



## Comparison of Three Nutraceutical Food Supplements for the Treatment of Infertility

Frank Comhaire<sup>1\*</sup>

<sup>1</sup>Department of Endocrinology, Ghent University, Brakelmeersstraat, 18 B 9830 Sint Martens-Latem, Belgium.

### Authors' contributions

The sole author designed, analyzed and interpreted and prepared the manuscript.

### Article Information

DOI: 10.9734/BJPR/2015/15105

Editor(s):

(1) Rafik Karaman, College of Pharmacy, Al-Quds University, Palestine.

Reviewers:

(1) Ganna Shayakhmetova, General Toxicology Department, SI "Institute of Pharmacology and Toxicology NAMS of Ukraine", Ukraine.

(2) Eugenio Ragazzi, Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Italy.  
Complete Peer review History: <http://www.sciencedomain.org/review-history.php?iid=881&id=14&aid=7446>

Original Research Article

Received 6<sup>th</sup> November 2014  
Accepted 4<sup>th</sup> December 2014  
Published 24<sup>th</sup> December 2014

### ABSTRACT

**Aims:** Approximately one out of every 8 couples is confronted with a problem of infertility. The diagnostic and therapeutic management, taking into account the WHO recommendations, may be complemented by nutraceutical food supplementation. The present study compares the original nutraceutical (Qualisperm®) with two recently marketed products (Proxceed plus®, and PROfertil®).

**Study Design:** The ingredients and their quantities of the three nutraceuticals were listed and compared, and their effectiveness on semen quality was assessed. The probability of conception per month was calculated, as were the numbers needed to treat, and the time to pregnancy, whenever available.

**Results:** All three nutraceuticals improve semen quality. The pregnancy rate per month of Proxceed plus was 3.7%, it was 5% for PROfertile, and 11% when Qualisperm was combined with WHO-recommended treatment of the male partner. The numbers needed to treat were 5.0 (CI: 3.58-8.18) for Proxceed plus, 9.4 (CI: 4.46-94.9) for PROfertil, and 2.8 (CI: 1.7-8.7) for Qualisperm added to WHO-recommended treatment. The combination of Proxceed plus with the non-steroidal anti-inflammatory agent Cinnoxicam generated a number needed to treat of 2.9 (CI: 2.32-3.98). The time to pregnancy was reduced to half when combining WHO-recommended treatment with Qualisperm, as compared to either WHO recommended treatment alone, or treatment with Proxceed plus with Cinnoxicam added. In a placebo-controlled double-blind randomised trial of in

\*Corresponding author: Email: [frank@comhaire.com](mailto:frank@comhaire.com);

vitro fertilisation the number needed to treat of Qualisperm, given together with a specific oil to both partners, was 4.

**Conclusion:** Since confounding factors may have influenced the findings of the present comparison, the results should be interpreted with care. It is concluded that all three nutraceuticals may improve fertility, but that the efficiency of Qualisperm is best documented.

**Keywords:** Nutraceutical; infertility; in vitro fertilisation; number needed to treat; time to pregnancy; food supplement.

## 1. INTRODUCTION

Several Nutritional Food Supplements (NFS) have been commercialised aiming at increasing or restoring fertility of the couple. In 2003, we were the first to introduce a judicious nutraceutical formulation [1] and to quantify its cost-efficiency [2]. In assessing the relative merits of each of the different NFS's, several aspects should be taken into account: the justification of the components and combinations of ingredients, the effects on semen characteristics, the results in terms of pregnancy rates per month, time to pregnancy (TTP), and numbers needed to treat (NNT) [3]. Also the effectiveness on the outcome of in vitro fertilisation (IVF) should be considered.

Thereby, the evidential value takes into account the generally accepted levels. Always the Class One recommendation regarding the treatment of the infertile couple consists of applying the guidelines of the "WHO manual for the standardized investigation, diagnosis and management of the infertile male" [4]. This, however, was not the case in a number of trials.

The comparison concerns the 3 NFS's that are presently available on the market, namely: Qualisperm (Qs; Nutriphyt Ltd., Oostkamp, Belgium), Proxceed plus (Px; Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Roma, Italy) and PROfert (Pf; Valentis, Vilnius, Lithuania). Qualisperm-Duo (DUO-Qs) adds linseed oil to the formulation for men, and fish oil to the formulation for women.

## 2. MATERIALS AND METHODS

The composition of the 3 nutraceuticals was reproduced from the publicity published by the manufacturers, and was listed in a comparative table indicating the recommended daily dosage. Both the results reported in published papers and those of personal studies were analysed, and the probability of conception per month (P/C-rate in %), the number needed to treat [5], and the time to pregnancy were calculated whenever possible.

The P/C-rate was calculated by dividing the number of pregnancies by the number of couple-months of treatment or observation. The NNT is the average number of patients or couples who need to be treated in order to attain one additional favourable outcome, being an ongoing pregnancy confirmed by ultrasound imaging. The lower the NNT, the more effective is the treatment. The number needed to treat was obtained by dividing 100 by the absolute difference of the percentage pregnancies in the treated group minus the percentage of pregnancies in the control group.

Statistics were performed using the MedCalc system for medical statistics (MedCalc Ltd, Ostend, Belgium).

All the data on patients were anonymous, and there was no ethical issue involved in analysing published results.

## 3. RESULTS AND CONSIDERATIONS

The listing of the ingredients (Table 1) was subdivided depending on whether they were present in all 3 nutraceuticals, though possibly in different quantities, or in one or two nutraceuticals only.

### 3.1 Common Ingredients Present in all 3 NFS's

**Carnitines:** Px contains L-carnitine and Acetyl-L-carnitine both in a relatively high quantity. Pf contains only L-carnitine, where as Qs contains only the acetyl-L-carnitine. Acetyl-L-carnitine was found to be more relevant for sperm function as it is concentrated in the epididymis [6], and it plays a pivotal role in the transportation of long-chain poly-unsaturated fatty acids into the mitochondria. There is no evidence that a dose higher than 100 mg/day adds functional benefits.

**Coenzyme ubiquinone Q10** is present in all 3 NFS's, but the daily dosage in Pf is somewhat lower than that in Qs and in Px.

**Table 1. This table lists the details of the formulation of PROfertile (Pf), Proxeed-plus (Px) and Qualisperm (Qs). The quantities listed correspond to the per day prescription dosage**

Agent	PROfertile	Proxeed_plus	Qualisperm
L-carnitine (mg)	440	3550	-
Acetyl-L-Carnitine (mg)	-	1000	100
Ubiquinone Q10 (mg)	15	40	25
Zinc (mg)	40	20	7,5
folic acid (Vit B9)(µg)	800	400	200
Selenium (µg)	60	100	-
Vit E (mg)	120	-	-
Glutathione (mg)	80	-	-
L-arginine (mg)	250	-	-
Cyancobalamine (Vit B12)(µg)	-	3	1,5
Fructose	-	2000	-
citric acid	-	100	-
Ascorbic acid (Vit C)(mg)	-	180	-
Pyridoxine (Vit B6)(mg)	-	-	3
Astaxanthin (mg)	-	-	8
Pine bark extract (mg)	-	-	100
Lepidii mmeyenii (Maca)(mg)	-	-	250
<b>DUO-Qs formulations</b>			
Linseed oil (mg)*	-	-	1000
Fish oil (mg)**	-	-	1000
Pregnancy/month (%)	4,9	2,3-4,9***	11***
Number needed to treat (NNT)	9,4	5	2,8 ***
In vitro fertilisation (IVF) (NNT)	-	-	4***

Legend to Table 1. The results of calculations of the pregnancy per month rate (P/C in %) and the number needed to treat (NNT) is also given. \* DUO-Qs for men, \*\* DUO-Qs for women, \*\*\* Combining WHO-recommended treatment and DUO's-Qs for men and women

Zinc should be given in the esterified formula that guarantees optimal intestinal uptake, namely zinc-picolinate [7]. This zinc-ester is used in Qs, but no information is available concerning the ester(s) included in Px and Pf, hampering the comparison between products.

Folic acid (Vit B9) is given in different quantities. Thereby Pf includes a relatively high dose (800 µg/day), which may be recommended during pregnancy, but has been suspected of possibly increasing the risk of a heart attack after long-term intake. The quantity used in Qs and in Px corresponds to the recommended daily dose.

### 3.2 Ingredients That are not Present in all 3 NFS's

Selenium is used in similar quantity in Px and Pf, both being close to the recommended adequate daily dosage. Selenium is not present in Qs.

Vit E is included in Pf, probably as the synthetic alfa-tocopherol-succinate. This vitamin E-surrogate can inhibit gap junctional intercellular communication [8] when given in the relatively

high dose such as the one used in Pf (120 mg/day). Vit E is not used in Px, nor in Qs.

Glutathione is included in Pf. It seems improbable that this substance reaches the reproductive organs when given orally [9], and there are no studies proving its effectivity in infertility treatment [10]. Glutathione is not included in Px nor in Qs.

L-arginine is an important constituent of Pf. There is little evidence that this semi-essential amino acid exerts beneficial effect on fertility [11]. Arginine is not used in Px nor in Qs.

Vitamin B12 is present in Qs and Px, but not in Pf. The quantity in Px is probably too high, as was observed when measuring the concentration of Vit B12 in blood (personal observation).

Fructose and Citric acid are included in Px. These substances are digested in the intestinal tract and have no other effect than, perhaps, taste correctors. They have no proven benefit for fertility, nor for semen quality.

*Vitamin C* is included in Px. There is some evidence from rodent studies that Vit C may protect testicular function against chemically-induced damage. However this water-soluble antioxidant was not found to be effective in the treatment of infertility, even when associated with Vit E [12]. Vit C is not included in Pf, nor in Qs.

*Vitamin B6* is part of the formulation of Qs only. Together with Vitamins B9 and B12 it lowers the homocysteine concentration in blood, hence reducing epigenetic hypermethylation. Vitamin B6 sustains the enzymatic activity of elongase and desaturase, which metabolise alpha-linolenic acid (ALA, 18:3 $\omega$ 3) into the long-chain poly-unsaturated omega-3 fatty acids docosahexaenoic acid (DHA, 22:6 $\omega$ 3) and eicosapentaenoic acid (EPA, 20:5 $\omega$ 3). These are generated in the seminiferous tubules and are of pivotal importance for optimal membrane function of the spermatozoa [13].

*Astaxanthin* (biomass of *Haematococcus pluvialis*) is present exclusively in Qs because of its potent anti-oxidant and complementary anti-inflammatory effect. It has been proven to be non-toxic, to improve sperm function [14], and to reduce oxidative damage of DNA [15].

*Pine bark extract*, rich in anthocyanidins, is included in Qs because of its strong anti-inflammatory activity and complementary anti-oxidant action, improving sperm function [16].

*Lepidium meyenii* or *Maca* is a phyto-adaptogen present in Qs, that protects proteins against the negative effects of stress and of oxidative overload.

*Essential fatty acids*. The DUO-formulation of Qs (Table 1) for men includes separate capsules with linseed (flaxseed)-oil, rich in the short chain fatty acid alpha-linolenic acid, that can pass through the blood-testis barrier. In the seminiferous tubules this fatty acid is metabolised into the long-chain poly-unsaturated fatty acids EPA and DHA by the elongase and desaturase enzymes. The function of these enzymes is reinforced by the cofactors Vit B6 and Zinc. The DUO-Qs formulation for women includes capsules of fish-oil that is rich in EPA and DHA. These act directly on the oocyte membrane, and EPA suppresses the inflammatory reaction that has been observed in e.g. endometriosis [17].

### 3.3 Effectivity

The effectivity of all 3 NFS's was evidenced by improved conventional sperm characteristics. Also the hyaluronan-binding ability was increased by Pf treatment [18] and the content of oxidized DNA of spermatozoa was decreased by Qs [15].

The overall pregnancy rate per month (P/C) of 4 major trials with Px is 2.3% (Fig. 1) [19]. A trial with the Px-plus formulation, that was recently made openly accessible, resulted in an estimated P/C of 3.7% [20]. In the same trial, patients treated with the combination of Px-plus with the non-steroidal-anti-inflammatory agent Cinnocicam added, had a P/C reaching 6.4%.

Our own double-blind placebo-controlled trial, complementing WHO-recommended treatment with Px, resulted in a P/C of 4.9% in the treated group, with 3 pregnancies in 61 couple-months, compared to 5.2% in the placebo-control group, with 3 pregnancies in 58 couple-months [19].

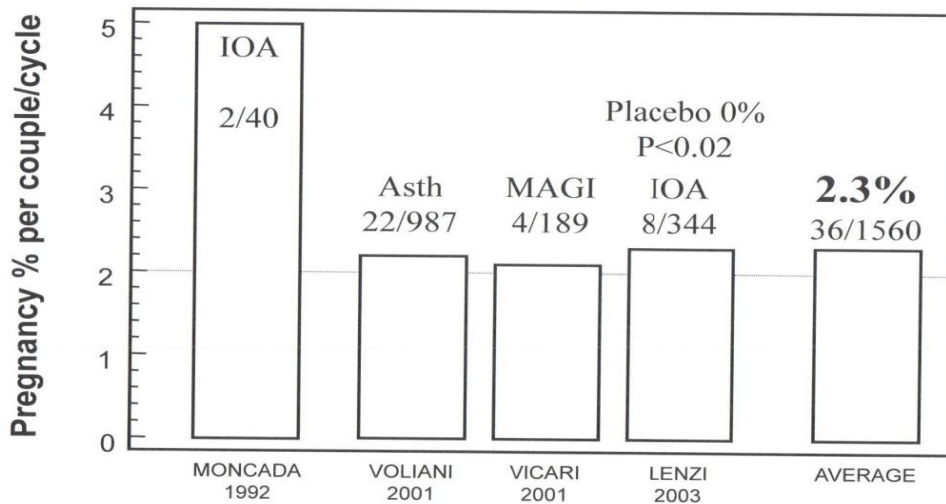
An open-label comparative trial with Pf has generated an estimated P/C of approximately 4.9% [21].

An open-label comparative trial has been performed with DUO-Qs for men, complementing WHO-recommended treatment [22]. The P/C-rate was 11% as compared to 1.9% in untreated controls, and to 3.9% in patients treated according to the WHO recommendations only, without Qs supplementation.

The most reliable single measure of effectivity of treatment is the number needed to treat (NNT). This can be estimated at 9.4 (95% confidence interval: 4.46-94.9) for Pf, at 5.0 (CI: 3.58-8.18) for Px, and at 2.8 (CI: 1.7-8.7) for Qs with WHO-recommended treatment. The NNT of the combined treatment with Px and the non-steroidal anti-inflammatory agent Cinnocicam was 2.9 (CI: 2.32-3.98) [20]. A lower NNT indicates a higher therapeutic effectivity, as less couples need to be treated to obtain one additional pregnancy.

Finally the time to pregnancy (TTP) can be estimated from the cumulative frequency distribution curves of successful pregnancies (Effective Cumulative Pregnancy Rate, Fig. 2). The cumulative pregnancy rate within 3 months after initiation of WHO recommended treatment,

## Pregnancy rates (Proxceed)



**Fig. 1.** This histogram represents the overall pregnancy rate per month in % (vertical axis) as calculated in 4 trials using Proxceed (Px) [graph from ref. 19]. The name of the first author of the respective papers and the year of publication are mentioned on the horizontal axis. The number of pregnancies and total number of couple-months is indicated. Patients included in the trials were recorded as suffering from: IOA meaning idiopathic oligo-asthenospermia, Asth meaning asthenozoospermie, and MAGI meaning male accessory gland infection. The trial by Lenzi et al. (2003) was placebo controlled with statistical significance ( $P<0.02$ ). In total 36 pregnancies have been reported in 1560 couple-months of treatment, with overall monthly pregnancy rate of 2.3%

either with the anti-oestrogen Tamoxifen in idiopathic oligozoospermia, or by varicocele embolization, was respectively 8% and 11%, and it increased to between approximately 20% and 30% after 6 months. In couples treated Px or Pf the ECPR attained between 25 and 35% in 6 months. It was 34% after 3 months of complementary treatment with DUO-Qs for men, reducing the time to pregnancy as compared to the other treatments that reached a similar cumulative pregnancy rate after 6 months or longer.

### 3.4 Treating Both Partners and Result of Assisted Reproduction Technology (ART)

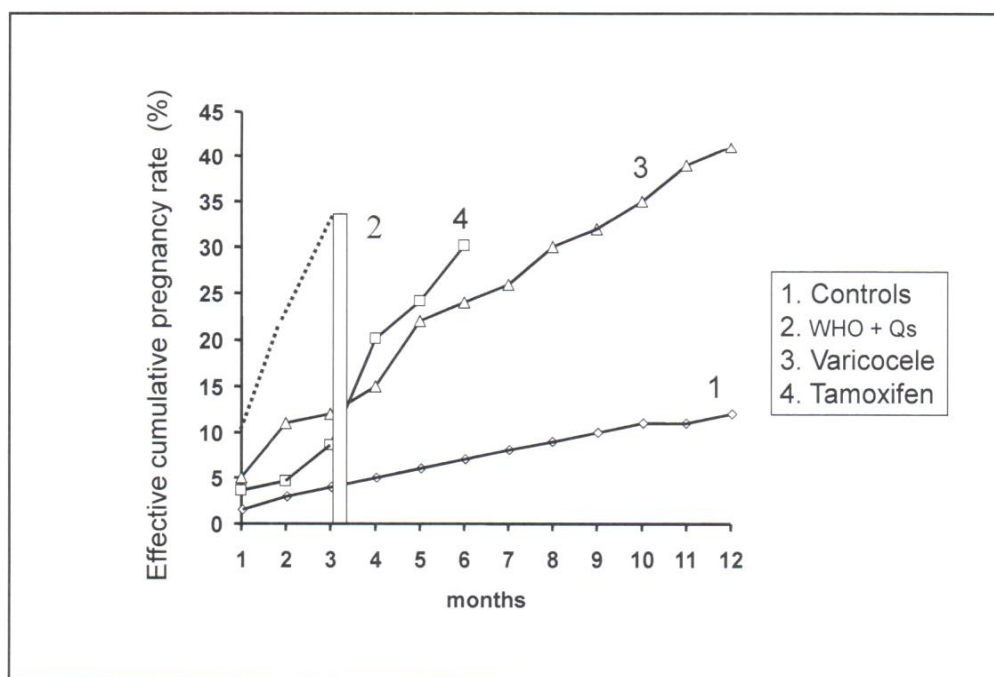
Infertility is a problem of the couple, and in one out of four cases there is a fertility-reducing factor on both partners (WHO). It is important to optimise fertility of the female partner together with that of the male partner. This is particularly important in case of advanced age of the women, or the presence of endometriosis, pelvic

inflammatory disease, or problems with ovulation due to polycystic ovary disease.

PROfertil-female contains the prescription pharmaceutical drug Clomiphene citrate that is indicated in cases of anovulation.

However, the pathological conditions of the female are accompanied by oxidative overload and chronic inflammation [23]. The DUO-Qs for women contains the ingredients described above, together with capsules of fish oil as a source of EPA and DHA. Use of this product in couple infertility is expected to increase the chances of pregnancy, both attained spontaneously or using techniques of assisted reproduction. Indeed, the probability of sperm-oocyte fusion will increase [24] and embryo quality will improve [25].

Qs is the only NFS that has been validated in assisted reproduction, particularly in In Vitro Fertilisation (IVF). There is evidence of its activity based on historical comparison, where treatment



**Fig. 2.** This figure represents the cumulative frequency distribution curve of “effective” pregnancies (ECPR in %, on the vertical axis) corresponding with the number of conceptions resulting in the birth of a healthy child. The controls (line 1) have been followed during the observation period of 12 months during which they were “counselled” and given “tender loving care”, but no other treatment. The horizontal axis displays the number of months after either varicocele cure by means of endovascular, trans-catheter embolization (line 3), or after initiation of treatment with Tamoxifen (line 4), because of idiopathic oligozoospermia. The bar at 3 months (and line 2) corresponds to the pregnancy rate after combined varicocele embolization or Tamoxifen treatment, plus intake of DUO-Qs for men

of both partners with the respective DUO-Qs formulations has increased the success rate, with NNT of 5.9 [3]. A similar NNT of 7 is obtained when comparing the results of IVF in DUO-Qs treated couples (42%) with the ongoing pregnancy rate after IVF observed in a comparable population of couples treated in other leading Belgian centres of reproductive technology (28%).

In a double-blind prospective randomised placebo-controlled trial of IVF, whereby both partners were treated with the respective DUO-Qs supplements, or received folic acid only, the chemical pregnancy rate (human chorionic gonadotropin-positive) was 55% in the active group, compared to 44% in the control group. The ongoing pregnancy rate (positive heart beat on ultrasound) was 45% in the treated group compared to 20% in the controls. Hence the NNT for one additional successful (ongoing) pregnancy was 4 [3].

#### 4. DISCUSSION

There are important differences in the composition of the three NFS's studied, and not every ingredient is equally well justified, whilst dosages may vary [26].

It has been possible to estimate the effectivity of the NFS's that are available on the market today. However, the comparison of effectivities is hampered by many factors that may have an important confounding influence. Indeed, in some trials the complementary nutraceutical food supplementation was given together with the WHO-recommended treatment, including varicocele embolization, antibiotic or anti-oestrogen treatment, but this was not the case in other trials.

Also the number of cases included was highly variable, and the study design was different. In addition, the diet taken by patients in the

Mediterranean region is known to differ from that consumed in middle and northern Europe, particularly regarding the intake of essential fatty acids. This may have influenced the success rate reported for Px, since the majority of the trials with this product were conducted in Italy.

In spite of these limitations, and considering due care in the interpretation of results, some general trends have emanated suggesting a somewhat lower effectiveness of Pf with NNT of approximately 9, compared to Px- with NNT of 5. The combination of Px with a non-steroidal anti-inflammatory agent, generating a NNT of 2.9, may be more effective than the nutraceutical supplementation with Px alone.

The DUO-Qs formulations include the ingredients that are probably most efficient in terms of anti-oxidative action, and in promoting sperm metabolism and biological composition. In addition Qs contains herbal preparations with potent anti-inflammatory effect, which is comparable to that of pharmaceutical agents. This may explain why its NNT is similar to that of Px plus Cinnoxiam.

The DUO-Qs combination for women may assist embryogenesis by counteracting oxidative stress of ovarian stimulation [27], and by providing supplementary energy during cell division. The latter may explain the favourable effect on the success-rate of IVF, particularly when considering the number of ongoing pregnancies.

## 5. CONCLUSION

It seems fair to conclude that nutraceutical food supplementation is effective for the treatment of the infertile couple. It is recommended to use NFS's in addition, and as a complementary remedy to the conventional treatment of the infertile couple recommended by WHO. NFS should also be advised to couples planning to undergo assisted reproductive technology, in vitro fertilisation in particular, with or without intra-cytoplasmic sperm injection (ICSI). Not only this should increase the successrate in terms of ongoing pregnancies, but it may also protect the embryo's from damage caused by the elevated concentration of oxidised DNA, and by epigenetic changes. In general, the supplementation of DUO-Qs to patients treated according to the WHO-recommended protocol seems to provide the best results when considering both the Number Needed to Treat (NNT) and the Time To Pregnancy (TTP).

## CONSENT

Not applicable.

## COMPETING INTERESTS

The author possesses the rights of intellectual property of Qs and receives royalty payments.

## REFERENCES

1. Comhaire F, Mahmoud A. The role of food supplementation in the treatment of the infertile man. *Reprod Biomed Online*. 2003;7:385-91.
2. Comhaire F, Decler W. Quantifying the effectiveness and cost-efficiency of food supplementation with antioxidants for male infertility. *Reprod Biomed Online*. 2011;23:361-2.
3. Comhaire F. Comparing the effectiveness of infertility treatments by numbers needed to treat (NNT). *Andrologia*. 2012;44:401-4.
4. Rowe P, Comhaire F, Hargreave T, Mahmoud A. WHO manual for the standardized investigation and management of the infertile male. *Publ. World Health Organization by Cambridge University Press*; 2000. ISBN 0-521-77474-8.
5. Laupacis A, Sacket DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med*. 1988;318:1726-33.
6. Vicari E, LaVigera S, Calogero A. Antioxidant treatment with carnitines is effective in infertile patients with prostate vesiculo epididymitis and elevated seminal leukocyte concentrations after treatment with nonsteroidal anti-inflammatory compounds. *Fertil Steril*. 2002;3:1203-8.
7. Barrie SA, Wright JV, Pizzorno JE, et al. Comparative absorption of zinc picolinate, zinc citrate and zinc gluconate in humans. *Agents Actions*. 1987;1(2):223-8.
8. Chaumontet C, Bex V, Véran F, Martel P. The vitamin E analog tocopherol succinate strongly inhibits gap junctional intercellular communication in rat liver epithelial cells (IAR203). *J Nutr Biochem*. 2008;19:263-8.
9. Witschi A, Reddy S, Sofer B, Lautenburg BH. The systemic availability of oral glutathione. *Eur J Pharmacol*. 1992;43:667-9.
10. Irvine DS. Glutathione as a treatment for male infertility. *Rev Reprod*. 1996;1:6-12.

11. Pryor JP, Blandy JP, Evans P, et al. Controlled clinical trial of arginine for infertile men with oligozoospermia. *Br J Urol.* 1978;50:47-50.
12. Rolf C, Cooper TG, Yeung CH, Nieschlag E. Antioxidant treatment of patients with asthenozoospermia or moderate oligoasthenozoospermia with high-dose vitamin C and vitamin E: A randomized, placebo-controlled, double-blind study. *Hum Reprod.* 1999;14:1023-33.
13. Zalata AA, Christophe AB, Depuydt CE, et al. The fatty acid composition of phospholipids of spermatozoa from infertile patients. *Mol Hum Reprod.* 1998;4:111-8.
14. Comhaire F, El Garem Y, Mahmoud A, et al. Combined conventional/antioxidant « Astaxanthin » treatment for male infertility: A double blind, randomized trial. *Asian J Androl.* 2005;7:257-62.
15. Comhaire FH, Christophe AB, Zalata AA, et al. The effects of combined conventional treatment, oral antioxidants and essential fatty acids on sperm biology in subfertile men. *Prostaglandins Leukot Essent Fatty Acids.* 2000;63:159-65.
16. Roseff SJ. Improvement in sperm quality and function with French maritime pine tree bark extract. *J Reprod Med.* 2002;47:821-4.
17. Netsu S, Konno R, Odagiri K, et al. Oral eicosapentaenoic acid supplementation as possible therapy for endometriosis. *Fertil Steril.* 2008;90(4 suppl):1496-502.
18. Lipovac M, Bodner F, Schütz A, et al. Increased hyaluronan binding ability of spermatozoa indicating a better maturity, morphology, and higher DNA integrity after micronutrient supplementation. *EMJ Urol.* 2014;1:60-5.
19. Comhaire F, Mahmoud A. Editorial Commentary. *J Androl.* 2004;25:771-2.
20. Cavalini G, Ferraretti AP, Gianaroli G, et al. Cinnoxiam and L-carnitine/acetyl-L-carnitine treatment for idiopathic and varicocele-associated oligoasthenospermia. *J Androl.* 2004;25:761-70.
21. Imhof M, Lackner J, Lipovac M, et al. Micronutrient supplementation increases sperm quality in the sub-fertile male. *Touch Briefings – European Urological Review.* 2011;1-4.
22. Comhaire F. The role of food supplementation in the treatment of the infertile couple and for assisted reproduction. *Andrologia.* 2010;42:331-40.
23. Gupta S, Ghulmiyyah J, Sharma R, et al. Power of proteomics in linking oxidative stress and female infertility. *Biomed Res Int.* 2014;9:16212.
24. Zalata A, Ahmed AH, Allamaneni SR, et al. Relationship between acrosin activity of human spermatozoa and oxidative stress. *Asian J Androl.* 2004;6:313-8.
25. Hammamiche F, Vujkovic M, Wijburg W, et al. Increased preconception omega-3 polyunsaturated fatty acid intake improves embryo morphology. *Fertil Steril.* 2011;95:1820-3.
26. Arcaniolo D, Favilla V, Tiscione D, et al. Is there a place for nutritional supplementation in the treatment of idiopathic male infertility? *Arch Ital Urol Androl.* 2014;86:164-70.
27. Younis A, Clower C, Nelsen D, et al. The relationship between pregnancy and oxidative stress markers on patients undergoing ovarian stimulation. *J Assist Reprod Genet.* 2012;29:1083-9.

© 2015 Comhaire; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:*  
<http://www.sciencedomain.org/review-history.php?iid=881&id=14&aid=7446>