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

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A B S T R A C T

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, carotinoids, 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 primorse, 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

https://doi.org/10.20546/ijcmas.2018.712.304
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 Thrastochoytrids.

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-linelonic 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 phycymycetes, and other sources such as *Pythium debaryannm* 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 Thraustochytrids**

*Thraustochytrids* 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**

*Thraustochytrids* 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 *Thraustochytrids*, with 14 of them utilizing carboxymethyl cellulose (CMC) as substrate. The hydrolysis of the substrate CMC affirms the presence and action of cellulase in *Thraustochytrids* (Nagano et al., 2011).

**Carotenoids**

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

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

**Extracellular polysaccharides**

*Thraustochytrids* 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| Mortierella sp.        | Suzuki et al., (2010)    |
| ALA        | 33-41   | Mortierella alliacea   | Jermsuntiea et al., (2011) |
| ALA        | 4.1-5.4 | Rhodotorula mucilaginosa| Gupta et al., (2011)    |
| ARA        | 11      | Mortierella alpinapeyrone| Kendrick and Ratledge (1992) |
| ARA        | 68.5-78.8| Mortierella alpina     | Totani and Oba (1987)   |
| DGLA       | 4.7-4.9 | Mortierella sp.        | Suzuki et al., (2010)    |
| DHA        | 0.7-0.8 | Colwellia sp.          | Bowman et al., (1997, 1998) |
| DHA        | 32      | Pichia methanolica     | Aoki et al., (2002)      |
| EPA        | 1.3-13  | Mortierella alliacea   | Jermsuntiea et al., (2011) |
| EPA/ARA    | 18/19   | Saprolegnia parasitica | Kendrick and Ratledge (1992) |
| EPA and DHA| 2.8 and 6.7 | Candida guilliermondii| Guo and Ota (2000)      |
| EPA        | 2-22    | Shwenella sp.          | Nichols and McMeekin (2002) |
| EPA        | 25.2    | Pythium irregular      | O’Brien et al., (1993)  |
| GLA        | 10.4    | Pythium debaryanum     | Shaw (1965)              |
| GLA        | 4.3-4.7 | Mortierella sp.        | Suzuki et al., (2010)    |
| Linoleic acid | 24.7 | Rhodotorula mucilaginosa | Gupta et al., (2011)    |
| Oleic acid | 45.4    |                        | Rhodotorula mucilaginosa |

Gupta et al., (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               |
|-------------------------|-----------|---------------------|------------------|----------|-------------------------|
| Thraustochytrids        | Screening for production of DHA | 107 | DHA creation fortified at high C:N greater than 1% glucose hinders T. aurem development. Lipid amassing was 25% and productivity rate was 0.48 g/l/day | 2.17 (g/l) | Bowels et al., (1999) |
| M. alpine               | Production of ARA on temperature and composition of media | 192 | The production of ARA was 1.14 g/l/day, when vegetable oil, NaNO₃ and soy flour were used as a medium in glucose fed batch cultures | 9.1 (g/l) | Singh and Ward (1997) |
| Mortierella ramanniana  | Submerged fermentation | 102 | M. ramanniana 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 Mn²⁺ (5 mg/ml) | 13.3 (g/l) | Dyal and Nairine (2005) |
| Cunninghamella echinulata | Parasite developed on tomato squander hydrolysate | 300 | C. echinulata found to produce of GLA more than 1 g/l in favour of glucose | 11.7 (g/l) | Fakas et al., (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        | Cunninghamella japonica    | 14.3                          | 29.1                                     | Emelyanova (1996)       |
| Orange peel +spent   | Mortierella isabelina      | 16.8                          | 4.23                                     | Stredansky et al., (2000) |
| malt grain           |                            |                               |                                          |                         |
| Pear barley          | Thamnidium elegans        | 15.6                          | 9.3                                      | Conti et al., (2001)    |
| Orange peel + glucose| Cunninghamella hamella    | -                             | 5.1                                      | Gema et al., (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)        | DHA            | Rhizomucor miehei     | Esterification   | Free fatty acids                       | Langholz et al., (1989); Gill and Valvety      |
| Cod liver (oil+ FFAs) | EPA/DHA        | Rhizomucor miehei     | Acidolysis       | Gs (Triglycerides)                     | Yamane et al., (1992); Gill and Valvety       |
| Cod liver (oil+ FFAs) | EPA/DHA        | Rhizomucor miehei     | Acidolysis       | Gs (Triglycerides)                     | Yamane et al., (1993); Gill and Valvety       |
| Cod liver (oil)       | EPA+DHA        | Pseudomonas sp.       | Alcoholysis      | Mono+Diglycerides+FFAs                 | Li and Ward (1993); Gill and Valvety (1997)    |
| Tuna (oil)            | DHA            | Candida cylindracea   | Hydrolysis       | Glycerides (di+triglycerides)          | Tanaka et al., (1993); Gill and Valvety       |
| Tuna (oil)            | EPA+ DHA       | Geotrichum candidum   | Hydrolysis       | Glycerides (triglycerides)             | Shimada et al., (1994); Gill and Valvety      |
| Menhaden (oil)        | EPA            | Pseudomonas sp.       | Hydrolysis       | Glycerides (mono glycerides)           | Maehr et al., (1994); Gill and Valvety        |
| Sardine (oil+ FFAs)   | EPA/DHA        | Rhizomucor miehei     | Acidolysis       | Glycerides (triglycerides)             | Hosokawa et al., (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 amoreliate 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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How to cite this article:

Naveena, K.C. and Ramalingappa. 2018. Production of Polyunsaturated Fatty Acids (PUFAs) from Microbes and their Secondary Metabolites. Int.J.Curr.Microbiol.App.Sci. 7(12): 2680-2689.
doi: https://doi.org/10.20546/ijemas.2018.712.304