

## Review Article

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## Production of Polyunsaturated Fatty Acids (PUFAs) from Microbes and their Secondary Metabolites

**K.C. Naveena\* and Ramalingappa***Department of Microbiology, Davangere University, Davangere-577007, Karnataka, India**\*Corresponding author*

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Polyunsaturated fatty acids (PUFAs) are the part of lipids produced from microorganisms, which have pulled in much consideration due to its beneficial consequences for human wellbeing. Polyunsaturated fatty acids have prompted the advancement of strategies for acquiring and controlling polyunsaturated lipids. Protein interceded responses have shown interesting points of interest over synthetic methodologies and business lipase. A few metabolites, for example, enzymes, carotenoids, and extracellular polysaccharides can likewise get from marine protists like *Thraustochytrids*. The present study briefly review relevant to polyunsaturated fatty acids produced, production in different fermentation process and its secondary metabolites.

### Introduction

Microbial lipids, particularly the single cell oils are generally acknowledged in the commercial center with the expansion in familiarity with the wellbeing benefits of PUFAs. The customer's interest for SCO oil is expanding and anticipated to grow constantly. The major nutraceuticals of these lipids classes are docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), Gamma linolenic acid (GLA) and arachidonic acid (ARA). Plants are not skilled to blend these long chain exceptionally unsaturated fats with the exception of GLA which is expectedly delivered from the seeds of night primrose,

borage and blackcurrant. As another option to plant and animal based oils, look into is being centered around screening and disengagement of new oleaginous microorganisms, which has investigated certain growths, microscopic organisms, green growth and yeasts blending microbial oils having long chain unsaturated fats (Syed *et al.*, 2006).

In generally polyunsaturated fatty acids (PUFAs) are constituents of the cell membrane and the primary structural components of the brain, skin, sperm, testicles, and retina (Liao *et al.*, 2016). PUFAs start from plants are expended in higher wealth than those from angle, with the goal that plant

omega-6 PUFA are devoured in higher amounts than omega-3 PUFA (Newton 1998). This over utilization of omega-6 with respect to omega-3 oil has been connected to expanded danger of tumor, diabetes, cardiovascular and neurodegenerative ailment (Simopoulos, 2006). To reestablish an adjust, utilization of omega-3 unsaturated fats ought to be expanded contrasted with omega-6 unsaturated fats. Omega 6 to omega-3 PUFA proportions of between 5:1 and 3:1 have been proposed as ideal for human utilization (Simopoulos, 2008).

The advancement of microbial lipid generation has essentially been focused on the living being determination and improvement of social conditions. Shockingly, less consideration has been centered on oil confinement, while most extraction strategies connected to microbial framework have been initially portrayed for creature tissues and plant materials. Accordingly, dependable procedures for recuperation and decontamination of microbial oils must be utilized to additionally build up this region of microbial biotechnology (Suzuki and Yokochi, 1989; Certik, 1996; Davies, 1988). A few investigations have tended to the remedial impacts of omega-3 PUFAs in tumor demonstrating that omega-3 PUFAs can enhance viability and fairness of chemotherapy (Bougnoux *et al.*, 2009; Nabavi *et al.*, 2015). DHA as a treatment methodology is regularly joined with chemotherapeutic medications since DHA in all probability upgrades the cytotoxic impacts of these medications (Nabavi *et al.*, 2015).

In the ongoing years, the structure of the cell film unsaturated fats has been explored, not just as a factor affecting the reaction to medications, yet additionally as a component impacting BC guess free of the treatment got (Bougnoux *et al.*, 2009, 2010; Straka *et al.*, 2015). Connecting BRCA to key dietary

variables, for example, omega-3 PUFAs, associated with the rate of BC (Brasky *et al.*, 2010; Molfino *et al.*, 2016), opens wide points of view for healthful avoidance in BC and in conceivably tweaking fiery status. As of late, Roy *et al.*, recorded positive relationship amongst erythrocyte and bosom tissue omega-3 unsaturated fats, and suggestive reverse relationship between erythrocyte long chain omega-3 PUFAs and tissue Creative protein (CRP) (Roy *et al.*, 2015). This review includes types fatty acids produced microorganisms, optimisation of PUFAs and secondary metabolites of *Thrastochytrids*.

### **Some polyunsaturated fatty acids obtained by microorganisms**

Many types of PUFAs have been obtained from different microorganisms including microalgae, bacteria, fungi and yeasts that produce omega-3 and omega-6 polyunsaturated fatty acids. Examples are arachidonic acid (ARA), gamma linolenic acid, ducosahexaenoic acid, eicosapentaenoic acid and linolenic acid (Gupta *et al.*, 2011) (Table 1).

### **Other polyunsaturated fatty acids**

For human health, plants were initially considered as the main source of PUFAs, especially gamma linolenic acid (GLA) which was accessible and economically high. The primary disadvantage of using PUFAs produced by plants is that many qualities are built to produce polyunsaturated fat for business purpose; without this innovation, there is low probability of DHA creation utilizing designed oil seed products (Alonso and Maroto, 2000).

Microbial long chain omega-6 polyunsaturated fatty acids for ex. Gamma linolenic acid (18:3), dihomo-gamma-linolenic acid (20:3) and arachidonic acid (20:4) have been

reported (Ratledge, 2001). The main business oil obtained from organisms that was gamma linolenic acid (GLA), predominantly GLA was extracted by growths of lower phycomycetes, and other sources such as *Pythium debaryanum* containing small amount of lipids (Shaw, 1965). *Schizochytrium* and *Cryptoconidium* sp., the source of DHA and *Mortierella* sp., are the major sources of ARA. These organisms are free from toxicity and pathogens; both DHA and ARA are used for infants (Ward, 2005).

### **Microbial polyunsaturated fatty acid (PUFAs) production**

To increase the product value of microbial lipids as compared to animal and plant derived oils, a variety of things have been done such as introduction of inexpensive agro-industrial substrates. Screening the potential oil producing organisms is the important step, which reduces the numerous strains of microbes for further study and they are essential for practical study. These strains can directly be used for optimization study. Production of maximum PUFAs depends on the availability of various nutrients and their compositions (Kennedy *et al.*, 1993). There are two basic processes involved in microbial lipid production, such as submerged and solid state fermentation.

#### **Submerged fermentation**

Submerged fermentation needs frequent nutrients and oxygen for the growth of aerobes. The cells growth and product formation of the microorganisms are influenced strongly by media components. In this process microbes are cultivated in a liquid medium under controlled conditions for the production of products. Submerged fermentation is used for microbial lipid production; particularly in single cell oil industries. The development of microbes

requires a procedure that comprises a few operation units, from microbial development in bioreactors to oil processing (Syed *et al.*, 2006) (Table 2). There are three essential operations which require extraordinary regard for the procedure advancement, inferable from the idea of oleaginous life forms: (1) Optimized conditions in fermentation; (2) Cell separation as intracellular oil; (3) Disruption of cells, extraction of oil and processing (refining).

Since the financial considerations of microbial PUFAs generations of microbial are seriously influenced by the cost of crude material feedstock, for the most part nitrogen constrained choice of development media is a vital stride. It ought to be noticed that obtaining satisfaction from the media for the screening procedure is unique in relation to expansive scale creation media under ideal fermented conditions (Certik, 1999).

#### **Solid state fermentation**

In the solid state fermentation, microbes are cultivated on a substrate of moist solid free from water; it allows the utilization of food and agro-industries' raw material and some other cheap raw materials as substrates (Pandey, 1992). Strong state aging is a minimal effort put in aging procedure; it is appropriate for agro mechanical buildups of the substrates in bio-processes. Solid state fermentation is known in the ancient Asian nations, yet it is almost disregarded in present day world (Pandey *et al.*, 2001).

Solid state fermentation forms are appropriate for the generation of hydrolytic chemical by filamentous growth, since they imitate normally the regular living states of parasites (Singhania *et al.*, 2009). Consideration towards this bioprocess is a result of many focal points in contrast to submerged maturation e.g. Littler bioreactor volume,

diminished downstream preparing cost, high efficiency, easier strategy, lessened vitality requirement, low waste water yield, etc. (Kim *et al.*, 1985; Burke and Cairney, 1997). In solid state fermentation (SSF), substrates are used as solid for cultivation, since the success of the procedure relies upon it to a great extent. The two most essential parts in solid state fermentation process are: Exchange of oxygen to the developing microorganisms and exchange of supplements and proteins inside the substrate strong mass; it also involves keeping of the coveted temperature by expelling the warmth created during aging. Generally, development of SSF involves following necessary steps. (1) Screening of isolated microorganisms; (2) Optimization studies through different parameters; (3) Establishment and designing of the pilot plant when scale up is necessary; (4) Data generation and commercial plant design; (5) Plant construction; (6) Regular plant operation for microbial metabolites production (Certik *et al.*, 1999).

A case of SSF is use of *Microsphaeropsis* sp., to deliver SCO from a substrate comprising of steam detonated wheat straw and wheat grain; there are likewise few reports on creation of GLA under SSF. The scale up region is under investigation and broad research is required on the path for microbial oils creation. This could quicken creation of advertisement for PUFA generation (Syed *et al.*, 2006) (Table 3).

Enriched glycerides, unsaturated fats and esters for biometrically and nutraceutical uses can be acquired by lipase catalyzed hydrolysis, alcoholysis, acidolysis, glycerolysis, and transesterification of fish, microbial oils and plant seed (Gill and Valvety, 1997) (Table 4).

### Secondary metabolites of *Thrastochytrids*

*Thrastochytrids* are able to create auxiliary metabolites e.g, steroids, sterols, carotenoids

and surfactants (Fan and Chen, 2007; Lewis *et al.*, 2001). Besides, they are additionally a wellspring of extracellular polysaccharides and biocatalysts.

### Enzymes

*Thrastochytrids* secrete a number of enzymes and compounds, for example, protease, esterase, lipase, corrosive and basic phosphate, cellulases and xylanases (Raghukumar, 2008). The additional cell lypolytic action was concentrated on 19 strains of *Thrastochytrids*, with 14 of them utilizing carboxymethyl cellulose (CMC) as substrate. The hydrolysis of the substrate CMC affirms the presence and action of cellulase in *Thrastochytrids* (Nagano *et al.*, 2011).

### Carotenoids

*Thrastochytrids* are promising well spring of carotenoids including PUFAs.

The generation of carotenoid colors, for example, astaxanthin, zeaxanthin, canthaxanthin, echinenone, phoenicoxanthin and  $\beta$ -carotene by *Thrastochytrium* sp. has been accounted (Burja *et al.*, 2006 and Carmona *et al.*, 2003). As  $\beta$ -carotene is a forerunner of vitamin A, adequate admission of  $\beta$ -carotene can prevent malady created by vitamin A inadequacy, including visual deficiency, safe brokenness and skin issue (Fierce *et al.*, 2008).

### Extracellular polysaccharides

*Thrastochytrids* are reported to produce extracellular polysaccharide (EPS) that incorporate sugars as the real part (39-53%) with the vicinity of proteins, lipids, uronic acids and sulfates (Jain *et al.*, 2005). EPS is an antitumor and antiviral agent and can likewise be utilized as a part of the corrective and nourishment commercial ventures (Sutherland, 1998).

**Table.1** Polyunsaturated fatty acids (% of total fatty acids) obtained from microorganisms

Fatty acid	TFA (%)	Microorganism	References
AA	25.9-53.8	<i>Mortierella</i> sp.	Suzuki <i>et al.</i> , (2010)
ALA	33-41	<i>Mortierella alliacea</i>	Jermstuntiea <i>et al.</i> , (2011)
ALA	4.1-5.4	<i>Rhodotorula muciliginosa</i>	Gupta <i>et al.</i> , (2011)
ARA	11	<i>Mortierella alpinapeyron</i>	Kendrick and Ratledge (1992)
ARA	68.5-78.8	<i>Mortierella alpine</i>	Totani and Oba (1987)
DGLA	4.7-4.9	<i>Mortierella</i> sp.	Suzuki <i>et al.</i> , (2010)
DHA	0.7-0.8	<i>Colwellia</i> sp.	Bowman <i>et al.</i> , (1997,1998)
DHA	32	<i>Pichia methanolica</i>	Aoki <i>et al.</i> , (2002)
EPA	1.3-13	<i>Mortierella alliacea</i>	Jermstuntiea <i>et al.</i> , (2011)
EPA/ARA	18/19	<i>Saprolegnia parasitica</i>	Kendrick and Ratledge (1992)
EPA and DHA	2.8 and 6.7	<i>Candida guilliermondii</i>	Guo and Ota (2000)
EPA	2-22	<i>Shwenella</i> sp.	Nichols and McMeekin (2002)
EPA	25.2	<i>Pythium irregular</i>	O'Brien <i>et al.</i> , (1993)
GLA	10.4	<i>Pythium debaryanam</i>	Shaw (1965)
GLA	4.3-4.7	<i>Mortierella</i> sp.	Suzuki <i>et al.</i> , (2010)
Linoleic acid	24.7	<i>Rhodotorula muciliginosa</i>	Gupta <i>et al.</i> , (2011)
Oleic acid	45.4		<i>Rhodotorula muciliginosa</i>
Gupta <i>et al.</i> , (2011)			

**Table.2** Polyunsaturated fatty acids produced from microbes through sub-merged fermentation

Microorganisms Involved	Parameter	Time of culture (h)	Analysis of PUFA	PUFA (%)	Reference
<i>Thraustochytrids</i>	Screening for production of DHA	107	DHA creation fortified at high C:N greater than 1% glucose hinders <i>T. aurem</i> development. Lipid amassing was 25% and productivity rate was 0.48 g/l/day	2.17 (g/l)	Bowels <i>et al.</i> , (1999)
<i>M. alpine</i>	Production of ARA on temperature and composition of media	192	The production of ARA was 1.14 g/l/day, when vegetable oil, NaNO <sub>3</sub> and soy flour were used as a medium in glucose fed batch cultures	9.1 (g/l)	Singh and Ward (1997)
<i>Mortierella ramanniana</i>	Submerged fermentation	102	<i>M. ramanniana</i> has to be excellent producer of gamma linolenic acid, when temperature was at 20 to 21° and media contain dextrose (5%), yeast extract (1%) and Mn <sup>2+</sup> (5 mg/ml)	13.3 (g/l)	Dyal and Nairine (2005)
<i>Cunninghamella echinulata</i>	Parasite developed on tomato squander hydrolysate	300	<i>C. echinulata</i> found to produce of GLA more than 1 g/l in favour of glucose	11.7 (g/l)	Fakas <i>et al.</i> , (2008)

**Table.3** Production of gamma linolenic acid under solid state fermentation

Substrate used	Investigated mould	Fermented biomass Oil (W/w %)	Gamma linolinic acid (%) in TFA (W/w %)	Reference
Soaked barley	<i>Cunninghamella japonica</i>	14.3	29.1	Emelyanova (1996)
Orange peel +spent malt grain	<i>Mortierella isabelina</i>	16.8	4.23	Stredansky <i>et al.</i> , (2000)
Pearl barley	<i>Thamnidium elegans</i>	15.6	9.3	Conti <i>et al.</i> , (2001)
Orange peel + glucose	<i>Cunninghamella japonica</i>	-	5.1	Gema <i>et al.</i> , (2002)

**Table.4** PUFAs in plants and animals lipid catalysed by lipase

Sources of lipid	PUFAs	Lipase catalyst	Reaction	PUFA product	Reference
Sand eel (oil) (1997)	DHA	<i>Rhizomucor miehei</i>	Esterification	Free fatty acids	Langholz <i>et al.</i> , (1989); Gill and Valvety
Cod liver (oil+ FFAs) (1997)	EPA/DHA	<i>Rhizomucor miehei</i>	Acidolysis	Gs (Triglycerides)	Yamane <i>et al.</i> , (1992); Gill and Valvety
Cod liver (oil+ FFAs) (1997)	EPA/DHA	<i>Rhizomucor miehei</i>	Acidolysis	Gs (Triglycerides)	Yamane <i>et al.</i> , (1993); Gill and Valvety
Cod liver (oil)	EPA+DHA	<i>Pseudomonas</i> sp.	Alcoholysis	Mono+Diglycerides+FFAs	Li and Ward (1993); Gill and Valvety (1997)
Tuna (oil) (1997)	DHA	<i>Candida cylindracea</i>	Hydrolysis	Glycerides (di+triglycerides)	Tanaka <i>et al.</i> , (1993); Gill and Valvety
Tuna (oil) (1997)	EPA+ DHA	<i>Geotrichum candidum</i>	Hydrolysis	Glycerides (triglycerides)	Shimada <i>et al.</i> , (1994); Gill and Valvety
Menhaden (oil) (1997)	EPA	<i>Pseudomonas</i> sp.	Hydrolysis	Glycerides (mono glycerides)	Maehr <i>et al.</i> , (1994); Gill and Valvety
Sardine (oil+ FFAs) (1997)	EPA/DHA	<i>Rhizomucor miehei</i>	Acidolysis	Glycerides (triglycerides)	Hosokawa <i>et al.</i> , (1995); Gill and Valvety

DHA, Docosahexaenoic acid, EPA, Eicosapentaenoic acid, FFAs, Free fatty acids.

EPS are found to assume a critical part in the cell life of *Thraustochytrids*. They may shield *Thraustochytrids* from drying up; help with the phone adherence to the marine substrate and serve as a source of vitality during starvation (Jain *et al.*, 2005). *Thraustochytrids* might likewise manage the cost of security against metal and poison sullying (Colaco *et al.*, 2006).

In conclusion, the pivotal role of biochemical parts of polyunsaturated fats has concentrated on PUFA ameliorate nutraceuticals and therapeutics and in light of the arrangement of

reasonable engineered systems for their creation. The diverse constituents of media assumed a vital part for creation of wanted lipid in any maturation procedure. It is inferred that supplement constraint, generally nitrogen, is the key figure inciting lipid aggregation oleaginous microorganisms. At show, the deficiency of expansive scale innovations for giving modest, decontaminated PUFAs has enormously confined endeavors toward this path. Be that as it may, modern interests in PUFA biomedical ought to quicken the improvement of biotechnological courses to high review

omega-3 and omega-6 PUFAs. Significant endeavors officially under approach to market lipase-interceded process, and this should, with the advancement of microbial and plant based generation frameworks, before long make vast amounts of PUFAs accessible for manufactured employments. *Thrastochytrids* can be utilizing full wellspring of omega-3 unsaturated fats, carotenoids, proteins and other important mixes.

### Conflict of Interests

The authors declare that they have no conflicts of interest for publication.

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