

Improvement in sperm DNA integrity with oral anti-oxidant therapy in patients with high DNA damage

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Introduction: Sperm DNA damage has been associated with reduced fertility potential. The challenge in the management of patients with elevated DNA damage increases proportionately with the rise of such damage. While oral anti-oxidants have been reported to be effective in patients with moderately elevated DNA damage (>15%); information concerning the response of patients with markedly elevated DNA damage is lacking. The purpose of this retrospective study was to evaluate the effect of oral anti-oxidant therapy in patients with high DNA damage (>60%).

Materials and methods: Following Institutional Research Ethics Board approval, 23 patients with a DNA fragmentation index (DFI) >60% were analyzed prior to and three months following oral anti-oxidant therapy. Four patients receiving concurrent therapy (antibiotics or varicocele surgery) between assessments were excluded from the study. Ten patients received Fertile One[®], a combination of vitamins, minerals and herbs, while nine patients received vitamins (C, E, folic acid) supplemented with zinc and selenium. Data were analyzed with Wilcoxon Signed Ranks Test and the results expressed as mean \pm SD.

Results: Improved DNA integrity was observed in 47% of patients following anti-oxidant treatment (60% on Fertile One[®] vs. 33% on vitamins alone). Patients who received Fertile One[®] showed a significant decrease in DFI ($69.5\% \pm 7.1$ vs. $63.9\% \pm 9.2$, $P < 0.05$). There was no significant difference in DFI after vitamins alone ($73.4\% \pm 14.6$ vs. $71.1\% \pm 12.1$).

While the group was diagnostically heterogeneous, no patients with particular pathology or idiopathic infertility had responded better to the oral anti-oxidant therapy.

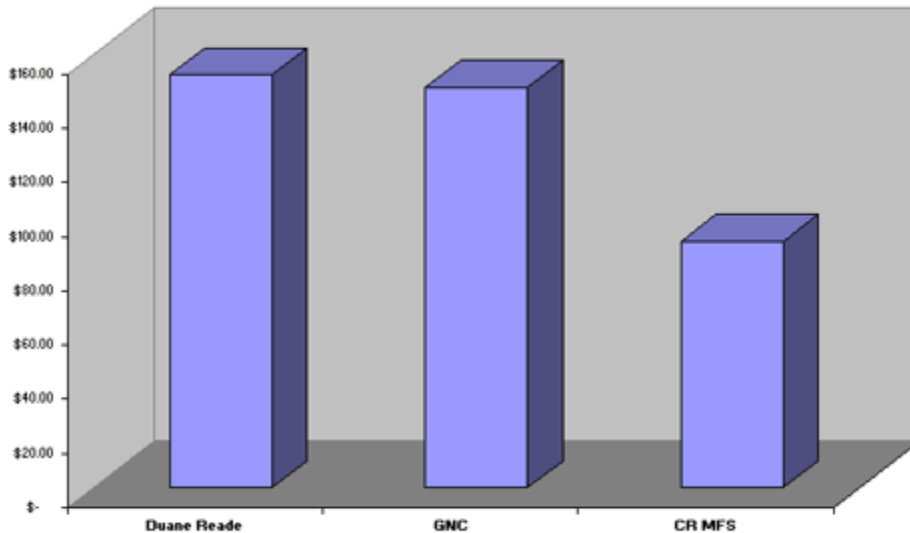
Conclusions: This non-randomized retrospective study suggests that the use of Fertile One[®] may reduce sperm DNA damage in men with markedly elevated DNA damage. While the reduction in damage was modest, there was significant improvement in nearly one-half of cases. Therefore, further study of oral anti-oxidant therapy is warranted in this patient population.

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COAST REPRODUCTIVE COST COMPARISON – This comparison uses standard size bottles of vitamins from the shelf of each retailer. The quantity of each vitamin needed is one or more per day. That is 13 separate components of one or more pills per day! Coast Reproductive’s Male Fertility Supplement contains all of the components in only **4 capsules per day** plus we guarantee the quality, purity and grade of our product.

	Duane Reade	GNC	CR MFS
Vitamin C	\$5.99	\$1.49	Included
Vitamin E	\$7.33	\$2.79	Included
Selenium	\$5.19	\$3.99	Included
Multi-Vitamin	\$9.49	\$23.99	Included
Folic Acid	\$9.78	\$6.99	Included
Co Q10	\$33.58	\$29.99	Included
Lycopene	\$11.58	\$19.99	Included
Vitamin B12	\$5.19	\$6.99	Included
Zinc	\$5.19	\$6.99	Included
Acetyl L-Carnitine	\$35.98	\$34.98	Included
Relora	N/A	N/A	Included
Vitamin A	\$2.59	\$2.49	Included
Glutathione	N/A	\$8.99	Included
L-Methionine	N/A	\$9.99	Included
Vitamin B3	3.17	\$4.99	Included
Vitamin B2	N/A	\$3.99	Included
	\$131.89	\$168.64	\$91.00

Retail Pricing Comparison
Pricing for individual components vs. CR MFS
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Effects of antioxidant treatment on DNA fragmentation index.

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OBJECTIVE: In addition to the standard semen analysis, the Sperm DNA integrity assay (SCSA) and Sperm DNA fragmentation index (DFI) have become more widely employed in the evaluation of male factor infertility. A (DFI) above 30% has been associated with a higher rate of pregnancy failure. Although no definite treatment exists for an elevated DFI, many Reproductive Endocrinologists empirically treat these patients with a course of antioxidant therapy (AOT), Fertile One™. To our knowledge, no published data exists evaluating the effects of AOT on the DFI. The objective of our study was to evaluate the association between treatment with antioxidants and the overall change in DNA fragmentation index in men seeking treatment for infertility.

DESIGN: We conducted a retrospective chart review of all of our patients from 5 IVF centers from January 2003 to January 2004.

MATERIALS AND METHODS: Men with male factor infertility or a history of no living children were offered the Sperm DNA integrity assay. Those with an initial DNA fragmentation index \geq 30% were included in the study. All together, 43 men met eligibility criteria. 17 of these men elected not to take AOT (Group A [controls]). 13 took AOT for 30 to 90 days (Group B) and 13 took AOT for greater than 90 days. All men had at least two sperm chromatin structural assays performed. The mean age of the men in the three groups was not statistically different. Statistical analysis was performed using the paired t test.

RESULTS: The mean duration of time between the two SCSA tests were 236 days for Group A, 64 days for group B, and 107 days for group C. The mean percent change for group B compared to group A was 10.2% (CI 3.7–16.7; $p < .005$). The mean percent change between group B and Group C was 5.5% (CI -2.4–13.3; $p = 0.25$).

CONCLUSION: Treatment of men with DFI $>$ 30% with a 30 to 90 day course of AOT (Fertile One™) was associated with a statistically significant decrease in the DFI. Extending the treatment beyond 90 days appeared to have no additional benefits on DFI.

Why we have Relora in our product...

Relora® is a natural proprietary blend of a patented (U.S. Patent No. US 6,582,735) extract of *Magnolia officinalis* and a proprietary extract from *Phellodendron amurense*. Relora® was developed as an ingredient for dietary supplements and functional foods that could be used in stress management and for stress-related appetite control. This patented blend of plant extracts is the result of screening more than fifty plant fractions from traditional plant medicines used around the world. Relora® has excellent stress management properties without causing sedation.

Safety Studies

An extensive literature review of the chemical constituents with the parent plant's use for hundreds of years indicates that this material is safe for its intended use. An acute toxicity study in rats (5g/kg) with 14-day observation revealed no untoward effects of the individual extracts or the combination in Relora® except mild diarrhea and slight sedation in female rats. No side effects are expected at the recommended human dosage.

Mechanism of Action

Relora® is a natural stress management ingredient that helps control stress-related eating and has the added value of being non-sedating. In central nervous system receptor binding assays the plant extracts in Relora® binds to several important targets associated with stress. It does not bind to the benzodiazepine receptors that would cause sedation, yet has the relaxing qualities that have been demonstrated in both animal and human studies. In addition, it normalizes hormone levels associated with stress-induced weight gain and eating behavior. Stress has been shown to play a significant role in a variety of conditions. A large percentage of overweight adults have excessive abdominal fat due to stress-related over eating. Relora® appears to maintain healthy hormone levels in stressed individuals and act as an aid in controlling weight and stress-related eating.

Animal Studies

The plant extracts in Relora® have been shown to be an effective non-sedating anti-stress product in an animal model known as the "Chick Social Separation Stress Procedure." The excellent results of the patent-pending extracts in Relora® using this model were published in *Psychopharmacology* (2001)153:219-234

Open Human Trials

The first formulation of Relora® was tested and found to be a safe, effective, and rapid acting, dietary supplement that helps control stress symptoms. Fifty subjects were treated with Relora® for two weeks. The recommended dosage was 200mg Relora® three times daily. (The new Relora® dosage is 750 mg daily in divided doses.) Based on pre-clinical studies, Relora® was designed and evaluated against the following concepts; Relora® helps control stress-related symptoms, such as:

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irritability; emotional ups and downs; restlessness; tense muscles; poor sleep; concentration difficulties. Post trial analysis revealed an excellent agreement (82%) with the pretrial concept. Relaxation was reported by 78% of the patients. The product does not cause significant sedation, however, 74% of the patients did

8 out of 10 people feel more relaxed.

report restful sleep. Only 24% reported drowsiness. Relora® was judged to be gentle on the stomach by 94% of the subjects. No significant side effects were reported. A second trial was undertaken to measure cortisol and DHEA levels in 12 patients with mild to moderate stress. Elevated cortisol levels and depressed DHEA levels are associated with chronic stress. A two-week regimen of Relora® caused a significant ($P= 0.003$) increase in salivary DHEA (227%) and a significant ($P = 0.01$) decrease in morning salivary cortisol levels (37%). Cortisol and DHEA levels were returned to normal in all subjects during the course of Relora®. A third trial of 49 subjects achieved similar results to the first trial regarding relaxation and restful sleep. In addition, Relora® reduced stress-related snacking of sweets, such as ice cream, cake, pie, and cookies by 76% in those individuals that claimed they ate these types of foods under stress.

Over 1,200 subjects at the Living Longer Clinic in Cincinnati have taken Relora® and rated its efficacy on a 5-point scale. Relora® was considered effective for stress, restful sleep and stress related eating if the subject rated the product 3 or higher. Ninety-one percent (91%) of the subjects reported Relora® helped them relax with a mean score of 3.5. Ninety percent (90%) reported Relora® helped them have a restful sleep with a mean score of 3.6. Eighty-six percent (86%) reported Relora® helped prevent stress related eating with a mean score of 3.5. Seventy-two percent (72%) of the subjects rated Relora® as effective in helping manage weight with a mean score of 3.1.

Clinical Trial

A double-blind placebo-controlled clinical trial with Relora® was completed in January 2004. The purpose of this study was to determine the effects of Relora® in overweight women who typically eat more in stressful situations. Twenty-eight subjects completed the study and Relora® was well tolerated. There was a significant weight gain during the study for the placebo group but no significant weight gain and some weight loss for the Relora® group. There was also a significant reduction in anxiety scores. The mechanism of action appears to be through reduction or normalization of stress hormone levels, and possibly perceived stress, thereby helping subjects maintain body weight.

Coast Reproductive Male Fertility Supplement – Fertile One®

Clinical Studies | Supporting Components

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