14(5):887-95. doi: 10.1111/ acel.12368. Epub 2015 Jun 26.

Coenzyme Q10 restores oocyte mitochondrial function and fertility during reproductive aging.

Ben-Meir A1,2, Burstein E1,2, Borrego-Alvarez A1, Chong J1, Wong E1,3, Yavorska T1,3, Naranian T1,3, Chi M4, Wang Y5, Bentov Y2,6, Alexis J7, Meriano J7, Sung HK1, Gasser DL8, Moley KH4, Hekimi S5, Casper RF1,2,3,6, Jurisicova A1,3,6

#### Abstract

Female reproductive capacity declines dramatically in the fourth decade of life as a result of an agerelated decrease in oocyte quality and quantity. The primary causes of reproductive aging and the molecular factors responsible for decreased oocyte quality remain elusive. Here, we show that aging of the female germ line is accompanied by mitochondrial dysfunction associated with decreased oxidative phosphorylation and reduced Adenosine tri-phosphate (ATP) level. Diminished expression of the enzymes responsible for CoQ production, Pdss2 and Cog6, was observed in oocytes of older females in both mouse and human. The age-related decline in oocyte quality and quantity could be reversed by the administration of CoQ10. Oocyte-specific disruption of Pdss2 recapitulated many of the mitochondrial and reproductive phenotypes observed in the old females including reduced ATP production and increased meiotic spindle abnormalities, resulting in infertility. Ovarian reserve in the oocyte-specific Pdss2-deficient animals was diminished, leading to premature ovarian failure which could be prevented by maternal dietary administration of CoQ10. We conclude that impaired mitochondrial performance created by suboptimal CoQ10 availability can drive age-associated oocyte deficits causing infertility.

# **RESVERATROLO: UN'AZIONE SPECIFICA SUL NUMERO** E SULLA QUALITÀ OVOCITARIA NELL'ETÀ MATERNA AVANZATA

Hum Reprod. 2013 Mar;28(3):707-17. doi: 10.1093/ humrep/des437. Epub 2013 Jan 4.

Resveratrol protects against ageassociated infertility in mice. Liu M1, Yin Y, Ye X, Zeng M, Zhao Q, Keefe DL, Liu L.

## **STUDY QUESTION:**

Does resveratrol counteract age-associated infertility in a mouse model of reproductive aging? administration of resveratrol protects against the reduction of fertility with reproductive aging in mice.

### WHAT IS KNOWN ALREADY:

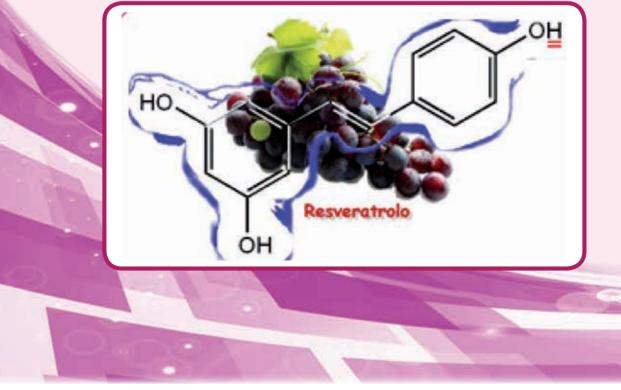
Loss of oocytes and follicles and reduced oocyte quality contribute to age-associated ovarian aging and infertility. Accumulation of free radicals with age leads to DNA mutations, protein damage, telomere shortening, apoptosis and accelerated ovarian aging. Increasing evidence shows that resveratrol, enriched in certain foods, for example red grapes and wine, has anti-tumor and anti-aging effects on

somatic tissues by influencing various signaling pathways, including anti-oxidation, as well as activating Sirt1 and telomerase. We investigated the potential of resveratrol to stave off ovarian aging in the inbred C57/BL6 mouse model.

## MAIN RESULTS AND THE ROLE OF CHANCE:

Young mice fed with resveratrol for 12 months retained the capacity to reproduce, while agematched controls produced no pups. Consistently, mice fed with resveratrol for 12 months exhibited a larger follicle pool than controls (P < 0.05). Furthermore, telomerase activity, telomere length and age-related gene expression in ovaries of mice fed with resveratrol resembled those of young mice,

but differed (P < 0.05) from those of age-matched old mice. Resveratrol improved (P < 0.05) the number and quality of oocytes, as evidenced by spindle morphology and chromosome alignment. Also, resveratrol affected embryo development in vitro in a dose-dependent manner.



# RESVERATROLO: UN'AZIONE SPECIFICA SUL NUMERO E SULLA QUALITÀ OVOCITARIA NELL'ETÀ MATERNA AVANZATA

Fertil Steril. 2015 Feb;103(2):570-9.e1. doi: 10.1016/j. fertnstert.2014.10.034. Epub 2014 Nov 20.

Effects of resveratrol on ovarian response to controlled ovarian hyperstimulation in ob/ob mice.

## <u>Cabello E1, Garrido P1, Morán J1, González del</u> <u>Rey C2, Llaneza P3, Llaneza-Suárez D4, Alonso A1,</u> <u>González C5.</u>

Plasma insulin and T levels decreased and Homeostatic Index of Insulin Resistance improved in ob/ ob mice treated with resveratrol. Interleukin-6 and tumor necrosis factor- $\alpha$  levels were significantly reverted back to near normalcy after resveratrol treatment in obese mice. Administration of resveratrol resulted in a significantly higher number of oocytes collected in wild-type mice. The number of primary, growing, preovulatory, and atretic follicles was found to be decreased in the group of obese mice treated with resveratrol when compared with the obese control group.

### CONCLUSION(S):

Resveratrol administration could exert benefits against loss of ovarian follicles, and these actions may be mediated, at least in part, via anti-inflammatory, insulin-sensitizing, and antihyperandrogenism effects.

These observations further validate the therapeutic potential of resveratrol to preserve ovarian reserve in conditions associated with obesity. Our results suggest the possible clinical use of resveratrol to enhance the ovarian response to COH in normalweight females.



Integratore alimentare a base di vitamine, inositolo, betaina, resveratrolo, coenzima Q10 e selenio.

Con edulcorante, senza glutine e senza lattosio

Disponibile in astuccio da 30 bustine

o da 20 bustine da 3,5 g l'una

**EFFETTO FISIOLOGICO:** Le Vitamine C, E e B2 ed il selenio contribuiscono alla protezione delle cellule dallo stress ossidativo; la Vitamina D, l'Acido folico e la Vitamina B12 intervengono nel processo di divisione delle cellule; la Vitamina B6 contribuisce alla regolazione dell'attività ormonale; il selenio contribuisce alla normale funzione tiroidea.

**INGREDIENTI:** Inositolo; Vitamina C (Acido L-ascorbico); Aroma; Betaina HCI; Acidificante: Acido citrico; Maltodestrine; Succo di Barbabietola disidratato in polvere; Agente antiagglomerante: Biossido di silicio; Vitamina E (Acetato di DL-alfa-tocoferile); Resveratrolo (da Fallopia japonica (Houtt.) Ronse Dec. radice); Coenzima Q10; Vitamina B2 (Riboflavina); Vitamina B12 (Cianocobalamina); Vitamina D (colecalciferolo); L-selenometionina; Edulcorante: Sucralosio; Vitamina B6 (cloridrato di piridossina); Folato da Coutrefolicº (acido (6S)-5-metilte-traidrofolico, sale della glucosammina).

**MODALITÀ D'USO**: Si consiglia di assumere fino ad un massimo di due bustine al giorno da far sciogliere in un bicchiere d'acqua (150 ml).

**AVVERTENZE:** Tenere fuori dalla portata dei bambini al di sotto dei tre anni di età. Gli integratori alimentari non vanno intesi come sostituti di una dieta variata ed equilibrata e di un sano stile di vita. Non eccedere la dose giornaliera raccomandata.

COMPOSIZIONE MEDIA		
COMPONENTI	Per 2 Bst	*VNR%
Inositolo	4,0 g	-
Vitamina C	500 mg	625%
Betaina	300 mg	-
Vitamina E	40 mg	333%
Resveratrolo	100 mg	-
Coenzima Q10	100 mg	-
Riboflavina	20 mg	1429%
Vitamina B12	20 µg	800%
Vitamina D	50 µg	1000%
Selenio	100 µg	182%
Vitamina B6	8 mg	571%
Folato da <b>\$\$Quotrefolic</b> °	400 µg	200%

\*Valore Nutritivo di Riferimento giornaliero (adulti) – Reg. UE 1169/2011

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