Progress in Lipid Research 64 (2016) 30–56

Contents lists available at ScienceDirect

Progress in Lipid Research

journal homepage: www.elsevier.com/locate/plipres

Metabolism and functional effects of plant-derived omega-3 fatty acids in humans

Ella J. Baker [a], Elizabeth A. Miles [a], Graham C. Burdge [a], Parveen Yaqoob [b], Philip C. Calder [a,c,*]

[a] Human Development and Health Academic Unit, Faculty of Medicine, University of Southampton, Southampton, United Kingdom
[b] Hugh Sinclair Unit of Human Nutrition, Department of Food and Nutritional Sciences and Institute for Cardiovascular and Metabolic Research, University of Reading, Reading, United Kingdom
[c] NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust and University of Southampton, Southampton, United Kingdom

ARTICLE INFO

Article history:
Received 31 May 2016
Received in revised form 28 July 2016
Accepted 29 July 2016
Available online 3 August 2016

Keywords:
Alpha-linolenic acid
Stearidonic acid
Omega-3
Human health
Fatty acid composition

ABSTRACT

Alpha-linolenic acid (ALA) is an essential fatty acid and the substrate for the synthesis of longer-chain, more unsaturated ω-3 fatty acids, eicosapentaenoic acid (EPA), docosapentaenoic acid and docosahexaenoic acid (DHA). EPA and DHA are associated with human health benefits. The primary source of EPA and DHA is seafood. There is a need for sustainable sources of biologically active ω-3 fatty acids. Certain plants contain high concentrations of ALA and stearidonic acid (SDA). Here we review the literature on the metabolism of ALA and SDA in humans, the impact of increased ALA and SDA consumption on concentrations of EPA and DHA in blood and cell lipid pools, and the extent to which ALA and SDA might have health benefits. Although it is generally considered that humans have limited capacity for conversion of ALA to EPA and DHA, sex differences in conversion to DHA have been identified. If conversion of ALA to EPA and DHA is limited, then ALA may have a smaller health benefit than EPA and DHA. SDA is more readily converted to EPA and appears to offer better potential for health improvement than ALA. However, conversion of both ALA and SDA to DHA is limited in most humans.

Contents

Abbreviations: AA, arachidonic acid; ALA, alpha-linolenic acid; CHD, coronary heart disease; CHF, congestive heart failure; CRP, C-reactive protein; CVD, cardiovascular disease; D5D, delta-5-desaturase; D6D, delta-6 desaturase; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; GM, genetically modified; IL-6, interleukin-6; LA, linoleic acid; MUFA, monounsaturated fatty acid; NEFA, non-esterified fatty acid; PUFA, polyunsaturated fatty acid; RBC, red blood cell; RCT, randomised control trial; sICAM-1, soluble intercellular cell adhesion molecule-1; sVCAM-1, soluble vascular cell-adhesion molecule-1; SAA, serum amyloid A; SDA, stearidonic acid; SFA, saturated fatty acid; TAG, triacylglycerol; VLC, very long-chain; ω-3, omega 3; WHO, World Health Organisation.

* Corresponding author at: Human Development and Health Academic Unit, Faculty of Medicine, University of Southampton, IDS Building, MP887 Southampton General Hospital, Tremona Road, Southampton SO16 6YD, United Kingdom.
E-mail address: pcc@soton.ac.uk (P.C. Calder).

http://dx.doi.org/10.1016/j.plipres.2016.07.002
0163-7827/

1. Introduction

Epidemiological studies and several randomised control trials (RCTs) demonstrate a positive relationship between consumption of very-long chain (VLC) ω-3 polyunsaturated fatty acids (PUFAs), specifically eicosapentaenoic acid (EPA; 20:5ω-3) and docosahexaenoic acid (DHA; 22:6ω-3), and long term health benefits [1], including a reduction in cardiovascular disease (CVD) morbidity and mortality [2–8], better visual and neurological development [9] and improvements in inflammatory conditions including arthritis [10] and asthma [11]. However, it is important to note that not all RCTs report reduced mortality in patients with existing CVD when they receive supplemental EPA and DHA [5,12,13]. Reasons for these inconsistencies have been discussed elsewhere [14].

The beneficial effects of EPA and DHA that have been reported involve modification of the biophysical properties of cell membranes [15–18], changes in specific cell signalling pathways and altered gene expression [19,20]. The primary source of EPA and DHA is seafood especially oily fish, although they are found in lower amounts in many other foods of animal origin. The World Health Organisation (WHO), as well as many other authorities, recommends consumption of oily fish once or twice a week in order to assure dietary intake of VLC ω-3 PUFAs with recognised health benefits [21]. However there are concerns about the sustainability of fish, and the current stocks of both farmed and wild fish are not likely to be sufficient to meet the needs of humans for VLC ω-3 PUFAs [22,23]. This has increased the interest in the metabolism, functional effects and health benefits of ω-3 PUFAs derived from plants, including alpha-linolenic acid (ALA; 18:3ω-3) and stearidonic acid (SDA; 18:4ω-3).

Sources of ALA include green plant tissues, some nuts (e.g. walnuts), rapeseed oil (also known as canola oil), soybean oil (in which ALA contributes 10% of total fatty acids), and flaxseeds and flaxseed oil (in which ALA contributes >50% of total fatty acids). ALA is the most abundant ω-3 PUFA in the diets of people who do not regularly consume oily fish or take concentrated VLC ω-3 PUFA supplements. Consumption of ALA in Europe, Australia and North America typically ranges from 0.6 to 2.3 g/d in adult men and 0.5 to 1.5 g/d in adult women [24–29]. Despite a higher dietary intake of ALA relative to EPA and DHA (approximately 25- and 15-fold greater [24]), concentrations of ALA within plasma and cell and tissue lipids are lower than those of EPA and DHA, apart from in adipose tissue stores. ALA is a metabolic precursor of EPA and DHA (Fig. 1). The biosynthetic pathway includes a series of desaturation, elongation and beta-oxidation reactions, with the rate-limiting enzyme considered to be that catalysed by delta-6 desaturase (D6D) (Fig. 1). However, it is also likely that there is regulation of other steps of the pathway, particularly the step involving translocation of 24:6ω-3 into the peroxisome. The observation that ALA levels in blood, cells and most tissues are much lower than the levels of EPA and DHA indicates that the primary biological role of ALA may be as a substrate for EPA and DHA synthesis. However, evidence suggests that conversion of

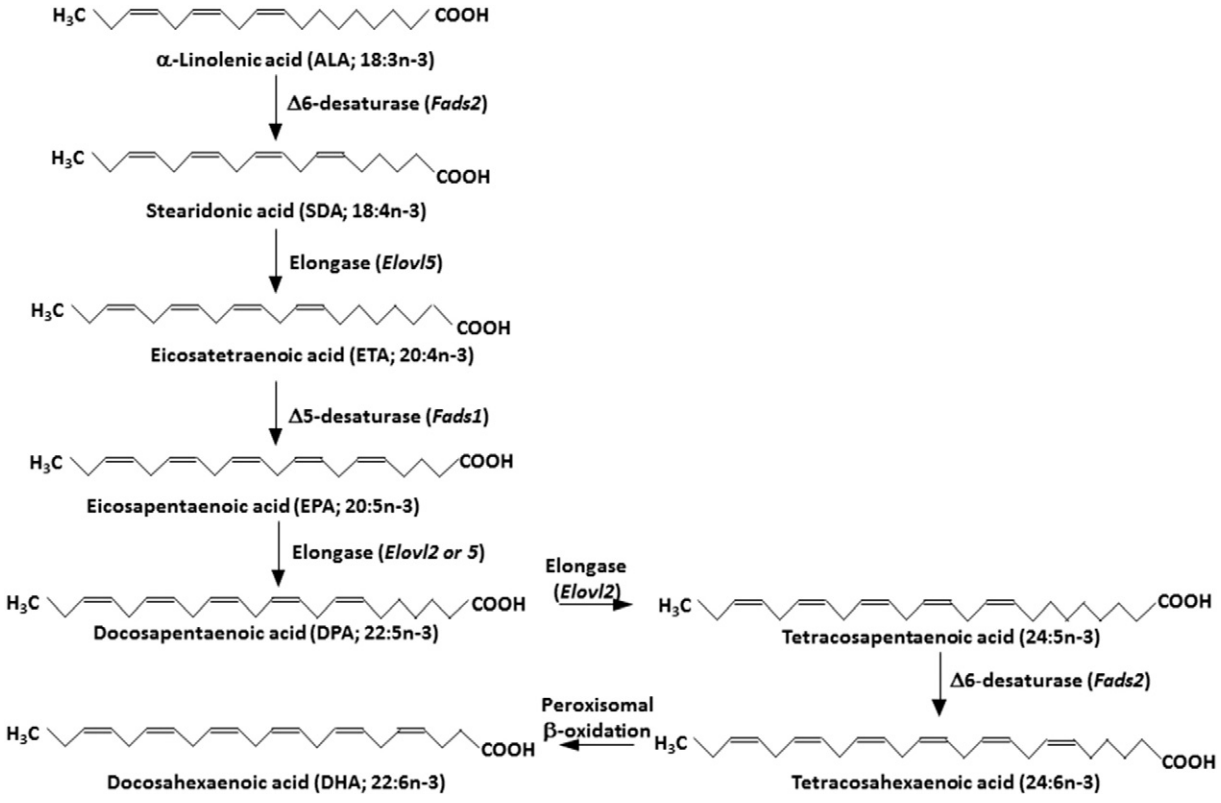

Fig. 1. The pathway of metabolic conversion of alpha-linolenic acid to longer-chain ω-3 polyunsaturated fatty acids. Genes encoding the various enzymes are shown in parentheses.