



Neview Oleaginous Yeasts as Cell Factories for the Sustainable Production of Microbial Lipids by the Valorization of Agri-Food Wastes

Antonio Caporusso ^{1,2}, Angela Capece ^{1,*} and Isabella De Bari ^{2,*}

- ¹ School of Agricultural, Forest, Food and Environmental Sciences, University of Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza, Italy; antonio.caporusso@unibas.it
- ² Italian National Agency for New Technologies, Energy and Sustainable Economic Development (ENEA), Laboratory for Processes and Technologies for Biorefineries and Green Chemistry, ENEA C.R. Trisaia S.S. 106 Jonica, 75026 Rotondella, Italy
- * Correspondence: angela.capece@unibas.it (A.C.); isabella.debari@enea.it (I.D.B.); Tel.: +39-0971-205686 (A.C.); +39-0835-974618 (I.D.B.)

Abstract: The agri-food industry annually produces huge amounts of crops residues and wastes, the suitable management of these products is important to increase the sustainability of agro-industrial production by optimizing the entire value chain. This is also in line with the driving principles of the circular economy, according to which residues can become feedstocks for novel processes. Oleaginous yeasts represent a versatile tool to produce biobased chemicals and intermediates. They are flexible microbial factories able to grow on different side-stream carbon sources such as those deriving from agri-food wastes, and this characteristic makes them excellent candidates for integrated biorefinery processes through the production of microbial lipids, known as single cell oils (SCOs), for different applications. This review aims to present an extensive overview of research progress on the production and use of oleaginous yeasts and present discussions on the current bottlenecks and perspectives of their exploitation in different sectors, such as foods, biofuels and fine chemicals.

Keywords: circular economy; biorefinery; single cells oils; agri-food byproduct; fatty acids; oleaginous yeasts; inhibitors; industrial application

1. Introduction

The growth of the world population has determined an inevitable increase in the demand for food, feed, fuels and all products of daily use of fossil origin with which an increasing amount of waste per capita and environmental impacts are associated. Many environmental issues raise the need to change the economic model and overcome the limits imposed by the classic production system of "taking, making and disposing". The new production model envisages the conversion of the value chain from linear to circular, improving the efficiency of resource use in order to offset the economic, environmental and social costs caused by the current linear use of resources. This new model offers several advantages, such as the valorization of waste and reduction of its environmental impact, production of bioenergy and biochemicals.

The FAO has estimated that, on average, about one-third of the food produced globally for human consumption is lost or wasted, and about 50% of these food wastes (FW) are fruit and vegetables [1]. In Europe, about 90 million tons of wastes such as olive mill wastewater (OMW), cheese whey (CW), and vegetable wastes are produced per year by the agri-food industry. Some estimations indicate that the total production of agricultural residues (parts of plants not used for food) in Europe reaches about 450 million tons [1]. Many of these residues are used on the farm as soil fertilizers, animal bedding, or animal feed, while others need to be treated to avoid environmental problems. Unutilized crop residues left in the field become a potential source of pollution due to eutrophication or, if burned openly, can cause severe air pollution such as greenhouse gas (GHG) emissions.



Citation: Caporusso, A.; Capece, A.; De Bari, I. Oleaginous Yeasts as Cell Factories for the Sustainable Production of Microbial Lipids by the Valorization of Agri-Food Wastes. *Fermentation* **2021**, *7*, 50. https:// doi.org/10.3390/fermentation7020050

Academic Editor: Tiziana Nardi

Received: 17 March 2021 Accepted: 31 March 2021 Published: 3 April 2021

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). The environmental pressures deriving from the disposal of waste materials, combined with the problem of high world population growth, make it necessary to speed up the development of systems for the sustainable use of these resources. One of the most virtuous ways for sustainable use of by-products is through biorefinery processes.

Different definitions and classifications of biorefineries are available (reviewed by [2]), but the more inclusive one used by the International Energy Agency (IEA) in Task 42 is "the sustainable transformation of biomass into a spectrum of marketable products (food, feed, materials, chemicals) and energy (fuels, energy, heat)". Among the different biorefinery processes, the most flexible for enhancing waste biomasses into marketable products and energy, are the biological conversion processes based on the use of specific microbial populations. Oleaginous microorganisms can be an interesting option to valorize many residual carbon sources. In the last years, single cell oils (SCOs) have attracted scientific and industrial attention as a consequence of their potential to replace fossil-based oils for multiple applications as "building blocks" for the synthesis of fuels, soaps, plastics, paints, detergents, textiles, rubbers, surfactants, lubricants, and additives for the food and cosmetic industry [3]. These oils have fatty acids (FAs) compositions similar to those of vegetable oils but they are considered more sustainable thanks to some advantages with respect to vegetable oils. In fact, the production of microbial lipids is unaffected by seasons, they can be produced in large quantities and with reduced space requirements, and they can be produced from a wide range of carbon sources. Production costs can be reduced by using low-cost carbon sources, even if the complex composition of many residual streams can negatively affect the microorganisms [4]. Although some applications of oleaginous microorganisms at an industrial scale already exist, their full potential still needs concerted research efforts to increase their overall feasibility.

This review provides an updated overview on the knowledge developed on the use of oleaginous microorganisms to convert many waste products into value-added oils and additional biobased products, describing the current limits and assessing future trends to make the process industrially feasible. In particular, the review will provide detailed information on the conversion of different agro-industrial residues and byproducts, such as lignocellulosic residues, CW, OMW, FW, along with analyses of the process aspects affecting the microorganisms' performance.

2. Oleaginous Microorganisms as Cell Factory

Some microorganisms are defined oleaginous as a result of their ability to accumulate lipids by as much as 20% of their dry cellular weight. This group includes several eukaryotic microorganisms (such as fungi, yeasts and algae) and some species of autotrophic and heterotrophic bacteria able to accumulate lipids in the form of triglycerides (TAGs) and free FAs. Although the first works concerning oleaginous microorganisms date back to 1870 [5,6], the economic competitiveness of microbial lipids with respect to vegetable oils was dubious [7]. More recently the concepts of bioeconomy and the circular economy decisively emerged and the number of research papers investigating this topic increased. Table 1 lists some recent papers regarding the production of lipids by different oleaginous species. The FAs profile of microbial oils are very similar to those of vegetable oils, making them interesting alternatives to oils produced through dedicated crops. Microalgae are very versatile organisms and their lipid content can vary in a range of 1–70%, although the common range is 20–50%. Promising and widely studied species able to accumulate high amounts of lipid include Botryococcus, Chlorella, Scenedesmus and Monoraphidium. Despite their large storage capacity, they need larger surfaces and longer growth time than bacterial and yeast cells.

Like microalgae, some bacteria can accumulate high titers of oils under specific environmental conditions, although the lipid composition is most different from other microbial oils. Bacteria mainly produce complex lipoids and few bacterial species can produce TAGs. The most abundant class of lipids accumulated by bacteria are polyhydroxyalkanoic acids, but several studies have documented TAGs accumulation by the genera *Rhodococcus* [8], *Streptomyces* [9], *Bacillus* [10], *Acinetobacter* [11] and *Nocardia* [12]. Recent developments in the formulation of microbial consortia for the production of polyhydroxyalkanoates have been reported by Ai et al. [13]. Bacterial species are characterized by fast growth rates and easy breeding, but their low lipid content, low biomass production, and difficulty in extracting lipids, still make the production of lipids from bacterial species unsustainable.

Oleaginous fungi include species belonging to Zygomycota and, in particular, to the genera *Mucor, Mortierella* and *Cunninghamella* [14] and, to a lesser extent, to Ascomycota, mainly referring to the genus *Aspergillus* [15]. Unlike other oleaginous species, fungi also produce long-chain polyunsaturated fatty acids (PUFA) of nutritional and pharmaceutical importance such as docosahexaenoic acid (DHA), γ -linolenic acid (GLA), eicosapentaenoic acid (EPA) and arachidonic acid (ARA) [16]. Fungi can accumulate high quantities of lipids, as much as 70% of their weight in optimized media [17]. One of the major problems related to the use of fungi lies in the difficulty of their cultivation, as in submerged cultures they show rheological problems due to the different morphological forms assumed depending on the medium and the cultivation conditions [18]. Therefore, fungi usually require solid-state cultivation with precise humidity control. The few available studies carried out on liquid cultivation reported low lipid accumulations [19].

Oleaginous yeasts represent interesting microbial factories. These are heterotrophic microorganisms able to grow and accumulate high levels of lipids, better known as single cell oils (SCOs). Their rapid growth, along with the ability to utilize a wide variety of raw materials and their easy cultivation in large fermenters, make them the best candidates for biorefinery processes compared to fungi, microalgae and bacteria. Oleaginous yeasts accumulate lipids, as neutral lipids in the form of monoacylglycerols, diacylglycerols and triacylglycerols. In general, the most abundant FAs produced by oleaginous yeasts are C16:0 (palmitic acid), C16:1 (palmitoleic acid), C18:0 (stearic acid), C18:1(oleic acid), and C18:2 (linoleic acid), whereas the fatty acids like C14:0 (myristic acid) and C18:3 (linolenic acid) are less abundant. In the last years, genetic engineering has been focusing on the production of PUFAs and long-chain fatty acids such as C20:0 (arachidic acid), C20:4 (arachidonic acid), C22:0 (behenic acid), and C24:0 (lignoceric acid) [20]. Furthermore, the interest toward these microorganisms is related also to their additional ability to produce polyols, organic acids and carotenoids [21–23].

Species	Organisms	Substrates	Lipid Contents % (w/w)	References
	Chlorella sp.	-	53.5	[24]
Microalgao	Botryococcus braunii	-	34.6	[25]
Microalgae	Monoraphidium sp	-	49.6	[26]
	Scenedesmus obliqus	-	18.5	[27]
	Rhodococcus opacus	molasses	30.0	[28]
Bacteria	Bacillus subtilis	cotton stalk	39.8	[10]
	Streptomyces	cellobiose	47.0	[9]
	Acinetobacter baylyi	glucose	61.0	[29]
	Mortariella isabellina	glucose	61.0	[30]
Funci	Cunninghamella echinulata	glucose	51.3	[31]
Tungi	Mucor moelleri	glycerol	24.0	[19]
	Aspergillus tubingensis	orange peel waste	16.0	[19]
	Yarrowia lipolitica	glucose	45.0	[32]
	Lipomyces tetrasporus	cardoon hydrolysate	47.0	[23]
Yeasts	Rhodosporidium toruloides	sugarcane molasses	61.0	[33]
	Lipomyces starkeiy	Arundo donax L	30.0	[34]
	Trichosporon oleaginous	glucose	54.0	[35]

Table 1. List of main oleaginous species and lipid accumulation performance.

3. Oleaginous Microorganisms as Cell Factory

The mechanisms related to direct conversion of substrate to TAGs production are essentially two: de novo synthesis and ex novo synthesis. De novo synthesis occurs when the microorganism is under nitrogen starvation and carbon excess conditions. This leads to metabolic switch whereby growth is stopped, favouring the lipogenic phase (Figure 1). On the contrary ex novo synthesis occurs when hydrophobic substrates (containing FAs, TAGs, sterol esters, etc.) are incorporated into the cell and are either used for energy purposes or accumulated as storage lipids [36].

3.1. De Novo Synthesis

All microorganisms are able to synthesize lipids using the same accumulation route, although only oleaginous yeasts are able to accumulate high lipid concentrations, equivalent to more than 20% of their dry cell weight (DCW). The lipid accumulation phase occurs when the microorganism is under conditions of excess of a carbon source and limitation of nitrogen or phosphorus, magnesium, zinc, iron and lead [37,38]. However, nitrogen limitation is the most effective form of inducing lipogenesis, leading to higher values of the substrate/lipid conversion yield and lipid content as internal biomass [39]. The lack of exogenous nitrogen is buffered by the activation of an endogenous pathway for cell nitrogen supply (Figure 1). AMP-deaminase, activated by nitrogen starvation, catalyzes the AMP cleavage to form IMP and NH4⁺ and thus supplies the cell with a nitrogen source. The subsequent decrease of AMP concentration has a negative feedback on the Krebs cycle, which stops at the level of isocitrate. Isocitrate dehydrogenase, the enzyme responsible for the conversion of isocitrate into α -ketoglutarate, loses its activity, since it is allosterically activated by intracellular AMP [17]. This leads to a mitochondrial isocitrate accumulation, which balances itself with citrate thanks to the enzyme aconitase and it is exported outside the mitochondria through the malate/citrate antiport. In the cytoplasm, citrate is converted into oxaloacetate and acetyl-CoA by ATP-citrate lyase (ACL) with ATP consumption. ACL, present only in oleaginous yeasts, is a key enzyme for the lipogenesis phase, and its absence limits the flux of carbon to FAs synthesis [17]. Acetyl-CoA is condensed with bicarbonate to form malonyl-CoA through acetyl-CoA carboxylase (ACCase). At this point the lipids synthesis starts through the binding of malonyl-CoA with acyl carrier protein (ACP), a component of the fatty acid synthase (FAS) complex. FAs are produced with cyclic reactions of condensation, reduction and dehydration. The stoichiometry of this cycle is shown below:

Acetyl-CoA + 7 malonyl-CoA + 14 NADPH \rightarrow Palmitoyl-CoA + 7 CO₂ + 14 NADP + 7 CoASH + 6 H₂O

As shown in the reaction, fourteen molecules of NADPH are required for the synthesis of palmitoyl-CoA. For each elongation step, two molecules of NADPH are required. The major sources of cytosolic NADPH are the pentose phosphate pathway (PPP) and the malic enzyme (ME). Although ME has always been considered the key enzyme in the supply of reducing equivalents useful for the synthesis of FAs [17], recent studies have shown that in *Yarrowia lipolytica* [40] and presumably also in *Rhodosporidium toruloides* [41], the microbial cell is supplied with NADPH by the PPP. The release of FA from ACP is catalysed by a thioesterase enzyme. The produced FAs can be released as free FAs or they can be activated by CoA as palmitoyl-CoA and stearoyl-CoA and shuttled to the endoplasmatic reticulum for TAGs synthesis, where further reactions result in elongation or desaturation. TAGs synthesis follows the Kennedy pathway and starts with glycerol-3-phosphate (G3P), supplied by glycolysis, and used as the glycerol backbone. In series, two acetyltransferases, G3P acyltransferase (GPAT) and lysophosphatidic acid acyltransferase (LPAAT), add two FAs to form phosphatidic acid (PA). Subsequently, PA is dephosphorylated by phosphatidate phosphatase (PAP) to produce diacylglycerol (DAG). Finally, the DAG is acylated either by diacylglycerol acyltransferase (DGAT) or phospholipid diacylglycerol acyltransferase to produce TAGs that are stored in the form of lipid droplets. The size, morphology and the number of these lipids droplets vary considerably among genera and even among closely related species [42].



Figure 1. Biochemistry of triglycerides (TAG) accumulation in oleaginous yeasts. Key enzymes in triglyceride synthesis are highlighted with red circles. Mitochondrial pathway in green, endoplasmic reticulum pathway in yellow and cytosolic pathway in black. Abbreviations: fatty acid synthase (FAS), isocitrate dehydrogenase (ICDH), malic enzyme (ME), acetyl-CoA carboxylase (ACCase), acetyl-CoA synthetase (ACS), glycerol-3-phosphate acyltransferase (GPAT), lysophosphatidic acid acyltransferase (LPAAT), phosphatidate phosphatase (PAP), diacylglycerol acyltransferase (DGAT). Adapted from [3,43,44].

3.2. Ex Novo Synthesis

Ex novo lipid biosynthesis involves the uptake of hydrophobic substrates, such as esters, TAGs, FAs, sterols, etc. The active transport of hydrophobic substrates into the cell is facilitated by secreted lipases, therefore only the microorganisms capable of producing lipases can incorporate free FAs. Once in the cell, free FAs can be used for energy purposes and then metabolized in peroxisomes by β -oxidation process or they can be incorporated into lipidic structures for storage. The selectivity and rate of free FAs uptake is often specific for some FAs allowing the modification of FA profiles over fermentation time. Selective FAs utilization, also known as fat biomodification, can be used to tailor the FAs profiles of hydrophobic substrates into value-added oils [36].

4. Oleaginous Yeasts: Characteristics of Main Species

Yeasts are widely distributed in natural ecosystems, such as soil and water, and are able to colonize the most extreme environments, such as the sea depths with low temperatures and scarce oxygen availability or even sites contaminated with oil, etc. Of the 1500 known species belonging to 100 different genera, about 30 of them are capable of accumulating lipids [45] and belong to diverse taxonomic groups, indicating that the metabolic capacity for lipid accumulation has evolved independently in basidiomycete and ascomycete fungi. The most known oleaginous yeasts include the genera *Yarrowia*, *Rhodotorula (Rhodosporidium), Lipomyces, Cryptococcus* and *Trichosporon*.

Yarrowia lipolytica is considered the model organism for this class of microorganisms due to its unique physiological characteristics [46]. Specifically, *Y. lipolytica* has emerged both as a convenient host for industrial processes and as a model organism for investigating lipid synthesis and accumulation in microbes and higher organisms. This is a hemias-

comycetous dimorphic yeast, belonging to the order Saccharomycetales. It is recognized as a generally regarded as safe (GRAS) microorganism, and for this reason Y. lipolytica is an attractive host for the production of dietary supplements and nutraceuticals. Yarrowia *lipolytica* is primarily isolated from foods with high proportions of fat and/or proteins, particularly (fermented) dairy products and meat, in consequence of its high lipolytic and proteolytic activities. The industrial use of Y. lipolytica for the large-scale production of high-quality protein by using *n*-alkanes as substrates [47] was already launched in the 1950s by British Petroleum. This species is able to metabolize a wide variety of substrates of industrial relevance such as lignocellulosic sugars, acetate [48], other volatile FAs coming from agro-industrial and municipal wastes [49,50], and also very hydrophobic substrates, such as FAs and TAGs obtained from animal fat and alkanes from petroleum sludge [51]. It also displays a high resistance to numerous stress factors, such as high concentrations of salt, wide ranges of pH, and shows tolerance to a variety of organic compounds [52–54]. The first genome sequence became available in 2004 [55] and the subsequently developed efficient genome editing tools and synthetic biology have contributed to improve its performances [56]. For this reason, it is widely used as host both in the production of typical lipids for biofuels [57] and oils with unusual FAs profiles or PUFA [58]. Yarrowia lipolyt*ica* can achieve a lipid content of up to 40%, with over 90% of those lipids stored in the form of TAGs [59]. Linoleic acid is the major PUFA synthesized by wild-type Y. lipolytica, but genetic engineering can be used to obtain recombinant strains overproducing, e.g., eicosapentaenoic acid, docosahexaenoic acid, arachidonic acid, conjugated linoleic acid or g-linolenic acid [60]. Furthermore, besides TAGs, Y. lipolytica can also produce organic acids, such as citric, isocitric, succinic, α -ketoglutaric, itaconic and acetic acids [61–63], polyols such as erythritol, mannitol, and arabitol [64,65] and enzymes, such as protease, RNase, phosphatase, esterase and lipase [66].

Rhodotorula toruloides, previously known as *Rhodosporidium toruloides*, is a red heterothallic, dimorphic yeast as it can exist both in the yeast form or as a mycelial form. It is classified in the Sporidiobolaceae family of the phylum Basidiomycota. This characteristic makes R. toruloides different from other yeasts widely used for biotechnological applications, such as Saccharomyces cerevisiae, Lipomyces starkeyi and Y. lypolytica, which are classified in the phylum Ascomycota. In addition to lipids, this yeast also produces carotenoids (responsible for the red color of the cells and providing antioxidant properties) and important enzymes. It was reported that the composition of neutral lipids of R. toruloides is the following: palmitic acid 23-30%, oleic acid 30-37%, stearic acid 32–37%, and linoleic acid 2–4% [36]. This species can grow in different ranges of temperatures (10-30) and pH (3-10) [67], on different carbon sources, such as lignocellulosic sugars [68], monosaccharides and disaccharides [69], glycerol [70], organic acids (acetate and lactate) [71,72], and long-chain FAs as well as D-galacturonic acid [68,73]. Rhodotorula toruloides displays high resistance in biomass hydrolysates containing inhibitors, producing lipids and carotenoids [74–76]. Despite the early discovery of the biotechnological potential of this yeast in 1950s, most application in bioprocesses for lipids production from diverse feedstocks have been carried out in the past decade and actually R. toruloides is considered an emerging industrial microorganism [77]. The use of this yeast by companies and research groups has increased exponentially in recent years as a result of recent improvements of genetic and metabolic engineering techniques and the availability of multiomics information on its genome and metabolism, as a consequence of the first publication of its genome sequence. The first sequenced genome of a *R. toruloides* strain became available in 2012, revealing a genome of 20.2 Mb in size with a GC content of 61.9%, containing 8171 protein-coding genes [78].

The genus *Lipomyces* is in the Lipomycetaceae family, order Sacharomycetales, phylum Ascomycota. To date, among the 16 species accepted as belonging to the genus *Lipomyces*, *L. starkeyi* (together with *L. lipofer* to a lesser extent) is the most extensively studied yeast of the genus [79]. *Lipomyces starkeyi* was originally isolated from soil, and is able to accumulate, under defined culture conditions, high amounts of TAGs (similar in composition to that

of palm oil) by up to 70% of the DCW [80]. It was reported that the strain *L. starkeyi* NBRC10381 is able to accumulate lipids by up to 85.1% of the DCW under nitrogen-limited conditions in media containing a mixture of 50 gL⁻¹ of each of glucose and xylose [81]. *Lipomyces starkeyi* can assimilate different carbon sources, such as lignocellulosic sugars [34], paper mill waste [82], glycerol [83], cellobiose [84] and acetic acid [85]. The prevalent FAs are C 16:0 and C 18:1, and PUFA, including C 18:2 and C 18:3. The complete sequencing of the genome was also achieved for this microorganism [86]. Moreover, numerous molecular genetic tools were developed to increase its lipid production [87], or modulate the FAs produced [88].

Cryptococcus curvatus, currently reclassified as *Cutaneotrichosporon curvatus*, is another of the best known oleaginous microorganisms. This yeast is widely diffused in nature and is isolated from foodstuffs, like raw milk and lettuce, or from marine sediments. This yeast is able to utilize different renewable carbon sources [89] lignocellulosic sugars [90], organic waste from the food industry [91], or active sludge [92], producing lipids in amounts up to 60% of its DCW [93]. The FA profile produced is composed of over 50% of unsaturated FAs, with a high quantity of oleic acid and about 10% of linolenic acid. The first draft genome sequence of *C. curvatus* was published in 2016 [94], allowing a noticeable progress in understanding the metabolism of this oleaginous yeast and in development of biomolecular tools [95] useful for increased lipid production.

The strain ATCC 20509, previously variously classified as Cryptococcus curvatus, Candida curvata or Apiotrichum curvatum, has recently been reclassified as Trichosporon oleaginosus [96]. Trichosporon species are basidiomycetes that belong to the order Tremellales. These yeasts have been isolated from environmental soil and milk whey samples, whereas recently some strains were isolated from immunocompromised hosts, raising the problem of potential pathogenicity. Mostly Trichosporon species grow as yeasts, but many of them were also able to form pseudohyphae or true hyphae and arthroconidia. *Trichosporon* oleaginosus has been extensively studied for its ability to accumulate TAGs by up to 70% of DCW [17], showing a FAs composition very similar to those of cocoa butter. This species can grow on different waste material feedstocks, such as whey permeate [96], crude glycerol [97], lignocellulosic sugars [98] and it differs from others oleaginous yeasts for the ability to use highly diverse carbon sources. This versatility is caused by the high tolerance to 5-HMF present in most undetoxified biomass hydrolysates, which at concentrations of 3 gL⁻¹ do not affect biomass and lipid production in *T. oleaginosus* [99]. Furthermore, detailed genome and transcriptome data for a T. oleaginosus strain were reported [100], which together with the innate metabolic versatility of this yeast, makes this microorganism an excellent candidate for the development of a super lipogenic microorganism.

5. Conversion of Low-Cost Carbon Sources

Oleaginous yeasts are able to produce SCOs heterotrophically from a variety of lowcost feedstocks, such as agricultural residues, FW and agro-industrial by-products [101]. In many cases the substrate needs some preliminary process to generate the carbon sources as the case of lignocellulosic hydrolysates. The multi-step conversion of the raw material into the final carbon source often implies the production of biomass degradation products that could inhibit microbial growth. In other cases, like CW, OMW, or FW, the substrate could require some preliminary treatment. The specific process to achieve the final carbon source from waste products is very important since it affects the medium composition, the overall microorganism performance and the process costs.

5.1. Lignocellulosic Agricultural Residues

Lignocellulosic biomasses are the largest sugars reservoir. They consist mainly of three polymers, cellulose (35–50%), hemicellulose (15–25%) and lignin (10–15%). Due to the complex hierarchical structure and recalcitrant nature of the lignocellulosic biomass, pretreatment steps are required before the enzymatic hydrolysis of the biomass polysaccharides. Typically, the flow chart for the conversion of lignocellulosic biomass involves

the following steps: biomass pretreatment, enzymatic hydrolysis of pretreated biomass, and finally conversion of sugars into lipids and lipid extraction. Pretreatment involves the application of physical, chemical, biological or physicochemical approaches. Several articles have reviewed methods for biomass pretreatment [102,103], green technologies [104], and emerging technologies [105]. Pretreatment technologies currently available at demonstration and even industrial scale include ammonia fiber expansion (AFEX), dilute acid (DA), steam explosion (SE), and organosoly. Depending on the type of raw material, method and severity of pretreatment, several undesirable compounds can be formed, such as furaldehyde, formaldehyde, phenols, aliphatic acids, vanillic acid, uronic acid, 4-hydroxybenzoic acid, acetic acid, and cinnamaldehyde which have an inhibitory effect on many microorganisms [106,107]. These undesirable compounds can be categorized into three groups: phenolic compounds produced from thermal degradation of lignin, furan aldehydes produced by dehydration of sugars (pentose and hexose), and carboxylic acids produced by hydrolysis of the acetyl group and further degradation of furan compounds. These compounds can also affect the activity of the hydrolytic enzymes used for the complete saccharification of lignocellulosic sugars [102]. Furthermore, they inhibit the growth of most microorganisms of industrial interest [4]. Some results related to the production of SCOs by oleaginous yeasts cultivated on lignocellulosic hydrolysates have been reported in Table 2. Although biomass hydrolysates are considered low-cost substrates, their complex chemical composition often require additional treatments (detoxification treatments), rising the process costs. The reduction of the toxicity of lignocellulosic hydrolysates can be achieved by removing the inhibitory compounds by means of different techniques, such as biological treatments, chemical additives, heating and vaporization, liquid-liquid extraction [108].

For the biological treatment, called bioabatement, good results were reported for the strain *Coniochaeta ligniaria* NRRL30616, which resulted able to metabolize several inhibitory compounds, such as furfural, 5-hydroxymethylfurfural (5-HMF), and aromatic and aliphatic acids [109,110]. The detoxification through the addition of Ca(OH)₂ was reported to reduce the concentration of furan and phenolic compound by approximately 20–30% [111].

Kim et al. [112] eliminated furan derivatives, organic acids and phenolic compounds by using polyethylene glycol (PEG) surfactant, activated carbon or ethyl acetate. Activated carbon has been shown to effectively absorb and remove approximately 90% of total phenols. Unfortunately, this technique has the disadvantage of also losing part of sugars, which can be adsorbed on the activated carbon [112]. Other authors [113] using ethyl acetate in the liquid-liquid extraction process, eliminated about 90% of acetic acid.

Although detoxification processes gave interesting results, side effects, such as the increase of production costs and decrease of assimilable sugars, compromise the economic feasibility of the process [114]. Some authors have evaluated the influence of cultivation parameters, such as the inoculum age, on the resistance to inhibitory compounds. For instance, Caporusso et al. [23] found that *L. tetrasporus* was not able to tolerate stress in cardoon hydrolysate (containing 0.42 gL⁻¹ furfural and 0.32 gL⁻¹ 5-HMF), but the inoculation of yeast cells in the stationary phase allowed the medium detoxification, with increased biomass and lipids yields. In contrast, the use of the same strategy was not effective for *C. curvatus*. Adaptive laboratory evolution was successfully applied to *Metschnikowia pulcherrima*, resulting in increased growth rates and reduced lag times under inhibiting conditions versus the progenitor [115].

However, not all the microorganisms are inhibited by lignocellulosic hydrolysates and different studies documented the SCOs production in undetoxified lignocellulosic hydrolysates.

Sitepu et al. [116] tested 45 different oleaginous yeast strains on simulated lignocellulosic hydrolysates and found that all the tested strains were able to grow well in media containing 0.5 gL⁻¹ of 5-HMF, whereas a significant growth reduction was observed when the concentration of 5-HMF increased further (1 gL⁻¹ and 2 gL⁻¹). Furfural showed the highest inhibition; in fact, about 20 tested strains were able to grow in 0.5 gL⁻¹, and only seven were able to grow in 1.0 gL^{-1} of furfural. Yu et al. [117] tested singularly the different by-products generated by the biomass thermal treatments (furfural, hydroxybenzaldehyde, vanillin and syringaldehyde) and found that furfural had the strongest inhibitory effect. At 1 gL⁻¹ of furfural, the cell biomass and lipid content of *T. oleaginosus* decreased by 78.4% and 61.0%, respectively. Among phenol derivatives, vanillin was the most toxic, followed by hydroxybenzaldehyde and syringaldehyde. The same results were found in *R. toruloides* Y4. Acetate, 5-HMF and syringaldehyde had slightly inhibitory effects, while hydroxybenzaldehyde and vanillin were toxic at concentrations higher than 10 mM. Again the most inhibiting molecule was furfural, which alone inhibited cell growth by 45% at a concentration of only 1 mM [118].

One recent investigation aimed at evaluating different oleaginous yeasts on sugarcane hydrolysates, demonstrated that the tolerance to inhibitory compounds is correlated to the nature and concentration of the compounds as well as the microorganisms. In fact, among the analysed strains, R. *toruloides DMKU-RE16* and *DMKU-RE124* showed the highest tolerance to furfural (1.0 gL^{-1}), while *R. fluviale DMKU-SP314* showed the highest tolerance to 5-HMF (4.0 gL^{-1}) and vanillin (1.0 gL^{-1}). Additionally, *R. toruloides DMKU-RE124* could also grow in the presence of 2.0 gL^{-1} acetic acid, although it exhibited a delayed growth [119].

Some authors found a synergistic interaction among inhibitors such as furfural and 5-HMF, whose effect is amplified when both are present in a mixture [4]. Conversely, Favaro et al. [120], revealed that antagonistic interactions exerted by inhibitor mixtures on microbial metabolism are strictly dependent on the strain and dose. Some authors [4] explained the inhibitory effect of weak acids as a consequence of the decoupling and accumulation of intracellular anions. Conversely, other studies reported the growth and lipids production using acetic acid as the sole C source with *R. toruloides AS 2.1389* [71], *C. curvatus MUCL 29819* [121], *L. starkeyi* [85], *Y. lipolytica* [48], and many other oleaginous yeasts species [122]. Furthermore, *T. cutaneum ACCC 20271*, in addition to metabolizing formic acid (15 gL⁻¹) and acetic acid (10 gL⁻¹), was able to convert high quantities of furfural and 5-HMF (3 gL⁻¹ for each) into the corresponding alcohols [123].

Adaptive evolution strategies can be used to increase both the inhibitors' tolerance and the sugar conversions into lipids. For example, in *Y. lipolytica* the produced lipids were increased of 30% in comparison to the initial strain [22]. Similar results were observed in *M. pulcherrima* [115], and *R. toruloides* [124].

Other than lipids, these microorganisms can produce additional compounds, such as carotenoids, ethanol, mannitol, arabitol, 2,3-butanediol, acetoin, citric acid, polysaccharides and polyols. Depending on the process, the production of lipids could be increased with respect to other products or vice versa.

Yeasts	Feedstock	Pretreatment	C Source gL ⁻¹	Inhibitors gL ⁻¹	Y Biomass% (w/w)	Y Lipid% (w/w)	Lipid Content % (w/w)	References
Candida albicans	Bagasse sugarcane	Steam explosion	reducing sugar 61.33	nd	31.8	10.	31.5	[125]
Cryptococcus albidus ATCC 10672	Sorghum stalks	Diluted alkali	Glucose 51.0 Xylose 30.0 Arabinose 2.9	Acetate 0.5	13.2	17.0	42.0	[126]
Geotrichum candidum NBT-1	Rice straw	Microwave assisted alkali	Glucose 22.0 Xylose 2.1 Galactose 17.0	nd	30.5	10.5	34.4	[127]
Yarrowia lipolytica ATCC 20460	Wheat straw	Dilute acid	Glucose 3.7 Xylose 19.6 Arabinose 4.7 Galactose 1.2	Acetate 4.0 5-HMF 0.1 Fur 0.4	26.7	1.4	4.6	[99]
Lipomyces starkeyi NRRL Y-1389	Wheat straw	Hydrothermal	Glucose 43.6 Xylose 12.3	Det	22.5	5.4	25.7	[21]
Lipomyces starkeyi ATCC 12659	Wheat straw	Dilute acid	Glucose 3.7 Xylose 19.6 Arabinose 4.7 Galactose 1.2	Acetate 4.0 5-HMF 0.1 Fur 0.4	50.3	15.8	31.2	[99]
Lipomyces Starkeyi ATCC 56304	Sorghum stalks	Diluted alkali	Glucose 51.0 Xylose 30.0 Arabinose 2.9	Acetate 0.5	21.5	16.0	44.0	[126]
Lipomyces Starkeyi ATCC 56305	Switchgrass	Diluted alkali	Glucose 58.0 Xylose 26.0	Acetate 0.5	19.8	17.0	39.0	[126]
Lipomyces tetrasporus	Douglas fir	Sulfite and diluted sulfuric acid	Glucose 8.5 Xylose 5.6 Galactose 4.8 Mannose 18.8	Acetate 6.7 5-HMF 1.8 Fur 1.4	35.5	11.4	23.9	[128]
Meyerozyma guilliermondii	Rice husk	Steam explosion	reducing sugar 63.15	nd	10.9	4.1	36.7	[125]

Table 2. Growth of different oleaginous yeasts strains on lignocellulosic hydrolysates with inhibitors and detoxified (Det).

Yeasts	Feedstock	Pretreatment	C Source gL ⁻¹	Inhibitors gL ⁻¹	Y Biomass% (w/w)	Y Lipid% (w/w)	Lipid Content % (w/w)	References
Pichia Kudriavzevii NBT-13	Rice straw	Microwave assisted alkali	Glucose 22.0 Xylose 2.1 Galactose 17.0	nd	17.6	6.7	37.5	[127]
Pichia kudriavzevii	Bagasse sugarcane	Steam explosion	Reducing sugar 61.3	nd	32.6	10.0	30.7	[125]
Pichia kudriavzevii	Rice husk	Steam explosion	Reducing sugar 63.15	nd	42.3	10.0	23.6	[125]
Pichia manshurica	Bagasse sugarcane	Steam explosion	Reducing sugar 61.3	nd	38.1	9.0	23.6	[125]
Pichia kudriavzevii	Bagasse sugarcane	Steame xplosion	Reducing sugar 61.3	nd	13.2	4.0	30.4	[125]
Rhodotorula Taiwanensis AM2352	Corncob hydrolysate	Hydrothermal + diluted acid	Glucose 7.2 Xylose 36.8	Det	33.9	16.9	50.1	[129]
Rhodotorula glutinis ATCC 204091	Wheat straw	Dilute acid	Glucose 3.7 Xylose 19.6 Arabinose 4.7 Galactose 1.2	Acetate 4.0 5-HMF 0.1 Fu 0.4	47.3	11.9	25.0	[99]
Rhodotorula glutinis ATCC 204091	Wheat straw	Dilute acid	Glucose 3.2 Xylose 14.0 Arabinose 3.7 Galactose 0.8	Det	54.4	11.1	20.7	[125]
Rhodosporidiobolus fluvialis DMKU-SP314	Sugarcane	Alkaline hydrogenperoxide	Glucose 18.6 Xylose 6.2 Glycerol 59.0	Det	33.6	21.2	63.3	[119]

Table 2. Cont.

Yeasts	Feedstock	Pretreatment	C Source gL ⁻¹	Inhibitors gL^{-1}	Y Biomass% (w/w)	Y Lipid% (w/w)	Lipid Content % (w/w)	References
Rhodosporidium toruloides NRRL Y-1091	Wheat straw	Hydrothermal	Glucose 43.6 Xylose 12.34	Det	32.1	5.0	18.7	[21]
Rhodosporidium toruloides DSMZ 4444	Corn stover	Dilute sodium hydroxide	Glucose 100.0 Xylose 10.0	Det	42.9	19.0	58.6	[130]
Rhodosporidium toruloides ATCC 10788	Wheat straw	Dilute acid	Glucose 3.2 Xylose 14.0 Arabinose 3.7 Galactose 0.8	Det	45.6	11.1	24.6	[125]
Rhodotorula mucilaginosa	Bagasse sugarcane	Steam explosion	Reducing sugar 61.3	nd	33.8	10.0	29.5	[125]
Rhodotorula mucilaginosa	Rice husk	Steam explosion	Reducing sugar 63.1	nd	40.9	10.0	24.4	[125]
Trichosporon Dermatis 32903	Corn stover	Dilute acid	Glucose 43.4 Xylose 22.7 Arabinose 3.8 Cellobiose 2.3	Acetate 2.3 5-HMF 2.6 Fur 1.3 Phenol 2.9	43.1	10.4	24.2	[131]
Trichosporon fermentans	Sweet sorghum	Enzymatic saccharification	Sucrose 27.2 Glucose 6.4 Fructose 6.4	nd	57.8	6.7	11.6	[132]
Trichosporon Oleaginosus ATCC 20509	Switchgrass	Diluted alkali	Glucose 58.0 Xylose 26.0	Acetate 0.5	25.1	27.0	58.0	[126]
Trichosporon Oleaginosus ATCC 20509	Wheat straw	Dilute acid	Glucose 3.2 Xylose 14.0 Arabinose 3.7 Galactose 0.8	Det	71.9	19.4	27.1	[99]

Table 2. Cont.

Y biomass = g dry cell weight/g sugars consumed; Y lipid = g lipids produced/g sugars consumed; Lipid content = g lipids produced/g dry cell weight.

5.2. Olive Mill Wastewater (OMW)

One of the main agricultural activities of the Mediterranean basin is olive oil production, which represents about 95% of the world's olive oil production. The chemical composition of OMW is very variable depending of several factors, such as the system used for oil extraction, the variety of olive trees, and the degree of fruit maturity at the time of processing. In general, OMW is composed by 83–92% of water, 4–16% of organic matter (polysaccharides, proteins, organic acids, phenols and polyphenols, aromatic molecules, lipids, and nitrogen) and 0.4–2.5% of salts [133]. All these molecules cause high levels of chemical oxygen demand (COD) and biological oxygen demand (BOD) in OMW, reaching values of more than 200 gL^{-1} and 100 gL^{-1} respectively [134]. Furthermore, other characteristics of OMW, such as the pH values (ranging from 3 to 6), the high content of polyphenols (up to 80 gL⁻¹) and high content of solid matter (up to 20 gL⁻¹ total solids), make these wastewaters hardly degradable and even toxic for most of the microorganisms and crops. In fact, although OMW could be temporarily stored in evaporation ponds [135], from which it can be distributed on agricultural lands, the direct disposal of OMW in nearby aquatic systems, or spreading on lands [136] have led to soil pollution, surface and ground water contamination, odor nuisances, and inhibition of aquatic life and vegetation [137]. For these reasons, OMW require pretreatment before their disposal, which currently can be accomplished by chemical-physical or biological methods. Chemical-physical methods, reviewed by Ochando-Pulido et al. [138], include simple evaporation, reverse osmosis, ultrafiltration, coagulation, oxidation, thermal drying and advanced oxidation processes (ozonation, Fenton process, electrochemical oxidizing methods); however, all these treatments are quite expensive. Biological methods offer the possibility to convert OMW into value-added products. They include anaerobic digestion, proposed as a promising technology for OMW treatment to produce energy (i.e., biogas), although many problems (such as growth inhibition of methanogens from phenolic compounds, low pH, alkalinity, low nitrogen content) still need to be overcome [139]. Other biological methods tested, such as aerobic treatment, composting and vermicompost yielded unsatisfactory results [140–142]. Other authors [143] studied the ability of two different wild-type strains of Yarrowia, W29 and IMUFRJ 50682, to convert OMW into the enzyme lipase. On OMW with COD of 19 gL⁻¹ and about 800 mgL⁻¹ of total polyphenols, the strain W29 showed the highest production of extracellular lipase, and the integration of medium with ammonium sulphate determined an improvement of lipase productivity, leading to 80% of COD degradation and 70% of total phenols reduction. Good results were obtained by biological methods based on the use of oleaginous microorganisms (Table 3). These microorganisms not only detoxify the substrate by reducing the polluting power, but they are able to convert these wastes into added-value products. The most studied yeast for OMW conversion was Y. lipolytica, which provided interesting results. For example, it was reported that on pure OMW, with a COD value of 105 mg O_2L^{-1} and a total polyphenol content of 650 mg L^{-1} , Y. *lipolytica* reduced the organic load by 41.22% and the content of polyphenolic compounds by 28.7% without dilutions and nutrient integration. The main metabolite was citric acid [144]. However, the results were variable among the different strains tested, as some of them did not reduce the organic load and were not able to overcome the stress conditions. Other studies reported interesting results [145,146], confirming the ability of some Y. lipolytica strains to reduce the polyphenols content present in OMW and the production of citric acid as the main metabolite. In medium with high polyphenol, an intracellular accumulation of lipid up to 48% was obtained [145]. A screening on oleaginous microorganisms belonging to different species [147], such as Y. lipolytica (6 strains), Candida tropicalis, Cryptococcus curvatus, Lipomyces lipofer, L. starkeyi and L. tetrasporus, showed that the tested microorganisms were not able to survive on OMW with initial polyphenol concentrations of 2000 mgL⁻¹. On diluted medium, although all microorganisms are able to grow, L. starkey and Y. lipolytica showed a fair ability to accumulate lipids, respectively 15 e 25%. Interestingly, the growth and metabolism of microorganisms could change by adding an alternative carbon source, such as glycerol or glucose. For one Y. lipolytica strain, the carbon flux in OMW + glucose

was directed to lipids synthesis (intracellular content of 20.5%), whereas on OMW + glycerol the carbon flux was directed towards the mannitol production, with a yield of 33.5% (g mannitol/g sugars consumed).

Table 3. Effect of oleaginous yeasts on OMW detoxification and product synthesis. * = mgL⁻¹, ** = (%, w/w)

Yeasts	OMW Composition (gL ⁻¹)	Organic Load Reduction (%, w/w)	Products (gL ⁻¹)	References
Candida tropicalis ATCC 750	COD 51.1 * Phenol 2.6 Sugars 13.2	COD reduction 68 Phenol reduction 39	Proteasi Lipasi Lipid content 78.7 **	[148]
Candida tropicalis LFMB 16	Phenol 1.5 Reducing sugars 7.0 + Commercial glucose 65.0	Decolorization of 16 Phenol reduction 58	Biomass 2.6 Ethanol 21.9 no lipids production	[147]
Cryptococcus curvatus ATCC 20509	Phenol 1.9 + Commercial xylose 100.0	Decolorization of 25 Phenol reduction 28	Biomass 23.8 Lipids 2.5 Lipid content 10.5 **	[149]
Lipomyces starkeyi DSM 702096	Phenol 1.9 + Commercial xylose 100.0	No decolorization Phenol reduction 28	Biomass 21.1 Lipids 5.9 Lipid content 27.9 **	[149]
Lipomyces starkeyi DSM 702096	Phenol 9.1 Reducing sugars 12.8	Phenol reduction 43	Lipid yield 22.4 **	[150]
Rhodotorula mucilaginosa CH4	COD range 11.6–24.6 *	COD reduction 95.7–56.7 Phenol reduction 83–45	Biomass 9.6 Lipids nd	[151]
Yarrowia lipolytica	Phenol 1.5	Decolorization of 63 Phenol reduction 34	Biomass 4.8 Lipid content 17.0 ** Citric acid 7.8	[146]
Yarrowia lipolytica A6	Phenol 1.9 Reducing sugars 7.0	Phenol reduction 16	Biomass 2.2 Lipid content 19.1* *	[147]
Yarrowia lipolytica A6	Phenol 1.9 Reducing sugars 7.0 + Glycerol 50.0	Phenol reduction 16 No uptake of OMW sugars	Biomass 5.6 Lipid content 14.9 ** Mannitol 13.4	[147]
Yarrowia lipolytica LGAM S	Phenol 2.0 Reducing sugars 7.0	No phenols reduction	Biomass 5.2 Lipid content 6.3 ** Citric acid 6.4	[147]

5.3. Cheese Whey (CW)

CW is a liquid waste of dairy industries, resulting from the cheese making process. The global production of CW is estimated to be over 1 billion tons per year [152]. In the European Union (EU), the total CW production is around 40 million tons/year. For 1 kg of cheese, approximately 10 L CW is produced. Although the chemical composition varies with the type of cheese, CW in general is composed of 5–8% of dry matter, mainly composed of lactose (45–50 gL⁻¹), proteins (6–8 gL⁻¹), lipids (4–5 gL⁻¹), and mineral salts (8–10% of dried extract). The latter includes several salts, such as NaCl and KCl (more than 50%), calcium salts and others [152]. Generally, CW is characterized by high COD and BOD, 50–102 gL⁻¹ and 27–60 gL⁻¹, respectively, because it retains about 55% of the total milk nutrients [153]. Though CW is nutrient-rich with high utilization potential, 50% of it is discarded without treatment. The other 50% is used as feedstock for animal feeding or to produce ricotta cheese, generating another by-product, similar in nutrient composition and pollution strength. Disposing of untreated CW leads to environmental problems like eutrophication or pollution problems [154,155]. This residue can be valorised

through physicochemical and biological treatments. Physicochemical processes consist of protein precipitation and membrane separation, useful for producing whey powder, whey protein concentrate, whey protein isolate, whey permeate, lactose, and minerals. Conversely, biological treatments involve the microbial conversion of lactose into high added value products [156,157]. As very few yeasts possess the lactose permease and β -galactosidase enzymes required for lactose metabolism [158], the growth of oleaginous yeast on CW medium is very limited (Table 4). Yeasts such as Y. lipolytica and C. curvatus, have been reported to accumulate lipids in CW medium [154,155]. A study performed on deproteinized CW showed that among 55 yeasts tested, only 11 were able to grow, and only six of them were oleaginous yeasts. Among these, the most effective in lipid accumulation (about 28% of DCW) was identified as Y. lipolytica. By means of the accurate control of process parameters, such as pH (5.5) and temperature (range of 5–15 °C), the yield increased up to 43% [155]. A study was performed with C. curvatus, comparing growth on pretreated and non-pretreated CW. A combined pretreatment (alkaline and hydrodynamic cavitation) was carried out in order to eliminate the bacterial flora that naturally populates the CW. In the raw CW, C. curvatus was not able to grow as it was inhibited by the dominant species of bacteria. In the pretreated CW, surprisingly C. curvatus produced high yields, about 200% more than those obtained on simple sugars, such as glucose, galactose and lactose, and an accumulation of about 65% of intracellular lipids was observed. Probably, the presence of some components such as lactic acid, citric acid, vitamins and minerals, which are toxic for some microorganisms [159], affected positively the C. curvatus growth [154]. Similarly, C. curvatus NRRL Y-1511 and C. laurentii UCD 68-201 resulted the most performing microorganism among the 18 strains analysed by Carota et al. [160]. A biomass yield and lipid content of 50% and 63%, respectively, were obtained with C. curvatus, and 52% and 72% with C. laurentii. Noteworthy, the scale-up of the process to 3 L bioreactor determined a significant change in FAME composition compared to shaken cultures, with a significant decrease in total saturated FAs (27.9 vs. 38.2%) and a 2.8-fold increase in linoleic acid (23.7 vs. 8.3%).

Table 4. Use of oleaginous yeasts on CW: effect on CW characteristics and products synthetized by yeasts metabolis
FA = fatty acid composition; De = Deproteinized; NDe = not Deproteinized. * = mgL ⁻¹ , ** = (%, w/w)

Yeasts	Treatment	CW Composition (gL ⁻¹)	Products (gL-1)	FA	References
Cystobasidium oligophagum JRC1	De	COD 66.4 * Reducing sugars 39.6	COD 66.4 * Biomass 12.8 Reducing sugars 39.6 ipid content 44.1 **		[161]
Cystobasidium oligophagum JRC1	NDe	COD 85.5 * Reducing sugars 56.5	Biomass 20.9 Lipids 4.6 Lipid content 21.8 **	5% C14:0–30% C16:0 10% C18:0–40% C18: 115% C18:2	[161]
Cryptoccoccus laurentii- 11	De	-	Biomass 4.6 Lipids 0.6 Lipid content 13.9 **	0.4% C14:0-0.3% C15:0 20.1% C16:0-0. 6% C17:0 27.5% C18:0-34.4% C18:1 4.8% C18:2-1.2% C20:0 0.8% C 22:0-4.8% C24:0	[162]
Debaryomyces etchellsii	De	COD 56.2 * Reducing sugars 25.2	Biomass 2.8 Lipid content 15.9 **	27% C16:0–5% C16:1 4% C18:0–53% C18:1 9% C18:2–2% other	[163]
Yarrowia lipolytica B9	De not sterile	Cheese whey + Lactose	Biomass 7.4 Lipids 4.2 Lipid content 58 **	16.9% C16:0–18.7% C16:1 8.4% C17:1–56.1% C18:1	[155]
Lipomyces starkeyi	De	BOD 21.1 * COD 50.8 * Lactose 56.0 Lactic acid 0.5	Biomass 9.2 Lipid content 18.2 **	24% C16:0–14.9% C18:0 49.6% C18:1–5.9% C18:2	[164]
Wickerhamomyces anomalus EC 28	De	COD 56.2 * Reducing sugars 32.0	Biomass 2.61 Lipid content 24.0 **	33% C16:0–5% C16:1 8% C18:0–32% C18:1 18% C18:2–4% C18:3	[165]

5.4. Food Waste (FW)

FW represents a great source of nutrients consisting mainly of carbohydrates, proteins, lipids and traces of inorganic components, which can be further digested into simpler organic compounds, i.e. glucose, amino acids, fatty acids [166,167] (Table 5). Like other biomasses, various pretreatments were developed for hydrolysis to obtain simple sugars. Physical, chemical, physico-chemical, enzymatic methods are usually adopted [168]. The composition of the hydrolysates produced can vary according to the origin and composition of FW, and the pretreatment method used. However, the main sugars present are glucose, fructose, galactose, and ribose, which are extracted mainly by enzymatic hydrolysis [169]. Low acid pretreatment is commonly applied directly or in combination with an enzymatic method to avoid the formation of inhibitory compounds, typically represented by furfural, 5-HMF, and phenols. Furthermore, a mixture of α -amylase, β -amylase, and glucoamylase enzymes is also used for the transformation of starch into monomeric sugars [170]. The most used strategy for FW treatment was anaerobic fermentation (AF), which leads to the production of CH_4 , H_2 , and volatile fatty acids (VFA). This pretreatment is widely used as it does not require sterile conditions and is relatively inexpensive. In the last years, some studies were no longer focused on the use of AF for the production of CH_4 but rather for VFA, used as a carbon source for several microorganisms. AF consists of several stages, each producing different by-products. In order to enhance the production of VFA, the last phase called methanogenesis can be suppressed [171]. The type of VFA mainly depends on the composition and degradation of FW. The degradation of some amino acid or the acidification of long chain FAs produces VFAs like acetic acid. On the other hand, the acidification of monosaccharides by anaerobic bacteria produces acetic, propionic, isobutyric, butyric, isovaleric, valeric and caproic acids [172]. Some studies have shown the toxicity of these VFAs in concentrations higher than 5 gL⁻¹ [50,173]. Differently, Huang et al. [71] tested a strain of R. toruloides (AS 2.1389), using acetate as the sole carbon source and found a strong inhibition at high concentrations of acetate (about 40 gL^{-1}), while between 5 gL⁻¹ and 20 gL⁻¹ *R. torudoiles* showed better lipid performance than growth performed on glucose media. By comparing the data between acetate and glucose (at 20 gL⁻¹), it was found that the microorganism was able to better convert sugars into biomass (biomass production 8.96 gL^{-1} , lipid content 13.7% and lipid yield 14.5%) and acetate in lipids (4.17 gL⁻¹, 23.5% and 18.7%, respectively).

Some studies have correlated the toxic effect of VFAs with the length of their chains [49]. For example, Liu et al. [91] found that *C. curvatus* can tolerate up to 30 gL^{-1} of acetic acid as sole C source, but only 15 gL⁻¹ was tolerated for propionic and butyric acid. In a mixture of VFAs, it was found that *C. curvatus* prefers acetic acid as sole carbon source. [174]. Differently, it was found that *Apiotrichum porosum DSM 27194* was able to assimilate different VFA mixtures containing acetic, propionic and butyric acids at different ratios for lipid production. A lipids content of 36.2% was obtained with the VFA ratio of 6:1:1 [175]. Noteworthily, many authors have found the production of unconventional FAs, i.e., odd chain FA, upon growth with VFA [176,177].

Table 5. Use of oleaginous yeasts on unreferit food wastes and main products derived from yeast metabolism. $= (76, a)$	Table 5. Use of oleaginous	yeasts on different food	l wastes and main	products derived from	yeast metabolism.	* = (%, w/w)
--	----------------------------	--------------------------	-------------------	-----------------------	-------------------	--------------

Yeasts	Feedstock	Pretreatment	C Source (gL ⁻¹)	Products (gL ⁻¹)	References
Apiotrichum porosum DSM27194	Corn stover	Diluted acid	Glucose 15.0 + VFA (acetic: propionic: butyric acid = 6:1:1)	Biomass 26.5 Lipid content 36.2 *	[175]
Apiotrichum porosum DSM27194	Corn stover	Diluted acid	Glucose 15.0 + VFA (acetic: propionic: butyric acid = 3:1:2)	Biomass 21.9 Lipid content 31.5 *	[175]
Cyberlindnera saturnu NRRL-Y-17396	Food waste	Anaerobic digestion	VFA 10.0 (acetic: propionic: butyric: valeric acid = 16:6.5:12.5:6)	Biomass yield 32.0 * Lipid yield 11.0 * Lipid content 33.9 *	[176]

Yeasts	Feedstock	Pretreatment	C Source (gL ⁻¹)	Products (gL ⁻¹)	References
Cutaneotrichosporon curvatum NRRL-Y-1511	Food waste	Anaerobic digestion	VFA 15.0 (acetic: propionic: butyric: valeric acid = 11:4:8:4)	Biomass yield 35.0 * Lipid yield 13.0 * Lipid content 36.9 *	[176]
Yarrowia lipolytica CICC 31596	Synthetic	-	Acetic acid 70.0	Biomass 37.1 Lipids 10.1 Lipid content 27.2 *	[178]
Yarrowia lipolytica CICC 31596	Food waste	Anaerobic digestion	VFA (acetic: propionic: butyric acid = 8:3:5)	Biomass 14.6 Lipid 3.2 Lipid content 21.8 *	[178]
Yarrowia lipolytica CICC 31596	Fruit and vegetable waste	Anaerobic digestion	VFA (acetic: propionic: butyric acid = 5:1:14)	Biomass 11.8 Lipid 3.1 Lipid content 26.0	[178]
Yarrowia lipolytica ACA DC 50109	Food waste	Anaerobic digestion	VFA 5.0 (acetic: propionic: butyric: valeric acid = 8:3:6:3)	Biomass yield 37.0 * Lipid yield 8 * Lipid content 20.1 *	[176]
Lipomyces lipofer NRRL-Y-11555	Food waste	Anaerobic digestion	VFA15.0(acetic: propionic: butyric: valeric acid = 11:4:8:4)	Biomass yield 30.0 * Lipid yield 5 * Lipid content 16.8 *	[176]
Rhodosporidium toruloides Y-27012	Potato peel	Biological hydrolysis	Glucose 80.0	Biomass 53.9 Lipids 26.7 Catotenoids nq	[179]
Rhodosporidium toruloides 2.1389	Food waste	Enzymatic hydrolysis	Reducing sugar 50.0 Fats 2.4 Acetic acid 0. 5 Lactic acid 4.0	Biomass 12.1 Lipid 6.4 Lipid content 52.7	[180]
Rhodosporidium toruloides Y2	Food waste	Diluted acid	Total sugars 36.7 Fats 10.7	Biomass 24.7 Lipid 7.3 Lipid content 22.9 *	[181]
Rhodotorula toruloides NRRL-Y-27012	Food waste	Anaerobic digestion	VFA 10.0 (acetic: propionic: butyric: valeric acid = 16:6.5:12.5:6)	Biomass yield 25 * Lipid yield 5 * Lipid content 25.7 *	[176]

Table 5. Cont.

6. Parameters Affecting Lipogenesis in Oleaginous Yeasts

Nitrogen limitation is reported as the main factor affecting the lipid accumulation in oleaginous microorganisms, but other parameters influencing the metabolism are involved in lipid accumulation. Among these, the main ones are the carbon source, nitrogen source [182], C/N ratio, oxygenation [183], temperature, pH [184], time of incubation and concentration of mineral salt. Obviously, the optimization of the process is necessary to improve the economic feasibility, that is influenced by the substrate cost, production rate, and lipid yields [185]. In the following sections, the effect of different parameters on SCO production will be discussed separately.

6.1. Effect of Type and Concentrations of Carbon Source

The type of carbon source inevitably influences the final yield of the process. The main sugars used by yeasts for their growth are glucose and xylose, followed by fructose, arabinose, mannose, galactose and in some cases also glycerol, hydrocarbons and oils. Considering glycolysis, the main biochemical pathway involved in sugar metabolism, two molecules of acetyl-CoA are generated from one molecule of glucose (or fructose); the same yield is obtained for galactose and mannose which are transformed into intermediates of glycolysis by the Leloir and mannose pathways. From 100 g (about 0.55 moles) of these

sugars (glucose, fructose, mannose and galactose), approximately 1.1 moles of acetyl-CoA can be generated, and if all this amount of acetyl-CoA converges to lipid synthesis, the theoretical maximum yield would be 0.32 g/g [36]. This value is slightly higher for xylose catabolism, about 0.34 g/g per 100 g (0.66 moles), in the case of exclusive presence of the phosphoketolase pathway, whereas for the pentose phosphate pathway (PPP), where around 1.0 mole of acetyl-CoA is formed per 100 g of xylose, the theoretical maximum yield would drop to 0.30 g/g. Also for glycerol, the maximum theoretical yield of SCO is around 0.30 g/g. Considering that not all acetyl-CoA produced is utilized for lipid synthesis because a portion is used for different metabolic processes, different studies report that, even under ideal conditions for the production of SCO by wild-type yeasts, the lipid yield on the glucose is expected to be around 0.22 g/g. The highest theoretical lipid yield derives from the use of acetate as a carbon source, from 100 g of acetate approximately 1.66 moles of acetyl-CoA are obtained, with a relative yield of 0.45 g/g. Not all acetyl-CoA can be channeled towards the lipid synthesis. Indeed, as studied by Liu et al. [48], during the lipogenic phase, high quantities of NAPDH are required, estimated at about 37.8 mol per 100 mol of acetate. This high amount of NADPH required, mainly produced by the PPP, greatly reduces the lipid yield. In fact, tight regulation of the metabolic cycle between energy synthesis and lipid production was observed in Y. lipolytica [48].

A recent study by Awad et al. [182] analysed the behavior of C. oleaginosus on different carbon sources. The highest biomass yield (18.4 gL^{-1}) was obtained on lactose, with a lipid content of 49.7%; when sorbitol was the only source of C, the lowest biomass and lipid yield was obtained, 4.5 gL^{-1} and 13.4%, respectively, whereas the best conversion of sugars into lipids was obtained with mannose (52% lipid content). Other authors [81] reported that L. starkeyi manages to accumulate 85% of intracellular lipids in the presence of a mixture of simple sugars (glucose and xylose), whereas in presence of only glucose the lipid accumulation was lower (about 79.6%). Likewise, Santek et al. [186] reported that the growth of *T. oleaginosus* in media containing xylose enhanced the lipid accumulation and reduced the cell growth, while the opposite effect was observed in media containing glucose. Furthermore, the increase of initial sugars concentration in media had the opposite effect on lipid and productivity. This effect was already observed in different oleaginous yeasts, such as Rhodotorula glacialis [187], Trichosporon cutaneum [188], L. starkeyi [189], and C. curvatus [90]. In a study reporting the use of L. tetrasporus [23], an inverse correlation between sugar concentration and lipid synthesis was observed, the decrease in lipid synthesis determined consequently an increase in the production of secondary products. The growth of L. tetrasporus in cardoon hydrolysates containing up to 45 gL^{-1} of total sugars, produced lipids with yields up to 20.9%, whereas for sugars concentration between 45 and 90 gL^{-1} , the lipids production decreased and the production of polyols increased [23]. Similarly, Tchakouteu et al. [190] documented polysaccharides accumulation in *C. curvatus* in media with high glucose concentrations. The accumulation of intracellular polysaccharides and polyols could be explained by changes in cellular metabolism in consequence of exposition to high osmotic stress.

Similar phenomena also occur in other yeast species. For example, in the widely investigated *S. cerevisiae* yeast osmotic stress induces a series of molecular, physiological and morphological events, the so-called response to osmotic stress, to maintain cellular activity. Yeast cells synthesize and accumulate small molecules, which are supposed to act as osmoprotectants [191]. In order to investigate the ability to utilize lignocellulosic carbon sources, tolerate inhibitory compounds, and grow in medium without integrated vitamins, Sitepu et al. [116] screened 48 oleaginous yeast strains belonging to 45 species. The study found that not all microorganisms were able to grow in low-cost carbon sources and high variability among different strains of the same species was found. For example, not all strains of the *Cryptococcus* family were able to grow on undetoxified lignocellulosic hydrolysates and not all *Cryptococcus* have been able to metabolize the various carbon sources. In this regard, between two *C. humicola* strains, one strain was able to metabolize and produce lipids on glycerol, while the other did not grown on this substrate. Glycerol,

a by-product of the biodiesel industry, has attracted a lot of interest in recent years. The flourished production of biodiesel, accompanied by the huge production of glycerol, stimulated research towards the enhancement of glycerol, used as the carbon source for SCO production [192].

6.2. Effect of Type and Concentrations of Nitrogen Source

Many studies regarding the influence of concentration and source of nitrogen on lipid biosynthesis are available. For example, Tkáčová et al. [193] reported that the C/N ratio did not have a significant impact on the growth of *T. oleaginous*, while it affects the total lipids content. However, the increase of C/N ratio in the growth media had the opposite effect on the bioprocess efficiency parameters; in fact, the lipid yields and productivity were increased, while biomass and growth rate were reduced. On the other hand, the production performances of Pichia guilliermondii increased until the value of C/N was 60 (maximum lipid concentration and productivity of $5.4 \,\mathrm{gL}^{-1}$ and $1.8 \,\mathrm{gL}^{-1} \,\mathrm{d}^{-1}$, respectively, lipid yield of 13%), whereas a reduction was observed with the ratio C/N of 80 (maximum lipid concentration and productivity of 3.1 gL^{-1} and $1.5 \text{ gL}^{-1} \text{ d}^{-1}$, respectively, lipid yield of 6%), with further decrease at higher C/N ratios. Similar results were reported for R. *glutinis* [194,195], which showed an increase in lipid accumulation in medium with C/Nratio from 20 to 70, and a negative effect on lipid accumulation was found when the C/N ratio was further increased to 100. Conversely, Awad et al. [182], evaluating the effect of a wide range of C/N ratios in C. oleaginosus, found that the best ratio C/N was 120. Among the different nitrogen sources studied, apart the organic sources (yeasts extract and tryptone), the best results were obtained with urea and NO_3 . Conversely, Chopra et al. [183] evaluated the influence of different inorganic N-sources, such as NH₄Cl, (NH₄⁺)₂SO₄ and NaNO₃, in *Pichia guilliermondii*. Although organic nitrogen sources (yeast extract, peptone, urea) have been proved to be better N-sources for both biomass and lipid production, they are not economically profitable. The study showed that NH₄Cl is the best source of nitrogen compared to NaNO₃. The lipid yield obtained with sodium nitrate (0.2 gL^{-1}) was significantly lower compared to that obtained with ammonium chloride (4.5 gL^{-1}) and $(NH4^+)_2SO_4$ as nitrogen sources. These results suggested that this microorganism preferred NH_4^+ as the N source.

6.3. Effect of Temperature

The ability to growth over a wide range of temperatures without negative effects on the growth rate is an appreciable feature in microorganisms used in large-scale fermentation processes. Furthermore, the ability of microorganisms to grow at high temperature is preferred for two main reasons: the reduction of costs necessary for cooling during the cultivation and to implement the process in simultaneous saccharification and fermentation (SSF) mode [196,197]. A study by Lamers et al. [197], performed on several strains of oleaginous yeasts, reported that two main behaviours were present among the different yeasts: strains with a relatively narrow temperature range and strains having a broad temperature range in which growth was marginally influenced. *Hansenula beijerinckii* and *Saccharomyces cerevisiae* (used as control) had a narrow optimum of 5 °C around the maximum growth achieved at 29 °C, a deviation from this temperature negatively affected cell growth. Differently, *Pichia anomala, Waltomyces lipofer*, and *Torulaspora delbrueckii* could vary the growth temperature by 9 °C from their optimum, without having a negative effect on growth and lipid production.

A recent paper by Abeln and Chuck [184] evaluated the influence of process temperature on oleaginous yeast *Metschnikowia pulcherrima*, the range of analysed temperatures ranged from 15 °C to 30 °C. It was found that with increasing temperature the biomass yield and the lipid yield decreased, while the yields in arabitol and glycerol increased. A similar correlation of arabitol formation with temperature was reported in *M. zobellii* [198] and *M. reukaufii* [199].

6.4. Effect of pH

Microbial assimilation of carbon source depends on the pH of the medium. The pH influences the surface properties of the cell membrane and thereby affects the carbon assimilation process. Several studies with *Y. lipolytica* showed that the pH range of 6 to 6.5 is suitable for lipid production [200,201]. A recent study demonstrated the significant influence of pH on lipid production since the lipid accumulation is favoured by a slightly acidic pH (5 to 6.5) [202]; similar results were obtained by Slininger et al. [203] for *L. terasporus* on lignocellulosic hydrolysates. Results from other authors [80] demonstrated that the optimal pH value differs among different strains and it depends also on the carbon source. In a study performed on *Rhodotorula glutinis* [204], no significant effect on synthesis of lipid or carotenoid was observed in the pH range from 4 to 7. Cultivation in medium with initial pH 3.0 resulted in a reduction in biomass and carotenoid production and a pH of 2 strongly inhibit the growth of microorganism.

6.5. Effect of Oxygenations

Few studies have analysed the influence of oxygen on lipid production, whose effects differ from one species to another. For example, in *C. curvatus* grown on casein whey, lipid yields decreased (from 20% to 15%) with lower oxygenation rates, in the range 8–2 mmol $O_2 L^{-1} h^{-1}$ [205]. In some cases, contradictory results were obtained among different studies. Naganuma et al. [206] found no correlation between oxygenation and lipid yield in *L. starkeyi*, whereas other authors [207] for the same species reported a decrease in lipids production at high levels of dissolved oxygen. Likewise, *R. glutinis* at high dissolved oxygen concentrations had a reduced lipid accumulation [208]. *Rhodotorula glutinis* cells cultivated in highly aerobic fermenters showed a fast growth rate and production of high cell mass, with a 50% reduction in average lipid content [209]. Saenge et al. [210] studied the effects of aeration rate on cell growth, lipids yield, carotenoids production, and glycerol consumption by *R. glutinis*, and found that an increase in aeration rate (from 0 to 2.0 vvm) enhanced biomass and lipids accumulation.

6.6. Effect of Mineral Salts and Other Components

Some authors [67,211] have reported that some ions, such as Mg^{+2} , Ca^{+2} , Mn^{+2} , Fe⁺³, Cu⁺² and Zn⁺², and mineral compounds [37] can affect the amount of biomass and lipid content. Zhao et al. [212] showed that MnSO₄, ZnSO₄, MgSO₄, CoCl₂, CuSO₄ and $FeSO_4$ in appropriate concentrations can increase cell growth and lipid accumulation. Each element has a different impact on growth and lipid production. Furthermore, their impact is influenced by the presence of other molecules. For example, it was found that in *R. toruloides* biomass production was not affected by MgSO₄, while KH₂PO₄ positively affected yeast biomass. However, it was seen that the increase in MgSO₄ and yeast extract concentrations affect positively biomass production until the MgSO₄ concentration was 0.25 gL^{-1} , after that no further increase in biomass production was observed, also if high yeast extract concentration was used. Similar effect was observed for glucose. In this case, the biomass was increased up to 0.35 gL^{-1} of MgSO₄, whereas at concentration higher of this value, no effect on biomass concentration was observed, also in presence of high glucose concentration [213]. The effect of KH_2PO_4 (0.4, 1.6, 1.8 and 2.8 gL⁻¹) on lipid production in *R. toruloides* was analysed by Kraisintu et al. [214], which found the highest lipid production (8.8 gL⁻¹) at 0.4 gL⁻¹ of KH₂PO₄.

6.7. Factors Affecting the Fatty Acids Profile

The most abundant fatty acids produced by oleaginous yeasts are C16:0, C16:1, C18:0, C18:1, C18:2. Their relative ratios, in some cases, are very similar to those of many vegetable oils of industrial interest (see Table 6). Furthermore, in addition to the ability to grow on different carbon sources, one of the characteristics for industrial interest in SCOs is the ability to modulate the profiles of FAs produced in function of different parameters. For example, Awad et al. [182] correlated the FAs produced by *C. oleaginous* with the

carbon source. Identical fatty acid profiles were obtained on mannose, maltose, lactose, and glucose, namely C 16:0 (30%), C 18:0 (10%), C 18:1 (52%), C18:2 (4%), others 4%. Using arabinose as carbon source, it was observed a reduction in C 18:0 (4%) and C 18:1 (7%) and an increase of C 18:2 (8%). The use of galactose as sole carbon source determined a decrease in C16:0 with a consequence increase in C18:0 and the highest fraction of C18:1 (57%). Furthermore, this study showed an increase of saturated FAs with ammonium salts as a N-source, which provides a new route to generate tailored FA profiles for specific oleochemicals or food applications [182]. Differently, Abeln and Chuck [184] correlated the FAs profile with the temperature. In fact, the decrease in cultivation temperature from 30 to 15 °C resulted in a higher degree of unsaturated FAs. In particular, it was observed the increase in oleic acid (C 18:1) and a decrease in shortchain FAs (C 14:0, C 16:0 and C 16:1), indicating that at low temperatures the activity of desaturases was favoured compared to elongases. As reported for S. cerevisiae, this behaviour might be correlated with genome regulation. At low temperatures, about 10 °C, transcription of genes encoding for desaturase is activated, probably in order to maintain the membrane fluidity [215]. In Y. lipolytica, the activity of D12-fatty acid desaturase enzyme was increased at decreasing the incubation temperature from 30 °C to 12 °C. Although the low incubation temperatures of 12 °C increase unsaturation, these temperatures do not favour lipid accumulation [216]. Kot et al. [204], found an inverse correlation between pH and oleic acid production. Although the ratio of unsaturated-to-saturated acids did not change, higher oleic acid production was achieved in medium with pH 3.0 (60%), while a lower amount was found in medium with pH 7.0 (48.1%). A similar effect was also found by Liu et al. [217] in T. fermentans; these authors reported a decrease of 10% in oleic acid production when the pH was increased from pH 4.5 to pH 6.5. Another interesting behaviour, found by several authors, is the correlation between oxygen concentration and fatty acid profile. Pan and Rhee [218] observed that under oxygen starvation conditions, the saturated FAs increased, whereas the increase of oxygen concentration increased the degree of FAs unsaturation. In agreement with these findings, Calvey et al. [207] and Davies et al. [205] observed in low aeration flasks a slight increase in the degree of saturation of FAs by *L. starkeiy* and *C. curvatus*. Probably, this behaviour could be correlated to the high activity of the FA desaturase that utilizes oxygen as substrate to insert the unsaturation [207]. In conclusion, the results obtained by different studies showed that the lipid profile can be modulated by changing the microorganism, the carbon and nitrogen source, the temperature, the pH, and the dissolved oxygen concentration.

	Fatty Acids (Relative %)							
Lipid Origin -	C14:0	C16:0	C16:1	C18:0	C18:1	C18:2	C18:3	– References
Soybean	-	10.1	-	4.3	22.3	53.7	8.1	[219]
Sunflower	-	5.2	0.1	3.7	33.7	56.5	-	[219]
Rapeseed oil	-	3.0	-	1.0	64.4	23.3	8.0	[220]
Corn	-	11.6	-	2.5	38.7	44.7	1.4	[219]
Jatropha	-	18.5	-	2.3	49.0	29.7	_	[220]
Cocoa butter	-	23.3	0.9	24.5	28.7	3.9	-	[220]
Palm oil	0.1	39.3	0.2	4.4	42.5	11.4	_	[221]
C. albidus ATCC 10672	-	20.0	-	5.0	42.0	25.0	8.0	[126]
C. curvatus ATCC 20509	-	25.9	-	15.2	47.7	6.4	-	[99]
Y. lipolytica ATCC 20460	-	6.0	-	2.0	56.0	19.9	-	[99]
L. starkeyi ATCC 56304	-	23.0	9.0	3.0	62.0	2.0	1.0	[126]
L. starkeyi ATCC 12659	-	36.2	-	4.5	46.3	3.4	-	[99]

Table 6. Comparison of composition in the main fatty acids of lipids from vegetable species and oleaginous yeasts.

Lipid Origin	Fatty Acids (Relative %)							Deferrer
	C14:0	C16:0	C16:1	C18:0	C18:1	C18:2	C18:3	- Kererences
L. tetrasporus DSM 70314	0.5	39.5	4.1	12.8	40.4	0.7	-	[23]
R. glutinis AS 2.1389	1.0	20.4	0.8	10.3	47.8	7.3	0.8	[222]
R. glutinis ATCC 204091	-	23.5	-	9.0	43.4	15.4	-	[99]
R. taiwanensis AM2352	16.7	24.4	1.4	2.9	46.8	6.5	-	[129]
R. toruloides DSMZ 4444	1.3	25.1	-	10.1	45.9	10.5	3.3	[130]
T. oleaginosus ATCC 20509	2.0	24.0	1.0	10.0	40.0	20.0	3.0	[126]

Table 6. Cont.

7. Applications of Microbial Oils

7.1. Food Applications

Currently, industrial production of microbial oils has been already launched by several companies such as DuPont, DSM (ex-Martek Bioscience Inc., Kaiseraugst, Switzerland), Cargill Alking Bioengineering (Wuhan, China) Co. Ltd. (CABIO), Nestle S.A., Nutricia, etc.

One of the first food applications of microbial lipids concerns the use as substitutes for cocoa butter. In addition to being used in the manufacture of chocolate, cocoa butter also finds various applications in the cosmetic field. At the turn of the 1980s and 1990s, the cost of cocoa butter was about 8, making profitable the production of a microbial substituent. Although the price subsequently dropped [223], the research continued as the price of this compound is characterized by strong variability. Numerous approaches have been tested in order to produce lipids with composition similar to those of cocoa butter, as mixtures of different fats of exotic plants (e.g., illipe', butter, mango fat, kokum butter) with fractions of palm oils, but no interesting results were obtained in consequence of the high price of exotic fats [224]. Given the composition of cocoa butter (Table 6), the lipids produced by oleaginous yeasts represent perfect cocoa butter substitute candidates. These have a very similar fatty acid profile, but the main drawback is linked to the low production of C 18:0. Numerous strategies have been developed to increase the amounts of C18:0 in microbial lipids. For example, Ward and Singh [36] have mutated a strain of C. curvatus to partially block the 1-9 desaturase, which converts stearate (18:0) to oleate (18:1) in order to increase the amount of stearate at the expense of oleate. Several authors reviewed the techniques used to increase the amounts of C18:0 in microbial lipids [20,225–227]. Similarly, many studies have focused on increasing the production of PUFAs in oleaginous microorganisms [228].

PUFAs affect different physiological functions in the human body [229]. They play important roles as structural components of membrane phospholipids and as precursors of the eicosanoids, which are hormone-like substances, influencing the cardiovascular, immune and central nervous systems, the brain, other than the involvement in inflammatory reactions. As mammals lack the ability to synthesize essential FAs, these must be obtained through the diet [230]. In the food industry, PUFAs are in highly demand and used as additives in infant foods, which is a still growing market, accounting for around \$52 billion in value. The main natural source of PUFAs is fish oil, widely used as an infant food supplement, but as a consequence of the pollution of the seas, and consequently of the fish, microbial PUFAs would be preferable to fish oil [39]. The first commercial product of microbial oils as a food supplement dates back to 1985. The oil, rich in linolenic acid, was supposed to be a substitute for evening primrose oil. Produced by the fungus Mucor *javanicus*, the product was sold under the trade name of "Oil of Javanicus" [39]. A few years later the microbial oil was replaced by borage oil (Borago officinalis), which has a higher percentage of linolenic acid. Only in 2001, when the Food and Drug Administration assigned GRAS status to SCOs, the infant formula market in the USA was invaded by

microbial oils. In February 2002, in the US market, over 50% of infant formula was fortified with SCOs [231]. Until 2010, it has been estimated that over 24 million babies consumed infant formulas containing microbial oils [93,232,233]. Currently, DSM is the company with the largest portfolio of commercial microbial products. For example, under the trade name of DHASCO-B, it sells docosahexaenoic acid (DHA), a major structural fat in the brain (97% of total fats) and eyes (93% of total fats). DHA is important for optimal infant brain, eye and nervous system development, and it has been shown to support a healthy pregnancy. A commercial product with the trade name life's[™]OMEGA (45; 60; 60-DS) is based on eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and is helpful in reducing the risk of cardiovascular diseases. Finally, arachidonic acid (ARA), a precursor of eicosanoids that play a role in immunity, blood clotting and other vital functions is distributed under the trade name ARASCO.

7.2. Oleochemical Application

SCOs can be converted by a variety of chemical, physical, and biochemical techniques to produce building blocks or final products at high value otherwise produced from fossil-based materials. SCOs from waste biomass or agri-food by-products represent a good candidate for biodiesel production and many scientific efforts have been made in this direction. Several studies reporting the transesterification of microbial oils into biodiesel are available [234]. For example, starch wastewater conversion by *Rhodotorula glutinis* [235] or orange peel waste conversion with *R. toruloides NRRL 1091* and *C. laurentii UCD 68-201* [236] resulted in high biodiesel yields. The use of *C. curvatus*, grown on office waste paper, suitably pre-treated for the extraction of sugars, produced biodiesel with characteristic features, such as cetane number, cold performance, density, and iodine value, which met the requirements of the international standard (EN14214) [222]. Similar results were obtained by growing a *R. glutinis* strain in palm oil mill effluent [219].

By comparing the microbial lipids profile with the profile of oils commonly used for biodiesel synthesis, i.e., soybean and rapeseed oils, in some cases the microbial lipids are more saturated. Soybean oil contains mostly linoleic and oleic acids (53.7 and 22.3%, respectively), while the content of these fatty acids in rapeseed oil are 23.3 and 64.4%, respectively [237]. In consequence of high saturation degree of the main FAs composing soybean and rapeseed oils, the biodiesel derived from these oils is characterized by favourable traits, such as an increased cetane number, decreased NOx emissions, shorter ignition delay time, and oxidative stability. The possibility to change the microbial lipid profile by modifying substrate, microorganism or growth conditions make microbial oils feasible option for biodiesel synthesis.

The petrochemical sector is responsible for more than 75% of the EU's GHGs emissions. Undoubtedly, the energy transition cannot be obtained without a deep change in the productive models and developing integrated biorefineries capable of utilizing a range of residue feedstocks and conversion platforms to produce not only fuels, but also chemicals, materials, and power.

SCOs can be converted in various chemical compounds by using different conversion processes. For example, through the hydrogenation and isomerization process, using lipids obtained by *R. toruloides*, a renewable diesel blendstock was obtained consisting in blend of naptha (C7–C11) and diesel (C12–C20) [3]. Monounsaturated FAs can be transformed via ozonolysis into dicarboxylic acids, which are important intermediates for polyester and polyamide synthesis [238]. In this regard, in Italy, the leading company in the circular economy field, namely Novamont, produces pelargonic and azelaic acids through ozonolysis of oleic acid. More in general, azelaic acid finds application as an active ingredient in products for the topical treatment of acne as it inhibits the growth of skin bacteria causing acne. Pelargonic acid is used as an intermediate for the production of herbicide, solvent, lubricant, and for the production of esters used in the perfume and flavor industry [239].

One of the biggest challenges in the oleochemical field is substituting phthalate esters, due to their harmful health effects on humans. Phthalate esters are commonly used as plasticizers in polymer formulation, in particular for poly(vinyl chloride) (PVC) formulation. A good alternative is the epoxidized microbial oils, which might substitute phthalate esters, since they demonstrated to be valid in various applications, eco-friendly and sustainable [240]. Epoxidation of fatty acids, i.e., oleic acid, can also be used to create polyesters and polymers to be used in the pharmaceutical field for drug delivery [241].

Through the hydrogenation of microbial oils, sustainable and green fatty alcohols were obtained [242]. Fatty alcohols are widely used for various applications and were used for the formulation of detergents, cosmetics and cleaning agents.

Many studies have been made for the conversion of vegetable oils to biolubricants [3] which, in comparison to traditional lubricants, have many advantages, such as excellent lubricity, higher viscosity index, less production of emission, less dermatological problems to humans and biodegradability. The versatility of the microbial fatty acid composition makes these compounds good substitute of vegetable oils for biolubricant synthesis [3].

8. Outlook

The conversion of agri-food wastes into SCOs could be a promising technology for their optimal and sustainable management. The use of agri-food wastes and their derivatives products as growth medium for oleaginous yeasts could reduce the environmental impact of several food chains. Moreover, thanks to numerous applications in the food and oleochemical fields, these processes would bring further environmental benefits. As widely described, the metabolism of these microorganisms is highly flexible and different final bioproducts can be achieved depending on the substrate and the process settings. Among food-related wastes and by-products, lignocellulosic feedstock has a huge potential since it is one of the most abundant raw material, containing important amounts of assimilable sugars. The main limit in the utilization of this renewable substrate is represented by the generation of some inhibitory products mainly during the pretreatment process. Optimized pretreatment process are necessary to reduce by-products and ensure high sugars yield. Overall, major efforts are needed to isolate microorganisms with increased stress tolerance. In this regard, the use of genetic engineering and adaptive evolutionary techniques would greatly reduce the current limitations on the exploitation of agri-food by-products. Technological advances in the conversion of agri-food by-products into SCO can contribute to alleviate environmental problems and increase the economic feasibility of production processes.

Author Contributions: Conceptualization, A.C. (Antonio Caporusso), A.C. (Angela Capece) and I.D.B.; investigation, A.C. (Antonio Caporusso), A.C. (Angela Capece) and I.D.B.; writing—original draft preparation, A.C. (Antonio Caporusso), A.C. (Angela Capece); writing—review and editing, A.C. (Antonio Caporusso), A.C. (Angela Capece) and I.D.B.; supervision, A.C. (Angela Capece) and I.D.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by regione Basilicata, "dottorati innovativi di ricerca con specializzazione in tecnologie abilitanti in industria 4.0".

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflict of interest.

References

- 1. Vanham, D.; Bouraoui, F.; Leip, A.; Grizzetti, B.; Bidoglio, G. Lost Water and Nitrogen Resources Due to EU Consumer Food Waste. *Environ. Res. Lett.* **2015**, *10*. [CrossRef]
- Diep, N.Q.; Sakanishi, K.; Nakagoshi, N.; Fujimoto, S.; Minowa, T.; Xuan, T.D. Biorefinery: Concepts, Current Status, and Development Trends. Int. J. Ofbiomass Renew. 2012, 1, 1–8.

- Probst, K.V.; Schulte, L.R.; Durrett, T.P.; Rezac, M.E.; Vadlani, P.V. Oleaginous Yeast: A Value-Added Platform for Renewable Oils. Crit. Rev. Biotechnol. 2016, 36, 942–955.
- Almeida, J.R.M.; Modig, T.; Petersson, A.; Hähn-Hägerdal, B.; Lidén, G.; Gorwa-Grauslund, M.F. Increased Tolerance and Conversion of Inhibitors in Lignocellulosic Hydrolysates by *Saccharomyces cerevisiae*. *J. Chem. Technol. Biotechnol.* 2007, *82*, 340–349.
 Einer O. H. Lee Der Ertte helt Der Metterherer Aufle Der Pharm. 1972, 202 [Conselb. 0].
- 5. Ficinus, O. Ueber Den Fettgehalt Des Mutterkorn. Arch. Der Pharm. 1873, 203. [CrossRef]
- Nägeli, C.; Loew, O. Ueber Die Chemische Zusammensetzung Der Hefe. Justus Liebigs Ann. Der Chem. 1878, 193, 322–348. [CrossRef]
- Bonatsos, N.; Marazioti, C.; Moutousidi, E.; Anagnostou, A.; Koutinas, A.; Kookos, I.K. Techno-Economic Analysis and Life Cycle Assessment of Heterotrophic Yeast-Derived Single Cell Oil Production Process. *Fuel* 2020, 264. [CrossRef]
- 8. Shields-Menard, S.A.; Amirsadeghi, M.; Sukhbaatar, B.; Revellame, E.; Hernandez, R.; Donaldson, J.R.; French, W.T. Lipid Accumulation by *Rhodococcus rhodochrous* Grown on Glucose. *J. Ind. Microbiol. Biotechnol.* **2015**, 42. [CrossRef]
- Röttig, A.; Hauschild, P.; Madkour, M.H.; Al-Ansari, A.M.; Almakishah, N.H.; Steinbüchel, A. Analysis and Optimization of Triacylglycerol Synthesis in Novel Oleaginous *Rhodococcus* and *Streptomyces* Strains Isolated from Desert Soil. *J. Biotechnol.* 2016, 225. [CrossRef]
- 10. Zhang, Q.; Li, Y.; Xia, L. An Oleaginous Endophyte *Bacillus subtilis HB1310* Isolated from Thin-Shelled Walnut and Its Utilization of Cotton Stalk Hydrolysate for Lipid Production. *Biotechnol. Biofuels* **2014**, 7. [CrossRef]
- 11. Santala, S.; Efimova, E.; Kivinen, V.; Larjo, A.; Aho, T.; Karp, M.; Santala, V. Improved Triacylglycerol Production in *Acinetobacter baylyi ADP1* by Metabolic Engineering. *Microb. Cell Factories* **2011**, *10*. [CrossRef]
- 12. Kumar, M.; Rathour, R.; Gupta, J.; Pandey, A.; Gnansounou, E.; Thakur, I.S. Bacterial production of fatty acid and biodiesel: Opportunity and challenges. In *Refining Biomass Residues for Sustainable Energy and Bioproducts: Technology, Advances, Life Cycle Assessment, and Economics*; Academic Press: Cambridge, MA, USA, 2020; pp. 21–49. [CrossRef]
- 13. Ai, M.; Zhu, Y.; Jia, X. Recent Advances in Constructing Artificial Microbial Consortia for the Production of Medium-Chain-Length Polyhydroxyalkanoates. *World J. Microbiol. Biotechnol.* **2021**, *37*, 1–14.
- 14. Ferreira, J.A.; Lennartsson, P.R.; Edebo, L.; Taherzadeh, M.J. Zygomycetes-Based Biorefinery: Present Status and Future Prospects. *Bioresour. Technol.* **2013**, 135. [CrossRef]
- 15. Hui, L.; Wan, C.; Hai-Tao, D.; Xue-Jiao, C.; Qi-Fa, Z.; Yu-Hua, Z. Direct Microbial Conversion of Wheat Straw into Lipid by a Cellulolytic Fungus of *Aspergillus oryzae A-4* in Solid-State Fermentation. *Bioresour. Technol.* **2010**, *101*. [CrossRef]
- Papanikolaou, S.; Aggelis, G. Sources of Microbial Oils with Emphasis to Mortierella (Umbelopsis) isabellina Fungus. World J. Microbiol. Biotechnol. 2019, 35, 63.
- 17. Ratledge, C.; Wynn, J.P. The biochemistry and molecular biology of lipid accumulation in oleaginous microorganisms. *Adv. Appl. Microbiol.* **2002**, *51*, 1–52.
- Troiano, D.; Orsat, V.; Dumont, M.J. Status of Filamentous Fungi in Integrated Biorefineries. *Renew. Sustain. Energy Rev.* 2020, 117, 109472.
- Carota, E.; Crognale, S.; D'Annibale, A.; Petruccioli, M. Bioconversion of Agro-Industrial Waste into Microbial Oils by Filamentous Fungi. Process Saf. Environ. Prot. 2018, 117. [CrossRef]
- 20. Ji, X.J.; Huang, H. Engineering Microbes to Produce Polyunsaturated Fatty Acids. Trends Biotechnol. 2019, 37, 344–346.
- 21. Liu, Z.; Feist, A.M.; Dragone, G.; Mussatto, S.I. Lipid and Carotenoid Production from Wheat Straw Hydrolysates by Different Oleaginous Yeasts. J. Clean. Prod. 2020, 249. [CrossRef]
- 22. Daskalaki, A.; Perdikouli, N.; Aggeli, D.; Aggelis, G. Laboratory Evolution Strategies for Improving Lipid Accumulation in *Yarrowia lipolytica*. *Appl. Microbiol. Biotechnol.* **2019**, 103. [CrossRef]
- Caporusso, A.; de Bari, I.; Valerio, V.; Albergo, R.; Liuzzi, F. Conversion of Cardoon Crop Residues into Single Cell Oils by *Lipomyces tetrasporus* and *Cutaneotrichosporon curvatus*: Process Optimizations to Overcome the Microbial Inhibition of Lignocellulosic Hydrolysates. *Ind. Crop. Prod.* 2021, 159. [CrossRef]
- 24. Feng, P.; Xu, Z.; Qin, L.; Asraful Alam, M.; Wang, Z.; Zhu, S. Effects of Different Nitrogen Sources and Light Paths of Flat Plate Photobioreactors on the Growth and Lipid Accumulation of *Chlorella Sp. GN1* Outdoors. *Bioresour. Technol.* 2020, 301. [CrossRef]
- 25. Nascimento, I.A.; Cabanelas, I.T.D.; dos Santos, J.N.; Nascimento, M.A.; Sousa, L.; Sansone, G. Biodiesel Yields and Fuel Quality as Criteria for Algal-Feedstock Selection: Effects of CO2-Supplementation and Nutrient Levels in Cultures. *Algal Res.* 2015, *8*. [CrossRef]
- Li, D.; Zhao, Y.; Ding, W.; Zhao, P.; Xu, J.W.; Li, T.; Ma, H.; Yu, X. A Strategy for Promoting Lipid Production in Green Microalgae Monoraphidium Sp. QLY-1 by Combined Melatonin and Photoinduction. Bioresour. Technol. 2017, 235. [CrossRef]
- Arbib, Z.; Ruiz, J.; Álvarez-Díaz, P.; Garrido-Pérez, C.; Perales, J.A. Capability of Different Microalgae Species for Phytoremediation Processes: Wastewater Tertiary Treatment, CO2 Bio-Fixation and Low Cost Biofuels Production. *Water Res.* 2014, 49. [CrossRef]
- 28. Saisriyoot, M.; Thanapimmetha, A.; Suwaleerat, T.; Chisti, Y.; Srinophakun, P. Biomass and Lipid Production by *Rhodococcus* opacus PD630 in Molasses-Based Media with and without Osmotic-Stress. J. Biotechnol. **2019**, 297. [CrossRef]
- 29. Salcedo-Vite, K.; Sigala, J.C.; Segura, D.; Gosset, G.; Martinez, A. *Acinetobacter baylyi ADP1* Growth Performance and Lipid Accumulation on Different Carbon Sources. *Appl. Microbiol. Biotechnol.* **2019**, 103. [CrossRef]
- 30. Gardeli, C.; Athenaki, M.; Xenopoulos, E.; Mallouchos, A.; Koutinas, A.A.; Aggelis, G.; Papanikolaou, S. Lipid Production and Characterization by *Mortierella (Umbelopsis) isabellina* Cultivated on Lignocellulosic Sugars. J. Appl. Microbiol. 2017, 123. [CrossRef]

- 31. Li, S.; Yu, H.; Liu, Y.; Zhang, X.; Ma, F. The Lipid Strategies in *Cunninghamella echinulata* for an Allostatic Response to Temperature Changes. *Process Biochem.* **2019**, *76*. [CrossRef]
- 32. Carsanba, E.; Papanikolaou, S.; Fickers, P.; Erten, H. Lipids by *Yarrowia lipolytica* Strains Cultivated on Glucose in Batch Cultures. *Microorganisms* **2020**, *8*, 1054. [CrossRef]
- Boviatsi, E.; Papadaki, A.; Efthymiou, M.N.; Nychas, G.J.E.; Papanikolaou, S.; da Silva, J.A.C.; Freire, D.M.G.; Koutinas, A. Valorisation of Sugarcane Molasses for the Production of Microbial Lipids via Fermentation of Two *Rhodosporidium* Strains for Enzymatic Synthesis of Polyol Esters. *J. Chem. Technol. Biotechnol.* 2020, 95. [CrossRef]
- 34. Di Fidio, N.; Ragaglini, G.; Dragoni, F.; Antonetti, C.; Raspolli Galletti, A.M. Integrated Cascade Biorefinery Processes for the Production of Single Cell Oil by *Lipomyces starkeyi* from *Arundo Donax L*. Hydrolysates. *Bioresour. Technol.* **2021**, 325. [CrossRef]
- 35. Capusoni, C.; Rodighiero, V.; Cucchetti, D.; Galafassi, S.; Bianchi, D.; Franzosi, G.; Compagno, C. Characterization of Lipid Accumulation and Lipidome Analysis in the Oleaginous Yeasts *Rhodosporidium azoricum* and *Trichosporon oleaginosus*. *Bioresour*. *Technol.* **2017**, 238. [CrossRef]
- 36. Papanikolaou, S.; Aggelis, G. Lipids of Oleaginous Yeasts. Part I: Biochemistry of Single Cell Oil Production. *Eur. J. Lipid Sci. Technol.* **2011**, *113*, 1031–1051.
- Beopoulos, A.; Cescut, J.; Haddouche, R.; Uribelarrea, J.L.; Molina-Jouve, C.; Nicaud, J.M. Yarrowia lipolytica as a Model for Bio-Oil Production. Prog. Lipid Res. 2009, 48, 375–387.
- Wu, S.; Hu, C.; Jin, G.; Zhao, X.; Zhao, Z.K. Phosphate-Limitation Mediated Lipid Production by *Rhodosporidium toruloides*. *Bioresour. Technol.* 2010, 101. [CrossRef]
- 39. Wynn, J.P.; Ratledge, C. Oils from Microorganisms. In *Bailey's Industrial Oil and Fat Products*; Shahidi, F., Ed.; John Wiley & Sons: Hoboken, NJ, USA, 2005.
- 40. Wasylenko, T.M.; Ahn, W.S.; Stephanopoulos, G. The Oxidative Pentose Phosphate Pathway Is the Primary Source of NADPH for Lipid Overproduction from Glucose in *Yarrowia lipolytica*. *Metab. Eng.* **2015**, *30*. [CrossRef]
- 41. Zhang, S.; Skerker, J.M.; Rutter, C.D.; Maurer, M.J.; Arkin, A.P.; Rao, C.V. Engineering *Rhodosporidium toruloides* for Increased Lipid Production. *Biotechnol. Bioeng.* **2016**, *113*. [CrossRef]
- 42. Arous, F.; Azabou, S.; Triantaphyllidou, I.E.; Aggelis, G.; Jaouani, A.; Nasri, M.; Mechichi, T. Newly Isolated Yeasts from Tunisian Microhabitats: Lipid Accumulation and Fatty Acid Composition. *Eng. Life Sci.* **2017**, *17*. [CrossRef]
- 43. Qin, L.; Liu, L.; Zeng, A.P.; Wei, D. From Low-Cost Substrates to Single Cell Oils Synthesized by Oleaginous Yeasts. *Bioresour. Technol.* 2017, 245, 1507–1519.
- 44. Jin, M.; Slininger, P.J.; Dien, B.S.; Waghmode, S.; Moser, B.R.; Orjuela, A.; Sousa, L.d.C.; Balan, V. Microbial Lipid-Based Lignocellulosic Biorefinery: Feasibility and Challenges. *Trends Biotechnol.* **2015**, *33*, 43–54.
- 45. Satyanarayana, T.; Gotthard, K. Yeast Biotechnology: Diversity and Applications, 1st ed.; Springer: New York, NY, USA, 2009.
- 46. Thevenieau, F.; Nicaud, J.M. Microorganisms as Sources of Oils. OCL Oilseeds Fats Crops Lipids 2013, 20, D603.
- 47. Madzak, C. Yarrowia lipolytica: Recent Achievements in Heterologous Protein Expression and Pathway Engineering. *Appl. Microbiol. Biotechnol.* **2015**, *99*, 4559–4577.
- Liu, N.; Qiao, K.; Stephanopoulos, G. 13C Metabolic Flux Analysis of Acetate Conversion to Lipids by *Yarrowia lipolytica*. *Metab.* Eng. 2016, 38. [CrossRef]
- 49. Gao, R.; Li, Z.; Zhou, X.; Cheng, S.; Zheng, L. Oleaginous Yeast *Yarrowia lipolytica* Culture with Synthetic and Food Waste-Derived Volatile Fatty Acids for Lipid Production. *Biotechnol. Biofuels* **2017**, *10*. [CrossRef]
- 50. Fontanille, P.; Kumar, V.; Christophe, G.; Nouaille, R.; Larroche, C. Bioconversion of Volatile Fatty Acids into Lipids by the Oleaginous Yeast *Yarrowia lipolytica*. *Bioresour. Technol.* **2012**, 114. [CrossRef]
- 51. Silverman, A.M.; Qiao, K.; Xu, P.; Stephanopoulos, G. Functional Overexpression and Characterization of Lipogenesis-Related Genes in the Oleaginous Yeast *Yarrowia lipolytica*. *Appl. Microbiol. Biotechnol.* **2016**, 100. [CrossRef]
- 52. Da Silva, L.V.; Coelho, M.A.Z.; Amaral, P.F.F.; Fickers, P. A Novel Osmotic Pressure Strategy to Improve Erythritol Production by *Yarrowia lipolytica* from Glycerol. *Bioprocess Biosyst. Eng.* **2018**, *41*. [CrossRef]
- Epova, E.; Guseva, M.; Kovalyov, L.; Isakova, E.; Deryabina, Y.; Belyakova, A.; Zylkova, M.; Shevelev, A. Identification of Proteins Involved in pH Adaptation in Extremophile Yeast *Yarrowia lipolytica*. In *Proteomic applications in biology*; Heazlewood, J.L., Petzold, C.J., Eds.; InTech: Rijeka, Croatia, 2012; pp. 209–224.
- 54. Walker, C.; Ryu, S.; Trinh, C.T. Exceptional Solvent Tolerance in *Yarrowia lipolytica* Is Enhanced by Sterols. *Metab. Eng.* **2019**, *54*. [CrossRef]
- 55. Dujon, B.; Sherman, D.; Fischer, G.; Durrens, P.; Casaregela, S.; Lafentaine, I.; de Montigny, J.; Marck, C.; Neuvéglise, C.; Talla, E.; et al. Genome Evolution in Yeasts. *Nature* **2004**, *430*. [CrossRef]
- 56. Markham, K.A.; Alper, H.S. Synthetic Biology Expands the Industrial Potential of *Yarrowia lipolytica*. *Trends Biotechnol.* **2018**, *36*, 1085–1095.
- 57. Blazeck, J.; Hill, A.; Liu, L.; Knight, R.; Miller, J.; Pan, A.; Otoupal, P.; Alper, H.S. Harnessing *Yarrowia lipolytica* Lipogenesis to Create a Platform for Lipid and Biofuel Production. *Nat. Commun.* **2014**, *5*. [CrossRef]
- Xie, D.; Jackson, E.N.; Zhu, Q. Sustainable Source of Omega-3 Eicosapentaenoic Acid from Metabolically Engineered Yarrowia lipolytica: From Fundamental Research to Commercial Production. Appl. Microbiol. Biotechnol. 2015, 99, 1599–1610.
- 59. Papanikolaou, S.; Aggelis, G. Lipid Production by *Yarrowia lipolytica* Growing on Industrial Glycerol in a Single-Stage Continuous Culture. *Bioresour. Technol.* **2002**, *8*2. [CrossRef]

- 60. Groenewald, M.; Boekhout, T.; Neuvéglise, C.; Gaillardin, C.; van Dijck, P.W.M.; Wyss, M. Yarrowia lipolytica: Safety Assessment of an Oleaginous Yeast with a Great Industrial Potential. *Crit. Rev. Microbiol.* **2014**, *40*, 187–206.
- 61. Ferreira, P.; Lopes, M.; Mota, M.; Belo, I. Oxygen Mass Transfer Impact on Citric Acid Production by *Yarrowia lipolytica* from Crude Glycerol. *Biochem. Eng. J.* **2016**, *110*. [CrossRef]
- 62. Rywińska, A.; Musiał, I.; Rymowicz, W.; Arowska, B.; Boruczkowski, T. Effect of Agitation and Aeration on the Citric Acid Production by *Yarrowia lipolytica* Grown on Glycerol. *Prep. Biochem. Biotechnol.* **2012**, *42*. [CrossRef]
- 63. Rzechonek, D.A.; Dobrowolski, A.; Rymowicz, W.; Mirończuk, A.M. Aseptic Production of Citric and Isocitric Acid from Crude Glycerol by Genetically Modified *Yarrowia lipolytica*. *Bioresour. Technol.* **2019**, 271. [CrossRef]
- 64. Rakicka, M.; Rywińska, A.; Cybulski, K.; Rymowicz, W. Enhanced Production of Erythritol and Mannitol by *Yarrowia lipolytica* in Media Containing Surfactants. *Braz. J. Microbiol.* **2016**, 47. [CrossRef]
- 65. Dulermo, T.; Lazar, Z.; Dulermo, R.; Rakicka, M.; Haddouche, R.; Nicaud, J.M. Analysis of ATP-Citrate Lyase and Malic Enzyme Mutants of *Yarrowia lipolytica* Points out the Importance of Mannitol Metabolism in Fatty Acid Synthesis. *Biochim. Et Biophys. Acta* -*Mol. Cell Biol. Lipids* **2015**, *1851*. [CrossRef]
- Carsanba, E.; Papanikolaou, S.; Fickers, P.; Erten, H. Screening Various Yarrowia lipolytica Strains for Citric Acid Production. Yeast 2019, 36. [CrossRef]
- 67. LI, Y.H.; LIU, B.; ZHAO, Z.B.; BAI, F.W. Optimization of Culture Conditions for Lipid Production by *Rhodosporidium toruloides*. *Chin. J. Biotechnol.* **2006**, 22. [CrossRef]
- Yaegashi, J.; Kirby, J.; Ito, M.; Sun, J.; Dutta, T.; Mirsiaghi, M.; Sundstrom, E.R.; Rodriguez, A.; Baidoo, E.; Tanjore, D.; et al. *Rhodosporidium toruloides*: A New Platform Organism for Conversion of Lignocellulose into Terpene Biofuels and Bioproducts. *Biotechnol. Biofuels* 2017, 10. [CrossRef]
- 69. Tsakona, S.; Papadaki, A.; Kopsahelis, N.; Kachrimanidou, V.; Papanikolaou, S.; Koutinas, A. Development of a Circular Oriented Bioprocess for Microbial Oil Production Using Diversified Mixed Confectionery Side-Streams. *Foods* **2019**, *8*, 300. [CrossRef]
- Tchakouteu, S.S.; Kalantzi, O.; Gardeli, C.; Koutinas, A.A.; Aggelis, G.; Papanikolaou, S. Lipid Production by Yeasts Growing on Biodiesel-Derived Crude Glycerol: Strain Selection and Impact of Substrate Concentration on the Fermentation Efficiency. J. Appl. Microbiol. 2015, 118. [CrossRef]
- Huang, X.F.; Liu, J.N.; Lu, L.J.; Peng, K.M.; Yang, G.X.; Liu, J. Culture Strategies for Lipid Production Using Acetic Acid as Sole Carbon Source by *Rhodosporidium toruloides*. *Bioresour. Technol.* 2016, 206. [CrossRef]
- 72. Sundstrom, E.; Yaegashi, J.; Yan, J.; Masson, F.; Papa, G.; Rodriguez, A.; Mirsiaghi, M.; Liang, L.; He, Q.; Tanjore, D.; et al. Demonstrating a Separation-Free Process Coupling Ionic Liquid Pretreatment, Saccharification, and Fermentation with: *Rhodosporidium toruloides* to Produce Advanced Biofuels. *Green Chem.* **2018**, 20. [CrossRef]
- 73. Xu, J.; Liu, D. Exploitation of Genus Rhodosporidium for Microbial Lipid Production. World J. Microbiol. Biotechnol. 2017, 33, 54.
- 74. SànchezNogué, V.; Black, B.A.; Kruger, J.S.; Singer, C.A.; Ramirez, K.J.; Reed, M.L.; Cleveland, N.S.; Singer, E.R.; Yi, X.; Yeap, R.Y.; et al. Integrated Diesel Production from Lignocellulosic Sugars: Via Oleaginous Yeast. *Green Chem.* 2018, 20, 4349–4365. [CrossRef]
- 75. Singh, G.; Sinha, S.; Bandyopadhyay, K.K.; Lawrence, M.; Paul, D. Triauxic Growth of an Oleaginous Red Yeast *Rhodosporidium toruloides* on Waste "extract" for Enhanced and Concomitant Lipid and β-Carotene Production. *Microb. Cell Factories* 2018, 17. [CrossRef]
- Lopes, H.J.S.; Bonturi, N.; Miranda, E.A. *Rhodotorula toruloides* Single Cell Oil Production Using Eucalyptus Urograndis Hemicellulose Hydrolysate as a Carbon Source. *Energies* 2020, 13, 795. [CrossRef]
- 77. Wen, Z.; Zhang, S.; Odoh, C.K.; Jin, M.; Zhao, Z.K. *Rhodosporidium toruloides*—A Potential Red Yeast Chassis for Lipids and Beyond. *FEMS Yeast Res.* 2020, 20, foaa038.
- 78. Zhu, Z.; Zhang, S.; Liu, H.; Shen, H.; Lin, X.; Yang, F.; Zhou, Y.J.; Jin, G.; Ye, M.; Zou, H.; et al. A Multi-Omic Map of the Lipid-Producing Yeast *Rhodosporidium toruloides*. *Nat. Commun.* **2012**, *3*. [CrossRef]
- 79. Sutanto, S.; Zullaikah, S.; Tran-Nguyen, P.L.; Ismadji, S.; Ju, Y.H. *Lipomyces starkeyi*: Its Current Status as a Potential Oil Producer. *Fuel Process. Technol.* **2018**, 177, 39–55.
- 80. Angerbauer, C.; Siebenhofer, M.; Mittelbach, M.; Guebitz, G.M. Conversion of Sewage Sludge into Lipids by *Lipomyces starkeyi* for Biodiesel Production. *Bioresour. Technol.* 2008, 99. [CrossRef]
- Juanssilfero, A.B.; Kahar, P.; Amza, R.L.; Miyamoto, N.; Otsuka, H.; Matsumoto, H.; Kihira, C.; Thontowi, A.; Ogino, C.; Prasetya, B.; et al. Effect of Inoculum Size on Single-Cell Oil Production from Glucose and Xylose Using Oleaginous Yeast *Lipomyces starkeyi*. J. Biosci. Bioeng. 2018, 125, 695–702. [CrossRef]
- Di Fidio, N.; Dragoni, F.; Antonetti, C.; de Bari, I.; Raspolli Galletti, A.M.; Ragaglini, G. From Paper Mill Waste to Single Cell Oil: Enzymatic Hydrolysis to Sugars and Their Fermentation into Microbial Oil by the Yeast *Lipomyces starkeyi*. *Bioresour. Technol.* 2020, 315. [CrossRef]
- Liu, L.p.; Zong, M.h.; Hu, Y.; Li, N.; Lou, W.y.; Wu, H. Efficient Microbial Oil Production on Crude Glycerol by *Lipomyces starkeyi* AS 2.1560 and Its Kinetics. Process Biochem. 2017, 58. [CrossRef]
- Gou, Q.; Tang, M.; Wang, Y.; Zhou, W.; Liu, Y.; Gong, Z. Deficiency of β-Glucosidase Beneficial for the Simultaneous Saccharification and Lipid Production by the Oleaginous Yeast *Lipomyces starkeyi*. *Appl. Biochem. Biotechnol.* 2020, 190. [CrossRef]
- 85. Xavier, M.C.A.; Coradini, A.L.V.; Deckmann, A.C.; Franco, T.T. Lipid Production from Hemicellulose Hydrolysate and Acetic Acid by *Lipomyces starkeyi* and the Ability of Yeast to Metabolize Inhibitors. *Biochem. Eng. J.* 2017, *118*. [CrossRef]

- 86. Riley, R.; Haridas, S.; Wolfe, K.H.; Lopes, M.R.; Hittinger, C.T.; Göker, M.; Salamov, A.A.; Wisecaver, J.H.; Long, T.M.; Calvey, C.H.; et al. Comparative Genomics of Biotechnologically Important Yeasts. *Proc. Natl. Acad. Sci. USA* **2016**, *113*. [CrossRef]
- Takaku, H.; Ebina, S.; Kasuga, K.; Sato, R.; Ara, S.; Kazama, H.; Matsuzawa, T.; Yaoi, K.; Araki, H.; Shida, Y.; et al. Isolation and Characterization of *Lipomyces starkeyi* Mutants with Greatly Increased Lipid Productivity Following UV Irradiation. *J. Biosci. Bioeng.* 2021. [CrossRef]
- Matsuzawa, T.; Maehara, T.; Kamisaka, Y.; Ara, S.; Takaku, H.; Yaoi, K. Identification and Characterization of Δ12 and Δ12/Δ15 Bifunctional Fatty Acid Desaturases in the Oleaginous Yeast *Lipomyces starkeyi*. Appl. Microbiol. Biotechnol. 2018, 102. [CrossRef]
- 89. Zhang, J.; Fang, X.; Zhu, X.L.; Li, Y.; Xu, H.P.; Zhao, B.F.; Chen, L.; Zhang, X.D. Microbial Lipid Production by the Oleaginous Yeast *Cryptococcus curvatus O3* Grown in Fed-Batch Culture. *Biomass Bioenergy* **2011**, *35*. [CrossRef]
- 90. Di Fidio, N.; Liuzzi, F.; Mastrolitti, S.; Albergo, R.; de Bari, I. Single Cell Oil Production from Undetoxified *Arundo Donax L. Hydrolysate by Cutaneotrichosporon curvatus. J. Microbiol. Biotechnol.* **2019**, 29. [CrossRef]
- 91. Liu, J.; Yuan, M.; Liu, J.N.; Huang, X.F. Bioconversion of Mixed Volatile Fatty Acids into Microbial Lipids by *Cryptococcus curvatus* ATCC 20509. Bioresour. Technol. 2017, 241. [CrossRef]
- Liu, J.; Mu, T.; He, W.; He, T.; Lu, L.; Peng, K.; Huang, X. Integration of Coagulation, Acid Separation and Struvite Precipitation as Fermentation Medium Conditioning Methods to Enhance Microbial Lipid Production from Dewatered Sludge. *Bioresour. Technol. Rep.* 2019, 7. [CrossRef]
- Meng, X.; Yang, J.; Xu, X.; Zhang, L.; Nie, Q.; Xian, M. Biodiesel Production from Oleaginous Microorganisms. *Renew. Energy* 2009, 34, 1–5.
- 94. Hofmeyer, T.; Hackenschmidt, S.; Nadler, F.; Thürmer, A.; Daniel, R.; Kabisch, J. Draft Genome Sequence of *Cutaneotrichosporon curvatus DSM 101032* (Formerly *Cryptococcus curvatus*), an Oleaginous Yeast Producing Polyunsaturated Fatty Acids. *Genome Announc.* **2016**, *4*. [CrossRef]
- 95. Wagner, J.M.; Alper, H.S. Synthetic Biology and Molecular Genetics in Non-Conventional Yeasts: Current Tools and Future Advances. *Fungal Genet. Biol.* 2016, 89. [CrossRef]
- 96. Gujjari, P.; Suh, S.O.; Coumes, K.; Zhou, J.J. Characterization of Oleaginous Yeasts Revealed Two Novel Species: *Trichosporon cacaoliposimilis Sp. Nov.* and *Trichosporon oleaginosus Sp. Nov. Mycologia* **2011**, 103. [CrossRef]
- 97. Zhang, X.; Chen, J.; Idossou, V.; Tyagi, R.D.; Li, J.; Wang, H. Lipid Accumulation from *Trichosporon oleaginosus* with Co-Fermentation of Washed Wastewater Sludge and Crude Glycerol. *Fuel* **2018**, 226. [CrossRef]
- Šantek, M.I.; Lisičar, J.; Mušak, L.; Špoljarić, I.V.; Beluhan, S.; Šantek, B. Lipid Production by Yeast *Trichosporon oleaginosus* on the Enzymatic Hydrolysate of Alkaline Pretreated Corn Cobs for Biodiesel Production. *Energy Fuels* 2018, 32. [CrossRef]
- 99. Yu, X.; Zheng, Y.; Dorgan, K.M.; Chen, S. Oil Production by Oleaginous Yeasts Using the Hydrolysate from Pretreatment of Wheat Straw with Dilute Sulfuric Acid. *Bioresour. Technol.* **2011**, *102.* [CrossRef]
- 100. Kourist, R.; Bracharz, F.; Lorenzen, J.; Kracht, O.N.; Chovatia, M.; Daum, C.; Deshpande, S.; Lipzen, A.; Nolan, M.; Ohm, R.A.; et al. Genomics and Transcriptomics Analyses of the Oil-Accumulating *Basidiomycete* Yeast *Trichosporon oleaginosus*: Insights into Substrate Utilization and Alternative Evolutionary Trajectories of Fungal Mating Systems. *mBio* 2015, 6. [CrossRef]
- 101. Ageitos, J.M.; Vallejo, J.A.; Veiga-Crespo, P.; Villa, T.G. Oily Yeasts as Oleaginous Cell Factories. *Appl. Microbiol. Biotechnol.* **2011**, 90, 1219–1227.
- 102. Chen, H.Z.; Liu, Z.H. Enzymatic Hydrolysis of Lignocellulosic Biomass from Low to High Solids Loading. *Eng. Life Sci.* 2017, 17, 489–499.
- 103. Kumar, A.K.; Sharma, S. Recent Updates on Different Methods of Pretreatment of Lignocellulosic Feedstocks: A Review. *Bioresour. Bioprocess.* 2017, *4*, 1–19.
- Capolupo, L.; Faraco, V. Green Methods of Lignocellulose Pretreatment for Biorefinery Development. *Appl. Microbiol. Biotechnol.* 2016, 100, 9451–9467.
- 105. Singh, R.; Krishna, B.B.; Kumar, J.; Bhaskar, T. Opportunities for Utilization of Non-Conventional Energy Sources for Biomass Pretreatment. *Bioresour. Technol.* **2016**, *199*, 398–407.
- 106. De Bari, I.; Liuzzi, F.; Villone, A.; Braccio, G. Hydrolysis of Concentrated Suspensions of Steam Pretreated *Arundo Donax*. *Appl. Energy* **2013**, *102*. [CrossRef]
- Ravindran, R.; Hassan, S.S.; Williams, G.A.; Jaiswal, A.K. A Review on Bioconversion of Agro-Industrial Wastes to Industrially Important Enzymes. *Bioengineering* 2018, 5, 93.
- Kim, D. Physico-Chemical Conversion of Lignocellulose: Inhibitor Effects and Detoxification Strategies: A Mini Review. *Molecules* 2018, 23, 309.
- 109. Nichols, N.N.; Sharma, L.N.; Mowery, R.A.; Chambliss, C.K.; van Walsum, G.P.; Dien, B.S.; Iten, L.B. Fungal Metabolism of Fermentation Inhibitors Present in Corn Stover Dilute Acid Hydrolysate. *Enzym. Microb. Technol.* **2008**, 42. [CrossRef]
- 110. Cao, G.; Ximenes, E.; Nichols, N.N.; Frazer, S.E.; Kim, D.; Cotta, M.A.; Ladisch, M. Bioabatement with Hemicellulase Supplementation to Reduce Enzymatic Hydrolysis Inhibitors. *Bioresour. Technol.* **2015**, *190*. [CrossRef]
- 111. Tsigie, Y.A.; Wang, C.Y.; Truong, C.T.; Ju, Y.H. Lipid Production from *Yarrowia lipolytica Po1g* Grown in Sugarcane Bagasse Hydrolysate. *Bioresour. Technol.* **2011**, *102*. [CrossRef]
- 112. Kim, Y.; Ximenes, E.; Mosier, N.S.; Ladisch, M.R. Soluble Inhibitors/Deactivators of Cellulase Enzymes from Lignocellulosic Biomass. *Enzym. Microb. Technol.* **2011**, *48*. [CrossRef]

- 113. Aghazadeh, M.; Ladisch, M.R.; Engelberth, A.S. Acetic Acid Removal from Corn Stover Hydrolysate Using Ethyl Acetate and the Impact on *Saccharomyces cerevisiae* Bioethanol Fermentation. *Biotechnol. Prog.* **2016**, *32*. [CrossRef]
- 114. Jönsson, L.J.; Alriksson, B.; Nilvebrant, N.O. Bioconversion of Lignocellulose: Inhibitors and Detoxification. *Biotechnol. Biofuels* **2013**, *6*, 16.
- 115. Hicks, R.H.; Sze, Y.; Chuck, C.J.; Henk, D.A. Enhanced Inhibitor Tolerance and Increased Lipid Productivity through Adaptive Laboratory Evolution in the Oleaginous Yeast *Metshnikowia pulcherrima. bioRxiv* 2020. [CrossRef]
- Sitepu, I.; Selby, T.; Lin, T.; Zhu, S.; Boundy-Mills, K. Carbon Source Utilization and Inhibitor Tolerance of 45 Oleaginous Yeast Species. J. Ind. Microbiol. Biotechnol. 2014, 41. [CrossRef]
- 117. Yu, X.; Zeng, J.; Zheng, Y.; Chen, S. Effect of Lignocellulose Degradation Products on Microbial Biomass and Lipid Production by the Oleaginous Yeast *Cryptococcus curvatus*. *Process Biochem*. **2014**, *49*. [CrossRef]
- 118. Hu, C.; Zhao, X.; Zhao, J.; Wu, S.; Zhao, Z.K. Effects of Biomass Hydrolysis By-Products on Oleaginous Yeast *Rhodosporidium* toruloides. Bioresour. Technol. 2009, 100. [CrossRef]
- Poontawee, R.; Limtong, S. Feeding Strategies of Two-Stage Fed-Batch Cultivation Processes for Microbial Lipid Production from Sugarcane Top Hydrolysate and Crude Glycerol by the Oleaginous Red Yeast *Rhodosporidiobolus fluvialis*. *Microorganisms* 2020, *8*, 151. [CrossRef]
- 120. Favaro, L.; Corte, L.; Roscini, L.; Cagnin, L.; Tiecco, M.; Colabella, C.; Berti, A.; Basaglia, M.; Cardinali, G.; Casella, S. A Novel FTIR-Based Approach to Evaluate the Interactions between Lignocellulosic Inhibitory Compounds and Their Effect on Yeast Metabolism. *Rsc Adv.* 2016, 6. [CrossRef]
- 121. Huang, X.f.; Shen, Y.; Luo, H.j.; Liu, J.n.; Liu, J. Enhancement of Extracellular Lipid Production by Oleaginous Yeast through Preculture and Sequencing Batch Culture Strategy with Acetic Acid. *Bioresour. Technol.* **2018**, 247. [CrossRef]
- Miranda, C.; Bettencourt, S.; Pozdniakova, T.; Pereira, J.; Sampaio, P.; Franco-Duarte, R.; Pais, C. Modified High-Throughput Nile Red Fluorescence Assay for the Rapid Screening of Oleaginous Yeasts Using Acetic Acid as Carbon Source. *Bmc Microbiol.* 2020, 20. [CrossRef]
- 123. Wang, J.; Gao, Q.; Zhang, H.; Bao, J. Inhibitor Degradation and Lipid Accumulation Potentials of Oleaginous Yeast *Trichosporon cutaneum* Using Lignocellulose Feedstock. *Bioresour. Technol.* **2016**, *218*. [CrossRef]
- Díaz, T.; Fillet, S.; Campoy, S.; Vázquez, R.; Viña, J.; Murillo, J.; Adrio, J.L. Combining Evolutionary and Metabolic Engineering in *Rhodosporidium toruloides* for Lipid Production with Non-Detoxified Wheat Straw Hydrolysates. *Appl. Microbiol. Biotechnol.* 2018, 102. [CrossRef]
- 125. Ananthi, V.; Siva Prakash, G.; Chang, S.W.; Ravindran, B.; Nguyen, D.D.; Vo, D.V.N.; La, D.D.; Bach, Q.V.; Wong, J.W.C.; Kumar Gupta, S.; et al. Enhanced Microbial Biodiesel Production from Lignocellulosic Hydrolysates Using Yeast Isolates. *Fuel* 2019, 256. [CrossRef]
- Lee, J.-E.; Vadlani, P.v.; Min, D. Sustainable Production of Microbial Lipids from Lignocellulosic Biomass Using Oleaginous Yeast Cultures. J. Sustain. Bioenergy Syst. 2017, 7. [CrossRef]
- Diwan, B.; Parkhey, P.; Gupta, P. From Agro-Industrial Wastes to Single Cell Oils: A Step towards Prospective Biorefinery. *Folia Microbiol.* 2018, 63, 547–568.
- 128. Dien, B.S.; Zhu, J.Y.; Slininger, P.J.; Kurtzman, C.P.; Moser, B.R.; O'Bryan, P.J.; Gleisner, R.; Cotta, M.A. Conversion of SPORL Pretreated Douglas Fir Forest Residues into Microbial Lipids with Oleaginous Yeasts. *RSC Adv.* **2016**, *6*, 20695–20705. [CrossRef]
- Miao, Z.; Tian, X.; Liang, W.; He, Y.; Wang, G. Bioconversion of Corncob Hydrolysate into Microbial Lipid by an Oleaginous Yeast Rhodotorula taiwanensis AM2352 for Biodiesel Production. Renew. Energy 2020, 161, 91–97. [CrossRef]
- Fei, Q.; O'Brien, M.; Nelson, R.; Chen, X.; Lowell, A.; Dowe, N. Enhanced Lipid Production by *Rhodosporidium toruloides* Using Different Fed-Batch Feeding Strategies with Lignocellulosic Hydrolysate as the Sole Carbon Source. *Biotechnol. Biofuels* 2016, 9. [CrossRef]
- 131. Yu, Y.; Xu, Z.; Chen, S.; Jin, M. Microbial Lipid Production from Dilute Acid and Dilute Alkali Pretreated Corn Stover via *Trichosporon dermatis. Bioresour. Technol.* **2020**, 295. [CrossRef]
- 132. Antonopoulou, I.; Spanopoulos, A.; Matsakas, L. Single Cell Oil and Ethanol Production by the Oleaginous Yeast *Trichosporon fermentans* Utilizing Dried Sweet Sorghum Stalks. *Renew. Energy* **2020**, *146*, 1609–1617. [CrossRef]
- 133. Dermeche, S.; Nadour, M.; Larroche, C.; Moulti-Mati, F.; Michaud, P. Olive Mill Wastes: Biochemical Characterizations and Valorization Strategies. *Process Biochem.* **2013**, *48*, 1532–1552.
- 134. Lee, Z.S.; Chin, S.Y.; Lim, J.W.; Witoon, T.; Cheng, C.K. Treatment Technologies of Palm Oil Mill Effluent (POME) and Olive Mill Wastewater (OMW): A Brief Review. *Environ. Technol. Innov.* **2019**, *15*, 100377.
- 135. Batuecas, E.; Tommasi, T.; Battista, F.; Negro, V.; Sonetti, G.; Viotti, P.; Fino, D.; Mancini, G. Life Cycle Assessment of Waste Disposal from Olive Oil Production: Anaerobic Digestion and Conventional Disposal on Soil. *J. Environ. Manag.* 2019, 237. [CrossRef]
- 136. Magdich, S.; Abid, W.; Boukhris, M.; ben Rouina, B.; Ammar, E. Effects of Long-Term Olive Mill Wastewater Spreading on the Physiological and Biochemical Responses of Adult Chemlali Olive Trees (*Olea Europaea* L.). *Ecol. Eng.* **2016**, *97*. [CrossRef]
- 137. Karaouzas, I.; Skoulikidis, N.T.; Giannakou, U.; Albanis, T.A. Spatial and Temporal Effects of Olive Mill Wastewaters to Stream Macroinvertebrates and Aquatic Ecosystems Status. *Water Res.* **2011**, *45*. [CrossRef]
- Ochando-Pulido, J.M.; Pimentel-Moral, S.; Verardo, V.; Martinez-Ferez, A. A Focus on Advanced Physico-Chemical Processes for Olive Mill Wastewater Treatment. Sep. Purif. Technol. 2017, 179, 161–174.

- Orive, M.; Cebrián, M.; Zufía, J. Techno-Economic Anaerobic Co-Digestion Feasibility Study for Two-Phase Olive Oil Mill Pomace and Pig Slurry. *Renew. Energy* 2016, 97. [CrossRef]
- 140. Muktadirul Bari Chowdhury, A.K.M.; Akratos, C.S.; Vayenas, D.v.; Pavlou, S. Olive Mill Waste Composting: A Review. *Int. Biodeterior. Biodegrad.* 2013, *85*, 108–119.
- 141. MacCi, C.; Masciandaro, G.; Ceccanti, B. Vermicomposting of Olive Oil Mill Wastewaters. Waste Manag. Res. 2010, 28. [CrossRef]
- 142. Tortosa, G.; Alburquerque, J.A.; Ait-Baddi, G.; Cegarra, J. The Production of Commercial Organic Amendments and Fertilisers by Composting of Two-Phase Olive Mill Waste ("alperujo"). J. Clean. Prod. 2012, 26. [CrossRef]
- 143. Lopes, M.; Araújo, C.; Aguedo, M.; Gomes, N.; Gonçalves, C.; Teixeira, J.A.; Belo, I. The Use of Olive Mill Wastewater by Wild Type Yarrowia lipolytica Strains: Medium Supplementation and Surfactant Presence Effect. J. Chem. Technol. Biotechnol. 2009, 84. [CrossRef]
- 144. Lanciotti, R.; Gianotti, A.; Baldi, D.; Angrisani, R.; Suzzi, G.; Mastrocola, D.; Guerzoni, M.E. Use of *Yarrowia lipolytica* Strains for the Treatment of Olive Mill Wastewater. *Bioresour. Technol.* **2005**, *96*. [CrossRef]
- 145. Sarris, D.; Stoforos, N.G.; Mallouchos, A.; Kookos, I.K.; Koutinas, A.A.; Aggelis, G.; Papanikolaou, S. Production of Added-Value Metabolites by *Yarrowia lipolytica* Growing in Olive Mill Wastewater-Based Media under Aseptic and Non-Aseptic Conditions. *Eng. Life Sci.* 2017, 17. [CrossRef]
- 146. Sarris, D.; Galiotou-Panayotou, M.; Koutinas, A.A.; Komaitis, M.; Papanikolaou, S. Citric Acid, Biomass and Cellular Lipid Production by *Yarrowia lipolytica* Strains Cultivated on Olive Mill Wastewater-Based Media. *J. Chem. Technol. Biotechnol.* 2011, 86, 1439–1448. [CrossRef]
- 147. Dourou, M.; Kancelista, A.; Juszczyk, P.; Sarris, D.; Bellou, S.; Triantaphyllidou, I.E.; Rywinska, A.; Papanikolaou, S.; Aggelis, G. Bioconversion of Olive Mill Wastewater into High-Added Value Products. *J. Clean. Prod.* **2016**, *139*, 957–969. [CrossRef]
- 148. Dias, B.; Lopes, M.; Ramôa, R.; Pereira, A.S.; Belo, I. *Candida tropicalis* as a Promising Oleaginous Yeast for Olive Mill Wastewater Bioconversion. *Energies* **2021**, *14*, 640. [CrossRef]
- Xenopoulos, E.; Giannikakis, I.; Chatzifragkou, A.; Koutinas, A.; Papanikolaou, S. Lipid Production by Yeasts Growing on Commercial Xylose in Submerged Cultures with Process Water Being Partially Replaced by Olive Mill Wastewaters. *Processes* 2020, *8*, 819. [CrossRef]
- Yousuf, A.; Sannino, F.; Addorisio, V.; Pirozzi, D. Microbial Conversion of Olive Oil Mill Wastewaters into Lipids Suitable for Biodiesel Production. J. Agric. Food Chem. 2010, 58, 8630–8635. [CrossRef]
- Jarboui, R.; Magdich, S.; Ayadi, R.J.; Gargouri, A.; Gharsallah, N.; Ammar, E. Aspergillus niger P6 and Rhodotorula mucilaginosa CH4 Used for Olive Mill Wastewater (OMW) Biological Treatment in Single Pure and Successive Cultures. Environ. Technol. 2013, 34. [CrossRef]
- 152. Carvalho, F.; Prazeres, A.R.; Rivas, J. Cheese Whey Wastewater: Characterization and Treatment. *Sci. Total Environ.* **2013**, 445–446, 385–396.
- 153. Mollea, C.; Marmo, L.; Bosco, F. Valorisation of Cheese Whey, a By-Product from the Dairy Industry. Food Industry 2013. [CrossRef]
- 154. Seo, Y.H.; Lee, I.; Jeon, S.H.; Han, J.I. Efficient Conversion from Cheese Whey to Lipid Using *Cryptococcus curvatus*. *Biochem. Eng. J.* **2014**, *90*. [CrossRef]
- 155. Taskin, M.; Saghafian, A.; Aydogan, M.N.; Arslan, N.P. Microbial Lipid Production by Cold-Adapted Oleaginous Yeast *Yarrowia lipolytica B9* in Non-Sterile Whey Medium. *BiofuelsBioprod. Biorefining* **2015**, *9*. [CrossRef]
- 156. Lappa, I.K.; Papadaki, A.; Kachrimanidou, V.; Terpou, A.; Koulougliotis, D.; Eriotou, E.; Kopsahelis, N. Cheese Whey Processing: Integrated Biorefinery Concepts and Emerging Food Applications. *Foods* **2019**, *8*, 347.
- 157. Zotta, T.; Solieri, L.; Iacumin, L.; Picozzi, C.; Gullo, M. Valorization of Cheese Whey Using Microbial Fermentations. *Appl. Microbiol. Biotechnol.* **2020**, *104*, 2749–2764.
- 158. Domingues, L.; Guimarães, P.M.R.; Oliveira, C. Metabolic Engineering of *Saccharomyces cerevisiae* for Lactose/Whey Fermentation. *Bioeng. Bugs* **2010**, *1*, 164–171.
- 159. Noike, T.; Takabatake, H.; Mizuno, O.; Ohba, M. Inhibition of Hydrogen Fermentation of Organic Wastes by Lactic Acid Bacteria. *Proc. Int. J. Hydrog. Energy* **2002**, 27.
- Carota, E.; Crognale, S.; D'Annibale, A.; Gallo, A.M.; Stazi, S.R.; Petruccioli, M. A Sustainable Use of Ricotta Cheese Whey for Microbial Biodiesel Production. *Sci. Total Environ.* 2017, 584–585. [CrossRef]
- 161. Vyas, S.; Chhabra, M. Assessing Oil Accumulation in the Oleaginous Yeast *Cystobasidium oligophagum JRC1* Using Dairy Waste Cheese Whey as a Substrate. *3 Biotech* 2019, *9*. [CrossRef]
- 162. Castanha, R.F.; de Morais, L.A.S.; Mariano, A.P.; Monteiro, R.T.R. Comparison of Two Lipid Extraction Methods Produced by Yeast in Cheese Whey. *Braz. Arch. Biol. Technol.* **2013**, *56*. [CrossRef]
- 163. Arous, F.; Frikha, F.; Triantaphyllidou, I.E.; Aggelis, G.; Nasri, M.; Mechichi, T. Potential Utilization of Agro-Industrial Wastewaters for Lipid Production by the Oleaginous Yeast *Debaryomyces etchellsii*. J. Clean. Prod. **2016**, 133, 899–909. [CrossRef]
- 164. Pirozzi, D.; Ausiello, A.; Zuccaro, G.; Sannino, F.; Yousuf, A. Culture of oleaginous yeasts in dairy industry wastewaters to obtain lipids suitable for the production of II-generation biodiesel. *Proc. World Acad. Sci. Eng. Technol.* **2013**, *8*, 57–61.
- 165. Arous, F.; Atitallah, I.b.; Nasri, M.; Mechichi, T. A Sustainable Use of Low-Cost Raw Substrates for Biodiesel Production by the Oleaginous Yeast *Wickerhamomyces anomalus*. *3 Biotech* **2017**, *7*. [CrossRef]

- 166. Lin, C.S.K.; Pfaltzgraff, L.A.; Herrero-Davila, L.; Mubofu, E.B.; Abderrahim, S.; Clark, J.H.; Koutinas, A.A.; Kopsahelis, N.; Stamatelatou, K.; Dickson, F.; et al. Food Waste as a Valuable Resource for the Production of Chemicals, Materials and Fuels. Current Situation and Global Perspective. *Energy Environ. Sci.* 2013, *6*, 426–464.
- 167. Dahiya, S.; Joseph, J. High Rate Biomethanation Technology for Solid Waste Management and Rapid Biogas Production: An Emphasis on Reactor Design Parameters. *Bioresour. Technol.* **2015**, *188*. [CrossRef]
- Krishna, D.; Kalamdhad, A.S. Pre-Treatment and Anaerobic Digestion of Food Waste for High Rate Methane Production-A Review. J. Environ. Chem. Eng. 2014, 2.
- Hafid, H.S.; Rahman, N.A.; Md Shah, U.K.; Baharudin, A.S. Enhanced Fermentable Sugar Production from Kitchen Waste Using Various Pretreatments. J. Environ. Manag. 2015, 156. [CrossRef]
- 170. Jiang, J.; Gong, C.; Wang, J.; Tian, S.; Zhang, Y. Effects of Ultrasound Pre-Treatment on the Amount of Dissolved Organic Matter Extracted from Food Waste. *Bioresour. Technol.* **2014**, 155. [CrossRef]
- 171. Sarkar, O.; Kumar, A.N.; Dahiya, S.; Krishna, K.V.; Yeruva, D.K.; Mohan, S.V. Regulation of Acidogenic Metabolism towards Enhanced Short Chain Fatty Acid Biosynthesis from Waste: Metagenomic Profiling. *RSC Adv.* **2016**, *6*. [CrossRef]
- 172. Magdalena, J.A.; Tomás-Pejó, E.; Ballesteros, M.; González-Fernandez, C. Volatile Fatty Acids Production from Protease Pretreated Chlorella Biomass via Anaerobic Digestion. *Biotechnol. Prog.* **2018**, *34*. [CrossRef]
- 173. Fei, Q.; Chang, H.N.; Shang, L.; dal rae Choi, J.; Kim, N.J.; Kang, J.W. The Effect of Volatile Fatty Acids as a Sole Carbon Source on Lipid Accumulation by *Cryptococcus albidus* for Biodiesel Production. *Bioresour. Technol.* 2011, 102. [CrossRef]
- 174. Vajpeyi, S.; Chandran, K. Microbial Conversion of Synthetic and Food Waste-Derived Volatile Fatty Acids to Lipids. *Bioresour. Technol.* **2015**, *188*. [CrossRef]
- 175. Qian, X.; Zhou, X.; Chen, L.; Zhang, X.; Xin, F.; Dong, W.; Zhang, W.; Ochsenreither, K.; Jiang, M. Bioconversion of Volatile Fatty Acids into Lipids by the Oleaginous Yeast *Apiotrichum porosum DSM27194*. *Fuel* **2021**, 290. [CrossRef]
- 176. Llamas, M.; Dourou, M.; González-Fernández, C.; Aggelis, G.; Tomás-Pejó, E. Screening of Oleaginous Yeasts for Lipid Production Using Volatile Fatty Acids as Substrate. *Biomass Bioenergy* **2020**, *138*. [CrossRef]
- 177. Annamalai, N.; Sivakumar, N.; Fernandez-Castane, A.; Oleskowicz-Popiel, P. Production of Microbial Lipids Utilizing Volatile Fatty Acids Derived from Wastepaper: A Biorefinery Approach for Biodiesel Production. *Fuel* **2020**, 276. [CrossRef]
- 178. Gao, R.; Li, Z.; Zhou, X.; Bao, W.; Cheng, S.; Zheng, L. Enhanced Lipid Production by *Yarrowia lipolytica* Cultured with Synthetic and Waste-Derived High-Content Volatile Fatty Acids under Alkaline Conditions. *Biotechnol. Biofuels* **2020**, *13*. [CrossRef]
- 179. Carmona-Cabello, M.; García, I.L.; Papadaki, A.; Tsouko, E.; Koutinas, A.; Dorado, M.P. Biodiesel Production Using Microbial Lipids Derived from Food Waste Discarded by Catering Services. *Bioresour. Technol.* **2021**, 323. [CrossRef]
- 180. Ma, X.; Gao, Z.; Gao, M.; Ma, Y.; Ma, H.; Zhang, M.; Liu, Y.; Wang, Q. Microbial Lipid Production from Food Waste Saccharified Liquid and the Effects of Compositions. *Energy Convers. Manag.* **2018**, 172. [CrossRef]
- Zeng, Y.; Bian, D.; Xie, Y.; Jiang, X.; Li, X.; Li, P.; Zhang, Y.; Xie, T. Utilization of Food Waste Hydrolysate for Microbial Lipid and Protein Production by *Rhodosporidium toruloides Y2. J. Chem. Technol. Biotechnol.* 2017, 92. [CrossRef]
- 182. Awad, D.; Bohnen, F.; Mehlmer, N.; Brueck, T. Multi-Factorial-Guided Media Optimization for Enhanced Biomass and Lipid Formation by the Oleaginous Yeast *Cutaneotrichosporon oleaginosus*. *Front. Bioeng. Biotechnol.* **2019**, 7. [CrossRef]
- Chopra, J.; Sen, R. Process Optimization Involving Critical Evaluation of Oxygen Transfer, Oxygen Uptake and Nitrogen Limitation for Enhanced Biomass and Lipid Production by Oleaginous Yeast for Biofuel Application. *Bioprocess Biosyst. Eng.* 2018, 41. [CrossRef]
- Abeln, F.; Chuck, C.J. The Role of Temperature, PH and Nutrition in Process Development of the Unique Oleaginous Yeast Metschnikowia pulcherrima. J. Chem. Technol. Biotechnol. 2020, 95. [CrossRef]
- Koutinas, A.A.; Chatzifragkou, A.; Kopsahelis, N.; Papanikolaou, S.; Kookos, I.K. Design and Techno-Economic Evaluation of Microbial Oil Production as a Renewable Resource for Biodiesel and Oleochemical Production. *Fuel* 2014, 116, 566–577. [CrossRef]
- 186. Ivančić Šantek, M.; Miškulin, E.; Petrović, M.; Beluhan, S.; Šantek, B. Effect of Carbon and Nitrogen Source Concentrations on the Growth and Lipid Accumulation of Yeast *Trichosporon oleaginosus* in Continuous and Batch Culture. *J. Chem. Technol. Biotechnol.* 2017, 92. [CrossRef]
- 187. Amaretti, A.; Raimondi, S.; Sala, M.; Roncaglia, L.; de Lucia, M.; Leonardi, A.; Rossi, M. Single Cell Oils of the Cold-Adapted Oleaginous Yeast *Rhodotorula glacialis DBVPG* 4785. *Microb. Cell Factories* **2010**, 9. [CrossRef]
- Hu, C.; Wu, S.; Wang, Q.; Jin, G.; Shen, H.; Zhao, Z.K. Simultaneous Utilization of Glucose and Xylose for Lipid Production by *Trichosporon cutaneum. Biotechnol. Biofuels* 2011, 4. [CrossRef]
- 189. Wild, R.; Patil, S.; Popović, M.; Zappi, M.; Dufreche, S.; Bajpai, R. Lipids from Lipomyces starkeyi. Food Technol. Biotechnol. 2010, 48.
- 190. Tchakouteu, S.S.; Chatzifragkou, A.; Kalantzi, O.; Koutinas, A.A.; Aggelis, G.; Papanikolaou, S. Oleaginous Yeast *Cryptococcus curvatus* Exhibits Interplay between Biosynthesis of Intracellular Sugars and Lipids. *Eur. J. Lipid Sci. Technol.* **2015**, *117*. [CrossRef]
- 191. Babazadeh, R.; Lahtvee, P.J.; Adiels, C.B.; Goksör, M.; Nielsen, J.B.; Hohmann, S. The Yeast Osmostress Response Is Carbon Source Dependent. *Sci. Rep.* **2017**, *7*. [CrossRef]
- 192. Dobrowolski, A.; Mituła, P.; Rymowicz, W.; Mirończuk, A.M. Efficient Conversion of Crude Glycerol from Various Industrial Wastes into Single Cell Oil by Yeast *Yarrowia lipolytica*. *Bioresour. Technol.* **2016**, 207. [CrossRef]
- 193. Ratledge, C. Yeasts, moulds, algae and bacteria as sources of lipids. In *Technological Advances in Improved and Alternative Sources of Lipids;* Springer: Boston, MA, USA, 1994; pp. 235–291.

- 194. Tkáčová, J.; Čaplová, J.; Klempová, T.; Čertík, M. Correlation between Lipid and Carotenoid Synthesis in Torularhodin-Producing *Rhodotorula glutinis. Ann. Microbiol.* **2017**, *67*. [CrossRef]
- 195. Braunwald, T.; Schwemmlein, L.; Graeff-Hönninger, S.; French, W.T.; Hernandez, R.; Holmes, W.E.; Claupein, W. Effect of Different C/N Ratios on Carotenoid and Lipid Production by *Rhodotorula glutinis*. *Appl. Microbiol. Biotechnol.* **2013**, 97. [CrossRef]
- 196. Gong, Z.; Shen, H.; Wang, Q.; Yang, X.; Xie, H.; Zhao, Z.K. Efficient Conversion of Biomass into Lipids by Using the Simultaneous Saccharification and Enhanced Lipid Production Process. *Biotechnol. Biofuels* **2013**, *6*. [CrossRef]
- 197. Lamers, D.; van Biezen, N.; Martens, D.; Peters, L.; van de Zilver, E.; Jacobs-van Dreumel, N.; Wijffels, R.H.; Lokman, C. Selection of Oleaginous Yeasts for Fatty Acid Production. *Bmc Biotechnol.* **2016**, 16. [CrossRef]
- Koganti, S.; Kuo, T.M.; Kurtzman, C.P.; Smith, N.; Ju, L.K. Production of Arabitol from Glycerol: Strain Screening and Study of Factors Affecting Production Yield. *Appl. Microbiol. Biotechnol.* 2011, 90. [CrossRef]
- 199. Nozaki, H.; Suzuki, S.I.; Tsuyoshi, N.; Yokozeki, K. Production of D-Arabitol by *Metschnikowia reukaufii AJ14787. Biosci. Biotechnol. Biochem.* 2003, 67. [CrossRef]
- 200. Papanikolaou, S.; Chevalot, I.; Komaitis, M.; Marc, I.; Aggelis, G. Single Cell Oil Production by *Yarrowia lipolytica* Growing on an Industrial Derivative of Animal Fat in Batch Cultures. *Appl. Microbiol. Biotechnol.* **2002**, *58*. [CrossRef]
- 201. Timoumi, A.; Cléret, M.; Bideaux, C.; Guillouet, S.E.; Allouche, Y.; Molina-Jouve, C.; Fillaudeau, L.; Gorret, N. Dynamic Behavior of *Yarrowia lipolytica* in Response to PH Perturbations: Dependence of the Stress Response on the Culture Mode. *Appl. Microbiol. Biotechnol.* 2017, 101. [CrossRef]
- 202. Kuttiraja, M.; Dhouha, A.; Tyagi, R.D. Harnessing the Effect of PH on Lipid Production in Batch Cultures of *Yarrowia lipolytica SKY7. Appl. Biochem. Biotechnol.* **2018**, *184.* [CrossRef]
- 203. Slininger, P.J.; Dien, B.S.; Kurtzman, C.P.; Moser, B.R.; Bakota, E.L.; Thompson, S.R.; O'Bryan, P.J.; Cotta, M.A.; Balan, V.; Jin, M.; et al. Comparative Lipid Production by Oleaginous Yeasts in Hydrolyzates of Lignocellulosic Biomass and Process Strategy for High Titers. *Biotechnol. Bioeng.* 2016, 113, 1676–1690. [CrossRef]
- Kot, A.M.; Błażejak, S.; Kurcz, A.; Bryś, J.; Gientka, I.; Bzducha-Wróbel, A.; Maliszewska, M.; Reczek, L. Effect of Initial PH of Medium with Potato Wastewater and Glycerol on Protein, Lipid and Carotenoid Biosynthesis by *Rhodotorula glutinis*. *Electron. J. Biotechnol.* 2017, 27. [CrossRef]
- 205. Davies, R.J.; Holdsworth, J.E.; Reader, S.L. The Effect of Low Oxygen Uptake Rate on the Fatty Acid Profile of the Oleaginous Yeast *Apiotrichum curvatum*. *Appl. Microbiol. Biotechnol.* **1990**, *33*. [CrossRef]
- 206. Naganuma, T.; Uzuka, Y.; Tanaka, K. Physiological Factors Affecting Total Cell Number and Lipid Content of the Yeast, *Lipomyces* starkeyi. J. Gen. Appl. Microbiol. **1985**, 31. [CrossRef]
- 207. Calvey, C.H.; Su, Y.K.; Willis, L.B.; McGee, M.; Jeffries, T.W. Nitrogen Limitation, Oxygen Limitation, and Lipid Accumulation in *Lipomyces starkeyi. Bioresour. Technol.* 2016, 200. [CrossRef]
- Yen, H.W.; Zhang, Z. Effects of Dissolved Oxygen Level on Cell Growth and Total Lipid Accumulation in the Cultivation of Rhodotorula glutinis. J. Biosci. Bioeng. 2011, 112. [CrossRef]
- 209. Yen, H.W.; Liu, Y.X. Application of Airlift Bioreactor for the Cultivation of Aerobic Oleaginous Yeast *Rhodotorula glutinis* with Different Aeration Rates. *J. Biosci. Bioeng.* 2014, 118. [CrossRef]
- 210. Saenge, C.; Cheirsilp, B.; Suksaroge, T.T.; Bourtoom, T. Potential Use of Oleaginous Red Yeast *Rhodotorula glutinis* for the Bioconversion of Crude Glycerol from Biodiesel Plant to Lipids and Carotenoids. *Process Biochem.* 2011, 46. [CrossRef]
- 211. Shuib, S.; Wan Nawi, W.N.N.; Taha, E.M.; Omar, O.; Abdul Kader, A.J.; Kalil, M.S.; Abdul Hamid, A. Strategic Feeding of Ammonium and Metal Ions for Enhanced GLA-Rich Lipid Accumulation in *Cunninghamella bainieri 2a1. Sci. World J.* 2014, 2014. [CrossRef]
- 212. Zhao, X.; Kong, X.; Hua, Y.; Feng, B.; Zhao, Z. Medium Optimization for Lipid Production through Co-Fermentation of Glucose and Xylose by the Oleaginous Yeast *Lipomyces starkeyi*. *Eur. J. Lipid Sci. Technol.* **2008**, 110. [CrossRef]
- 213. Saran, S.; Mathur, A.; Dalal, J.; Saxena, R.K. Process Optimization for Cultivation and Oil Accumulation in an Oleaginous Yeast *Rhodosporidium toruloides A29. Fuel* **2017**, *188.* [CrossRef]
- 214. Kraisintu, P.; Yongmanitchai, W.; Limtong, S. Selection and Optimization for Lipid Production of a Newly Isolated Oleaginous Yeast, *Rhodosporidium toruloides DMKU3-TK16. Kasetsart J. Nat. Sci.* **2010**, *44*, 436–445.
- 215. Nakagawa, Y.; Sakumoto, N.; Kaneko, Y.; Harashima, S. Mga2p Is a Putative Sensor for Low Temperature and Oxygen to Induce OLE1 Transcription in *Saccharomyces cerevisiae*. *Biochem. Biophys. Res. Commun.* **2002**, 291. [CrossRef]
- 216. Tezaki, S.; Iwama, R.; Kobayashi, S.; Shiwa, Y.; Yoshikawa, H.; Ohta, A.; Horiuchi, H.; Fukuda, R. Δ12-Fatty Acid Desaturase Is Involved in Growth at Low Temperature in Yeast Yarrowia lipolytica. Biochem. Biophys. Res. Commun. 2017, 488. [CrossRef]
- 217. Liu, Z.J.; Liu, L.P.; Wen, P.; Li, N.; Zong, M.H.; Wu, H. Effects of Acetic Acid and PH on the Growth and Lipid Accumulation of the Oleaginous Yeast *Trichosporon fermentans*. *BioResources* **2015**, *10*. [CrossRef]
- 218. Gu Pan, J.; Shick Rhee, J. Kinetic and Energetic Analyses of Lipid Accumulation in Batch Culture of *Rhodotorula glutinis*. J. Ferment. *Technol.* **1986**, *64*. [CrossRef]
- 219. Issariyakul, T.; Dalai, A.K. Biodiesel from Vegetable Oils. Renew. Sustain. Energy Rev. 2014, 31, 446–471.
- 220. Fassinou, W.F.; Sako, A.; Fofana, A.; Koua, K.B.; Toure, S. Fatty Acids Composition as a Means to Estimate the High Heating Value (HHV) of Vegetable Oils and Biodiesel Fuels. *Energy* **2010**, *35*. [CrossRef]
- 221. Heikal, E.K.; Elmelawy, M.S.; Khalil, S.A.; Elbasuny, N.M. Manufacturing of Environment Friendly Biolubricants from Vegetable Oils. *Egypt. J. Pet.* 2017, 26. [CrossRef]

- 222. Saenge, C.; Cheirsilp, B.; Suksaroge, T.T.; Bourtoom, T. Efficient Concomitant Production of Lipids and Carotenoids by Oleaginous Red Yeast *Rhodotorula glutinis* Cultured in Palm Oil Mill Effluent and Application of Lipids for Biodiesel Production. *Biotechnol. Bioprocess Eng.* **2011**, *16*. [CrossRef]
- Kaphueakngam, P.; Flood, A.; Sonwai, S. Production of Cocoa Butter Equivalent from Mango Seed Almond Fat and Palm Oil Mid-Fraction. J. Food Agro-Ind. 2009, 2, 441–447.
- 224. Ward, O.P.; Singh, A. Omega-3/6 Fatty Acids: Alternative Sources of Production. Process Biochem. 2005, 40. [CrossRef]
- 225. Kothri, M.; Mavrommati, M.; Elazzazy, A.M.; Baeshen, M.N.; Moussa, T.A.A.; Aggelis, G. Microbial Sources of Polyunsaturated Fatty Acids (PUFAs) and the Prospect of Organic Residues and Wastes as Growth Media for PUFA-Producing Microorganisms. *FEMS Microbiol. Lett.* 2020, 367, 367.
- 226. Uemura, H. Synthesis and Production of Unsaturated and Polyunsaturated Fatty Acids in Yeast: Current State and Perspectives. *Appl. Microbiol. Biotechnol.* 2012, 95, 1–12.
- 227. Zhu, Q.; Xue, Z.; Yadav, N.; Damude, H.; Pollak, D.W.; Rupert, R.; Seip, J.; Hollerbach, D.; Macool, D.; Zhang, H.; et al. Metabolic Engineering of an Oleaginous Yeast for the Production of Omega-3 Fatty Acids. In *Single Cell Oils: Microbial and Algal Oils*, 2nd ed.; AOCS Press: Urbana, IL, USA, 2010; pp. 51–73.
- Bellou, S.; Triantaphyllidou, I.E.; Aggeli, D.; Elazzazy, A.M.; Baeshen, M.N.; Aggelis, G. Microbial Oils as Food Additives: Recent Approaches for Improving Microbial Oil Production and Its Polyunsaturated Fatty Acid Content. *Curr. Opin. Biotechnol.* 2016, 37, 24–35.
- Laoteng, K.; Čertík, M.; Cheevadhanark, S. Mechanisms Controlling Lipid Accumulation and Polyunsaturated Fatty Acid Synthesis in Oleaginous Fungi. *Chem. Pap.* 2011, 65, 97–103.
- 230. Béligon, V.; Christophe, G.; Fontanille, P.; Larroche, C. Microbial Lipids as Potential Source to Food Supplements. *Curr. Opin. Food Sci.* **2016**, *7*, 35–42.
- 231. Fichtali, J.; Senanayake, S.P.J.N. Development and Commercialization of Microalgae-Based Functional Lipids. In *Functional Food Product Development*; Wiley-Blackwell: Oxford, UK, 2010; Volume 2, pp. 206–225.
- Madani, M.; Enshaeieh, M.; Abdoli, A. Single Cell Oil and Its Application for Biodiesel Production. *Process Saf. Environ. Prot.* 2017, 111, 747–756.
- Martinez-Silveira, A.; Villarreal, R.; Garmendia, G.; Rufo, C.; Vero, S. Process Conditions for a Rapid in Situ Transesterification for Biodiesel Production from Oleaginous Yeasts. *Electron. J. Biotechnol.* 2019, 38. [CrossRef]
- Xue, F.; Gao, B.; Zhu, Y.; Zhang, X.; Feng, W.; Tan, T. Pilot-Scale Production of Microbial Lipid Using Starch Wastewater as Raw Material. *Bioresour. Technol.* 2010, 101. [CrossRef]
- 235. Carota, E.; Petruccioli, M.; D'Annibale, A.; Gallo, A.M.; Crognale, S. Orange Peel Waste–Based Liquid Medium for Biodiesel Production by Oleaginous Yeasts. *Appl. Microbiol. Biotechnol.* **2020**, *104*. [CrossRef]
- 236. Annamalai, N.; Sivakumar, N.; Oleskowicz-Popiel, P. Enhanced Production of Microbial Lipids from Waste Office Paper by the Oleaginous Yeast *Cryptococcus curvatus*. *Fuel* **2018**, 217. [CrossRef]
- 237. Kruger, J.S.; Cleveland, N.S.; Yeap, R.Y.; Dong, T.; Ramirez, K.J.; Nagle, N.J.; Lowell, A.C.; Beckham, G.T.; McMillan, J.D.; Biddy, M.J. Recovery of Fuel-Precursor Lipids from Oleaginous Yeast. ACS Sustain. Chem. Eng. 2018, 6. [CrossRef]
- 238. Brenna, E.; Colombo, D.; di Lecce, G.; Gatti, F.G.; Ghezzi, M.C.; Tentori, F.; Tessaro, D.; Viola, M. Conversion of Oleic Acid into Azelaic and Pelargonic Acid by a Chemo-Enzymatic Route. *Molecules* **2020**, *25*, 1882. [CrossRef]
- 239. Hosney, H.; Nadiem, B.; Ashour, I.; Mustafa, I.; El-Shibiny, A. Epoxidized Vegetable Oil and Bio-Based Materials as PVC Plasticizer. *J. Appl. Polym. Sci.* **2018**, 135, 46270. [CrossRef]
- Perez-Sena, W.Y.; Wärnå, J.; Eränen, K.; Tolvanen, P.; Estel, L.; Leveneur, S.; Salmi, T. Use of Semibatch Reactor Technology for the Investigation of Reaction Mechanism and Kinetics: Heterogeneously Catalyzed Epoxidation of Fatty Acid Esters. *Chem. Eng. Sci.* 2021, 230. [CrossRef]
- Munkajohnpong, P.; Kesornpun, C.; Buttranon, S.; Jaroensuk, J.; Weeranoppanant, N.; Chaiyen, P. Fatty Alcohol Production: An Opportunity of Bioprocess. *Biofuels Bioprod. Biorefining* 2020, 14, 986–1009. [CrossRef]
- Owuna, F.J.; Dabai, M.U.; Sokoto, M.A.; Dangoggo, S.M.; Bagudo, B.U.; Birnin-Yauri, U.A.; Hassan, L.G.; Sada, I.; Abubakar, A.L.; Jibrin, M.S. Chemical Modification of Vegetable Oils for the Production of Biolubricants Using Trimethylolpropane: A Review. *Egypt. J. Pet.* 2020, 29, 75–82.