Review Article

# Is There a Role for Nutritional Supplements in Dry Eye?

Sanjay Srinivasan,[1,2] *MBBS, MRCSEd, MMed (Ophthal)*, Chee-Chew Yip,[1-3] *MBBS, FRCSEd, MMed (Ophthal)*

## Abstract

**Introduction: Dry eye syndrome is a prevalent eye condition whereby the terminology, classification and treatment are not yet clearly elucidated. Methods: Literature review was done with Pubmed search engine with key words " dry eye", "nutritional supplements" and "treatment" for articles related to the pathogenesis of dry eye and the use of nutrients in treatment of dry eye. Results: Increased inflammatory cytokines may contribute to the pathogenesis of ocular surface and lacrimal gland inflammation. Nutritional supplementation with omega-3 fatty acids at an appropriate consumption ratio with omega-6 fatty acids was found to have a reduced incidence of dry eye due to its anti-inflammatory effects. Conclusions: The role of nutritional supplements in the treatment of dry eyes remains unknown. Omega-3 fatty acids may be considered as an adjunct therapy to conventional tear substitutes. Further research and clinical studies are necessary to validate the efficacy and safety of these nutritional supplements.**

**Ann Acad Med Singapore 2007;36(Suppl):45-9**

**Key words: Dry eye, Nutritional supplements, Omega fatty acids**

## Introduction

The possible role of nutritional supplementation in preventing or halting the progression of ocular disease is of interest to healthcare professionals and patients. Nutritional supplements are available in many forms such as vitamins A, B, C and E, carotenoids (beta-carotene, lutein, and zeaxanthin), minerals such as selenium and zinc, and the herb, ginkgo biloba. Traditionally, nutritional supplements have been used in the treatment of various eye diseases including glaucoma, cataract, age-related macular degeneration (AMD) and dry eye.[1]

Patients with intermediate risk of AMD or advanced AMD in one eye were recommended Age-Related Eye Disease Study (AREDS) formulation which was successful in preventing the advancement of AMD by 25%. The formulation consisted of vitamins C, E, beta-carotene and zinc.[2] Improvement in the visual function of patients with AMD has been noted with lutein and zeaxanthin supplementation.[3] Ginkgo biloba has been reported to improve pre-existing visual field damage in some patients with normal tension glaucoma.[3]

Essential fatty acids such as omega-3 fatty acids are important in retinal development and in the prevention of cardiovascular diseases.[3] A high ratio of omega-3 to omega-6 fatty acids and polyunsaturated fat appear to increase the risk of primary open-angle glaucoma.[4] The essential omega-6 fatty acid, gamma-linolenic acid (GLA), is useful in Sjögren's syndrome and may help in other dry eye conditions.[3] It is therefore useful to review the role of nutritional supplements in the treatment of dry eye.

Literature review was done with pubmed using the key words " dry eye", "nutritional supplements" and "treatment" for articles related to the pathogenesis of dry eye and the use of nutrients in the treatment of dry eye.

## Dry Eye

Dry eye is caused by abnormalities in the quality and/or the quantity of the tear film causing ocular surface dysfunction and desquamation. The tear film serves many functions to maintain the health of the ocular surface. It acts as a lubricant to reduce friction between the eyelid and the ocular surface besides washing away debris, noxious agents and inflammatory mediators.

Sack et al[5] identified over 80 chemokines, cytokines, growth factors (such as epidermal growth factor), monocyte chemoattractant protein-1, interleukin 8 (IL-8) and tissue

[1] Ophthalmology and Visual Sciences, Alexandra Hospital, Singapore
[2] Eye Clinic, Jurong Medical Centre, Singapore
[3] Department of Ophthalmology, Tan Tock Seng Hospital, Singapore
Address for Correspondence: Dr Yip Chee Chew, Ophthalmology and Visual Sciences, 378, Alexandra Road, Alexandra Hospital, Singapore 159964.
Email: chee_chew_yip@alexhosp.com.sg

inhibitor of metalloproteinase-1 and -2 in the tears. Numerous other previously undetected tear components include angiogenin, growth factors, chemokines, gamma inducible protein-10, growth-related oncogene, epithelial neutrophil-activating protein-78, and macrophage inflammatory protein-3 alpha. Some of these, such as interleukins, function as inflammatory mediators and may contribute towards the pathogenesis of dry eyes.

A normal healthy tear film is essential for clear vision, as the tear film is the first converging lens system that light encounters as it enters the eye. The 3 layers of the tear film from outer to inner include the lipid, the aqueous and the mucin layers. Abnormalities of one or more layers of the tear film may affect the ocular surface causing dry eye symptoms.

## Pathogenesis

Dry eye is highly prevalent, affecting 14% to 33% of the population worldwide depending on the study and the definition used.[6-9] International specialists on dry eye used a modified, 2-round Delphi panel approach to propose an appropriate terminology, devise a classification system and develop treatment recommendations for different levels of disease severity.[10] The panelists unanimously recommended dysfunctional tear syndrome as a more appropriate term for this disease.

On the basis of known pathophysiology, symptoms, and clinical presentation, all panelists agreed that the term dry eye did not reflect the events occurring in the eye.[10] Specifically, all patients with this condition did not necessarily suffer from reduced tear volume but rather may have abnormalities of the tear film composition that include the presence of pro-inflammatory mediators.[11-13] Patients with dry eye syndrome have been shown to possess increased concentration of interleukin1 (IL-1), interleukin 6 (IL-6) and tumour necrosis factor alpha (TNF $\alpha$) in the tear film.[14] The balance of cytokines in the tear fluid and the conjunctival epithelium is altered in Sjögren's syndrome/kerato-conjunctivitis sicca.[15] The severity of keratoconjunctivitis sicca increases as the tear fluid epidermal growth factor concentration decreases and the levels of inflammatory cytokines in the conjunctival epithelium increase. These findings provide new insight into the pathogenesis of keratoconjunctivitis sicca and provide potential targets for therapy.[15] Stern et al[16] showed that dry eye is an inflammatory disease with gradual progression to diminished tear production.

## Treatment

The treatment of dry eye is challenging and the treatment algorithms are often complicated. Multiple therapeutic agents and treatment strategies are available for the treatment of different stages of same disease. To the clinician that manages dry eye patients on a daily basis, the treatment can sometimes be frustrating and unrewarding.

The conventional treatment of dry eye with artificial tears is based on the concept of volume replacement of diminished tear quantity. However, some dry eye patients do not tolerate artificial tears on a long-term basis, especially those containing preservatives such as benzalkonium

Table 1. Treatment Recommendations for Dysfunctional Tear Syndrome (DTS) on the Basis of Level of Severity[10]

| DTS severity | Patient profiles* | Treatment recommendations | |
|---|---|---|---|
| Level 1 | Mild to moderate symptoms and no signs<br>Mild to moderate conjunctival signs | No treatment<br>Preserved tears<br>Environmental management<br>Allergy drops | Use of hypoallergenic products<br>Water intake<br>Psychological support<br>Avoidance of drugs contributing to dry eye |
| Level 2 | Moderate to severe symptoms<br>Tear film signs<br>Mild corneal punctate staining<br>Conjunctival staining<br>Visual signs | Unpreserved tears<br>Gels<br>Ointments<br>Nutritional support (flaxseed/fatty acids) | Secretagogues<br>Topical steroids<br>Topical cyclosporine A |
| Level 3 | Severe symptoms<br>Marked corneal punctate staining<br>Central corneal staining<br>Filamentary keratitis | Tetracyclines<br>Punctal plugs | |
| Level 4 | Severe symptoms<br>Severe corneal staining erosions<br>Conjunctival scarring | Surgery<br>Systemic anti-inflammatory therapy<br>Oral cyclosporine<br>Moisture goggles | Punctal cautery<br>Acetylcysteine<br>Contact lenses |

* Levels of severity of DTS without lid margin disease according to symptoms and signs

chloride. Ocular surface toxicity and intolerance due to preservatives in the eye drops become more significant in cases of severe dry eye that require frequent instillation of artificial tears. Preservative-free tear substitutes such as Refresh Plus® (Allergan, Irvine) and Tears Naturale Free® (Alcon, Dallas), and eye drops containing fast disappearing preservatives like Purite® (such as Refresh Tears™ (Allergan, Irvine) and Refresh Liquigel® (Allergan, Irvine) eye drops) are alternatives that can be considered in this intolerant group of patients. Nonetheless, the former being more expensive may pose a financial burden to the patient in view of the need for long-term treatment.

Trehalose solution was also reported to be an effective and safe eye drop in improving the symptoms and signs of patients with moderate to severe dry eye compared to saline.[17] Trehalose solution at a concentration of 100-mM improved tear film breakup time, fluorescein scores and rose bengal scores.[17] Recently, cyclosporin A emulsion eye drop is being used in dry eye therapy to suppress lacrimal and ocular surface inflammation.[18,19] Corticosteroids[20] are beneficial in cases of severe dry eye but prolonged use is complicated by undesirable ocular side effects such as cataract and glaucoma.

Yoon et al[21] found that umbilical cord serum contained essential tear components. Umbilical cord serum eye drops were effective and safe for the treatment of severe dry eye syndrome. In a randomised study by Noble et al,[22] autologous serum was found to be beneficial in severe ocular surface disorders. For most of these patients, autologous serum was superior to conventional treatment for improving ocular surface health and comfort.

The treatment recommendations for dysfunctional tear syndrome[10] based on the level of severity is shown in Table 1. There is a poor correlation between symptoms and signs. The efficacy criteria to determine the stage of the disease are often not uniform.

## Omega Fatty Acids

Long-chain polyunsaturated fatty acids are classified based on their chemical structure into two groups: omega-3 fatty acids and omega-6 fatty acids. The omega-3 notation means that the first double bond is three carbons from the methyl end of the molecule. The omega-3 and omega-6 fatty acids are essential fatty acids that are required to be consumed in the diet or as supplements as they are not synthesised in the body.

### *Omega 3 Fatty Acids*

The two best sources of omega-3 fatty acids are flaxseed and dark, cold-water fish like salmon, mackerel and tuna. Flaxseed and cold-water fish each provide a different type of omega-3 fatty acid. Flaxseed provides "short-chain" omega-3 fatty acid while cold-water fish provides "long-chain" omega-3 fatty acid.[23] Omega-3 polyunsaturated fatty acid possesses the most potent immunomodulatory activity amongst all omega-3 fatty acids, especially those that are derived from fish oil such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The only good sources are fish, seafood and "omega-3" eggs.[24] EPA and DHA, are more biologically potent than alpha-linolenic acid (ALA).[25] The amounts of EPA and DHA in the diet vary greatly from person to person.

Omega-3 fatty acids act by either modulating the amount and types of eicosanoids synthesised or by eicosanoid-independent mechanisms. The latter include actions upon intracellular signaling pathways, transcription factor activity and gene expression.[25] Simopoulos[26] reported that dietary intake of omega-3 fatty acids at an appropriate ratio of consumption with omega-6 fatty acids (recommended ratio 2.3:1) affects the overall level of inflammatory activity in the body. In an meta analysis of the analgesic effects of omega-3 fatty acids, Goldberg and Katz[27] suggested that omega-3 fatty acid is an attractive adjunctive treatment for joint pain associated with rheumatoid arthritis, inflammatory bowel disease, and dysmenorrhoea.

### *Omega 6 Fatty Acids*

Linoleic acid and its derivative GLA are two omega-6 fatty acids obtained from plant source, including unprocessed, unheated oil, such as corn, sunflower seed, safflower, soy, sesame, cottonseed, black currant seed, and borage oils.[27] Animal sources of omega-6 fatty acids, although in smaller amounts than in plants, are lean meats, organ meats and breast milk. The administration of linoleic and GLA as dietary supplements have been reported to have a beneficial effect in the treatment of chronic inflammatory disorders, such as rheumatoid arthritis.[27]

Gamma-linolenic acid does not accumulate in significant amounts in cell membranes, even when it is provided in the diet. It is converted to dihomo-GLA (DGLA), a substrate for cyclooxygenase (that gives rise to a prostaglandin $E_1$ series) and 15-lipoxygenase (that gives rise to 15-hydroxy-DGLA). Prostaglandin $E_1$ exerts several anti-inflammatory effects, including the inhibition of superoxide, tumour necrosis factor, interleukin-1 β (IL-1β), and IL-6.[28] 15-hydroxy-DGLA is an inhibitor of 5-lipoxygenase and 12-lipoxygenase and thus can decrease the synthesis of some arachidonic acid (ARA)-derived mediators, such as leukotriene $B_4$, which is a potent pro-inflammatory compound.

The administration of linoleic and GLA as dietary supplements reduces the levels of inflammatory ARA oxidation products and produces less active prostanoids.[28] Black currant seed oil rich in both GLA and ALA, have

been shown to modulate membrane lipid composition and eicosanoid production.[29]

The mechanism by which omega-3 fatty acid reduces pain is not known. Evidence is equivocal for an EPA/ DHA mediated reduction in cytokine secretion in humans. Kelley et al[30] reported that high-dose EPA or DHA resulted in a suppression of TNF-α or IL-1β release by monocytes, whereas Kew et al[31] failed to detect any changes in cytokine release.

**The Role of Omega Fatty Acids in Age-related Macular Degeneration**

The long chain fatty acid DHA is found in high concentration in the photoreceptor outer segments and is constantly shed and turned over during the normal visual cycle. A deficiency of DHA might therefore impair retinal function and promote AMD.[32] In fact, several previous epidemiologic studies and clinical trials suggested that high dietary intake of fat was associated with a higher incidence of AMD whereas high intakes of fish or omega-3 fatty acids were associated with lower rates.[33,34] The US twin study of AMD provided evidence that cigarette smoking increased the risk while fish consumption and omega-3 fatty acid intake reduced the risk of AMD.[35]

**The Role of Omega Fatty Acids in Dry Eye**

Aqueous tear deficient dry eye syndrome is an inflammatory disorder that affects the ocular surface and the lacrimal gland. Ocular surface can become a target of the immune system and exhibit signs of inflammation in autoimmune diseases (such as Sjögren's syndrome), organ transplantation (graft versus host disease), and ageing.[36] The hallmarks of lacrimal gland inflammation are the presence of focal lymphocytic infiltrates and increased production of pro-inflammatory cytokines. The mechanisms leading to lacrimal gland dysfunction are still poorly understood. Apoptosis, the production of autoantibodies, hormonal imbalance, alterations in signaling molecules, neural dysfunction and increased levels of pro-inflammatory cytokines have been postulated mechanisms to account for the lacrimal gland insufficiency in various disease states.[36]

Boerner[37] treated 116 patients in a open-label clinical trial with omega-3 supplements and found that 98% of dry eye patients reported an improvement in their symptoms. Miljanovic et al[38] reported the relationship between dietary omega-3 and omega-6 fatty acids and clinically diagnosed dry eye syndrome and suggested that higher dietary intake of omega-3 fatty acid was associated with decreased incidence of dry eyes in women.

DGLA, ARA and EPA are omega-3 fatty acid-derived precursors of eicosanoids that function as modulators of inflammation. The omega-3 fatty acids may also have a direct effect on the polar portion of the lipid layer by increasing the amount of omega-3 fatty acid present or affecting the omega-6 to omega-3 fatty acid ratio.[39] The intake of omega- 3 fatty acids may decreases the endogenous oestrogen levels[40] which influence the risk of developing dry eye.[41] The omega-3 fatty acid deficient individuals usually have a thick meibomian gland secretion that results in evaporative tear loss.[42] Pinna et al[43] studied the effect of oral linoleic acid and GLA, the omega-6 essential fatty acids, on meibomian gland dysfunction. Treatment with linoleic acid and GLA tablets along with eyelid hygiene improved symptoms and reduced eyelid margin inflammation more than either omega-6 fatty acids or eyelid hygiene alone.[43]

**Safety of Omega Fatty Acids**

Safety concerns have been raised regarding long-term omega fatty acid supplementation. Bays[44] reported a theoretical risk of bleeding (due to the antithrombotic effect of omega fatty acids), toxicity, patient intolerance (due to potential oxidation of the omega fatty acids supplements) and contamination of the fish oils with environmental toxins like mercury and dioxins. It is advisable to warn the patients of these potential risks and avoid the use of omega fatty acid supplements in individuals on anti-platelet or anti-coagulant therapy or with bleeding disorders.

**Conclusions**

Omega fatty acids are essential fatty acids present in the diet or in nutritional supplements. They may be potential therapeutic options to augment tear substitutes in the management of dry eye. Supplementation of omega fatty acids works via multiple mechanisms to relieve the symptoms of dry eye. It improves the quality of meibomian gland secretion and stimulates aqueous tear secretion via its anti-inflammatory and anti-apoptotic actions on the dysfunctional lacrimal gland. Further clinical trials are necessary to validate the risks and benefits of omega fatty acids. Eye-care practitioners should be aware of the potential side effects of these ocular nutritional supplements and to discuss them with patients before the commencement of treatment.

REFERENCES

1. Bartlett H, Eperjesi F. An ideal ocular nutritional supplement? Ophthalmic Physiol Opt 2004;24:339-49.
2. Coleman H, Chew E. Nutritional supplementation in age-related macular degeneration. Curr Opin Ophthalmol 2007;18:220-3.
3. Brown NA, Bron AJ, Harding JJ, Dewar HM. Nutrition supplements and the eye. Eye 1998;12(Pt 1):127-33.
4. Kang JH, Pasquale LR, Willett WC, Rosner BA, Egan KM, Faberowski

N, et al. Dietary fat consumption and primary open-angle glaucoma. Am J Clin Nutr 2004;79:755-64.
5. Sack RA, Conradi L, Krumholz D, Beaton A, Sathe S, Morris C. Membrane array characterization of 80 chemokines, cytokines, and growth factors in open- and closed-eye tears: angiogenin and other defense system constituents. Invest Ophthalmol Vis Sci 2005;46: 1228-38.
6. Schein OD, Munoz B, Tielsch JM, Bandeen-Roche K, West S. Prevalence of dry eye among the elderly. Am J Ophthalmol 1997;124:723-8.
7. Schaumberg DA, Sullivan DA, Buring JE, Dana MR. Prevalence of dry eye syndrome among US women. Am J Ophthalmol 2003;136:318-26.
8. Lin PY, Tsai SY, Cheng CY, Liu JH, Chou P, Hsu WM. Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. Ophthalmology 2003;110:1096-101.
9. Brewitt H, Sistani F. Dry eye disease: the scale of the problem. Surv Ophthalmol 2001;45:S199-S202.
10. Dysfunctional tear syndrome study group. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea 2006;25: 900-7.
11. Pflugfelder SC. Anti-inflammatory therapy for dry eye. Am J Ophthalmol 2004;137:337-42.
12. Baudouin C. The pathology of dry eye. Surv Ophthalmol 2001;45 (Suppl 2):S211-S220.
13. Lemp MA. Evaluation and differential diagnosis of keratoconjunctivitis sicca. J Rheumatol Suppl 2000;61:11-4.
14. Pflugfelder SC, Jones D, Ji Z, Afonso A, Monroy D. Altered cytokine balance in the tear fluid and conjunctiva of patients with Sjögren's syndrome keratoconjunctivitis sicca. Curr Eye Res 1999;19:201-11.
15. Solomon A, Dursun D, Liu Z, Xie Y, Macri A, Pflugfelder SC. Pro- and ante-inflammatory forms of interleukin-1 in the tear fluid and conjunctiva of patients with dry-eye disease. Invest Ophthalmol Vis Sci 2001;42: 2283-92.
16. Stern ME, Beuerman RW, Fox RI, Gao J, Mircheff AK, Pflugfelder SC. The pathology of dry eye: The interaction between the ocular surface and lacrimal glands. Cornea 1998;17:584-9.
17. Matsuo T, Tsuchida Y, Morimoto N. Trehalose eye drops in the treatment of dry eye syndrome. Ophthalmology 2002;109:2024-9.
18. Sall K, Stevenson OD, Mundorf TK, Reis BL. Two multicenter, randomised studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate to severe dry eye disease. Ophthalmology. 2000;107:631-9.
19. Kunert KS, Tisdale AS, Gilpson IK. Goblet cell numbers and epithelial proliferation in the conjunctiva of patients with dry eye syndrome treated with cyclosporin. Arch Ophthalmol 2002;120:330-7.
20. Avunduk AM, Avunduk MC, Varnell ED, Kaufman HE. The comparison of efficacies of topical corticosteroids and nonsteroidal anti-inflammatory drops on dry eye patients: a clinical and immunocytochemical study. Am J Ophthalmol 2003;136:593-602.
21. Yoon KC, Im SK, Park YG, Jung YD, Yang SY, Choi J. Application of umbilical cord serum eyedrops for the treatment of dry eye syndrome. Cornea 2006;25:268-72.
22. Noble BA, Loh RS, MacLennan S, Pesudovs K, Reynolds A, Bridges LR, et al. Comparison of autologous serum eye drops with conventional therapy in a randomised controlled crossover trial for ocular surface disease. Br J Ophthalmol 2004;88:647-52
23. Available at: http://www.theratears.com/nutrition-in-depth.aspx. Accessed 23 June 2007.
24. Balk EM, Horsley TA, Newberry SJ, Lichtenstein AH, Yetley EA, Schachter HM, et al. A collaborative effort to apply the evidence-based review process to the field of nutrition: challenges, benefits, and lessons learned. Am J Clin Nutr 2007;85:1448-56.
25. Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. J Am Coll Nutr 2002;21:495-505.
26. Simopoulos AP. Human requirement for n-3 poly unsaturated fatty acids. Poult Sci 2000;79:961-70.
27. Goldberg RJ, Katz J. A meta-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain. Pain 2007;129:210-23.
28. Calder PC, Zurier RB. Polyunsatered fatty acids and rheumatoid arthritis. Curr Opin Clin Nutr Metab Care 2001;4:115-21.
29. Wu D, Meydani M, Leka LS, Nightingale Z, Handelman GJ, Blumberg JB, et al. Effect of dietary supplementation with black currant seed oil on the immune response of healthy subjects. Am J Clin Nutr 1999;70: 536-43.
30. Kelley DS, Taylor PC, Nelson GJ, Schmidt PC, Ferretti A, Erickson KL, et al. Docosahexaenoic acid ingestion inhibits natural killer cell activity and production of inflammatory mediators in young healthy men. Lipids 1999;34:317-24.
31. Kew S, Mesa MD, Tricon S, Buckley R, Minihane AM, Yaqoob P. Effects of oils rich in eicosapentaenoic and docosahexaenoic acids on immune cell composition and function in healthy humans. Am J Clin Nutr 2004;79:674-81.
32. Guymer RH, Chong EW. Modifiable risk factors for age-related macular degeneration. Med J Aust 2006;184:455-8.
33. Mares JA, Moeller SM. Diet and age-related macular degeneration: expanding our view. Am J Clin Nutr 2006;83:733-4.
34. Chua B, Flood V, Rochtchina E, Wang JJ, Smith W, Mitchell P. Dietary fatty acids and the 5-year incidence of age-related maculopathy. Arch Ophthalmol 2006;124:981-6.
35. Seddon JM, George S, Rosner B. Cigarette smoking, fish consumption, omega-3 fatty acid intake, and associations with age-related macular degeneration: the US Twin Study of Age-Related Macular Degeneration. Arch Ophthalmol 2006;124:995-1001.
36. Zoukhri D. Effect of inflammation on lacrimal gland function. Exp Eye Res 2006;82:885-98.
37. Boerner CF. Dry eye successfully treated with oral flaxseed oil. Ocular Surg News 2000;147-8.
38. Miljanovic B, Trivedi KA, Dana MR, Gilbard JP, Buring JE, Schaumberg DA. Relation between dietary n-3 and n-6 fatty acids and clinically diagnosed dry eye syndrome in women. Am J Clin Nutr 2005;82:887-93.
39. Sullivan BD, Cermak JM, Sullivan RM, Papas AS, Evans JE, Dana MR, et al. Correlations between nutrient intake and the polar lipid profiles of meibomian gland secretions in women with Sjogren's syndrome. Adv Exp Med Biol 2002;506:441-7.
40. Noble LS, Takayama K, Zeitoun KM, Putman JM, Johns DA, Hinshelwood MM, et al. Prostaglandin E2 stimulates aromatase expression in endometriosis-derived stromal cells. J Clin Endocrinol Metab 1997; 82:600-6.
41. Schaumberg DA, Buring JE, Sullivan DA, Dana MR. Hormone replacement therapy and dry eye syndrome. JAMA 2001;286:2114-9.
42. Nutritional supplement stimulates tear production. Ophthalmology Times 15 May 2003;Vol 28, No. 10.
43. Pinna A, Piccinini P, Carta F. Effect of oral linoleic and gamma-linolenic acid on meibomian gland dysfunction. Cornea 2007;26:260-4.
44. Bays HE. Safety considerations with omega-3 fatty acid therapy. Am J Cardiol 2007;99:35C-43C.