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Standards of Practice
Ocular Abnormalities

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This CET has been approved for one point by the GOC. It is open to all FBDO members, and associate member optometrists. The multiple-choice questions (MCQs) for this month's CET are available **online only** from 1 November 2021, to comply with the GOC's Good Practice Guidance for this type of CET. Insert your answers to the six MCQs online at www.abdo.org.uk. After member login, scroll down and you will find CET Online within your Personalised Dashboard. **Questions will be presented in random order**. Please ensure that your email address and GOC number are up-to-date. The pass mark is 60 per cent. The answers will appear in the March 2022 issue of *Dispensing Optics*. The closing date is 18 December 2021.

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For Optometrists

C-79288 Approved for one CET Point

Can plant-based sources of Omega-3 **benefit patients with dry eye?**

By Anna Wheatley BSc (Hons), FBDO

In 2017, the respected Tear Film and Ocular Surface (TFOS) DEWS II Report detailed that dry eye disease (DED) is thought to affect between five to 50 per cent of the population. This figure is influenced by multiple risk factors including[1]:

- Increasing age
- Race
- Sex
- Contact lens wear
- Environment
- Screen use

Whilst often considered as a minor eye condition, evidence indicates that quality of life may be negatively affected by DED due to its impact on both discomfort and vision[1]. Therefore, patients with some form of DED will be regularly encountered in High Street optical practice.

Molina-Leyva *et al*, amongst others, have suggested that omega fatty acids (OFA) could be used in the treatment of DED to alter the inflammatory process[2], although the efficacy of OFAs has also been questioned[3] – suggesting further studies are required.

In the 2017 DEWS II Report, Stapleton *et al* noted the increased level of interest around the use of dietary supplements and modification of essential fatty acids (EFAs) as possible sources for preventing and treating DED[1]. However, the report cautioned that the ratio of Omega-6 (n-6) to Omega-3 (n-3) should also be considered. This statement was based on the evidence that EFAs had displayed anti-inflammatory properties at a systemic level. However, a 2019 Cochrane systematic review warned that, although there was evidence that long-chain Omega-3 played some role in the management of DED, further study was recommended[4].

The Association of British Dispensing Opticians (ABDO) suggests that omega supplements may improve the quality of the lipid constituent of tears[5], whereas the College of Optometrists class the strength of the recommendation regarding OFA supplementation as weak due to the evidence being classed as moderate[6]. It is notable that the College of Optometrists' advice is based on the findings of DEWS II Report and a further randomly controlled trial, whereas it is not clear what evidence the ABDO advice is based upon.

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TEAR HYPEROSMOLARITY AND OCULAR SURFACE INFLAMMATION

The TFOS DEWS II Report redefined DED as an ocular surface disease resulting from multiple factors[7,8]. Characteristics identified included:

- Instability of the tear film
- Increased osmolarity (hyperosmolarity) of the tears
- Abnormal neurosensory behaviour causing pain/discomfort
- Inflammation of the ocular surface leading to damage

Tear hyperosmolarity occurs when there is an imbalance in the constituents (mucus, aqueous and lipid) of the tear film. TFOS DEWS II categorises DED as[9]:

- Evaporative dry eye (EDE)
- Aqueous deficient dry eye (ADDE)
- A combination of the two types

Hyperosmolarity is regarded as one of the main considerations in DED due to its role in inflammation of the ocular surface[9]. When measuring osmolarity, a 'normal' value would be in the range of 270-315mOsm/L (milliosmoles per litre) conducive to the homeostasis (the normal balance) of the tear film[10]. A difference between each eye exceeding 8mOsm/L would indicate an imbalance in the tear film homeostasis[11]. Changes to ocular osmolarity are initiated by tear deficiency, excess evaporation or a combination of the two.

Some causes considered in studies have included:

- Temperature
- Dehydration
- Medications (systemic)
- Contact lens use
- Meibomian gland dysfunction (MGD)
- Tear film instability
- Humidity
- High altitudes
- Sleep deprivation

Problems caused by hyperosmolarity can include:

- An increase in cytokine interferon-gamma (a defence mechanism) resulting in epithelial cell apoptosis (cell death), damaging the tissue and nerves of the ocular surface[11]
- Pain can be present as a result of nerve stimulation along with increased lacrimation due to the inflammatory stimulation of the lacrimal gland[12]
- The combination of chronic inflammation and goblet cell loss having an impact on mucin production is thought to result in tear film instability[10]

Figure 1. The Sea Buckthorn plant is used to make Omega-3 supplements

These are all considered a part of the cycle of DED[13]. The TFOS DEWS II Pathophysiology Report[8] explains that the epithelial cells of the cornea, when in a state of hyperosmolarity, initiate the inflammatory mediators along with proteases responsible for cell destruction.

The TFOS DEWS II Management and Therapy Report[14] provides a four-stage recommendation for management and treatment. Stage one includes:

- Education
- Environmental modification
- Dietary consideration including EFA supplementation
- Consideration of medication-related risk factors
- Ocular lubricants
- Lid hygiene/warm compress

SOURCES OF OMEGA FATTY ACIDS

The majority of OFAs are sourced from marine life. However, due to concerns including sustainability, allergies and dietary requirements, there is a demand for alternative sources[15]. As a dispensing optician in practice, it is necessary to maintain current knowledge in order to deliver evidence-based practice[16] – including which supplements are suitable and effective for patients. Whilst the efficacy of OFAs is not universally agreed, it is one of the more popular recommendations amongst eyecare professionals.

This article considers whether plant-based sources of omega fatty acids are effective in the management of inflammation, which is a part of DED. A literature review study was conducted to provide a greater understanding of the availability and effectiveness of plant-based sources of Omega-3 that could be used in the management of inflammatory factors associated with DED.

There is currently little research available to be able to compare the efficacy of plant and marine-based sources Omega-3 when considering inflammation in DED. Four studies were identified that highlight the following sources of plant-based Omega-3

- Sea Buckthorn oil (SB) **(Figure 1)**
- Flaxseed oil (FS)
- Algal oil (AO)

Questionnaires	Number of questions	Author/owner
Ocular Surface Disease Index (OSDI)	12	Outcome Research Group @ Allergen Inc
National Eye Institute Visual Function Questionnaire-25 (NEI-25)	25	National Eye Institute
Standard Patient Evaluation of Eye Dryness Questionnaire (SPEED)	8	Korb & Blackie
Dry Eye Questionnaire (DEQ-5)	5	Begley *et al*

Table 1: *Examples of dry eye questionnaires*

Feature under test	Test title	Test description
TEAR STABILITY	**Tear break-up time (TBUT)**	Assesses if the tear film is stable by observing the time taken for the tear film to 'break-up' between blinks. This can be measured with the use of a keratometer observing the time taken for the mires to distort. Another option would be to use specialised equipment such as the Tearscope Plus, which projects a pattern onto the ocular surface. The pattern is observed to assess the speed of distortion occurring. Normal TBUT is considered at 15-20 seconds[21].
TEAR VOLUME	**Meniscometry/tear meniscus height (TMH)**	The height of the tear meniscus can be measured with the use of a slit lamp beam through the lower tear prism. This can confirm excessive/reduced tear production. A normal TMH is considered to be between 0.2 and 0.4mm[21].
	Schirmer strips	Involves the insertion of a Schirmer strip (paper 5x35mm) in the lower lid. This is then measured after five minutes to observe tear quantity. If administered without anaesthesia, reflex tearing may occur possibly impacting the reliability of the test[11].
TEAR OSMOLARITY	**Osmometry**	The osmolarity can be measured using an osmometer such as that produced by TearLab[10]. A sample of tears is collected by the device and analysed to assess the osmolarity of the tears[7].
OCULAR SURFACE INTEGRITY	**Ocular surface staining**	This uses dyes such as sodium fluorescein and lissamine green. The dyes are instilled to highlight areas of epithelial damage with the use of a slit lamp. Due to the invasive nature of this type of examination, reflex tearing may occur[21].

Table 2: *Examples of dry eye examination procedures*

The four studies were:

- 'Oral Sea Buckthorn oil attenuates tear film osmolarity and symptoms in individuals with dry eye' by Larmo et al (2010)[17]
- 'The role of Omega-3 dietary supplementation in blepharitis and meibomian gland dysfunction (an AOS thesis)' by Macsai (2008)[18]
- 'Algal-oil supplements are a viable alternative to fish-oil supplements in terms of docosahexaenoic acid (22:6n-3; DHA)' by Ryan and Symington (2014)[19]
- 'Comparative anti-inflammatory effects of plant- and marine-derived omega-3 fatty acids explored in an endothelial cell line' by Baker *et al* (2020)[20]

Two of the studies compare plant and marine-based sources of Omega-3 whilst two concentrate on the results of a plant-based source. Due to the different study designs, direct comparison is limited. Two of the studies concentrate on the effect of Omega-3 at a cellular level. One assessed the blood lipid levels including Omegas 3 and 6 along with levels of the EFA Docosahexaenoic acid (DHA). The other looked at the effect of four EFAs on inflammation at a cellular level using human umbilical vein endothelial cells (HUVEC). This included:

- Docosahexaenoic acid (DHA)
- Alpha-linolenic acid (ALA)
- Stearidonic acid (SDA)
- Eicosapentaenoic acid (EPA)

It is possible, however, to assess the study results to support an improved understanding of any anti-inflammatory effects beneficial to the management of DED.

TEAR FILM ASSESSMENTS

Examples of some of the tests utilised in the two studies considering DED are detailed in **Tables 1 and 2**. As recommended, within the Diagnostic Methodology TFOS DEWS II paper, tests for DED should be carried out in an order from least to most invasive to reduce the risk of reflex tearing impacting the results[11] – as follows:

- Screening through triage and questionnaire
- Homeostasis assessment: i) NIBUT (non-invasive tear break-up time); ii) osmolarity; iii) ocular surface staining

- Assessment of subtype to classify aqueous deficient (ADDE), evaporative (EDE) or a combination

WHAT DOES THE EVIDENCE SAY?

First, it should be noted that not all sources provide the same OFA. **Table 3** shows which EFAs are contained in the sources studied.

The four studies reviewed provide us with the following evidence:

- The Sea Buckthorn oil study showed no significant improvement compared to the placebo group other than slight objective improvement in burning sensation and redness
- The Flaxseed oil study, considering the effect of Omega-3 dietary supplementation in blepharitis and meibomian gland dysfunction (MGD), showed no significant improvement in ocular testing compared with the placebo group nor in the objective assessments. A systemic change in levels of Omega-3:Omega-6 was reported to a significant level
- The Algal oil supplementation study compared the supplement with that of a fish oil source. This study suggested that the DHA available in both sources worked to a similar level, resulting in an improved systemic balance in the participants who followed a vegetarian or plant-based diet. The improvement could be considered interesting, as the levels of Omega-3 in the supplements was 400mg higher in the fish oil supplement compared to the plant-based. This was a short, two-week study that may benefit from a longer study
- The cellular study compared ALA and SDA from an unspecified plant-based source with that of EPA and DHA from a marine-based source. It suggested that ALA and SDA were less effective than EPA and DHA, which significantly inhibited four and five inflammatory mediators respectively. This study did not consider dietary intake or supplementation but provided evidence towards the effect of these fatty acids on inflammation

Whilst there are varying views on the effectiveness of OFAs in the management of DED, support of therapeutic use is stated in the first step of the TFOS DEWS II Management and Therapy report, 'Recommended management and treatment protocol'[14]. This protocol provides a structured four-step approach offering guidance to professionals, transferable into daily practice prompting further reading of this article. It should, however, be considered that other more recent studies may be available to add to the evidence base.

Source	Omega-3 contained within
Fish oil	DHA and EPA
Sea Buckthorn oil	ALA
Flaxseed oil	ALA
Algal oil	DHA and EPA

Table 3: *Sources of Omega-3*

Other considerations may be required for future studies on the subject, taking into account the environmental seasonal influences such as central heating or allergies and current dietary intake of Omega-3. Consideration of the two main classifications of DED (being evaporative to which MGD belongs and aqueous tear deficient) may also provide more focus[22].

Some significant points that can be taken from the review are:

- DHA appeared to be the most effective OFA in creating an anti-inflammatory effect when compared with ALA, SDA and EPA[20]
- DHA is mostly found in marine-based sourced OFAs with an exception being algae
- The results suggested that Algal-oil, whilst not bioequivalent to fish oil, proved a good source of DHA for those not receiving a marine-based source of OFAs from dietary intake

DHA, from dietary sources, has been studied further concerning immune-driven DED considering the pro-inflammatory pathway amongst other factors[23]. A brief search of optical consumable suppliers provided five sources of OFA oral supplements marketed to manage DED **(Table 4)**. Three plant-based sources containing Algal oil as the source of Omega-3 (DHA and EPA) were also identified, although these were not marketed for dry eye **(Table 5)**.

An optimal lower ratio of Omega-6:Omega-3, which has been discussed in relation to reduced inflammation [17,18], is supported by Miljanovic *et al* who evidenced a higher ratio of Omega-6 consumption leading to a significant risk of DED ($p=0.01$) in women[24]. Algal oil appeared to improve this balance, reducing n-6 significantly in the vegetarian/vegan group ($p<0.05$) and increasing Omega-3 significantly across the groups[19].

Currently, in the UK, no recommendation is provided regarding the dosage of Omega-3 supplements. The Association of UK Dieticians suggests 450mg of EPA and DHA daily for an adult[25]. Within the human studies reviewed, the dosages varied from 6g to 600mg. As the studies were conducted in various countries (Finland, America and England) the recommendations may have differed.

The daily amount of Omega-3 from each of the supplements identified varied greatly from DHA 80mg, EPA 122mg in one source to DHA 500mg, EPA 300mg in another. When considering this, combined with dietary intake, the resultant amount may be variable and difficult to regulate. A possible solution to assess individual dietary intake was discussed in a recent study where the results of the dietary questionnaire was shown to be comparable to those of a 'Dried Blood Spot' test[26], suggesting this step may be useful in creating a treatment plan without the need for blood tests.

Concerns have previously been raised that a high dosage of Omega-3 may have contraindications with some medications[27] although this has been countered by later research[28]. One identified contraindication cited in National Institute for Health and Care Excellence (NICE) guidance states that patients with familial hypercholesterolaemia (high cholesterol[29]) should not be recommended Omega-3 supplementation[30].

Interestingly, these studies only involved marine-based sources leading to the question of how plant-based sources would perform in comparison.

Supplement Name	Supplier	Ingredients	Dose levels
LAGAD LACRIMA	**Lagard Vision Laboratory**	Fish oil rich in polyunsaturated fatty acids, Omega-3, fish gelatine, refined oil of seed of Borago officinalis, glycerol (moistener), alpha-lipoic acid, refined soybean oil, ascorbic acid, colloidal silica (thickener), microencapsulated Zinc Sulphate, water, dl-alpha-tocopheryl (Natural Vitamin E), sunflower lecithin (emulsifier), titanium dioxide (colourant), sodium copper chlorophyllin (colourant), patent blue V (colourant), quinoline yellow (colourant).	**PER DAILY DOSE (dosage: twice daily)** **ALA – 100mg n-3 total – 422mg Providing: EPA – 122mg DHA – 80mg Borage oil providing GLA – 40mg**
OCUVITE COMPLETE	**Bausch + Lomb**	Fish oil containing DHA; L-ascorbic acid (vitamin C); lutein suspension 20 per cent from marigold flowers (Tagetes erecta L.) in sunflower oil; dl-alpha-tocopheryl acetate (vitamin E); thickeners: mono and diglycerides of fatty acids (E471); zinc sulphate (zinc); thickener: silicon dioxide (nano); zeaxanthin suspension 20 per cent from marigold flowers (Tagetes erecta L.) in soy oil. Shell contains: shell agent: fish gelatine; firming agent: glycerol (E422); colouring agent: Iron oxide and hydroxide.	**PER DAILY DOSE (dosage: one daily)** **EPA – 140mg DHA – 360mg**
OMEGA VISION	**Scope**	Omega 3 fish oil, fish gelatine, thickener: glycerol, anti-oxidant: tocopherol rich extract, AquaPur (water)	**PER DAILY DOSE (dosage: two daily)** **Fish oil providing: EPA – 600mg DHA – 400mg Additional Omega-3 –200mg**
VITEYES 2 PLUS OMEGA 3	**Butterflies Healthcare**	Fish oil (fish), gelatin (bovine), ascorbic acid crystals, yellow beeswax, d-alpha-tocopherol, glycerin, soybean oil, purified water, zinc oxide, lutein, lecithin, colour: caramel, zeaxanthin, copper oxide.	**PER DAILY DOSE (dosage: 3 daily)** **Fish oil providing: Omega-3 – 1,000mg EPA – 650mg DHA – 350mg**
VITEYES OMEGA BLEND	**Butterflies Healthcare**	Fish oil, organic flaxseed oil, gelatin (bovine), yellow beeswax, glycerin, purified water, vitamin E (contains soy), carob, turmeric, borage oil, vitamin B6, colour: titanium dioxide.	**PER DAILY DOSE (dosage: one daily)** **Fish oil providing: EPA – 150mg DHA – 100mg Flaxseed oil providing: ALA – 250mg borage seed oil providing: GLA – 2mg**

Table 4: *Omega fatty acid oral supplements marketed for people with dry eye*

This highlights a requirement of further investigation for the considerations of patient safety before recommendation of specific plant-based supplements.

EVIDENCE AND FURTHER CONSIDERATIONS

Any recommendation of supplementation by a dispensing optician should be evidence-based and conducted within their scope of practice. The availability of plant-based sources of Omega-3 for use in the management of DED, as a recommended oral supplement, may be considered an important factor by some patients. As a result of this, providing patient-centred care in this situation requires current knowledge of ingredients, sources and suppliers.

Patients trust the knowledge of the professional to provide them with individualised care, therefore, the professional should feel confident in the information they refer to. A recent study found inconsistencies in recommendations of practitioners in Australia and New Zealand regarding dosage and source, supporting the requirement for structured protocols to guide practitioners[31]. Dosage and contraindications require additional consideration if these have not already been researched in ongoing or unpublished studies.

Due to the limited results and different study designs of the research in this review, the comparison was challenging. However, through the overlap of themes within the studies, it was possible to draw the findings together and gain an increased understanding of the situation.

Though limited, and not without weakness in design, the studies reviewed have provided base evidence that the available plant-based sources of OFAs may be effective in reducing inflammatory mediators associated with some classifications of DED. Whilst suggesting a positive impact on DED, many factors for further consideration have been identified. Having not provided a definite answer to the question, the findings have raised further issues for consideration that could influence future research.

If any additional research were located that supported the selected

Supplement Name	Supplier	Ingredients	Dose levels
OPTI3	**Vegetology**	Opti3 complex (microalgal oils, Helianthus annuus oil), antioxidants (rosemary extract, tocopherols, ascorbyl palmitate), cholecalciferol, vegetarian capsule shell (modified starch, vegan glycerol, carrageenan, sodium carbonate).	**PER DAILY DOSE (dosage: two daily)** EPA – 300mg DHA – 500mg Total n-3 – 835mg Vitashine D3 - 5µg (200iu) (100 per cent EU RDA)
VEGAN OMEGA-3	**BioCare**	Life's OMEGA (Algal oil, high oleic sunflower oil, antioxidants), natural mixed tocopherols and ascorbyl palmitate, rosemary extract, capsule shell (modified corn starch, glycerol, carrageenan [seagel cap], sodium carbonate).	**PER DAILY INTAKE (dosage: one to two daily)** Algal oil – 556mg Providing: DHA – 167mg EPA – 83mg
VEGAN ALGAL OIL 3-6-9	**Holland & Barrett**	Algal oil, olive oil, capsule shell (modified corn starch, glycerol, carrageenan, sodium carbonate), evening primrose oil, safflower oil, sunflower oil, vitamin E (as d-alpha-tocopherol and mixed tocopherols), rosemary extract, vitamin C (as ascorbyl palmitate).	**PER CAPSULE (dosage: one to three daily)** Algal oil – 680mg Providing: DHA – 204mg EPA – 102mg

Table 5: *Omega fatty acid oral supplements from plant-based sources*

studies, it would be prudent to focus on DHA, as this demonstrated the most efficacy in inflammatory mediator reduction at a cellular level. Improved balance in omega-6:omega-3 was evidenced in both human Flaxseed and Algal oil trials. However, combining the results of the studies would suggest an aim towards a further investigation of Algal oil being a source of DHA. The effect of Algal oil on the objective tests frequently used in the assessment of DED would build on the understanding of efficacy. A study of the effect on patient declared symptoms would also add strength to the results.

The question as to the efficacy of currently available sources cannot be answered fully due to the limitations discussed. Algal oil supplements appear to be the standard source available, in a DED setting, for those patients who are unable or disinclined to rely on marine-based sources.

A move towards patient-centred care, recommended by NICE, involves a more individualised service relating to patient's requirements including their preferences, belief system and lifestyle[32]. A dispensing optician is part of a multi-disciplinary team providing patient-centred care. An example of this is their role in the management of DED, which can assist in the preparation for cataract surgery, due to the need for an 'optimal ocular surface' before surgery, reducing the risk of post-operative complications[33].

Further work on this subject would be recommended to provide professionals with valid evidence to support advice given to patients. This action would be beneficial in maintaining the best interest of the patients as required to maintain professional standards of care.

Considerations for dispensing opticians in practice include:

- Understanding the classifications of DED to enable appropriate advice to be given
- Awareness of supplement availability including source and dosage
- Contraindications relating to medication or existing health issues

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