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# Microbial lipids as potential source to food supplements

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For centuries, men have used microorganisms for their activities and abilities to produce metabolites of interest such as antibiotics or pigments. Lipids are now under the spotlight as applications can be found in several domains such as in biofuels. Lipids formed by microorganisms can also be interesting from a dietary point of view, as some microorganisms (yeast, fungi, microalgae and Thraustochytrids) are able to produce polyunsaturated fatty acids (PUFAs). These PUFAs, such as those belonging to the omega-3 and omega-6 series, are known for their benefits to human health. The use of microorganisms represents a promising way to produce PUFAs at lower cost and with a higher yield. This manuscript discusses various potent microorganisms for single cell oils production designed for the dietary domain.

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## Introduction

Various types of microorganisms are able to accumulate lipids as intracellular storage compounds: yeasts, fungi, moulds and microalgae [1]. Lipids obtained from these oleaginous organisms are often referred to as single cell oils (SCO). They form lipid droplets that can be found in the intracellular medium or in chloroplasts for algae [2]. Analysis of their fatty acids profiles reveal interesting points, especially because they are similar to those obtained from vegetable oils which represent the main feedstock for first-generation biodiesel production. The other important characteristic of SCO fatty acids profiles is the significant presence of essential fatty acids. These essential fatty acids are polyunsaturated fatty acids (PUFAs) which cannot be synthesized by mammals and must be therefore brought by food. For a larger accessibility to population, essential fatty acids are also available as dietary supplements.

This manuscript will discuss the single-cell oils produced by oleaginous microorganisms which can be used as food supplement. It will present the PUFAS, the biosynthesis of PUFAs and the different types of microorganisms involved in the production of the lipids of interest.

## PUFAs

They are gathered into omega-3 and omega-6 families. The omega-3 family (also referred to as ω-3 or *n*-3) includes α-linolenic acid (ALA or C18:3*n*-3), eicosapentaenoic acid (EPA or C20:5*n*-3) and docosahexaenoic acid (DHA or C22:6*n*-3) while the omega-6 family (ω-6 or *n*-6) gathers γ-linolenic acid (GLA or C18:3*n*-6), linoleic acid (LA), arachidonic acid (ARA or C20:4*n*-6) and conjugated linolenic acid (CLA). The fatty acids differ by the length of the aliphatic chain, the degree of unsaturation, the location and the conformation *cis* or *trans* of double bonds. Their nomenclature involves the number of carbons present in the aliphatic chain, the number of double bonds, their positions and their configurations. Some authors specify the position changes by referring to the carboxylic acid function (Δ) of the molecule, but others prefer to refer to the terminal methyl (indicated by *n*- or ω-).

ALA and LA are, for each family, the precursors of the other family members. Their health benefits have been described and make them indispensable to a proper development [4–7]. EPA and DHA actions against cardiovascular diseases have been proven as they reduce arterial LDL-cholesterol delivery participate in the inflammatory response through resolvins and neuroprotectins generation and suppress vascular smooth muscle cell proliferation [7]. DHA is also a major structural component of the grey matter of the brain and the eye retina. Therefore DHA is essential to ensure optimum neural and visual functions [8]. However, using fish oils as nutritional supplements, and notably for infants, is debatable because of the presence of environmental pollutants such as dioxins, PCBs and heavy metals which might be taken up by fish and concentrated in their livers and other organs. The other important source of DHA is mother's milk. Also rich in ARA, mother's milk brings the indispensable fatty acids for neural development and visual acuity to new-borns. DHA and ARA are absent from cow's milk used in place of mother's milk. Therefore, they should be added to the diet of babies to ensure a normal development. LA acts as a precursor for the synthesis of more highly unsaturated and longer-chained omega-6 family. LA is virtually found in every food we eat and is the predominant PUFA in land-based meats, dairy, vegetables, vegetable oils, cereals, fruits, nuts, legumes, seeds and breads. GLA is produced in the body as a product of LA metabolism but can also be found in some plants oils such as evening primrose and borage oils and is incorporated into infant formula and for treatments ranging from atopic eczema, rheumatoid arthritis, multiple sclerosis and premenstrual tension [9]. ARA is the most abundant PUFA in humans, present in organs, muscle and blood tissue and has a major role as a structural lipid associated predominantly with phospholipids. It is also the principal omega-6 fatty acid present in the brain. ARA is a direct precursor of a number of eicosanoids regulating lipoprotein metabolism, blood rheology, leucocyte function and platelet activation.

## Biosynthesis and accumulation

With the ongoing interest in PUFAs, the world wholesale market for infant formula has increased tremendously. PUFAs naturally brought by human milk have to be supplied in infant formulas in order to warrant a normal development of babies. Traditional sources of PUFAs are well-known [3•,6,7] (Table 1), however, the search for cheaper, more accessible alternative sources of production began a few decades ago. Oleaginous organisms produce long chain fatty acids such as PUFAs [3•,7]. Therefore, using these oleaginous microorganisms represents a promising way to produce PUFAs. But, understanding the metabolic pathway implied in the biosynthesis of PUFAs and how microorganisms are able to accumulate lipids of interest is of crucial importance in order to achieve the highest yield and productivity possible.

**Table 1**

**Dietary sources of functional lipids.**

| Family | PUFA | Dietary sources |
|---|---|---|
| Omega-3 | ALA | Vegetable oil (flaxseed oil, chia seed oil, canola oil, egg, meat, walnut, hazelnut) |
| | | Fatty fish oil |
| | EPA | Fatty fish oil |
| | DHA | Fatty fish oil |
| | | Breast milk |
| Omega-6 | LA | Vegetable oil |
| | | Nuts |
| | GLA | Evening primrose oil |
| | | Borage oil |
| | ARA | Egg yolk |
| | | Animal fat |
| | | Breast milk |

### Biosynthesis of PUFAs

The process of lipogenesis for oleaginous yeasts, fungi, Microalgae and Thraustochytrids is well known [2,10–13,14••,15] and more efforts are needed for a better knowledge of bacterial accumulation of PUFAs [16]. The process can be divided into two parts (Figure 1): the first one is the production of acetyl-CoA and the second one involves the conversion of acetyl-CoA into lipids. Acetyl-CoA obtained is converted into palmitic acid by lipogenesis pathway, which is the primer for longer-chained saturated or unsaturated fatty acids and acts as the primer for the synthesis of malonyl-Acyl Carrier Protein (ACP) and acetyl-ACP.

The overall equation is:

$$\begin{aligned} &2\text{acetyl-CoA} + 7\text{malonyl-CoA} + 14\text{NADPH} \\ &\quad + 14\text{H}^+ \rightarrow \text{palmiticacid} + 7\text{CO}_2 + 8\text{CoA} \\ &\quad + 14\text{NADP}^+ + 6\text{H}_2\text{O} \end{aligned}$$

Many pathways are involved in the lipogenesis, they are well explained in many publications [10,11••,15, 17–19]. After the lipogenesis specific enzymes, desaturases and/or elongases convert palmitic acid into unsaturated or polyunsaturated fatty acids (PUFAs) or into longer fatty acyl chains. Desaturase catalyzes the introduction of double bond(s) into the fatty acid chain and elongase in a sequence similar to that of C2-unit cycling addition. Two distinct schemes (Figures 2 and 3) for the production of PUFAs have been identified: the elongation/desaturation pathway which involves elongase and desaturase and the anaerobic polyketide pathway which occurs mainly in thraustochytrids and are large-celled marine heterokonts.

### Accumulation of PUFAs and cultivation system to produce PUFAs

In mainly oleaginous microorganisms, lipid accumulation is triggered when the carbon source is present in excess and an element in the growth medium becomes limiting. The limitation of many elements can induce lipid accumulation but usually it is nitrogen limitation which is used for this purpose because it is the most efficient type of limitation for inducing lipid accumulation. Under these conditions, the carbon flux is diverted towards lipid synthesis, leading to an accumulation of triacylglycerols within discrete lipid bodies in the cells [21,22•].

For lipid accumulation in oleaginous microorganisms, different modes of biomass production [10,15,23•] can be considered: batch [22•,24–27], fed-batch [28,29,30•] and continuous [31] culture modes (Table 2). The mode of culture is an important parameter that will be crucial for optimizing lipid production and will therefore have a direct economic impact on the process. The tools of