Received: 6 May 2022 | Revised: 6 July 2022 | Accepted: 18 September 2022

DOI: 10.1002/bit.28245

REVIEW

BIOTECHNOLOGY AND BIOENGINEERING WILEY

Fungal lipases as biocatalysts: A promising platform in several industrial biotechnology applications

Amira Mahfoudhi | Sameh Benmabrouk | Ahmed Fendri | Adel Sayari

Laboratory of Biochemistry and Enzymatic Engineering of Lipases, Engineering National School of Sfax (ENIS), University of Sfax, Sfax, Tunisia

Correspondence
Ahmed Fendri, Laboratory of Biochemistry and Enzymatic Engineering of Lipases, Engineering National School of Sfax (ENIS), University of Sfax, Sfax. Tunisia.
Email: ahmed_fendri@yahoo.fr

Abstract

Many researchers have found fungi as a reliable source of lipase due to the versatility of their properties, ease of mass production, thermal stability, pH stability, broad substrate specificity, retained activity in organic solvents, and their low-cost extraction procedure. This review paper presents an overview about the main aspects of fungal lipases screened from several types of strains as well as their use as biocatalysts. Additionally, some biochemical properties will be reported. As commonly known, lipases can be produced from animals, plants, and microorganisms. Compared to other lipases, those obtained from fungi have been found to be more productive, a fact that encouraged the massive production of most fungal lipases due to their considerable commercial importance during the past few years. This paper is concerned about some of the major characteristics that made fungal lipases desirable products in the industrial fields. Due to the enantioselective properties of fungal lipases and their ability to remain active under extreme temperature, pH, and organic solvents, enzymes are capable to synthesize esters as well as to catalyze a variety of chemical reactions that include esterification, transesterification, acidolysis and aminolysis in aqueous and nonaqueous media. Furthermore, lipases are considered to have a commercial importance for biotechnological application fields, which makes them increasingly popular in food, detergent, cosmetic, organic synthesis, and pharmaceutical domains. The biotechnological potential of lipases has made the latter a coveted choice in industries for the present and future as biocatalysts. In addition, a classification of these fungal enzymes is also highlighted in this review. Moreover, the impact of an immobilization strategy of these fungal strains to achieve higher yields and to improve their production is discussed. Finally, fungal enzymes have played a crucial role from ancient times to today in different fields using several types of biological systems, which gives them a great interest for the production of these enzymes in large amounts with low cost and easy viability to enlarge their use in many industries. Likewise, some future perspectives on lipase production will also be discussed by focusing on special cases on lipase engineering.

KEYWORDS

biocatalysts, biochemical properties, biotechnological applications, fungal lipase, lipase engineering, review

1 | INTRODUCTION

Lipases (triacylglycerol acylhydrolases EC 3.1.1.3) are a class of hydrolases that are able to catalyze the hydrolysis of triglycerides to glycerol and free fatty acids over an oil–water interface. Besides, lipases are capable to synthesize esters as well as to catalyze transesterification reactions and present enantioselective properties. These lipolytic enzymes are also able to perform a very specific chemical transformation (biotransformation). Microbial lipases are considered to have a commercial interest for biotechnological applications that make them increasingly popular in the food, detergent, cosmetic, organic synthesis, and pharmaceutical industries (Mosbah et al., 2005; Sayari et al., 2007; Thakur, 2012).

Joseph et al. (2008) report that lipases have been deemed to be one of the leading biocatalysts with proven potential for contributing to the multibillion dollar underexploited lipid technology of bio-industry. Indeed, they have been used in lipid in situ metabolism and multifaceted ex situ industrial applications.

Since the 1980s, the number of available lipases has progressively increased due to the huge achievements made in the cloning and expression of enzymes from microorganisms, as well as to an increasing demand for these biocatalysts with novel and specific properties such as specificity and stability at various pH and temperatures (Bornscheuer et al., 2002; Menoncin et al., 2010).

Lipases can be produced from animals, plants, microorganisms (Dutra et al., 2008; Griebeler et al., 2011). Thanks to their stability, selectivity, and broad substrate specificity, microbial lipases have drawn special industrial attention. According to Abada (2008), the main microorganisms producers of extracellular lipases are bacteria and fungi. Fungal lipolytic enzymes have been produced traditionally by submerged fermentation (SF) because the recovery of extracellular enzymes and determination of biomass are facilitated by being performed by simple filtration or centrifugation. Solid-state fermentation (SSF) has also been used for the production of lipases from fungi (Coradi et al., 2013).

The importance of lipases can be observed by the recent great number of published articles. In fact, over the last few years, there has been an increase in the number of publications related to industrial applications of lipase-catalyzed reactions, achieved in common organic solvents, ionic liquids, or even in nonconventional solvents.

Additionally, the developing industrial order for lipases has led to the identification of new and prospective highly lipase-productive microbial strains together with rational enzyme properties. These enzymes are designed to achieve huge levels of activity and substrate specificity, and have engendered a great concern in applying rapid, reliable, specific, selective, and sensitive analytical methods for lipases activity evaluation (Stoytcheva et al., 2012). Among the diverse biological sources of the lipases studied, filamentous fungi are found to be the best useful source for the industrial field due to the properties of these lipases that are usually extracellular and soluble (Fibriana et al., 2013).

Pollardo et al. (2018) show that lipases have largely been used as biocatalysts for various reactions like esterification, transesterification, acidolysis, interesterification, alcoholysis, aminolysis, oximolysis, thiotransesterification, and ammoniolysis in anhydrous organic solvent.

Interestingly, the immobilization of enzymes on magnetic support has many advantages such as selective and safe recovery with magnetic force from the medium. Thus, it eliminates the expensive techniques like filtration, liquid chromatography, and centrifugation to separate the compound (Jambulingam et al., 2019).

The present study focuses on fungal lipases screened from different types of strains. Added to that, the use of these fungal enzymes as biocatalysts and their main biochemical properties have been described, without forgetting to mention their importance in different biotechnological application fields. However, review articles on fungal lipases are still scarce; for example, there is a need for an assortment of reports on the fungal lipase production, molecular structures, purification, and industrial applications.

2 | FUNGAL LIPASES AS BIOCATALYSTS

Among the microorganisms, fungi are identified as one of the best lipase sources (Tan et al., 2003). Recently, fungal lipases have been given significant attention in the industries due to their unique substrate specificity and stability under varied chemical and physical conditions. Besides, fungal lipolytic enzymes are extracellular in nature and can be extracted easily, which paves the way to the minimization of their cost and makes this microbial source preferred over bacteria (Mehta et al., 2017).

Aspergillus niger, *Candida rugosa*, *Humicola lanuginosa*, *Mucor miehei*, *Rhizopus arrhizus*, *Rhizopus delemar*, *Rhizopus japonicus*, *Rhizopus niveus*, and *Rhizopus oryzae* are screened in large scale for lipase production and, as a biological catalyst, have given a favorable vision in meeting the needs for a lot of industrial applications (Chandra et al., 2020). Fungal commercial lipases shed light on several biotechnological fields such as food and dairy products, detergent, pharmaceutical, agrochemical, and oleochemical industries, in bioremediation, in biodiesel production, and in paper and leather industry. Moreover, fungal lipases can be used in some medical applications.

The use of fungal lipases as biocatalysts for the production of biomolecules has a tremendous potential benefit for future developments. The most essential merits are:

- evaluation of high efficacy of lipases under mild reaction conditions;
- usability in “natural” reaction systems and products;
- reduction of environmental pollution;
- availability of lipases from different fungal sources;
- improvement of lipases by genetic engineering.

3 | CLASSIFICATION OF FUNGAL LIPASES

Lipase classification has been first presented as bacterial on the basis of the latter protein topology as these enzymes have high sequence diversity and physiological properties (Verma et al., 2021). Lipases are classified into eight families. This classification has been revised several times and, currently, there are 15 families that are a part of ESTHER database available on http://bio-web.ensam.inra.fr/esther (Fu et al., 2013; Handrick et al., 2001). ESTHER is a broad database containing information on a large diversity of α/β hydrolases fold superfamily that includes lipases (Lenfant et al., 2012).

In addition to what has been proposed by Arpigny and Jaeger, a new classification is recently reported in the Lipase Engineering Database (LED) about sequences based on a comparatively simplified version of lipase data (http://www.led.uni-stuttgart.de) that integrates information on sequence and structure of lipases and related proteins sharing the same α/β hydrolases fold to facilitate protein engineering (Lenfant et al., 2012).

This classification divides these enzymes into three classes based on the oxyanion hole pattern: GX, GGGX, and Y classes (Fischer, 2003). Based on this classification and on the amino-acid sequence similarities, fungal lipases have been grouped into five different subclasses (Figure 1): Two in the GX class, two in the GGGX class, and one in the Y class (Borrelli & Trono, 2015; Gupta et al., 2015).

4 | FACTORS INFLUENCING FUNGAL LIPASES PRODUCTION

The lipase production by fungi differs depending on the strain, the composition of the growth medium (the kind of carbon and nitrogen sources used), cultivation conditions, temperature, and pH (Treichel et al., 2010).

In addition, Ramos-Sánchez et al. (2015) demonstrate that fungi behave more efficiently in SSF and present greater productivities when compared to SF. Although there are some limitations when using the SSF, some analysis and optimization of several factors were included to overcome the latter.

Likewise, Mehta et al. (2017) show that most fungal lipases present an optimum of pH ranging from 4 to 11 and are stable over a wide range of temperatures from 10°C to 96°C.

Besides, the production of extracellular and cell-bound lipases depends on the carbon and nitrogen sources in the growth medium (Chandra et al., 2020; Vakhlu & Kour, 2006).

5 | BIOCHEMICAL PROPERTIES OF SOME FUNGAL LIPASES

Various special characteristics of microbial lipases like their substrate specificity, temperature, and pH dependency, stability in the presence of metal ion and organic solvents and nontoxic nature lead to their main role in several industrial applications (Verma et al., 2012). The most common characteristics of the microbial lipases are:

- their ability to use all mono-, di-, and tri-acylglycerols in addition to the free fatty acids in transesterification reactions;
- little inhibition by product;
- high activity/yield in nonaqueous media;
- little reaction time;
- tolerance to altered pH, temperature, organic solvents, and metal ions (Kumar et al., 2012).

The fungal lipases display variable biochemical properties. Table 1 summarizes the main biochemical properties of some previously studied fungal lipases.

5.1 | Effect of temperature on lipase activity and stability

Many studies carried out on fungal lipases have shown that these enzymes are more active and stable at temperatures ranging from 30°C to 40°C. In 1995, Comménil et al. show that *Botrytis cinerea* produces a temperature-sensitive lipase with a maximum activity occurring at 38°C. The enzyme is completely inactivated above 60°C.

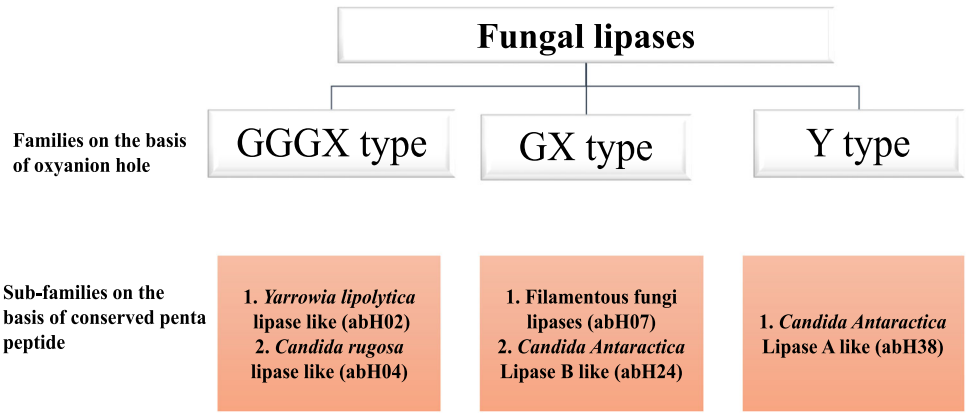

FIGURE 1 Classification of fungal lipases based on lipase engineering database.

TABLE 1 Biochemical properties of some fungal lipases

Source	MW (kDa)	pH opt	Temperature opt (°C)	Specific activity (U/mg)	Other characteristics	References
Botrytis cinerea	-	6	32–40	-	– Calcium-independent lipase	Commenil et al. (1995)
Aspergillus niger MZKI Al 16	65	7	45	nd	– Specificity towards short – chain of TG. – 1,3 positional specificity	Pokorny et al. (1997)
Rhizopus rhizopdiformis	-	-	-	43	-	Cordova et al. (1998)
Rhizopus pusillus	-	-	-	10.8	-	Cordova et al. (1998)
Penicillium restrictum	-	-	-	30	-	Gombert et al. (1999)
Candida rugosa *DMS 2031*	LipA-64 LipB-62 LipC-60	7.8 7.8 7.8	35–40 - -	- - -	- - -	Benjamin and Pandey (2001)
Rhizopus oryzae	32	8	37	10,000 (olive oil)	– Specificity towards long chain TG	A. B. Salah et al. (2001)
Fusarium solani FS1	-	-	-	0.45	-	Maia (2001)
Aspergillus niger	32	3–5	25–35	627 (Tricaprylin)	– Thermostable – *Sn*-1 specificity	Van Heerden et al. (2002)
Rhizopus oligosporus TUV-31	-	-	-	76.6	-	Iftikhar (2001)
Rhizopus oligosporus ISUUV-16	-	-	-	81.2	-	Awan et al. (2003)
Aspergillus carneus	27	9	37	502 (olive oil)	– 1,3 positional specificity – Alkaline lipase	Saxena et al. (2003)
Penicillium aurantiogriseum	28	8	60	17.8–25 (TC_4)	– Stable in organic solvents	Lima et al. (2003, 2004)
Penicillium camemberti Thom PG-3	28	6.4	48	nd	– 1.3 positional specificity.	Tan et al. (2004)
Geotrichum sp.	-	-	-	20	-	Burkert (2004)
Penicillium simplicissimum	- -	- -	- -	 21 30	- -	Basheer et al. (2004) Gutarra et al. (2007)
Aspergillus oryzae	21.6	9	55	694 (pNP-butyrate)	– Degradation of bioplastics	Maeda et al. (2005)
Aspergillus carneu	-	-	-	12.7	-	Kaushik et al. (2006)
Antrodia cinnamomea	60	8	45	187.5	– Alkaline lipase	Shu et al. (2006)

(Continues)

TABLE 1 (Continued)

Source	MW (kDa)	pH opt	Temperature opt (°C)	Specific activity (U/mg)	Other characteristics	References
BCRC 35396				(p-NPP)		
Rhizopus homothalicus	-	-	-	826	-	Rodriguez et al. (2006)
Rhizopus oryzae. W	29	8	37	3500 (olive oil)	– Doesn't show the mechanism of interfacial activation	R. B. Salah et al. (2006)
Candida cylindracea	-	-	-	23.7	-	B. S. Kim and Hou (2006) Brozzoli et al. (2009)
Candida cylindracea NRRLY 17506	-	-	-	20.4	-	
Rhizopus chinensis CCTCC M201021	-	6.4 (fully entangled filaments) and 6.8 (for dispersed mycelia)	30	101.2–691 U/g	– An efficient biocatalyst in biosynthesis of short-chain fatty esters in n-heptane	Teng and Xu (2008)
Penicillium verrucosum	-	-	-	40	-	Kempka et al. (2008)
Aureobasidium pullulans HN2.3	63.5	8.5	35	88.6 (p-NPL)	– Inhibited by – Hg^{2+}, Fe^{2+} and – Zn^{2+}	Z. Liu et al. (2008)
Candida rugosa	-	-	-	3.8	-	Rajendran et al. (2008)
Aspergillus niger NCIM 1207	32.2	2.5	50	1373.13 (p-NPP)	– Acidic lipase – Specific for 3-position in the ester bond	Mhetras et al. (2009)
Rhizopus sp. *JK-1*	-	7.5	30	30.38	– Has the second highest activity of lipase produced by *Rhizopus* sp.	Kantak et al. (2011)
Aspergillus awamori	-	-	-	495	-	Basheer et al. (2011)
Penicillium chrysogenum	-	-	-	46	-	S. Kumar et al. (2011)
Cladosporium tenuissimum	46	6	60	37.2	-	Saranya and Ramachandra (2020)

Abbreviations: p-NPL, *p*-nitrophenyl-laurate; pNP, *p*-nitrophenol butyrate; pNPP, *p*-nitrophenyl palmitate.

Besides, the *B. cinerea* lipase is stable at room temperature and 98% of the initial activity remains after an incubation of 48 h.

Additionally, fungal lipases purified from *R. oryzae* and *E. ashbyii*exhibit optimum activity at 30°C (A. K. Sharma et al., 2016; Vijayalakshmi & Kalindhi, 2015). Moreover, Falony et al. (2006) find that a lipase isolated from *A. niger* is highly active at 40°C and then the lipolytic activity starts to decline drastically after 60°C and is completely lost at 90°C. Another extracellular lipase derived from *A. niger* has an optimal reaction temperature at 35°C and the enzyme activity decreases when the temperature was beyond 50°C (Xing et al., 2020). Similarly, *A. japonicus* produces a lipase with an optimum temperature of 40°C (Jayaprakash & Ebenezer, 2012). As for the Rhizomucor *variabilis* lipase, it shows its maximal activity at 30°C (Bancerz et al., 2018).

Some other previous studies have reported the characterization of thermo-tolerant fungal lipases. In fact, intracellular lipase extracted from *Aspergillus westerdijkiae* (de Castro et al., 2017), *Nomuraea rileyi* (Supakdamrongkul et al., 2010), and *Rhizopus oryzae* (Saranya & Ramachandra, 2020) exhibit their maximal activities at 60°C, and fairly high stabilities are recorded at 50°C. Moreover, an interesting lipase was isolated from *T. lanuginosus* that is both thermo-tolerant and organic solvent resistant. The optimal temperature for this lipase is 60°C and it maintains 90% of its activity at 60°C for 24 h (Facin et al., 2018).

Similarly, Saranya and Ramachandra (2020) have isolated and purified a lipase from *Cladosporium tenuissimum* that reaches the maximum of its activity at 60°C.

5.2 | Effect of pH on lipase activity and stability

Most previous studies have shown that fungal lipases are in general active and stable in a wide range of pH. A lipase purified from *A. niger MYA135*is found to be active within the pH range of 2.0–10.0 with an optimum activity obtained at pH 6.5 (Pera et al., 2006). The purified lipase is more stable within the pH range of 2.0–10.0 when pre-incubated for 1 h at 37°C. Moreover, Jayaprakash and Ebenezer (2012) investigate the influence of different pH ranging from 3 to 12 on the activity and stability of a lipase purified from *A. japonicus*. The optimal activity and stability of this enzyme is found to beat neutral pH values. As previously reported by A. K. Sharma et al. (2016), the lipase secreted by *A. niger* is highly active between pH 4.5 and 5.5 and fully stable in the pH range from 3 to 10.5 at 30°C for 24 h.

Furthermore, other studies prove that a heat and organic solvent-tolerant lipase from *Thermomyces* exhibits the highest activity at pH 7 and maintains stability between pH 5.0 and 9.0 (Facin et al., 2018). Another lipase from *T. lanuginosus* shows an optimum pH of 8.5, although high activity is maintained within the pH range of 8–10 (A. Kumar et al., 2019). A lipase isolated from *Rhyzopus oryzae* revealed an optimum pH of 9.0 (Asmat et al., 2018).

Interestingly, a lipase isolated from *Candida viswanathii* displays its highest activity at pH 4. It maintains 80% and 90% of its activity at pH 3.5 and 4.5, respectively. However, at pH 2.0–3.0, the enzyme activity was reduced to 15%–40% (A. F. Almeida et al., 2018). The same behavior is obtained with a lipase from *A. niger* that exhibits its highest activity at pH 4, with 90% of this activity maintained at higher pH values (Zubiolo et al., 2014).

5.3 | Effect of metal ions

Metal ions play different important roles in influencing the structure and function of enzymes including lipases. Transition metal ions are a challenge to study in enzymology because of problems associated with solubility, oxidation, high binding, poor buffering, changes of redox state, and attaining appropriate free activities in solution (Aslamkhan & Ebenezer, 2002). Different behaviors towards metal ions are obtained with many fungal lipases. In fact, the effect of different metal ions (1 mM) is investigated on the stability of a lipase purified from *A. japonicus* (Jayaprakash & Ebenezer, 2012). The activity of this fungal enzyme is inhibited by incubating with Mn^{2+} and Hg^{2+} while the *A. japonicus* lipase is found to be stable after pre-incubation for 1 h with calcium. Also, Katiyar and Ali (2013) report that an increase in catalytic activity of *Candida rugosa* lipase was obtained in the presence of Ca^{2+}. This might be due to the fact that the *A. japonicus* and *Candida rugosa* lipases require calcium as a cofactor for their biological activities. However, Xing et al. (2021) prove that the activity of lipase from *Aspergillus niger* GZUF36 is inhibited up to 75% by 5 mM of Ca^{2+}. In addition, neither Ca^{2+} (5, 10, and 30 mM), Mg^{2+} (10, 50, and 100 mM), Na^{+} (0.1, 0.5, and 1 M), nor K^{+} (0.1, 0.5, and 1 M) has an effect on the action of a lipase screened from *C. tenuissimum* (Saranya & Ramachandra, 2020).

5.4 | Effect of surfactants

Long-chain ionic liquids like surfactants have a tendency to alter the physicochemical properties of lipases by internal alteration of charges from cationic to anionic and vice versa (Saranya & Ramachandra, 2020). In other cases, these surfactants aid in providing enzymes with access to substrates through interfacial area stabilization, which enhances the catalytic reaction of lipases (Gaur et al., 2008).

Furthermore, Supakdamrongkul et al. (2010) prove that surfactants are important components for emulsion preparations during lipase assays at every stage from enzyme production, purification, and characterization. Besides, some lipases show variation in affinities to the substrate when different concentrations of surfactants like Triton X100, SDS, Tween 80 and Tween 20 are added (Saranya & Ramachandra, 2020). The lipase isolated from the fungus *Nomuraea rileyi* presents an activity that is enhanced in the presence of SDS and Tween 80 whereas the lipase extracted from the thermophilic *Rhizopus oryzae* strain is inhibited when introducing SDS and Tween 80 (Supakdamrongkul et al., 2010).

5.5 | Effect of organic solvents on stability of fungal lipases

The stability of lipases in organic solvents is an important parameter for industrial applications such as transesterification reactions (Ranganathan et al., 2008). Currently, suitable performance of enzymes in non-polar solvents has been established in different biocatalytic processes (Hernández-Rodríguez et al., 2009). However, the availability of lipases that are active and stable in polar solvents could open new opportunities in biocatalysis with polar substrates.

In addition, Pera et al. (2006) have studied the impact of various organic solvents (methanol, ethanol, acetone, butanol, hexane, and heptane) on the stability of *A. niger* lipase. The enzyme shows high stability in the presence of all solvents with the highest residual activity with acetone when pre-incubated for 1 h at 37°C. Besides, different organic solvents (at a concentration of 10% and 20% v/v) are experimented on a lipase purified from *A. japonicus*. This enzyme retains 90% of its activity after incubation with methanol, acetone, chloroform, ethanol, and hexane. The highest residual activity (95%) is obtained in the presence of methanol when pre-incubated for 1 h (Jayaprakash & Ebenezer, 2012). Moreover, a lipase derived from *Rhizomucor miehei* was found to tolerate organic solvents including low concentrations of methanol, ethanol, propanol, and isopropanol, which had little impact on its catalytic activity (Tako et al., 2017). Interestingly, the residual activity of *Aspergillus niger* GZUF36 lipase is higher in non-polar solvents, particularly in *n*-hexane (106.02% ± 1.05% at 4°C for 2 h). It maintains 88.86% of its activity in dimethyl sulfoxide (polar solvent). However, this fungal lipase is completely inactivated in dichloromethane (non-polar solvent) (Xing et al., 2021).

5.6 | Enzyme immobilization

The use of several methods of immobilized fungal enzymes has increased considerably in recent years, mainly as a strategy to boost the biocatalyst stability and facilitate the recovery/reuse steps (Fibriana et al., 2013; Rodrigues et al., 2019).

The most common methods used for immobilized fungal enzymes are adsorption, covalent bonding, encapsulation, and cross-linking (Ali et al., 2018; Boudrant et al., 2020). Different enzyme immobilization methods are listed in Figure 2 (Contesini et al., 2020).

Adsorption is a simple and low-cost technique used to bond the enzyme to a support through weak forces such as van der Waals forces, hydrogen bonds, electrostatic, and hydrophobic interactions. Covalent bonding methods, in contrast, are based on the formation of strong covalent bonds between enzyme and support, usually involving amino acid chains and functional groups (F. L. C. Almeida et al., 2021; Mulinari et al., 2020). In encapsulation processes, the enzyme is enclosed within the support matrix without chemically reacting with the support. Finally, cross-linking processes use a bifunctional agent to create bonds between enzyme molecules, yielding a carrier-free enzyme complex (Eş et al., 2015; Facin et al., 2019).

There have been considerable advances in fungal lipase immobilization for industrial applications, accompanied by an increasing number of technical documents and scientific research on the topic (J. Liu et al., 2020; Osbon & Kumar, 2019).

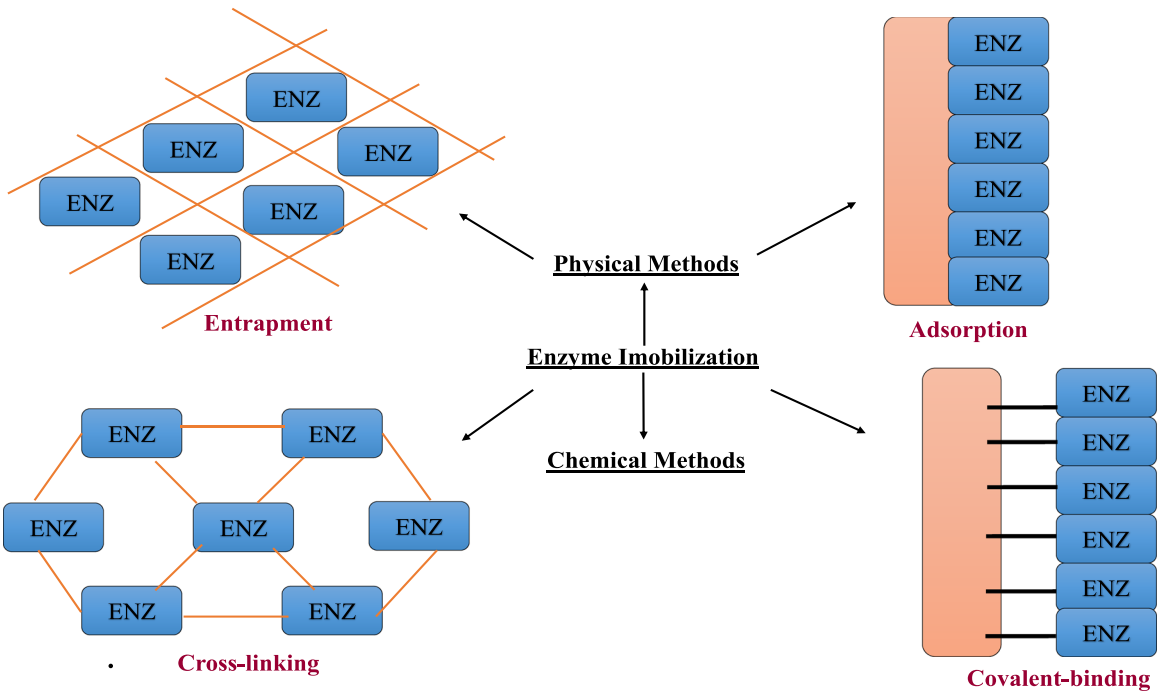

FIGURE 2 Several methods of enzyme immobilization

TABLE 2 The benefits and the drawbacks of immobilized enzymes in the industrial field

Benefits	Drawbacks
✓ Easy dissociation of biocatalyst	✓ Compared to the native enzyme it has a slow enzyme activity
✓ In downstream processing costs reduced	✓ For carriers and immobilization, additional costs needed
✓ The reusing of biocatalyst (reutilizing)	✓ The reaction rates are slow compared to native enzymes
✓ Toward organic solvents and higher temperatures, it presents better stability	✓ Subject to fouling
✓ Doesn't need the membrane to isolate enzyme from product use of the fixed bed or batch reactors	✓ Exhausted immobilized enzyme incinerated (disposed)
✓ With other enzymes co-immobilization is faisable	

In this respect, it is critical to shed light on the advantages and disadvantages of immobilized enzymes (summarized in Table 2; Enespa et al., 2022).

6 | BIOTECHNOLOGICAL APPLICATIONS

The upsurge in the demand for fungal lipases has steadily grown in industrial applications due to their innate versatility (Hasan et al., 2006; Kapoor & Gupta, 2012; Ray, 2015; Thakur, 2012).

Fungal lipases are widely known by their enzymatic properties and substrate specificity, which make them a versatile tool for industrial applications. They present an important group of biotechnological enzymes because of the versatility of their properties and their easy mass production (Figure 3).

6.1 | Fungal lipases in food processing industry

Thanks to some unique properties such as the specificity towards several substrates, temperature and pH dependency, and nontoxic nature, the fungal lipases are used in different areas of modern food industries such as the production of sugar fatty acid esters.

The mostly used fungal lipases in the development of dairy products and in the processing of other foods are those screened from *Aspergillus niger*, *Rhizopus oryzae*, *Candida rugosa* (Jooyandeh et al., 2009). Fungal lipases are frequently applied in the dairy industry for the selective hydrolysis of milk triacylglycerols during cheese ripening. Particularly, a recombinant lipase from *R. miehei* expressed in *A. oryzae* is commercially available with the trade name Palatase M (Novozymes) and used in the dairy industry to improve cheese properties. Lipase (Est_p6) isolated from a metagenomic library from marine sediments was produced in *E. coli* and applied to well hydrolyze milk fat and impart a desirable and distinctive flavor to milk products (Peng et al., 2014).

Immobilized lipases from *Candida antaractica B (CAL-B)*, *Candida cylindracea AY30*, and *Geotrichum candidum* are used for the esterification of functionalized phenols and the synthesis of lipophilic antioxidants in sunflower oils (Buisman et al., 1998; Mehta et al., 2017). Furthermore, some fungal lipases are used for the enhancement of aroma in Black tea (Ramarethinam et al., 2002).

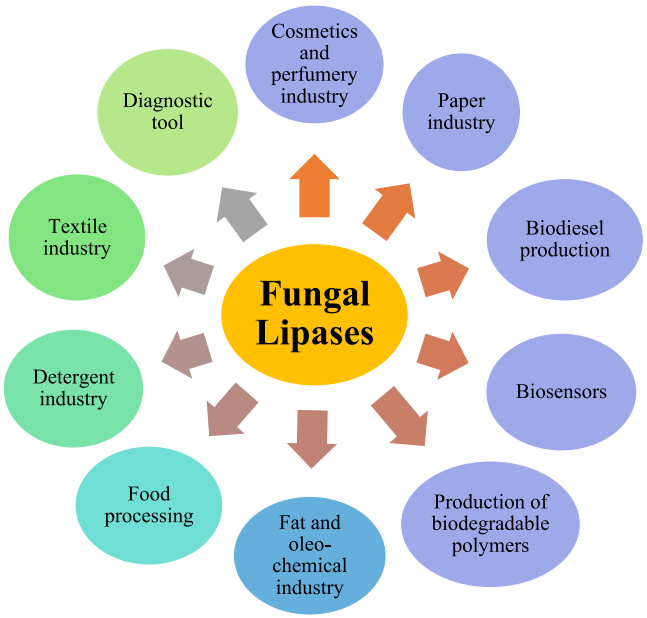

FIGURE 3 Main applications of fungal lipases

Penicillium camembertii lipase is used for the production of glycerol-glycolipid from a mixture containing glycosidases and fatty acid (Sharma et al., 2011). Likewise, lipases from *Thermomyces lanuginosa* and *Candida Antarctica B* are used as potentially reliable catalysts for sugar ester production (Chandra et al., 2020; Ferrer et al., 2005). A *Penicillium cyclopium* lipase produced in *Pichia pastoris* (J. Huang et al., 2013) has been used for the synthesis of mono- and diacylglycerols and showed its potential for food emulsifier preparations. The commercial enzyme Novozym 435, an immobilized lipase from *C. antarctica* expressed in *A. niger*, has been successfully used to produce sugar esters (Neta et al., 2012).

The interesterification by 1,3-regioselective fungal lipases has also been used to enrich low-cost fats like palm-oil fractions into 1, (3) palmitoyl, 2-oleoyl,3, (1) stearoyl glycerol and 1, (3) steraroyl, 2-oleoyl 3, (1) stearoyl glycerol (Rajendran et al., 2009).

Interestingly, Ghide et al. (2022) have used *Rhizomucor miehei* lipase immobilized on magnetic multi-walled carbon the synthesis of 1,3-dioleoyl-2-palmotoylglycerol (OPO)-rich human milk fat substitutes nanotubes suggest that the immobilized fungal lipase is a

promising biocatalyst for the synthesis of OPO-rich triacylglycerols with potential use in infant formulas.

In the food processing industry, recombinant lipases are highly encouraged and some have been found with GRAS status and introduced in several food fields, showing that the application of lipases directly to food tends to increase and will be expanded in the coming years (Salgado et al., 2022).

6.2 | Fungal lipases in fats and oleo-chemical industry

The use of lipases in the field of fats and oleo-chemical industry is rapidly expanding as it saves energy and minimizes thermal degradation during several reactions such as hydrolysis, esterification, acidolysis, alcoholysis, interesterification, and aminolysis (Bornscheuer, 2018).

Besides, lipases are designed by their ability to hydrolyze ester bonds in triacyglycerols in the presence of excess water. Additionally, these lipolytic enzymes can catalyze the esterification reaction (ester synthesis) in a low-water environment. Esterification and interesterification are used to get value-added products between the lipolytic transformation of oils and fats like specialty fats and partial glycerides using the positional and fatty acid detailed lipases (Chandra et al., 2020). Furthermore, depending on the nature of the substrates, lipases can catalyze alcoholysis (an acyl moiety displaced between an acyl glycerol and an alcohol), acidolysis (an acyl moiety displaced between an acyl glycerol and a carboxylic acid), and transesterification (two acyl moieties exchanged between two acylglycerols) (R. Sharma et al., 2001; Figure 4).

The modification of fats and oil is one of the essential parts in food processing industry that requires novel economic and green technologies (Gupta et al., 2003). Several studies have shown that the use of different fungal lipases for the modification of oils and the upgrade of cheap oils and fats is essential to synthesize lipids (Authority, 2014).

Additionally, Gupta et al. (2003) demonstrate that among some commercial fungal lipolytic enzymes, lipase from *Rhizopus niveus* shows an important potential for the production of interesterified butter fat with an increased proportion of oleic acid at the *sn*-2 position.

Similarly, Komatsu et al. (2004) find that the phospholipid microemulsion systems using soybean lecithin as the amphiphilic component are used in the interesterification reaction of olive oil with palmitic acid catalyzed by the *Rhizopus delemar* lipase. Likewise, another lipase from *Rhizopus* genus (*R. japonicus*) is used to produce butter suitable for chocolate manufacture by interesterification of palm oil with methyl stearate (Pogori, et al., 2007.

Andualema and Gessesse (2012) prove that lipases isolated from *R. miehei* are used for the hydrolysis of oils and fats to produce free fatty acids and glycerol compounds which are later used for soap production, generating flavor in various types of foods and as precursors of various medicines in the pharmaceutical industry. As for Singh and Mukhopadhyay (2012), they state that some fungal lipases are generally used in the production of a variety of products, ranging from fruit juices to vegetable fermentation. In addition, some fungal lipases facilitate the removal of fat from meat and fish products (R. Sharma et al., 2001).

Fungal lipases are also important biocatalysts with which to modify oil substances used in the food industry. Although there are studies on the ability of lipases to release fatty acids in some edible oils, the bioactive properties of the produced hydrolysis products have not yet been characterized as far as we know. Kotogán et al. (2022) have showed that the *R. miehei* lipase treatment may be a suitable approach to developing bioactive lipid mixtures with antioxidative and antimicrobial activities from vegetable and fish oil substances. The health-protective fatty acid compounds obtained after an extraction can be used as additives in functional food products.

6.3 | Fungal lipases in pulp and paper industries

The use of enzymes in the pulp and paper industries has been ranged extensively (Chandra et al., 2020). Farrell et al. (1997) report that "Pitch" is a term used to describe collectively the hydrophobic compounds of wood, namely triglycerides and waxes, which causes severe problems for production in this field. A unique enzymatic pitch control system used in lipases has been developed to degrade triglycerides present in mechanical pulp slurry (Singh & Mukhopadhyay, 2012). For example, a recombinant lipase (the Resinase A) expressed in *Aspergillus* sp from Novozymes A/S and another lipase obtained from *C. rugosa* are used as pitch controls in paper industry (Mehta et al., 2017; Singh & Mukhopadhyay, 2012). Similarly, a method has been developed by one of Japan's major paper industries, "Nippon", to manage contamination from wood pitch by effecting their hydrolysis (90%) using fungal lipase from *Candida rugosa* (Patel et al., 2019).

Resin is frequently detected in pulp and paper processing. This fact can be the result of its deposition on the paper stock, raw material in the storage tank, and oils from the roller resin binder. All these factors may cause paper destruction, which is an unstable and downtime operation. Resins and oils also present obstacles with respect to machine cleaning and protection, and typically result in great inconvenience. Resin deposition will also reduce the effectiveness of washing, screening, and purification of pulp. Lipase might be employed to eliminate esters from pulp, and consequently, improving the quality and production capacity (Horchani et al., 2012).

In the papermaking industry, adding fungal lipases can eliminate only the contaminating resins and oils in the paper. This will provide the reduction of breakage and guarantee paper quality and output (A. F. Almeida et al., 2018). Lipase can also treat anion residue and bitumen deposition in papermaking so as to avoid negative effects on the operation of papermaking equipment (Demuner et al., 2011; Liu et al., 2012).

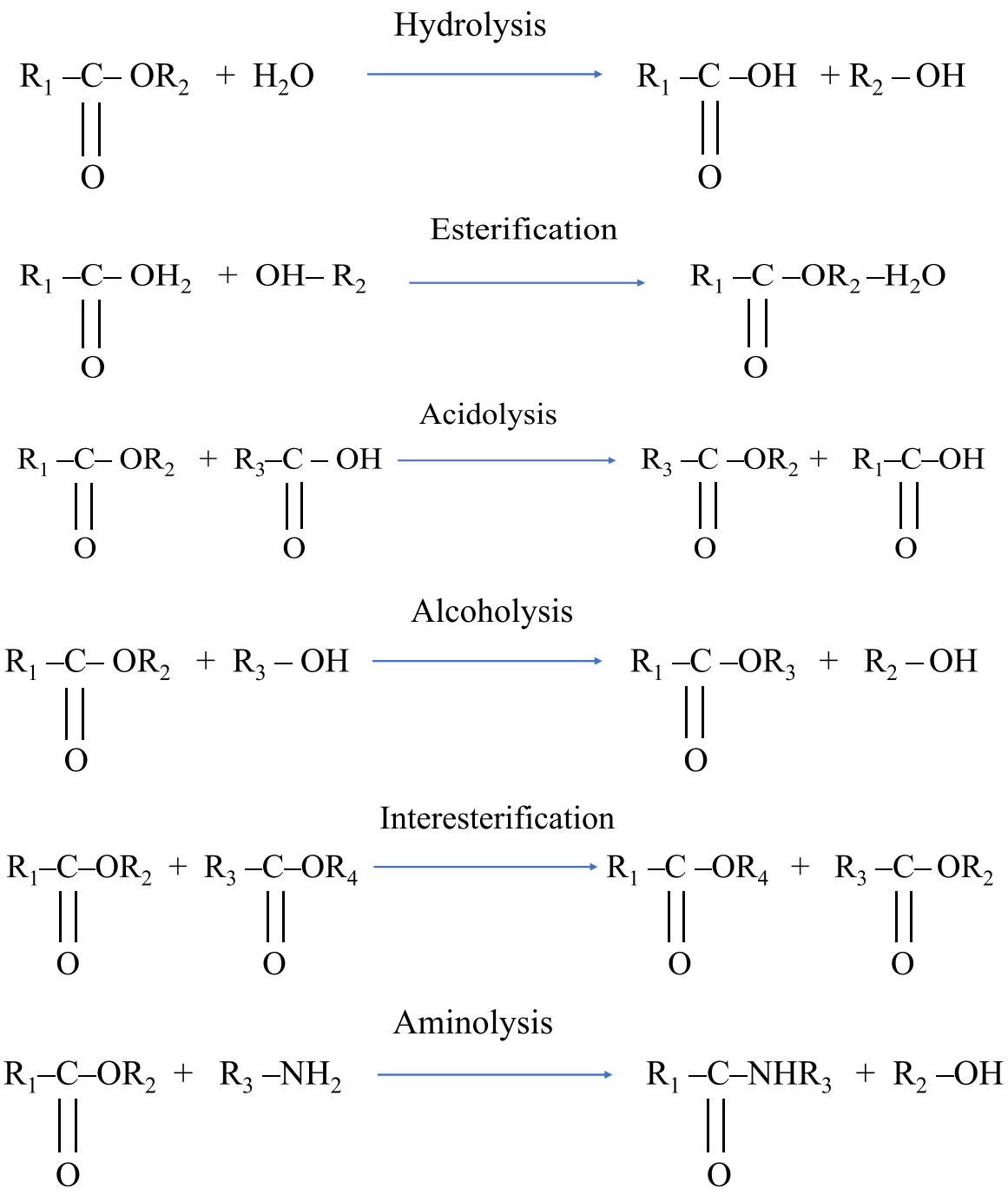

FIGURE 4 Diverse lipase-mediated reactions

6.4 | Use of fungal lipase in textile industry

Fungal lipases are widely used in the leather Industry, since they are able to transform the natural fats present in the skins into free fatty acids and triacylglycerols (Pérez et al., 2019). These fungal enzymes are also used to help in the removal of size lubricants to provide the fabric with better absorbency for enhanced levelness of dyeing. Additionally, some commercial preparations used for the desizing of denim and other cotton fabrics contain fungal lipases (Hasan et al., 2006).

Afşar and Cetinkaya (2008) prove that polyester is one of the most valued fabrics in the industrial field, due to its high resistance to stretch, stains, and abrasion. Moreover, enzymatic treatments of polyester fiber by lipases help to increase the latter's ability to absorb dyes and cationic chemical compound that aid in tissue preservation, antimicrobial, and chemical formulations. For example, *Aspergillus oryzae* lipase is able to modify PET (polyethylene terephthalate) fabrics, improving their polarity and anti-static ability (Mehta et al., 2017; X. Wang et al., 2008).

6.5 | Fungal lipases in detergent industry

Fungal lipases present a main role when they are used as additives in household detergents and for industrial laundry (Mehta et al., 2017). Other studies have shown that these fungal lipolytic enzymes can reduce an environmental load of detergent products as they gain energy that enables the use of a lower wash temperature (Singh & Mukhopadhyay, 2012; Vakhlu & Kour, 2006). In addition, lipases from *Aspergillus oryzae*, *Humicola lanuginosa*, and *R. oryzae*are used in detergents, allowing better washing performances and energy saving (Hasan et al., 2010).

Das et al. (2016) tested the ability of *A. tamarii* lipase to clean the peanut oil stain used for deep frying. These authors emphasized that the lipolytic enzyme was able to improve the capacity of detergents to eliminate stains. Nevertheless, they stated that the effectiveness of removing oil stains in the presence of detergent and enzyme was the same in cold and hot water.

A previous study showed that a lipase produced by *Fusarium oxysporum* increased the cleaning efficacy with various commercial detergents (Prazeres et al., 2006). Hemachander and Puvanakrishnan (2000) also reported that the presence of detergents with a lipase produced by *Ralstonia pickettii* increased the effectiveness of removing stains by 24%–27% compared to its treatment with only detergents.

6.6 | Production of biodegradable polymers

Pérez et al. (2019) demonstrate that biopolymers such as polyphenols, polysaccharides, and polyesters show a considerable degree of diversity and complexity. Actually, these biopolymers have become a major focus of researchers because they are biodegradable and are produced from renewable natural resources.

In addition, fungal lipases are used as biocatalysts in the production of useful biodegradable compounds. To reduce the viscosity of biodiesel in winter use, 1-butyl oleate is synthesized by direct esterification of butanol and oleic acid (Singh & Mukhopadhyay, 2012). This compound minimizes the viscosity of biodiesel allowing a better use at low temperatures. Similarly, trimethylolpropane esters are also synthesized as lubricants by some lipolytic enzymes (Hasan et al., 2006).

In addition, the performance of fungal lipases as biocatalysts in the synthesis of esters and transesterification reactions in organic solvent systems allows the use of these lipolytic enzymes to catalyze the degradation of polyesters (Pérez et al., 2019). Besides, functional polyesters are synthesized through the specific catalysis of lipases, and their properties and functions are evaluated. Enantio- and regioselective polycondensations by fungal lipases have produced chiral and sugar-containing polyesters, respectively (Chandra et al., 2020; Uyama & Kobayashi, 2002).

6.7 | Fungal lipases as biosensors

A biosensor based on the enzyme-catalyzed dissolution of biodegradable polymer films has been developed. Three polymer-enzyme systems are investigated (Sumner et al., 2001):

- A dextran hydrogel, which is degraded by dextranase.
- A poly (ester amide), which is degraded by the proteolytic enzyme α-chymotrypsin.
- A poly (trimethylene) succinate, degraded by a lipase.

Several applications of such sensor systems are based on the detection of the enzyme concentration and the construction of disposable enzyme-based immunosensors using the polymer-degrading enzyme as a biocatalyst label (Singh & Mukhopadhyay, 2012; Sumner et al., 2001).

As biosensors and fungal lipases have been proved to be highly practical in some industrial applications, different methods have been recently developed using lipolytic enzymes. For example, in the pharmaceutical and food industries, the determination of triglyceride levels present in a sample of human fluids or food has been possible by using lipases from fungus. Thanks to their unique properties, which make them able to convert the triglycerides into glycerol, the latter compound can be quantified using several methods such as chemical, enzymatic, or colorimetric methods (Pérez et al., 2019).

In addition, fungal lipases as biosensors are also used to determine lipid levels in the clinical diagnosis (Saxena et al., 2004). For example, *Candida rugosa* lipase is developed as a DNA probe (Benjamin and Pandey, 2001). In another research, the same fungal enzyme is immobilized on a mesoporous silica as a matrix for the detection of triglyceride levels (X. R. Huang et al., 2001). Moreover, the *Candida rugosa* strain is used as a catalyst and a biosensor for the detection of β-hydroxyacid esters and triglycerides in blood serum (Califano et al., 2014; Mehta et al., 2017).

In some other studies, the *C. rugosa* lipase is also developed as a potentiometric biosensor and applied to detect both triglycerides and organophosphorous pesticides (Kartal et al., 2007; Ouertani et al., 2012).

6.8 | Fungal lipases in cosmetics and perfume industries

Marion and Oliver (2013) report that lipases have been used in the cosmetic sector for personal care such as cleaning, softening, aroma, and coloring. Additionally, K. K. Kim et al. (1997) state that a patent Nippon Oil and Fats have been obtained from a preparation of propylene-glycerol mono-fatty acid ester in the presence of lipases. This ester has been used as emulsifier and a pearling agent in cosmetic and food fields. Besides, lipases present a beneficial role in hair waving preparation (Momsia & Momsia, 2013) and are used as

ingredients in topical anti-obese creams (August, 1972) or in oral administration (Andualema & Gessesse, 2012).

In addition, Mouad et al. (2016) also report that immobilized *Rhizomucor meihei* lipase is used as a biocatalyst in personal care products such as skin creams and bath oils, and so forth. Moreover, a lipase isolated from *Candida antarctica B* synthesizes amphiphilic compounds received great attention in cosmetic industry due to a range of beneficial properties for skin (Mouad et al., 2016).

Another nonspecific lipase derived from *Candida antartica*, marketed as Novozym 435, was determined to be highly suitable for the enzymatic synthesis of isopropyl myristate (Vadgama et al., 2015). Immobilized *Rhizomucor meihei* lipase was used as a biocatalyst in personal care products such as skin and sun-tan creams, bath oils, and so forth.

Interestingly, immobilized *Candida antarctica B* lipase (Novozym 435) is successfully used for the acylation of retinol by reverse hydrolysis, alcoholysis, acidolysis, and inter-esterification with several bifunctional acylating agents (Rejasse et al., 2003). Retinyl palmitate is also synthesized in organic solvents by an immobilized *Candida* sp. lipase (Yin et al., 2006; Ouertani et al., 2012).

Similarly, hollow spheres of inorganic silica have been found to be promising materials for fungal lipase encapsulation due to their high strength, low cost, and the pleasing hand feel of the resulting cosmetic formulations (Ansorge-Schumacher & Thum, 2013; Pérez et al., 2019).

Furthermore, lipases used in the medical and pharmaceutical sectors can be isolated from various sources such as bacteria, fungi, and some protozoa. Lipases from the fungus *C. rugosa* and immobilized on nylon supports in the presence of organic solvents are capable of synthesizing lovastatin, a drug widely used in the treatment of serum cholesterol reduction (Mehta et al., 2017). Moreover, S. Sharma and Kanwar (2014) who have isolated a lipase from *Serratia marcescens* showed that the latter is able to produce a chiral 3-phenylglycidic acid through an enantioselective hydrolysis. This is an intermediate compound in the synthesis of diltiazem hydrochloride, a drug used in many countries as a coronary vasodilator (Pérez et al., 2019).

Another important aspect shows that fungal lipases, due to their ability to emulsify fats, can be used in the treatment of digestive disorders together with other enzymes like proteases (Hasan et al., 2006). In addition, chirality is a key feature in the efficiency of many pharmaceutical products, and consequently, single enantiomers of chiral intermediates are produced by fungal lipases. The use of this type of lipolytic enzymes has become increasingly widespread in the pharmaceutical industry (Kazi et al., 2010; Okuma et al., 2009).

Recently, Mehta et al. (2017) have shown that lipases isolated from fungi can be used as therapeutics in the treatment of gastrointestinal disturbances, dyspepsias, and cutaneous manifestations of digestive allergies.

6.9 | Fungal lipases as diagnostic tools (in medical and pharma sectors)

Lipases play a great role as diagnostic tools because they increase levels that indicate some diseases. These are important drug targets or marker enzymes in the medical sector. In fact, lipase levels in blood serum are used as a diagnostic tool for detecting pathological situations such as pancreatic injury and acute pancreatitis (Jawed et al., 2019). Lipase activity/level determination is also important in the diagnosis of heart ailments (McNeill et al., 1991; Singh & Mukhopadhyay, 2012).

6.10 | Fungal lipases in biodiesel production

Biofuels, including biodiesel, have become a renewable alternative to fossil fuels (Bilal et al., 2021; Shuba & Kifle, 2018). Biodiesel is a group of esters produced by transesterification reactions between fatty acids and an alcohol in the presence of a catalyst (Filho et al., 2019; Ismail et al., 2021; Figure 5). The biodiesel produced from waste and nonedible vegetable oil helps to minimize the risks of food byproducts pollution and boost energy security, and is considered as an important step in recycling waste oil (Gashaw et al., 2015; Narwal & Gupta, 2013).

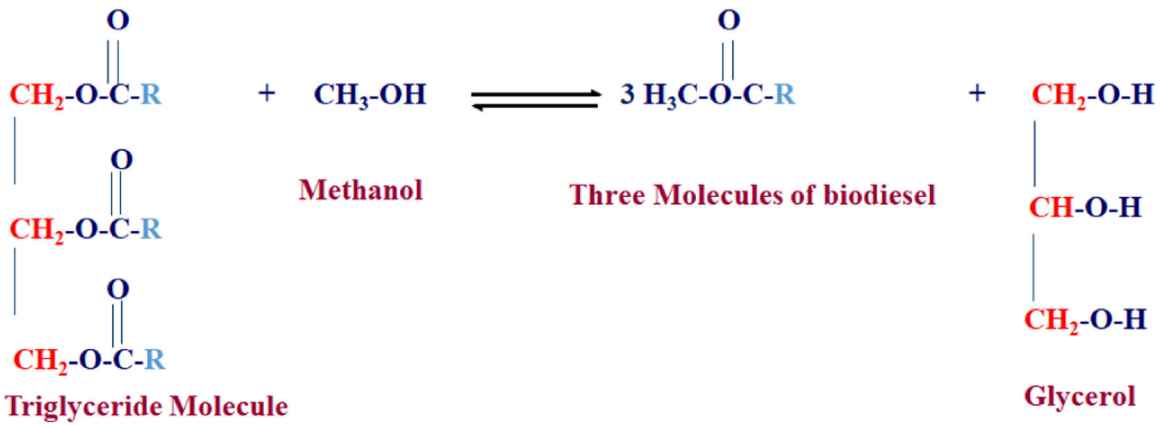

FIGURE 5 Schematic illustration of lipase-catalyzed biodiesel production

Biodiesel can be obtained from different sources such as vegetable oils (from soybean, jatropha, rapeseed, palm, sunflower, corn, peanut, canola, and cottonseed), animal fat (bovine tallow, lard), used cooking oil, grease (trap grease, float grease), and algae (Filho et al., 2019; Pérez et al., 2019).

Nowadays, biodiesel is produced principally by alkaline and supercritical fluid catalysis (Mandolesi De Araújo et al., 2013). Biocatalysis by lipolytic enzymes has been used in the industrial production of biodiesel (Q. Li et al., 2020; Santos et al., 2020; Talavari et al., 2020). Edible waste oil and methanol are also converted into biodiesel and glycerin via the actions of fungal lipases (Karmee et al., 2015). For instance, lipase produced by *T. lanuginosus*-catalyzed methanolysis of waste oil for the production of biodiesel (K. Tian et al., 2017). Using the commercial lipase Novozyme® 435, edible waste oil was used as raw material to produce biodiesel via enzyme-catalyzed regeneration (Sorte et al., 2020). Moreover, M. Tian et al. (2021) proved that *Rhizomucor miehei* lipase, which is a single-chain α/β-type protein, was found to be widely used in biodiesel production due to its catalytic activity and methanol tolerance. One year later, the same authors have used a semirational directed evolution method combined with N-glycosylation to enhance catalytic activity and methanol tolerance (M. Tian et al., 2022). Mutant N267 of *R. miehei* lipase retained 64% activity after incubation in 50% methanol for 8 h, which was 48% greater than the wild type. The same mutant achieved biodiesel yields of 99.33% (colza oil) and 81.70% (waste soybean oil) for 24 h, which was much higher than WT (51.6% for rapeseed oil and 44.73% for wasted soybean oil).

Besides, the production of biodiesel is obtained by the employ of different immobilized fungal lipases such as *B. cepacia* and *C. antarctica* lipases on magnetic nanoparticle (G. Li et al., 2017; Mehrasbi et al., 2017), *C. rugosa* lipase on Fe_3O_4 nanocomposite (Xie & Huang, 2018), *R. oryzae* lipase on magnetic graphene oxide (Nematian et al., 2020), *C. antarctica* and *R. miehei* lipases on silica (Shahedi et al., 2019), and *Fusarium heterosporum* lipase on bio-support beads (Quayson et al., 2020).

Table 3 shows some promising results of the use of fungal lipase in the biodiesel field.

6.11 | Other sectors

In recent years, lipases have been applied in soaking, dehairing, bating, and degreasing operations in leather making (Mehta et al., 2017). In addition, other studies have confirmed the use of lipases in bioremediation such as environmental management (in waste, effluent and sewage treatment) (Chandra et al., 2020; Pérez et al., 2019; Singh & Mukhopadhyay, 2012). Furthermore, Gupta et al. (2015) state that lipolytic enzymes have shown a beneficial role in cellular physiology and biofilm use.

Promising strategies to increase the productivity of bioprocesses and reduce costs is the production of recombinant lipases by heterogonous expression systems for industrial applications (lipase engineering) have been reported (Valero, 2012). For example, an overview on recombinant *Rhizopus oryzae* lipase, one of the most common lipases used in biocatalysis, is shown. In this case, *P. pastoris* represents the most promising host system (Valero, 2012). Additionally, the demand and market of enzymes used in the industrial field, emerging techniques of enzyme engineering, and high throughput technologies for enzyme screening have increased (Madhavan et al., 2020). In such cases, recombinant forms are favored to conquer the demand of purification protocols (Lotti & Alberghina, 2007). For example, some new results have shown that N-glycosylation modification in the α-helix structure of *Rhizomucor miehei* lipase proved to be an effective strategy for improving the performance of this lipolytic enzyme in biodiesel applications (M. Tian et al., 2021).

Likewise, nowadays, the metagenome-based sequencing technologies are very powerful for the identification of several novel biocatalysts and for analyzing the dark matter to find other novel natural beneficial products (Verma et al., 2021).

7 | HOST FUNGAL STRAINS USED IN HETEROLOGOUS LIPASE PRODUCTION

Compared with bacteria, the fungi hosts are considered as a supplementary approach. In this topic, strains such as genera *Mucor*, *Rhizopus*, *Geotrichum*, *Rhizomucor*, *Aspergillus*, and *Penicillium* are the major lipase-producing sources (Table 4).

Higher plasmid copy number, plasmid stability, and higher ability to secrete extracellular proteins as compared to other heterologous hosts are unique properties typical to Filamentous fungi. Among different fungi species, *Aspergillus* sp. And *Trichoderma* sp. are generally used for lipase production in several application fields (Adachi et al., 2011, 2013). Prathumpai et al. (2004) reported the presence of two recombinant strains of *Aspergillus niger* producing a heterologous lipase from *Thermomyces lanuginosus* using the TAKA amylase promoter from *Aspergillus oryzae*. The most studied filamentous fungi host is *Aspergillus oryzae*, for example, CalB with high esterification activity has been heterologously produced by *Aspergillus oryzae* and immobilized for whole-cell biocatalyst for enzymatic biodiesel production (Prathumpai et al., 2004).

Moreover, *Trichoderma reesei* has gained attention for recombinant protein production in recent years using cbh1 promoter (B. Wang & Xia, 2011), and is subsequently recommended as a new host for recombinant lipase production.

Furthermore, G. Li et al. (2018) highlighted a strategy that combined computational algorithms to predict single-point mutations and disulfide bonds in RML without losing its catalytic activity. Thanks to this method, an RML variant with a significantly enhanced thermostability was obtained. This study provides a competitive alternative for wild-type RML in practical applications and further a rapid and a new approach for thermostability engineering.

TABLE 3 Summary of the biodiesel production with some fungal lipase as a main biocatalyst

Substrates	Lipase	Immobilization support	Reactor type	Stepwise addition	Biodiesel generation	Yield (Y)-conversion/ operational stability	Ref.
Soybean, safflower, linseed, corn, and palm oil	*Candida* sp. *99–125*	Cotton membrane	-	-	-	Y: ≥88.5%	Tan et al. (2006)
Soybean oil	*Rhizopus oryzae* mixed with *Candida rugosa*	Silica gel	-	-	-	Y: >99%	D. H. Lee et al. (2006)
Waste activated, bleaching earth	*Candida cylindracea*	-	-	-	-	Y: 97%	Park et al. (2008)
Sun flower oil	*Candida antarctica*	Acrylic resin	-	-	-	Y: >99%	Ognjanovic et al. (2009)
Soybean oil	*Candida antarctica*	Macroporous acrylic resin	-	-	-	Y: 84.9%	(Seong et al. (2011)
Soybean oil	*Rhizomucor miehei* mixed with *Thermomyces lanuginosus* (TLL)	-	-	-	-	Y: 90%	Rodrigues and Ayub (2011)
Pomace oil	*Thermomyces lanuginosus*	Olive pomace	-	-	-	Y: 93%	Yücel (2011)
Soybean oil	*Burkholderia cenocepacia*	Macroporous resin NKA	-	-	-	Y: 98%	
Palm oil	*Candida antarctica*	Macroporous acrylic resin	-	-	-	Y: 96%	Talukder et al. (2011)
Pistacia chinensis bge seed oil	*Rhizopus oryzae*	Macroporous resin	-	-	-	Y: 92%	X. Li et al. (2012)
Pistacia chinensis bge seed oil	*Rhizopus oryzae*	Anion exchange resin	-	-	-	Y: 94%	X. Li et al. (2012)
Waste cooking oil	*Rhizopus oryzae*	Calcium alginate beads	-	-	-	Y: 84%	Balasubramaniam et al. (2012)
Waste cooking oil	*Candida Antarctica*	Macroporous acrylic resin	-	-	-	Y: 94.3%	Hama et al. (2013)
Corn oil	*Candida antarctica*	Macroporous acrylic resin	-	-	-	Y: 81.3%	Ciftci and Temelli (2013)
WCO + iso-propanol	proROL	WCB IE into calcium alginate beads	BR	-	3rd	Y: 71%	Bharathiraja et al. (2014)
WCO + iso-butanol	proROL	WCB IE into calcium alginate beads	BR	-	3rd	Y: 62%	Bharathiraja et al. (2014)
WCO + iso-amyl alcohol	proROL	WCB IE into calcium alginate beads	BR	-	3rd	Y: 43%	Bharathiraja et al. (2014)
Nannochloropsis gaditana algal lipid	*Rhizopus oryzae*	Macroporous acrylic resin	-	-	-	Y: 94.7%	Navarro López et al. (2015)
Oil extracted from *Chlorella vulgaris* + MeOH	proROL	IA into MGO-AP	BR	Yes	3rd	Y: 54% OS: after 5 cycles Y decreased to 25%	Nematian et al. (2020)

Abbreviations: BR, red reactor; IE, entrapment immobilization; MeOH, methanol; MGO-AP, magnetic nanoparticles and graphene oxide-3-aminopropyl triethoxysilane; ROL, *Rhizopus oryzae* lipase; WCB, whole cell biocatalyst; WCO, waste cooking oil.

TABLE 4 The main fungal host strains used for heterologous lipase production

Host strains from fungi	Source		References
	Genus	Species	
Aspergillus niger	*Thermomyces*	*T. lanuginosus*	Prathumpai et al. (2004)
Aspergillus Oryzae	*Fusarium* and *Aspergillus*	*F. heterosporum* and *A. oryzae*	Adachi et al. (2011) Adachi et al. (2013)
	Candida	*C. antarctica*	
Trichoderma reesei	*Fusarium*	*F. heterosporum*	Hama et al. (2007)
	Aspergillus	*A. niger*	Qin et al. (2012)
	Penicillium	*P. allii*	Bradner et al. (2003)

8 | HOST STRAIN ENGINEERING

To use lipases in several industrial applications, a scale-up lipase productivity is required and a number of approaches have been adopted for this purpose. In this respect, the various processes and metabolic engineering techniques to perform the production of fungal lipase are summarized below.

Commercial lipases are mainly obtained from extracellular lipases. Therefore, the optimization of these lipases is required for the genetic manipulation of host strains.

In some previous studies, the production of free-type lipase was focused, primarily, on the performance in batch cultures where the optimization of medium and operating conditions are the main parameters (Hwang et al., 2014). Recently, a huge increase of fungal lipase productivity *Cryptococcus flavescens* has been performed by a fed-batch fermentation process (Elegado et al., 2019).

In addition, some limitations are recorded in the production of wild-type lipases generally known by their low productivity and high cost. Besides, wild-type lipolytic enzymes typically lack optimal specificities and desirable catalytic properties for industrial feedstock.

Therefore, to meet the standards of quantity and manipulation of industrial processes, other alternatives such as cloning and the expression of the recombinant lipase genes to obtain significant amounts of pure lipases are to be opted for.

Hwang et al. (2014) showed that, promoter optimization is a commonly used technique which significantly improves the production of lipases. Gene modification that makes the genes adaptable for expression in the recombinant host cells has also been utilized. Chang et al. (2006) performed codon optimization on the lip3 gene and improved the lipase yield by 50- to 70-fold. Yaver et al. (2000) utilized a restriction enzyme-mediated integration (REMI) as a mutagen to generate insertion mutant libraries in a recombinant *Aspergillus oryzae* strain expressing *Thermomyces lanuginosus* lipase (Yaver et al., 2000). They found that the disruption of palB gene could result in increased lipase expression, while complementation of palB leads to a decrease in lipase production. These results proved that genetic modifications can be used to modulate the expression of heterologous proteins (Yaver et al., 2000).

Although the improvement of lipase production can be performed from the recombinant lipase, the recombinant protein yield is limited by many posttranslational events, such as disulfide bond formation, solubility, misfolding, secretion, proteolysis, and even the toxicity to host cells (Makrides, 1996). Thus, genetic and metabolic engineering can play a significant role to increase the production of the recombinant lipase by reducing or discarding these limitations.

In addition, lipase production can also be improved by the efficient and convenient techniques of scale-up fermentation. A significantly enhanced production of *Candida rugosa* lipase in the constitutive recombinant *Pichia pastoris* was achieved by Zhao et al. (2008) in both laboratory and pilot scales by the optimization of the fermentation conditions. In this research, fermentation was scaled up from 5 to 800 L using the exponential feeding, which was combined with pH-stat strategy and a two-stage fermentation strategy, which empowers an excellent balance between the expression of recombinant lipase and the growth of host cells. An optimum lipase activity of approximately 14,000 IU/ml was obtained and a cell weight of 500 g/L at the 800 L scale. In large-scale fermentation of recombinant lipases, the cell growth rate can be effectively controlled by tuning cell lyses and proteolytic sensitivity of the lipases (Narayanan & Chou, 2009).

The upgrading of lipase production by metabolic engineering has been a considerable interest in improving biofuels production (Atsumi & Liao, 2008; S. K. Lee et al., 2008). It has also been used in the amelioration of the production of therapeutic proteins (Dyer et al., 2002; Jordà et al., 2012).

To conclude, this review has covered some fungal host strains used for the production of lipase. Regardless of the hosts adopted, the application of metabolic engineering represents a profitable direction to maximize the production rate of lipase.

9 | DISCUSSION AND CONCLUSION

Until now, there have not been enough papers that deal with the fungal enzymes used as biocatalysts in the industrial field. Based on this topic, the isolation of lipolytic fungi is an alternative to discover novel species with high levels of lipase secretion, catalytic activity, high affinity for substrates, and high velocity of products obtained from hydrolysis and transesterification reactions due to their characteristics.

Lipase is often used in several industrial fields and has become a commercial enzyme. Although lipase can be produced from

microorganisms and plants, fungal lipases, which are obtained from various different media, are still poorly explored.

Additionally, the major benefit of fungal lipases is that they are simply acquiescent to separation because of their extracellular nature, which considerably decreases their overall cost and makes them more interesting than bacterial lipases. Moreover, it is important to study the optimization of the fungal lipase production to obtain better-quality new lipases that are produced less costly and have a wider range of applications in the industrial field.

However, the global demand of commercial enzymes, about 75% of which are hydrolytic enzymes (including lipases), is expected to rise by about 5% in the next decade (Dewan, 2017). Therefore, an increase in the availability of these enzymes is expected, which should significantly contribute to an important expansion of lipase use in many fields of applications (Contesini et al., 2020). This challenge can be addressed by screening for novel lipase-producing microorganisms and performing metabolic engineering.

In this respect, recent advances in screening techniques have enabled fast identification of high-yield of fungi microbes and the application of synthetic biology to maximize the lipase production, which is expected to overcome traditional engineering techniques and become a better alternative by using the most suitable features of natural and artificial microbial systems with some rational designs that are extensible, comprehensive, and efficient.

A promising field for future research is the integration of different techniques to develop desired characteristics in lipases, with low-cost production, making them excellent biocatalysts in industrial processes. Therefore, lipase immobilization strategies are growing rapidly and these by-products can also be used in several sectors, allowing for cheaper, more efficient and more reusable reaction conditions.

Moreover, immobilization protocols are used to increase the ability of lipase to withstand higher temperatures in the presence of organic solvents. Immobilization protocols can offer mechanical stability and the possibility of reusability. However, the formulation of desired immobilization system still needs further research (Balbool et al., 2021; Ismail et al., 2021; Santos et al., 2022).

It is worth mentioning that the major challenge is to commercially purify the new low-cost fungal lipases. A genuine effort from process engineers is essential to design specialized reactors and optimize cost-effective processes.

AUTHOR CONTRIBUTIONS

Amira Mahfoudhi and Prof. Adel Sayari conceived the presented idea. Amira Mahfoudhi prepared the manuscript. Dr. Sameh Ben Mabrouk and Prof. Adel Sayari contributed to the analysis of the results. Prof. Ahmed Fendri supervised the findings of the work. All authors approved the final draft of the manuscript.

ACKNOWLEDGMENTS

This study is a part of a doctoral thesis by Amira Mahfoudhi whose research was financially supported by the Ministry of Higher Education and Scientific Research (Tunisia) through a grant to the Laboratory of Biochemistry and Enzymatic Engineering of Lipases—Engineering National School of Sfax (ENIS).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of the study are available within the review.

ORCID

Ahmed Fendri http://orcid.org/0000-0001-5199-1893

REFERENCES

Abada, E. A. E.-M. (2008). Production and characterization of a mesophilic lipase isolated from *Bacillus stearothermophilus* AB-1. *Pakistan Journal of Biological Sciences*, *11*, 1100–1106.

Adachi, D., Hama, S., Nakashima, K., Bogaki, T., Ogino, C., & Kondo, A. (2013). Production of biodiesel from plant oil hydrolysates using an *Aspergillus oryzae* whole-cell biocatalyst highly expressing *Candida antarctica* lipase B. *Bioresource Technology*, *135*, 410–416.

Adachi, D., Hama, S., Numata, T., Nakashima, K., Ogino, C., Fukuda, H., & Kondo, A. (2011). Development of an *Aspergillus oryzae* whole-cell biocatalyst coexpressing triglyceride and partial glyceride lipases for biodiesel production. *Bioresource Technology*, *102*, 6723–6729.

Afşar, A., & Cetinkaya, F. (2008). A research on increasing the effectiveness of degreasing process by using enzymes. *Textile and Apparel*, *18*, 278–283.

Ali, Z., Li, T., Khan, M., Ali, N., & Zhang, Q. (2018). Immobilization of lipase on iron oxide organic/inorganic hybrid particles: A review article. *Reviews on Advanced Materials Science*, *53*(1), 106–117. https://10.1016/10.1515/rams-2018-0008

Almeida, A. F., Terrasan, C. R. F., Terrone, C. C., Tauk-Tornisielo, S. M., & Carmona, E. C. (2018). Biochemical properties of free and immobilized *Candida viswanathii* lipase on octyl-agarose support: Hydrolysis of triacylglycerol and soy lecithin. *Process Biochemistry*, *65*, 71–80. https://10.1016/10.1016/j.procbio.2017.10.019

Almeida, F. L. C., Castro, M. P. J., Travália, B. M., & Forte, M. B. S. (2021). Erratum to "Trends in lipase immobilization: Bibliometric review and patent analysis". *Process Biochemistry*, *110*, 37–51. https://doi.org/10.1016/j.procbio.2021.07.005

Andualema, B., & Gessesse, A. (2012). Microbial lipases and their industrial applications. *Biotechnology(Faisalabad)*, *11*, 100–118. https://doi.org/10.3923/biotech.2012.100.118

Ansorge-Schumacher, M. B., & Thum, O. (2013). Immobilised lipases in the cosmetics industry. *Chemical Society Reviews*, *42*, 6475–6490. https://doi.org/10.1039/c3cs35484a

Aslamkhan, A. G., Aslamkhan, A., & Ahearn, G. A. (2002). Preparation of metal ion buffers for biological experimentation: A methods approach with emphasis on iron and zinc. *Journal of Experimental Zoology*, *292*, 507–522. https://doi.org/10.1002/jez.10068

Asmat, S., Husain, Q., & Khan, M. S. (2018). A polypyrrole–methyl anthranilate functionalized worm-like titanium dioxide nano-composite as an innovative tool for immobilization of lipase: Preparation, activity, stability and molecular docking investigations. *New Journal of Chemistry*, *42*, 91–102. https://doi.org/10.1039/C7NJ02951A

Atsumi, S., & Liao, J. C. (2008). Metabolic engineering for advanced biofuels production from *Escherichia coli*. *Current Opinion in Biotechnology*, *19*, 414–419. https://doi.org/10.1016/j.copbio.2008.08.008

August, P. (1972). Lipase containing defatting creams (West Germany Patent, 2, 064 940).

Authority, E. N. F. (2014). Scientific opinion on lipase from a genetically modified strain of *Aspergillus oryzae* (strain NZYM-LH). *EFSA Journal*, *12*, 3763. https://doi.org/10.2903/j.efsa.2014.3763

Awan, U. F., Shafiq, K., Mirza, S., Ali, S., Rehman, A., & Haq, I. (2003). Mineral constituents of culture medium for lipase production by *Rhizopus oligosporous* fermentation. *Asian Journal of Plant Sciences*, *2*, 913–915. https://doi.org/10.3923/ajps.2003.913.915

Balasubramaniam, B., Sudalaiyadum Perumal, A., Jayaraman, J., Mani, J., & Ramanujam, P. (2012). Comparative analysis for the production of fatty acid alkyl esterase using whole cell biocatalyst and purified enzyme from *Rhizopus oryzae* on waste cooking oil (sunflower oil). *Waste Management*, *32*, 1539–1547.

Balbool, B. A., Abo Nouh, F. A., Gezaf, S. A., Mohamed, A. H., & Abdel-Azeem, A. M. (2021). Bioprospecting of thermophilic fungal enzymes and potential applications. In A. M. Abdel-Azeem, A. N. Yadav, N. Yadav, & Z. Usmani (Eds.), *Industrially Important Fungi for Sustainable Development* (pp. 347–375). Springer.

Bancerz, R., Osińska-Jaroszuk, M., Jaszek, M., Sulej, J., Wiater, A., Matuszewska, A., & Rogalski, J. (2018). Fungal polysaccharides as a water-adsorbing material in esters production with the use of lipase from *Rhizomucor variabilis*. *International Journal of Biological Macromolecules*, *118*, 957–964. https://doi.org/10.1016/j.ijbiomac.2018.06.162

Basheer, S. M., Chellappan, S., Beena, P. S., Sukumaran, R. K., Elyas, K. K., & Chandrasekaran, M. (2011). Lipase from marine *Aspergillus awamori* BTMFW032: Production, partial purification and application in oil effluent treatment. *New Biotechnology*, *28*, 627–638. https://doi.org/10.1016/j.nbt.2011.04.007

Benjamin, S., & Pandey, A. (2001). Isolation and characterization of three distinct forms of lipases from *Candida rugosa* produced in solid state fermentation. *Brazilian Archives of Biology and Technology*, *44*, 213–221. https://doi.org/10.1590/S1516-89132001000200016

Bharathiraja, B., Ranjithkumar, R., Chakravarthy, M., Yogendran, D., Vivek, P., Yuvaraj, D., & Palani, S. (2014). Kinetic analysis of fatty acid alkyl esters using whole cell biocatalyst and lipase catalyzed transesterification from waste cooking oil. *Asian Journal of Microbiology, Biotechnology & Environmental Sciences*, *16*, 745–752.

Bilal, M., Fernandes, C. D., Mehmood, T., Nadeem, F., Tabassam, Q., & Ferreira, L. F. R. (2021). Immobilized lipases-based nano-biocatalytic systems—A versatile platform with incredible biotechnological potential. *International Journal of Biological Macromolecules*, *175*, 108–122. https://doi.org/10.1016/j.ijbiomac.2021.02.010

Bornscheuer, U. T. (2018). Enzymes in lipid modification. *Annual Review of Food Science and Technology*, *9*, 85–103. https://doi.org/10.1146/annurev-food-030117-012336

Bornscheuer, U. T., Bessler, C., Srinivas, R., & Hari Krishna, S. (2002). Optimizing lipases and related enzymes for efficient application. *Trends in Biotechnology*, *20*, 433–437. https://doi.org/10.1016/S0167-7799(02)02046-2

Borrelli, G., & Trono, D. (2015). Recombinant lipases and phospholipases and their use as biocatalysts for industrial applications. *International Journal of Molecular Sciences*, *16*, 20774–20840. https://doi.org/10.3390/ijms160920774

Boudrant, J., Woodley, J. M., & Fernandez-Lafuente, R. (2020). Parameters necessary to define an immobilized enzyme preparation. *Process Biochemistry*, *90*, 66–80. https://doi.org/10.1016/j.procbio.2019.11.026

Brozzoli, V., Crognale, S., Sampedro, I., Federici, F., D'annibale, A., & Petruccioli, M. (2009). Assessment of olive-mill wastewater as a growth medium for lipase production by *Candida cylindracea* in bench-top reactor. *Bioresource Technology*, *100*, 3395–3402. https://doi.org/10.1016/j.biortech.2009.02.022

Buisman, G. J. H., Van Helteren, C. T. W., Kramer, G. F. H., Veldsink, J. W., Derksen, J. T. P., & Cuperus, F. P. (1998). Enzymatic esterifications of functionalized phenols for the synthesis of lipophilic antioxidants. *Biotechnology Letters*, *20*, 131–136. https://doi.org/10.1023/A:1005368222340

Burkert, J. (2004). Optimization of extracellular lipase production by *Geotrichum* sp. using factorial design. *Bioresource Technology*, *91*, 77–84. https://doi.org/10.1016/S0960-8524(03)00152-4

Califano, V., Bloisi, F., Aronne, A., Federici, S., Nasti, L., Depero, L., & Vicari, L. (2014). Biosensor applications of MAPLE deposited lipase. *Biosensors*, *4*, 329–339. https://doi.org/10.3390/bios4040329

Chandra, P., Enespa, R., Singh, R., & Arora, P. K. (2020). Microbial lipases and their industrial applications: A comprehensive review. *Microbial Cell Factories*, *19*, 169. https://doi.org/10.1186/s12934-020-01428-8

Chang, S. W., Lee, G. C., & Shaw, J. F. (2006). Efficient production of active recombinant *Candida rugosa* LIP3 lipase in *Pichia pastoris* and biochemical characterization of the purified enzyme. *Journal of Agricultural and Food Chemistry*, *54*, 5831–5838. https://doi.org/10.1021/jf060835e

Ciftci, O. N., & Temelli, F. (2013). Enzymatic conversion of corn oil into biodiesel in a batch supercritical carbon dioxide reactor and kinetic modeling. *The Journal of Supercritical Fluids*, *75*, 172–180. https://doi.org/10.1016/j.supflu.2012.12.029

Comménil, P., Belingheri, L., Sancholle, M., & Dehorter, B. (1995). Purification and properties of an extracellular lipase from the fungus *Botrytis cinerea*. *Lipids*, *30*, 351–356. https://doi.org/10.1007/BF02536044

Contesini, F. J., Davanço, M. G., Borin, G. P., Vanegas, K. G., Cirino, J. P. G., Melo, R. R., Mortensen, U. H., Hildén, K., Campos, D. R., & Carvalho, P. O. (2020). Advances in recombinant lipases: Production, engineering, immobilization and application in the pharmaceutical industry. *Catalysts*, *10*, 1032. https://doi.org/10.3390/catal10091032

Coradi, G. V., da Visitação, V. L., de Lima, E. A., Saito, L. Y. T., Palmieri, D. A., Takita, M. A., de Oliva Neto, P., & de Lima, V. M. G. (2013). Comparing submerged and solid-state fermentation of agro-industrial residues for the production and characterization of lipase by *Trichoderma harzianum*. *Annals of Microbiology*, *63*, 533–540. https://doi.org/10.1007/s13213-012-0500-1

Cordova, J., Nemmaoui, M., Ismaïli-Alaoui, M., Morin, A., Roussos, S., Raimbault, M., & Benjilali, B. (1998). Lipase production by solid state fermentation of olive cake and sugar cane bagasse. *Journal of Molecular Catalysis B: Enzymatic*, *5*, 75–78. https://doi.org/10.1016/S1381-1177(98)00067-8

Das, A., Shivakumar, S., Bhattacharya, S., Shakya, S., & Swathi, S. S. (2016). Purification and characterization of a surfactantcompatible lipase from *Aspergillus tamarii* JGIF06 exhibiting energy-efficient removal of oil stains from polycotton fabric. *3Biotech*, *6*, 131.

de Castro, F. F., Pinheiro, A. B. P., Nassur, C. B., & Barbosa-Tessmann, I. P. (2017). Mycelium-bound lipase from a locally isolated strain of *Aspergillus westerdijkiae*. *Biocatalysis and Agricultural Biotechnology*, *10*, 321–328. https://doi.org/10.1016/j.bcab.2017.04.009

Demuner, B. J., Pereira Junior, N., & Antunes, A. M. S. (2011). Technology prospecting on enzymes for the pulp and paper industry. *Journal of technology management & innovation*, *6*, 148–158. https://doi.org/10.4067/S0718-27242011000300011

Dewan, S. S. (2017). *Global markets for enzymes in industrial applications*. BCC Research.

Dutra, J. C. V., da C. Terzi, S., Bevilaqua, J. V., Damaso, M. C. T., Couri, S., Langone, M. A. P., & Senna, L. F. (2008). Lipase production in solid-state fermentation monitoring biomass growth of *Aspergillus niger* using digital image processing. *Applied Biochemistry and Biotechnology*, *147*, 63–75. https://doi.org/10.1007/s12010-007-8068-0

Dyer, J., Chapital, D., Kuan, J., Mullen, R., & Pepperman, A. (2002). Metabolic engineering of *Saccharomyces cerevisiae* for production of

novel lipid compounds. *Applied Microbiology and Biotechnology*, *59*, 224–230. https://doi.org/10.1007/s00253-002-0997-5

Elegado, F., Legaspi, C. L., Paet, J. M., Querubin, F., Tolentino, J. E., Vilela, J., Paguio, A. Jr., Maloles, J., & Zarate, J. (2019). Screening, identification and optimization of extracellular lipase production of yeast (Cryptococcus flavescens) isolated from a tree canopy fern in the Mount Makiling Forest Reserve, Philippines. *AIP Conf Proc*, *2155*, 020029. https://doi.org/10.1063/1.5125533

Enespa, I., Chandra, P., & Singh, D. P. (2022). Sources, purification, immobilization and industrial applications of microbial lipases: An overview. *Critical Reviews in Food Science and Nutrition*, 1–34. https://doi.org/10.1080/10408398.2022.2038076

Eş, I., Vieira, J. D. G., & Amaral, A. C. (2015). Principles, techniques, and applications of biocatalyst immobilization for industrial application. *Applied Microbiology and Biotechnology*, *99*, 2065–2082. https://doi.org/10.1007/s00253-015-6390-y

Facin, B. R., Melchiors, M. S., Valério, A., Oliveira, J. V., & Oliveira, D. (2019). Driving immobilized lipases as biocatalysts: 10 years state of the art and future prospects. *Industrial & Engineering Chemistry Research*, *58*, 5358–5378. https://doi.org/10.1021/acs.iecr.9b00448

Facin, B. R., Valério, A., Bresolin, D., Centenaro, G., de Oliveira, D., & Oliveira, J. V. (2018). Improving reuse cycles of *Thermomyces lanuginosus* lipase (NS-40116) by immobilization in flexible polyurethane. *Biocatalysis and Biotransformation*, *36*, 372–380. https://doi.org/10.1080/10242422.2018.1458842

Falony, G., Armas, J. C., Mendoza, J. C. D., & Hernández, J. L. M. (2006). Production of extracellular lipase from *Aspergillus niger* by solid-state fermentation. *Food Technology and Biotechnology*, *44*, 235–240.

Farrell, R. L., Hata, K., & Wall, M. B. (1997). Solving pitch problems in pulp and paper processes by the use of enzymes or fungi. In K.E.L. Eriksson (Ed.), *Biotechnology in the pulp and paper industry* (Vol. 57, pp. 197–212).

Ferrer, M., Soliveri, J., Plou, F. J., López-Cortés, N., Reyes-Duarte, D., Christensen, M., Copa-Patiño, J. L., & Ballesteros, A. (2005). Synthesis of sugar esters in solvent mixtures by lipases from *Thermomyces lanuginosus* and *Candida antarctica B*, and their antimicrobial properties. *Enzyme and Microbial Technology*, *36*, 391–398. https://doi.org/10.1016/j.enzmictec.2004.02.009

Fibriana, F., Upaichit, A., & Hongpattarakere, T. (2013). *Optimization of bioprocess variables for fungal lipase production using statistical experimental design: A mini review*. In ASEAN/Asian Academic Society International Conference Proceeding Series, Vol. 2 (pp. 64–67).

Filho, D. G., Silva, A. G., & Guidini, C. Z. (2019). Lipases: Sources, immobilization methods, and industrial applications. *Applied Microbiology and Biotechnology*, *103*, 7399–7423. https://doi.org/10.1007/s00253-019-10027-6

Fischer, M. (2003). The lipase engineering database: A navigation and analysis tool for protein families. *Nucleic Acids Research*, *31*, 319–321. https://doi.org/10.1093/nar/gkg015

Fu, J., Leiros, H. K. S., de Pascale, D., Johnson, K. A., Blencke, H. M., & Landfald, B. (2013). Functional and structural studies of a novel cold-adapted esterase from an Arctic intertidal metagenomic library. *Applied Microbiology and Biotechnology*, *97*, 3965–3978. https://doi.org/10.1007/s00253-012-4276-9

Gashaw, A., Getachew, T., & Teshita, A. (2015). A review on biodiesel production as alternative fuel. *Journal of Forest Products and Industries*, *4*, 80–85.

Gaur, R., Gupta, A., & Khare, S. K. (2008). Purification and characterization of lipase from solvent tolerant *Pseudomonas aeruginosa* PseA. *Process Biochemistry*, *43*, 1040–1046. https://doi.org/10.1016/j.procbio.2008.05.007

Ghide, M. K., Li, K., Wang, J., Abdulmalek, S. A., & Yan, Y. (2022). Immobilization of *Rhizomucor miehei* lipase on magnetic multiwalled carbon nanotubes towards the synthesis of structured lipids rich in sn-2 palmitic acid and sn-1,3 oleic acid (OPO) for infant formula use. *Food Chemistry*, *390*, 133171. https://doi.org/10.1016/j.foodchem.2022.133171

Gombert, A. K., Pinto, A. L., Castilho, L. R., & Freire, D. M. G. (1999). Lipase production by *Penicillium restrictum* in solid-state fermentation using babassu oil cake as substrate. *Process Biochemistry*, *35*, 85–90. https://doi.org/10.1016/S0032-9592(99)00036-9

Griebeler, N., Polloni, A. E., Remonatto, D., Arbter, F., Vardanega, R., Cechet, J. L., Di Luccio, M., de Oliveira, D., Treichel, H., Cansian, R. L., Rigo, E., & Ninow, J. L. (2011). Isolation and screening of lipase-producing fungi with hydrolytic activity. *Food and Bioprocess Technology*, *4*, 578–586. https://doi.org/10.1007/s11947-008-0176-5

Gupta, R., Kumari, A., Syal, P., & Singh, Y. (2015). Molecular and functional diversity of yeast and fungal lipases: Their role in biotechnology and cellular physiology. *Progress in Lipid Research*, *57*, 40–54. https://doi.org/10.1016/j.plipres.2014.12.001

Gupta, R., Rathi, P., & Bradoo, S. (2003). Lipase mediated upgradation of dietary fats and oils. *Critical Reviews in Food Science and Nutrition*, *43*, 635–644. https://doi.org/10.1080/10408690390251147

Gutarra, M. L. E., Godoy, M. G., Castilho, L. R., & Freire, D. M. G. (2007). Inoculum strategies for *Penicillium simplicissimum* lipase production by solid-state fermentation using a residue from the babassu oil industry. *Journal of Chemical Technology & Biotechnology*, *82*, 313–318. https://doi.org/10.1002/jctb.1674

Hama, S., Yoshida, A., Tamadani, N., Noda, H., & Kondo, A. (2013). Enzymatic production of biodiesel from waste cooking oil in a packed-bed reactor: An engineering approach to separation of hydrophilic impurities. *Bioresource Technology*, *135*, 417–421. https://doi.org/10.1016/j.biortech.2012.06.059

Handrick, R., Reinhardt, S., Focarete, M. L., Scandola, M., Adamus, G., Kowalczuk, M., & Jendrossek, D. (2001). A new type of thermoalkalophilic hydrolase of *Paucimonas lemoignei* with high specificity for amorphous polyesters of short chain-length hydroxyalkanoic acids. *Journal of Biological Chemistry*, *276*, 36215–36224. https://doi.org/10.1074/jbc.M101106200

Hasan, F., Shah, A. A., & Hameed, A. (2006). Industrial applications of microbial lipases. *Enzyme and Microbial Technology*, *39*, 235–251. https://doi.org/10.1016/j.enzmictec.2005.10.016

Hasan, F., Shah, A. A., Javed, S., & Hameed, A. (2010). Enzymes used in detergents: Lipases. *African Journal of Biotechnology*, *9*(31), 4836–4844.

Hemachander, C., & Puvanakrishnan, R. (2000). Lipase from *Ralstonia pickettii* as an additive in laundry detergent formulations. *Process Biochemistry*, *35*, 809–814. https://doi.org/10.1016/S0032-9592(99)00140-5

Hernández-Rodríguez, B., Córdova, J., Bárzana, E., & Favela-Torres, E. (2009). Effects of organic solvents on activity and stability of lipases produced by thermotolerant fungi in solid-state fermentation. *Journal of Molecular Catalysis B: Enzymatic*, *61*, 136–142. https://doi.org/10.1016/j.molcatb.2009.06.004

Horchani, H., Aissa, I., Ouertani, S., Zarai, Z., Gargouri, Y., & Sayari, A. (2012). *Staphylococcal* lipases: Biotechnological applications. *Journal of Molecular Catalysis B: Enzymatic*, *76*, 125–132. https://doi.org/10.1016/j.molcatb.2011.11.018

Huang, J., Yang, Z., Guan, F., Zhang, S., Cui, D., Guan, G., & Li, Y. (2013). A novel mono-and diacylglycerol lipase highly expressed in *Pichia pastoris* and its application for food emulsifier preparation. *Process Biochemistry*, *48*, 1899–1904. https://doi.org/10.1016/j.procbio.2013.08.021

Huang, X. R., Li, Y. Z., Yang, G. L., Liu, L. L., Qu, Y. B., & Zhang, W. J. (2001). A novel method for fabrication of a glass-electrode-based lipase sensor. *Chinese Chemical Lett*, *12*, 453–456.

Hwang, H. T., Qi, F., Yuan, C., Zhao, X., Ramkrishna, D., Liu, D., & Varma, A. (2014). Lipase-catalyzed process for biodiesel production: Protein engineering and lipase production. *Biotechnology and Bioengineering*, *111*, 639–653. https://doi.org/10.1002/bit.25162

Iftikhar, T., & Hussain, A. (2001). Effects of nutrients on the extracellular lipase production by mutant strain of *Rhizopus oligosporous* TUV-31. *Biotechnology(Faisalabad)*, *1*, 15–20. https://doi.org/10.3923/biotech.2002.15.20

Ismail, A. R., Kashtoh, H., & Baek, K. H. (2021). Temperature-resistant and solvent-tolerant lipases as industrial biocatalysts: Biotechnological approaches and applications. *International Journal of Biological Macromolecules*, *187*, 127–142. https://doi.org/10.1016/j.ijbiomac.2021.07.101

Jambulingam, R., Shalma, M., & Shankar, V. (2019). Biodiesel production using lipase immobilised functionalized magnetic nanocatalyst from oleaginous fungal lipid. *Journal of Cleaner Production*, *215*, 245–258. https://doi.org/10.1016/j.jclepro.2018.12.146

Jawed, A., Singh, G., Kohli, S., Sumera, A., Haque, S., Prasad, R., & Paul, D. (2019). Therapeutic role of lipases and lipase inhibitors derived from natural resources for remedies against metabolic disorders and lifestyle diseases. *South African Journal of Botany*, *120*, 25–32. https://doi.org/10.1016/j.sajb.2018.04.004

Jayaprakash, A., & Ebenezer, P. (2012). Purification and characterization of *Aspergillus japonicus* lipase from a pig fat production medium. *Journal of Academia and Industrial Research*, *1*, 1–7.

Jooyandeh, H., Amarjeet, K., & Minhas, K. S. (2009). Lipases in dairy industry: a review. *Food Science and Technology*, *46*, 181–189.

Jordà, J., Jouhten, P., Cámara, E., Maaheimo, H., Albiol, J., & Ferrer, P. (2012). Metabolic flux profiling of recombinant protein secreting *Pichia pastoris* growing on glucose: Methanol mixtures. *Microbial Cell Factories*, *11*, 57. https://doi.org/10.1186/1475-2859-11-57

Joseph, B., Ramteke, P. W., & Thomas, G. (2008). Cold active microbial lipases: Some hot issues and recent developments. *Biotechnology Advances*, *26*, 457–470. https://doi.org/10.1016/j.biotechadv.2008.05.003

Kantak, J. B., Bagade, A. V., Mahajan, S. A., Pawar, S. P., Shouche, Y. S., & Prabhune, A. A. (2011). Isolation, identification and optimization of a new extracellular lipase producing strain of *Rhizopus sp*. *Applied Biochemistry and Biotechnology*, *164*, 969–978. https://doi.org/10.1007/s12010-011-9188-0

Kapoor, M., & Gupta, M. N. (2012). Lipase promiscuity and its biochemical applications. *Process Biochemistry*, *47*, 555–569. https://doi.org/10.1016/j.procbio.2012.01.011

Karmee, S., Patria, R., & Lin, C. (2015). Techno-economic evaluation of biodiesel production from waste cooking oil—a case study of Hong Kong. *International Journal of Molecular Sciences*, *16*, 4362–4371. https://doi.org/10.3390/ijms16034362

Kartal, F., KilinÇ, A., & Timur, S. (2007). Lipase biosensor for tributyrin and pesticide detection. *International Journal of Environmental Analytical Chemistry*, *87*, 715–722. https://doi.org/10.1080/03067310701327741

Katiyar, M., & Ali, A. (2013). Effect of metal ions on the hydrolytic and transesterification activities of *Candida rugosa* lipase. *Journal of Oleo Science*, *62*, 919–924. https://doi.org/10.5650/jos.62.919

Kaushik, R., Saran, S., Isar, J., & Saxena, R. K. (2006). Statistical optimization of medium components and growth conditions by response surface methodology to enhance lipase production by *Aspergillus carneus*. *Journal of Molecular Catalysis B: Enzymatic*, *40*, 121–126. https://doi.org/10.1016/j.molcatb.2006.02.019

Kazi, B., Kiss, L., Forró, E., & Fülöp, F. (2010). Synthesis of orthogonally protected azepane β-amino ester enantiomers. *Tetrahedron Letters*, *51*, 82–85. https://doi.org/10.1016/j.tetlet.2009.10.072

Kempka, A. P., Lipke, N. L., da Luz Fontoura Pinheiro, T., Menoncin, S., Treichel, H., Freire, D. M. G., Luccio, M. D., & de Oliveira, D. (2008). Response surface method to optimize the production and characterization of lipase from *Penicillium verrucosum* in solid-state fermentation. *Bioprocess and Biosystems Engineering*, *31*, 119–125. https://doi.org/10.1007/s00449-007-0154-8

Kim, B. S., & Hou, C. T. (2006). Production of lipase by high cell density fed-batch culture of *Candida cylindracea*. *Bioprocess and Biosystems Engineering*, *29*, 59–64. https://doi.org/10.1007/s00449-006-0058-z

Kim, K. K., Song, H. K., Shin, D. H., Hwang, K. Y., & Suh, S. W. (1997). The crystal structure of a triacylglycerol lipase from *Pseudomonas cepacia* reveals a highly open conformation in the absence of a bound inhibitor. *Structure*, *5*, 173–185. https://doi.org/10.1016/S0969-2126(97)00177-9

Komatsu, T., Nagayama, K., & Imai, M. (2004). Interesterification activity of *Rhizopus delemar* lipase in phospholipid microemulsions. *Colloids and Surfaces B: Biointerfaces*, *38*, 175–178. https://doi.org/10.1016/j.colsurfb.2004.01.017

Kotogán, A., Furka, Z. T., Kovács, T., Volford, B., Papp, D. A., Varga, M., Huynh, T., Szekeres, A., Papp, T., Vágvölgyi, C., Mondal, K. C., Kerekes, E. B., & Takó, M. (2022). Hydrolysis of edible oils by fungal lipases: An effective tool to produce bioactive extracts with antioxidant and antimicrobial potential. *Foods*, *11*, 1711. https://doi.org/10.3390/foods11121711

Kumar, A., Park, G. D., Patel, S. K. S., Kondaveeti, S., Otari, S., Anwar, M. Z., Kalia, V. C., Singh, Y., Kim, S. C., Cho, B. K., Sohn, J. H., Kim, D. R., Kang, Y. C., & Lee, J. K. (2019). SiO_2 microparticles with carbon nanotube-derived mesopores as an efficient support for enzyme immobilization. *Chemical Engineering Journal*, *359*, 1252–1264. https://doi.org/10.1016/j.cej.2018.11.052

Kumar, A., Sharma, P., & Kanwar, S. S. (2012). Lipase catalyzed esters syntheses in organic media: A review. *International Journal of Institutional Pharmacy and Life Sciences*, *2*, 91–119.

Kumar, S., Katiyar, N., Ingle, P., & Negi, S. (2011). Use of evolutionary operation (EVOP) factorial design technique to develop a bioprocess using grease waste as a substrate for lipase production. *Bioresource Technology*, *102*, 4909–4912. https://doi.org/10.1016/j.biortech.2010.12.114

Lee, D. H., Kim, J. M., Shin, H. Y., Kang, S. W., & Kim, S. W. (2006). Biodiesel production using a mixture of immobilized *Rhizopus oryzae* and *Candida rugosa* lipases. *Biotechnology and Bioprocess Engineering*, *11*, 522–525. https://doi.org/10.1007/BF02932077

Lee, S. K., Chou, H., Ham, T. S., Lee, T. S., & Keasling, J. D. (2008). Metabolic engineering of microorganisms for biofuels production: From bugs to synthetic biology to fuels. *Current Opinion in Biotechnology*, *19*, 556–563. https://doi.org/10.1016/j.copbio.2008.10.014

Lenfant, N., Hotelier, T., Velluet, E., Bourne, Y., Marchot, P., & Chatonnet, A. (2012). ESTHER, the database of the α/β-hydrolase fold superfamily of proteins: Tools to explore diversity of functions. *Nucleic Acids Research*, *41*, D423–D429. https://doi.org/10.1093/nar/gks1154

Li, G., Fang, X., Su, F., Chen, Y., Xu, L., & Yan, Y. (2018). Enhancing the thermostability of *Rhizomucor miehei* lipase with a limited screening library by rational-design point mutations and disulfide bonds. *Applied and Environmental Microbiology*, *84*, e02129-17. https://doi.org/10.1128/AEM.02129-17

Li, G., Li, K., Liu, A., Yang, P., Du, Y., & Zhu, M. (2017). 3D flower-like β-MnO_2/reduced graphene oxide nanocomposites for catalytic ozonation of dichloroacetic acid. *Scientific Reports*, *7*, 43643. https://doi.org/10.1038/srep43643

Li, Q., Chen, Y., Bai, S., Shao, X., Jiang, L., & Li, Q. (2020). Immobilized lipase in bio-based metal-organic frameworks constructed by biomimetic mineralization: A sustainable biocatalyst for biodiesel

synthesis. *Colloids and Surfaces B: Biointerfaces*, *188*, 110812. https://doi.org/10.1016/j.colsurfb.2020.110812

Li, X., He, X. Y., Li, Z. L., Wang, Y. D., Wang, C. Y., Shi, H., & Wang, F. (2012). Enzymatic production of biodiesel from *Pistacia chinensis bge* seed oil using immobilized lipase. *Fuel*, *92*, 89–93. https://doi.org/10.1016/j.fuel.2011.06.048

Lima, V. M. G., Krieger, N., Mitchell, D. A., & Fontana, J. D. (2004). Activity and stability of a crude lipase from Penicillium aurantiogriseum in aqueous media and organic solvents. *Biochem. Engineering Journal*. *18*, 65–71. https://doi.org/10.1016/S1369-703X(03)00165-7

Lima, V. M., Krieger, N., Sarquis, M. I. M., Mitchell, D. A., Ramos, L. P., & Fontana, J. D. (2003). Effect of nitrogen and carbon sources on lipase production by *Penicillium aurantiogriseum*. *Food Technology and Biotechnology*, *41*, 105–110.

Liu, J., Ma, R. T., & Shi, Y. P. (2020). "Recent advances on support materials for lipase immobilization and applicability as biocatalysts in inhibitors screening methods"—a review. *Analytica Chimica Acta*, *1101*, 9–22. https://doi.org/10.1016/j.aca.2019.11.073

Liu, K., Zhao, G., He, B., Chen, L., & Huang, L. (2012). Immobilization of pectinase and lipase on macroporous resin coated with chitosan for treatment of whitewater from papermaking. *Bioresour Technol*, *123*, 616–619. https://doi.org/10.1016/j.biortech.2012.07.074

Liu, Z., Chi, Z., Wang, L., & Li, J. (2008). Production, purification and characterization of an extracellular lipase from *Aureobasidium pullulans* HN2.3 with potential application for the hydrolysis of edible oils. *Biochemical Engineering Journal*, *40*, 445–451. https://doi.org/10.1016/j.bej.2008.01.014

Lotti, M., & Alberghina, L. (2007). Lipases: Molecular structure and function. In J. Polaina, & A. P. MacCabe (Eds.), *Industrial enzymes* (pp. 263–281). Springer.

Madhavan, A., Arun, K. B., Binod, P., Sirohi, R., Tarafdar, A., Reshmy, R., Awasthi, M. K., Sindhu, R. (2020). Design of novel enzyme biocatalysts for industrial bioprocess: Harnessing the power of protein engineering, high throughput screening and synthetic biology. *Bioresource Technology*, *325*, 124617.

Maeda, H., Yamagata, Y., Abe, K., Hasegawa, F., Machida, M., Ishioka, R., Gomi, K., & Nakajima, T. (2005). Purification and characterization of a biodegradable plastic-degrading enzyme from *Aspergillus oryzae*. *Applied Microbiology and Biotechnology*, *67*, 778–788. https://doi.org/10.1007/s00253-004-1853-6

Maia, M. (2001). Effect of culture conditions on lipase production by *Fusarium solani* in batch fermentation. *Bioresource Technology*, *76*, 23–27. https://doi.org/10.1016/S0960-8524(00)00079-1

Makrides, S. C. (1996). Strategies for achieving high-level expression of genes in *Escherichia coli*. *Microbiological Reviews*, *60*, 512–538. https://doi.org/10.1128/mr.60.3.512-538.1996

Mandolesi De Araújo, C. D., De Andrade, C. C., de Souza e Silva, E., & Dupas, F. A. (2013). Biodiesel production from used cooking oil: A review. *Renewable and Sustainable Energy Reviews*, *27*, 445–452. https://doi.org/10.1016/j.rser.2013.06.014

Marion, B. A. S., & Oliver, T. (2013). Review article: immobilized lipases in the cosmetics industry. *Chemical Society Reviews*, *42*, 6406–6442.

McNeill, G. P., Shimizu, S., & Yamane, T. (1991). High-yield enzymatic glycerolysis of fats and oils. *Journal of the American Oil Chemists' Society*, *68*, 1–5. https://doi.org/10.1007/BF02660298

Mehrasbi, M. R., Mohammadi, J., Peyda, M., & Mohammadi, M. (2017). Covalent immobilization of *Candida antarctica* lipase on core-shell magnetic nanoparticles for production of biodiesel from waste cooking oil. *Renewable Energy*, *101*, 593–602. https://doi.org/10.1016/j.renene.2016.09.022

Mehta, A., Bodh, U., & Gupta, R. (2017). Fungal lipases: A review. *Journal of Biotech Research*, *8*, 58–77.

Menoncin, S., Domingues, N. M., Freire, D. M. G., Toniazzo, G., Cansian, R. L., Oliveira, J. V., Di Luccio, M., de Oliveira, D., & Treichel, H. (2010). Study of the extraction, concentration, and partial characterization of lipases obtained from *Penicillium verrucosum* using solid-state fermentation of soybean bran. *Food and Bioprocess Technology*, *3*, 537–544. https://doi.org/10.1007/s11947-008-0104-8

Mhetras, N. C., Bastawde, K. B., & Gokhale, D. V. (2009). Purification and characterization of acidic lipase from *Aspergillus niger* NCIM 1207. *Bioresource Technology*, *100*, 1486–1490. https://doi.org/10.1016/j.biortech.2008.08.016

Momsia, T., & Momsia, P. (2013). A review on microbial lipase-versatile tool for industrial applications. *International Journal of Life Sciences Biotechnology and Pharma Research*, *2*, 18.

Mosbah, H., Sayari, A., Mejdoub, H., Dhouib, H., & Gargouri, Y. (2005). Biochemical and molecular characterization of *Staphylococcus xylosus* lipase. *Biochimica et Biophysica Acta (BBA) - General Subjects*, *1723*, 282–291. https://doi.org/10.1016/j.bbagen.2005.03.006

Mouad, A. M., Taupin, D., Lehr, L., Yvergnaux, F., & Porto, A. L. M. (2016). Aminolysis of linoleic and salicylic acid derivatives with *Candida antarctica* lipase B: A solvent-free process to obtain amphiphilic amides for cosmetic application. *Journal of Molecular Catalysis B: Enzymatic*, *126*, 64–68. https://doi.org/10.1016/j.molcatb.2016.01.002

Mulinari, J., Oliveira, J. V., & Hotza, D. (2020). Lipase immobilization on ceramic supports: An overview on techniques and materials. *Biotechnology Advances*, *42*, 107581. https://doi.org/10.1016/j.biotechadv.2020.107581

Narayanan, N., & Chou, C. P. (2009). Alleviation of proteolytic sensitivity to enhance recombinant lipase production in *Escherichia coli*. *Applied and Environmental Microbiology*, *75*, 5424–5427. https://doi.org/10.1128/AEM.00740-09

Narwal, S. K., & Gupta, R. (2013). Biodiesel production by transesterification using immobilized lipase. *Biotechnology Letters*, *35*, 479–490. https://doi.org/10.1007/s10529-012-1116-z

Navarro López, E., Robles Medina, A., González Moreno, P. A., Jiménez Callejón, M. J., Esteban Cerdán, L., Martín Valverde, L., Castillo López, B., & Molina Grima, E. (2015). Enzymatic production of biodiesel from *Nannochloropsis gaditana* lipids: Influence of operational variables and polar lipid content. *Bioresource Technology*, *187*, 346–353. https://doi.org/10.1016/j.biortech.2015.03.126

Nematian, T., Shakeri, A., Salehi, Z., & Saboury, A. A. (2020). Lipase immobilized on functionalized superparamagnetic few-layer graphene oxide as an efficient nanobiocatalyst for biodiesel production from *Chlorella vulgaris* bio-oil. *Biotechnology for Biofuels*, *13*, 57. https://doi.org/10.1186/s13068-020-01688-x

Neta, N. A. S., Santos, J. C. S., Sancho, S. O., Rodrigues, S., Gonçalves, L. R. B., Rodrigues, L. R., & Teixeira, J. A. (2012). Enzymatic synthesis of sugar esters and their potential as surface-active stabilizers of coconut milk emulsions. *Food Hydrocolloids*, *27*, 324–331. https://doi.org/10.1016/j.foodhyd.2011.10.009

Ognjanovic, N., Bezbradica, D., & Knezevic-Jugovic, Z. (2009). Enzymatic conversion of sunflower oil to biodiesel in a solvent-free system: Process optimization and the immobilized system stability. *Bioresource Technology*, *100*, 5146–5154. https://doi.org/10.1016/j.biortech.2009.05.068

Okuma, K., Ono, A. M., Tsuchiya, S., Oba, M., Nishiyama, K., Kainosho, M., & Terauchi, T. (2009). Assymetric synthesis of (2S, 3R)-and (2S, 3S)-[2-13C; 3-2H] glutamic acid. *Tetrahedron Letters*, *50*, 1482–1484. https://doi.org/10.1016/j.tetlet.2009.01.062

Osbon, Y., & Kumar, M. (2019). Biocatalysis and strategies for enzyme improvement, *Biophysical chemistry—advance applications* (pp. 1–22). Intech.

Ouertani, S., & Horchani, H. (2012). Fungal lipases: Versatile tools for biocatalysis Lipase: Functions. *Synthesis and Role in Disease*, 111–136.

Park, E. Y., Sato, M., & Kojima, S. (2008). Lipase-catalyzed biodiesel production from waste activated bleaching earth as raw material in a pilot plant. *Bioresource Technology*, *99*, 3130–3135. https://doi.org/10.1016/j.biortech.2007.05.059

Patel, N., Rai, D., Shivam, I., Shahane, S., & Mishra, U. (2019). Lipases: Sources, production, purification, and applications. *Recent Patents on Biotechnology*, *13*, 45–56. https://doi.org/10.2174/1872208312666181029093333

Peng, Q., Wang, X., Shang, M., Huang, J., Guan, G., Li, Y., & Shi, B. (2014). Isolation of a novel alkaline-stable lipase from a metagenomic library and its specific application for milkfat flavor production. *Microbial Cell Factories*, *13*, 1–9. https://doi.org/10.1186/1475-2859-13-1

Pera, L. M., Romero, C. M., Baigori, M. D., & Castro, G. R. (2006). Catalytic properties of lipase extracts from *Aspergillus niger*. *Food Technology & Biotechnology*, *44*, 247–252.

Pogori, N., Xu, Y., & Cheikhyoussef, A. (2007). Potential aspects of lipases obtained from *Rhizopus* fungi. *Research Journal of Microbiology*, *2*, 101–116. https://doi.org/10.3923/jm.2007.101.116

Pokorny, D., Cimerman, A., & Steiner, W. (1997). *Aspergillus niger* lipases: Induction, isolation and characterization of two lipases from a MZKI A116 strain. *Journal of Molecular Catalysis B: Enzymatic*, *2*, 215–222. https://doi.org/10.1016/S1381-1177(96)00031-8

Pollardo, A. A., Lee, H., Lee, D., Kim, S., & Kim, J. (2018). Solvent effect on the enzymatic production of biodiesel from waste animal fat. *Journal of Cleaner Production*, *185*, 382–388. https://doi.org/10.1016/j.jclepro.2018.02.210

Prathumpai, W., Flitter, S. J., McIntyre, M., & Nielsen, J. (2004). Lipase production by recombinant strains of *Aspergillus niger* expressing a lipase-encoding gene from *Thermomyces lanuginosus*. *Applied Microbiology and Biotechnology*, *65*, 714–719. https://doi.org/10.1007/s00253-004-1699-y

Prazeres, J. N., Cruz, J. A. B., & Pastore, G. M. (2006). Characterization of alkaline lipase from *Fusarium oxysporum* and the effect of different surfactants and detergents on the enzyme activity. *Brazilian Journal of Microbiology*, *37*, 505–509. https://doi.org/10.1590/S1517-83822006000400019

Pérez, M. M., Gonçalves, E. C. S., Vici, A. C., Salgado, J. C. S., & de Moraes, M. D. L. T. (2019). Fungal lipases: Versatile tools for white biotechnology. In A. N. Yadav, S. Mishra, S. Singh, & A. Gupta (Eds.), *Recent advancement in white biotechnology through fungi* (Vol. 2, pp. 361–404). Springer.

Quayson, E., Amoah, J., Rachmadona, N., Hama, S., Yoshida, A., Kondo, A., & Ogino, C. (2020). Biodiesel-mediated biodiesel production: A recombinant *Fusarium heterosporum* lipase-catalyzed transesterification of crude plant oils. *Fuel Processing Technology*, *199*, 106278. https://doi.org/10.1016/j.fuproc.2019.106278

Rajendran, A., Palanisamy, A., & Thangavelu, V. (2008). Evaluation of medium components by Plackett-Burman statistical design for lipase production by *Candida rugosa* and kinetic modeling. *Chinese Journal of Biotechnology*, *24*, 436–444. https://doi.org/10.1016/S1872-2075(08)60024-2

Rajendran, A., Palanisamy, A., & Thangavelu, V. (2009). Lipase catalyzed ester synthesis for food processing industries. *Brazilian Archives of Biology and Technology*, *52*, 207–219. https://doi.org/10.1590/S1516-89132009000100026

Ramarethinam, S., Latha, K., & Rajalakshmi, N. (2002). Use of a fungal lipase for enhancement of aroma in black tea. *Food Science and Technology Research*, *8*, 328–332. https://doi.org/10.3136/fstr.8.328

Ramos-Sánchez, L. B., Cujilema-Quitio, M. C., Julian-Ricardo, M. C., Cordova, J., & Fickers, P. (2015). Fungal lipase production by solid-state fermentation. *J Bioprocessing and Biotechniques*, *5*, 1.

Ranganathan, S. V., Narasimhan, S. L., & Muthukumar, K. (2008). An overview of enzymatic production of biodiesel. *Bioresource Technology*, *99*, 3975–3981. https://doi.org/10.1016/j.biortech.2007.04.060

Ray, S. (2015). Applications of extracellular microbial lipases—a review. *Int J Res Biotechnol Biochem*, *5*, 6–12.

Rejasse, B., Maugard, T., & Legoy, M. D. (2003). Enzymatic procedures for the synthesis of water-soluble retinol derivatives in organic media. *Enzyme and Microbial Technology*, *32*, 312–320. https://doi.org/10.1016/S0141-0229(02)00289-2

Rodrigues, R. C., & Ayub, M. A. Z. (2011). Effects of the combined use of *Thermomyces lanuginosus* and *Rhizomucor miehei* lipases for the transesterification and hydrolysis of soybean oil. *Process Biochemistry*, *46*, 682–688. https://doi.org/10.1016/j.procbio.2010.11.013

Rodrigues, R. C., Virgen-Ortíz, J. J., Dos Santos, J. C. S., Berenguer-Murcia, Á., Alcantara, A. R., Barbosa, O., Ortiz, C., & Fernandez-Lafuente, R. (2019). Immobilization of lipases on hydrophobic supports: Immobilization mechanism, advantages, problems, and solutions. *Biotechnology Advances*, *37*, 746–770. https://doi.org/10.1016/j.biotechadv.2019.04.003

Rodriguez, J. A., Mateos, J. C., Nungaray, J., González, V., Bhagnagar, T., Roussos, S., Cordova, J., & Baratti, J. (2006). Improving lipase production by nutrient source modification using *Rhizopus homothallicus* cultured in solid state fermentation. *Process Biochemistry*, *41*, 2264–2269. https://doi.org/10.1016/j.procbio.2006.05.017

Salah, A. B., Sayari, A., Verger, R., & Gargouri, Y. (2001). Kinetic studies of *Rhizopus oryzae* lipase using monomolecular film technique. *Biochimie*, *83*, 463–469. https://doi.org/10.1016/S0300-9084(01)01283-4

Salah, R. B., Mosbah, H., Fendri, A., Gargouri, A., Gargouri, Y., & Mejdoub, H. (2006). Biochemical and molecular characterization of a lipase produced by *Rhizopus oryzae*. *FEMS Microbiology Letters*, *260*, 241–248. https://doi.org/10.1111/j.1574-6968.2006.00323.x

Salgado, C. A., Dos Santos, C. I. A., & Vanetti, M. C. D. (2022). Microbial lipases: Propitious biocatalysts for the food industry. *Food Bioscience*, *45*, 101509. https://doi.org/10.1016/j.fbio.2021.101509

Santos, M. R., Hirata, D. B., & Angelotti, J. A. F. (2022). Lipases: Sources of acquisition, ways of production, and recent applications. *Catalysis Research*, *2*(2), 35. https://doi.org/10.21926/cr.2202013

Santos, S., Puna, J., & Gomes, J. (2020). A review on bio-based catalysts (immobilized enzymes) used for biodiesel production. *Energies*, *13*, 3013. https://doi.org/10.3390/en13113013

Saranya, G., & Ramachandra, T. V. (2020). Novel biocatalyst for optimal biodiesel production from diatoms. *Renewable Energy*, *153*, 919–934. https://doi.org/10.1016/j.renene.2020.02.053

Saxena, R. K., Davidson, W. S., Sheoran, A., & Giri, B. (2003). Purification and characterization of an alkaline thermostable lipase from *Aspergillus carneus*. *Process Biochemistry*, *39*, 239–247. https://doi.org/10.1016/S0032-9592(03)00068-2

Saxena, R. K., Malhotra, B., & Batra, A. (2004). Commercial importance of some fungal enzymes. *Handbook Fungal Biotechnol*, *0*, 287–298.

Sayari, A., Mosbah, H., & Gargouri, Y. (2007). Importance of the residue Asp 290 on chain length selectivity and catalytic efficiency of recombinant *Staphylococcus simulans* lipase expressed in. *Molecular Biotechnology*, *36*, 14–22. https://doi.org/10.1007/s12033-007-0008-2

Seong, P. J., Jeon, B. W., Lee, M., Cho, D. H., Kim, D. K., Jung, K. S., Kim, S. W., Han, S. O., Han, S. O., Kim, Y. H., & Park, C. (2011). Enzymatic coproduction of biodiesel and glycerol carbonate from soybean oil and dimethyl carbonate. *Enzyme and Microbial Technology*, *48*, 505–509. https://doi.org/10.1016/j.enzmictec.2011.02.009

Shahedi, M., Yousefi, M., Habibi, Z., Mohammadi, M., & As'habi, M. A. (2019). Co-immobilization of *Rhizomucor miehei* lipase and *Candida antarctica* lipase B and optimization of biocatalytic biodiesel production from palm oil using response surface methodology. *Renewable Energy*, *141*, 847–857. https://doi.org/10.1016/j.renene.2019.04.042

Sharma, A. K., Sharma, V., & Saxena, J. (2016). A review on properties of fungal lipases. *International Journal of Current Microbiology and Applied Sciences*, *5*(12), 123–130. https://doi.org/10.20546/ijcmas.2016.512.014

Sharma, D., Sharma, B., & Shukla, A. K. (2011). Biotechnological approach of microbial lipase: A review. *Biotechnol*, *10*, 23–40. https://doi.org/10.3923/biotech.2011.23.40

Sharma, R., Chisti, Y., & Banerjee, U. C. (2001). Production, purification, characterization, and applications of lipases. *Biotechnology Advances*, *19*, 627–662. https://doi.org/10.1016/S0734-9750(01)00086-6

Sharma, S., & Kanwar, S. S. (2014). Organic solvent tolerant lipases and applications. *Scientific World Journal*, *2014*, 625258.

Shu, C. H., Xu, C. J., & Lin, G. C. (2006). Purification and partial characterization of a lipase from *Antrodia cinnamomea*. *Process Biochemistry*, *41*, 734–738. https://doi.org/10.1016/j.procbio.2005.09.007

Shuba, E. S., & Kifle, D. (2018). Microalgae to biofuels: 'Promising' alternative and renewable energy, review. *Renewable and Sustainable Energy Reviews*, *81*, 743–755. https://doi.org/10.1016/j.rser.2017.08.042

Singh, A. K., & Mukhopadhyay, M. (2012). Overview of fungal lipase: A review. *Applied Biochemistry and Biotechnology*, *166*, 486–520. https://doi.org/10.1007/s12010-011-9444-3

Sorte, S., Ribeiro, J. P., Coutinho, J. A. P., & Nunes, M. I. (2020). Study of fame production from waste cooking oil: Operation in batch and continuous regime with regeneration of enzyme catalyst. *Energy Reports*, *6*, 751–756. https://doi.org/10.1016/j.egyr.2019.09.062

Stoytcheva, M., Montero, G., Zlatev, R., A. Leon, J., & Gochev, V. (2012). Analytical methods for lipases activity determination: A review. *Current Analytical Chemistry*, *8*, 400–407. https://doi.org/10.2174/157341112801264879

Sumner, C., Krause, S., Sabot, A., Turner, K., & McNeil, C. J. (2001). Biosensor based on enzyme-catalysed degradation of thin polymer films. *Biosensors and Bioelectronics*, *16*, 709–714. https://doi.org/10.1016/S0956-5663(01)00210-X

Supakdamrongkul, P., Bhumiratana, A., & Wiwat, C. (2010). Characterization of an extracellular lipase from the biocontrol fungus *Nomuraea rileyi* MJ, and its toxicity toward *Spodoptera litura*. *Journal of Invertebrate Pathology*, *105*, 228–235. https://doi.org/10.1016/j.jip.2010.06.011

Tako, M., Kotogan, A., Papp, T., Kadaikunnan, S., Alharbi, N. S., & Vagvolgyi, C. (2017). Purification and properties of extracellular lipases with transesterification activity and 1,3-regioselectivity from *Rhizomucor miehei* and *Rhizopus* oryzae. *Journal of Microbiology and Biotechnology*, *27*, 277–288. https://doi.org/10.4014/jmb.1608.08005

Talavari, R., Hosseini, S., & Moradi, G. (2020). Low-cost biodiesel production using waste oil and catalyst. *Waste Management & Research: The Journal for a Sustainable Circular Economy*, *39*, 250–259. https://doi.org/10.1177/0734242X20935174

Talukder, M. M. R., Das, P., Fang, T. S., & Wu, J. C. (2011). Enhanced enzymatic transesterification of palm oil to biodiesel. *Biochemical Engineering Journal*, *55*, 119–122. https://doi.org/10.1016/j.bej.2011.03.013

Tan, T., Nie, K., & Wang, F. (2006). Production of biodiesel by immobilized *Candida* sp. lipase at high water content. *Applied Biochemistry and Biotechnology*, *128*, 109–116. https://doi.org/10.1385/ABAB:128:2:109

Tan, T., Zhang, M., Wang, B., Ying, C., & Deng, L. (2003). Screening of high lipase producing *Candida sp.* and production of lipase by fermentation. *Process Biochemistry*, *39*, 459–465. https://doi.org/10.1016/S0032-9592(03)00091-8

Tan, T., Zhang, M., Xu, J., & Zhang, J. (2004). Optimization of culture conditions and properties of lipase from *Penicillium camembertii Thom* PG-3. *Process Biochemistry*, *39*, 1495–1502. https://doi.org/10.1016/S0032-9592(03)00296-6

Teng, Y., & Xu, Y. (2008). Culture condition improvement for whole-cell lipase production in submerged fermentation by *Rhizopus chinensis* using statistical method. *Bioresource Technology*, *99*, 3900–3907. https://doi.org/10.1016/j.biortech.2007.07.057

Thakur, S. (2012). Lipases, its sources, properties and applications: A review. *International Journal of Scientific and Engineering Research*, *3*, 1–29.

Tian, K., Tai, K., Chua, B. J. W., & Li, Z. (2017). Directed evolution of *Thermomyces lanuginosus* lipase to enhance methanol tolerance for efficient production of biodiesel from waste grease. *Bioresource Technology*, *245*, 1491–1497. https://doi.org/10.1016/j.biortech.2017.05.108

Tian, M., Yang, L., Lv, P., Wang, Z., Fu, J., Miao, C., Li, Z., Li, L., Liu, T., Du, W., & Luo, W. (2022). Improvement of methanol tolerance and catalytic activity of *Rhizomucor miehei* lipase for one-step synthesis of biodiesel by semi-rational design. *Bioresource Technology*, *348*, 126769. https://doi.org/10.1016/j.biortech.2022.126769

Tian, M., Yang, L., Wang, Z., Lv, P., Fu, J., Miao, C., Li, M., Liu, T., Liu, T., & Luo, W. (2021). Improved methanol tolerance of *Rhizomucor miehei* lipase based on N-glycosylation within the α-helix region and its application in biodiesel production. *Biotechnology for Biofuels*, *14*, 237. https://doi.org/10.1186/s13068-021-02087-6

Treichel, H., de Oliveira, D., Mazutti, M. A., Di Luccio, M., & Oliveira, J. V. (2010). A review on microbial lipases production. *Food and Bioprocess Technology*, *3*, 182–196. https://doi.org/10.1007/s11947-009-0202-2

Uyama, H., & Kobayashi, S. (2002). Enzyme-catalyzed polymerization to functional polymers. *Journal of Molecular Catalysis B: Enzymatic*, *19-20*, 117–127. https://doi.org/10.1016/S1381-1177(02)00158-3

Vadgama, R. N., Odaneth, A. A., & Lali, A. M. (2015). Green synthesis of isopropyl myristate in novel single phase medium Part I: Batch optimization studies. *Biotechnology Reports*, *8*, 133–137. https://doi.org/10.1016/j.btre.2015.10.006

Vakhlu, J., & Kour, A. (2006). Yeast lipases: Enzyme purification, biochemical properties and gene cloning. *Electronic Journal of Biotechnology*, *9*, 69–85. https://doi.org/10.2225/vol9-issue1-fulltext-9

Valero, F. (2012). Heterologous expression systems for lipases: A review. In G. Sandoval (Ed.), *Lipases and phospholipases* (pp. 161–178). Humana Press.

Van Heerden, E., Litthauer, D., & Verger, R. (2002). Biochemical characterisation and kinetic properties of a purified lipase from *Aspergillus niger* in bulk phase and monomolecular films. *Enzyme and Microbial Technology*, *30*, 902–909. https://doi.org/10.1016/S0141-0229(02)00031-5

Verma, N., Thakur, S., & Bhatt, A. K. (2012). Microbial lipases: Industrial applications and properties (a review). *Int. Res. J Biol. Sci. 1*, 88–92.

Verma, S., Meghwanshi, G. K., & Kumar, R. (2021). Current perspectives for microbial lipases from extremophiles and metagenomics. *Biochimie*, *182*, 23–36. https://doi.org/10.1016/j.biochi.2020.12.027

Vijayalakshmi, S., & Kalindhi, K. (2015). Isolation and purification of lipase from the riboflavin overproducing fungus *Eremothecium ashbyii*. *Journal of The Analgesics*, *3*, 1–8. https://doi.org/10.14205/2311-0317.2015.03.01.1

Wang, B., & Xia, L. (2011). High efficient expression of cellobiase gene from Aspergillus niger in the cells of *Trichoderma reesei*. *Bioresource Technology*, *102*, 4568–4572. https://doi.org/10.1016/j.biortech.2010.12.099

Wang, X., Lu, D., Jönsson, L. J., & Hong, F. (2008). Preparation of a PET-hydrolyzing lipase from *Aspergillus oryzae* by the addition of bis(2-hydroxyethyl) terephthalate to the culture medium and enzymatic

modification of PET fabrics. *Engineering in Life Sciences*, *8*, 268–276. https://doi.org/10.1002/elsc.200700058

Xie, W., & Huang, M. (2018). Immobilization of *Candida rugosa* lipase onto graphene oxide Fe_3O_4 nanocomposite: characterization and application for biodiesel production. *Energy Conversion and Management*, *159*, 42–53. https://doi.org/10.1016/j.enconman.2018.01.021

Xing, S., Zhu, R., Cheng, K., Cai, Y., Hu, Y., Li, C., Zeng, X., Zhu, Q., & He, L. (2021). Gene expression, biochemical characterization of a *sn*-1,3 extracellular lipase from *Aspergillus niger* GZUF36 and its model-structure analysis. *Frontiers in Microbiology*, *12*, 633489. https://doi.org/10.3389/fmicb.2021.633489

Xing, S., Zhu, R., Li, C., He, L., Zeng, X., & Zhang, Q. (2020). Gene cloning, expression, purification and characterization of a sn-1,3 extracellular lipase from Aspergillus niger GZUF36. *Journal of Food Science and Technology*, *57*, 2669–2680. https://doi.org/10.1007/s13197-020-04303-x

Yaver, D. S., Lamsa, M., Munds, R., Brown, S. H., Otani, S., Franssen, L., Johnstone, J. A., & Brody, H. (2000). Using DNA-tagged mutagenesis to improve heterologous protein production in *Aspergillus oryzae*. *Fungal Genetics and Biology*, *29*, 28–37. https://doi.org/10.1006/fgbi.1999.1179

Yin, C., Liu, T., & Tan, T. (2006). Synthesis of vitamin A esters by immobilized *Candida sp.* lipase in organic media. *Chinese Journal of Chemical Engineering*, *14*, 81–86. https://doi.org/10.1016/S1004-9541(06)60041-4

Yücel, Y. (2011). Biodiesel production from pomace oil by using lipase immobilized onto olive pomace. *Bioresource Technology*, *102*, 3977–3980. https://doi.org/10.1016/j.biortech.2010.12.001

Zhao, W., Wang, J., Deng, R., & Wang, X. (2008). Scale-up fermentation of recombinant *Candida rugosa* lipase expressed in *Pichia pastoris* using the GAP promoter. *Journal of Industrial Microbiology & Biotechnology*, *35*, 189–195. https://doi.org/10.1007/s10295-007-0283-8

Zubiolo, C., Santos, R. C. A., Carvalho, N. B., Soares, C. M. F., Lima, A. S., & Santana, L. C. L. D. A. (2014). Encapsulation in a sol-gel matrix of lipase from *Aspergillus niger* obtained by bioconversion of a novel agricultural residue. *Bioprocess and Biosystems Engineering*, *37*, 1781–1788. The Lipase Engineering Database. http://www.led.uni-stuttgart.de

How to cite this article: Mahfoudhi, A., Benmabrouk, S., Fendri, A., & Sayari, A. (2022). Fungal lipases as biocatalysts: A promising platform in several industrial biotechnology applications. *Biotechnology and Bioengineering*, 119, 3370–3392. https://doi.org/10.1002/bit.28245