



# Production strategies and biotechnological relevance of microbial lipases: a review

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## Abstract

Lipases are enzymes that catalyze the breakdown of lipids into long-chain fatty acids and glycerol in oil-water interface. In addition, they catalyze broad spectrum of bioconversion reactions including esterification, inter-esterification, among others in non-aqueous and micro-aqueous milieu. Lipases are universally produced from plants, animals, and microorganisms. However, lipases from microbial origin are mostly preferred owing to their lower production costs, ease of genetic manipulation etc. The secretion of these biocatalysts by microorganisms is influenced by nutritional and physicochemical parameters. Optimization of the bioprocess parameters enhanced lipase production. In addition, microbial lipases have gained intensified attention for a wide range of applications in food, detergent, and cosmetics industries as well as in environmental bioremediation. This review provides insights into strategies for production of microbial lipases for potential biotechnological applications.

**Keywords** Lipases · Microorganisms · Microbial lipases · Bioprocess parameters · Biotechnological applications

## Introduction

Lipases (triacylglycerol acylhydrolases, EC 3.1.1.3) are a class of enzymes that catalyze the hydrolysis of triglycerides into diglycerides, monoglycerides, glycerol, and free fatty acids at the organic-aqueous interface [1]. In addition, they catalyze a plethora of reactions including esterification, inter-esterification, trans-esterification, alcoholysis, acidolysis, and aminolysis in non-aqueous and micro-aqueous milieu [2]. Lipases represent the third most commercialized enzymes, after proteases and carbohydrases, and account for more than one-fifth of the global enzyme market [3, 4]. They are commonly secreted from plants, animals, and microorganisms [1]. However, microbial lipases represent the most widely used class of enzymes in biotechnology owing

to their stability at broad ranges of temperature and pH, substrate specificity, high yields, lower production costs, and ease of genetic manipulation [5]. In addition, the microorganisms can be cultivated in huge amounts in a relatively short time by an established fermentation process for mass production of the enzyme.

Microbial lipases are serine hydrolases and their activities rely on a catalytic triad, comprising of Ser-Asp/Glu-His with a consensus sequence (Gly-x-Ser-x-Gly) [6, 7]. The three-dimensional structure of lipases reveals the characteristic  $\alpha/\beta$  hydrolase fold [8]. The active site of the  $\alpha/\beta$  hydrolase fold enzymes consists of three catalytic residues namely, nucleophilic residue, catalytic acid residue, and histidine residue [9]. Furthermore, microbial lipases exhibit chemo-specificity, regio-selectivity, and enantio-selectivity toward substrates [10]. They are employed for a variety of biotechnological applications in biodiesel, food, nutraceutical, detergent, bioremediation, agriculture, cosmetics, leather, and paper industries [11]. Therefore, the present review discusses on the techniques for detection of lipase production from a diversity of microorganisms. It further reveals bioprocess parameters influencing microbial lipase production coupled with strategies for optimization of the biocatalysts for industrial and environmental applications.

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## Lipase-producing microorganisms

Many microorganisms including bacteria, fungi, yeasts, and actinomycetes produce lipases [12]. Among bacteria, lipase production has been reported from members of the genera *Acinetobacter* [13], *Bacillus* [14], *Burkholderia* [15], *Pseudomonas* [16], *Staphylococcus* [17], *Microbacterium* [18], *Lactobacillus* [19], *Serratia* [20], *Aeromonas* [21], *Arthrobacter* [22], *Stenotrophomonas* [23], and *Thermosyntropha* [24] etc. However, genera *Bacillus* and *Pseudomonas* are recognized as the most prominent lipase producers [5]. In addition, lipase secretion from fungal and yeast strains has been extensively studied in the last decades. Among fungi, lipases from *Aspergillus*, *Mucor*, *Penicillium*, *Rhizopus*, *Fusarium*, and *Geotrichum*, have been reported [25–30]. Yeasts including members of the general *Candida*, *Cryptococcus*, *Trichosporon*, *Aureobasidium*, and *Rhodotorula* have been adequately investigated for their lipase-producing potentials [31–35]. These lipase-producing microorganisms are domiciled in different habitats including industrial wastes, vegetable oil mill effluent, dairy effluent, oil-contaminated sites, decaying foods, hot spring etc. [36–38]. A list of lipase-producing microorganisms and their sources of isolation is presented in Table 1.

## Methods for detection of microbial lipase production

Several techniques have been developed for the screening of microorganisms for lipase production. These methods either involve the use of microbial strains under study or measurement of lipase activity from crude or purified enzyme [61, 62]. Numerous approaches employed for detection of microbial lipase production or measuring lipolytic activity are discussed in details below:

### Qualitative screening of microorganisms on selective growth media

In this technique, lipolysis is detected by changes in the appearance of the substrates (such as tributyrin and triolein) that are emulsified in the growth media [63]. The formation of clear halos around the colonies cultivated on the agar plate is an indication of lipase production [64]. *Pseudomonas fluorescens* RB02-3 and *Acinetobacter haemolyticus* NS02-30 were screened for lipolytic activity on tributyrin agar [48, 53]. Lipolytic *Bacillus* sp. LBN 4 was isolated on tributyrin agar medium using glycerol tributyrate as substrate [65]. Lipase production by *Bacillus aryabhattai* SE3-PB was detected on Tween-20 agar plate as visible precipitates of calcium salts around the agar wells, resulting from formation of fatty acid from lipid hydrolysis [14]. In addition, solid media

supplemented with dyes such as phenol red, Victoria Blue B, Spirit blue, or Nile blue sulfate as pH indicators are also used for determination of lipolytic activity. The drop in pH due to the release of fatty acid is indicated by a change in the color of the indicators. Phenol red agar, consisting of phenol red dye (0.01%, w/v), olive oil (0.1%, v/v), CaCl<sub>2</sub> (0.1%, w/v), and Agar (2%, w/v), has been used for screening of *Bacillus* strain [39]. *Geobacillus zalihae* sp. nov. was screened for lipolytic activity using triolein agar plate, comprising of triolein (0.25%, v/v), agar (1%, w/v), nutrient broth (0.8%, w/v), and Victoria Blue (0.01%, w/v) [52]. Furthermore, fluorescent dye Rhodamine B is also employed for the detection of lipolytic organisms in plate assay containing emulsified olive oil as substrate. The formation of orange fluorescent halos around colonies under ultraviolet irradiation suggests production of lipase [66]. Castro-Ochoa et al. [44] screened *Bacillus thermoleovorans* CCR11 for lipolytic activity on Rhodamine B agar consisting of Rhodamine B (0.001%, w/v), nutrient broth (0.8%, w/v), NaCl (0.4%, w/v), olive oil (3%, v/v), and agar (1%, w/v). Spirit blue agar medium has also been used for the detection of lipolytic activity of *Serratia rubidaea* and *Acinetobacter* sp. [46, 67]. This chromogenic method is simple and rapid. However, acidification of the medium resulting from the production of free fatty acids from microbial lipases gives false results [63].

### Quantitative titrimetric assay

Lipase activity is measured quantitatively on a continuously stirred triacylglyceride emulsion by neutralization of free fatty acids released following addition of titrated NaOH (in order to maintain the pH at a constant end point value) [10, 63]. Several authors have reported the use of olive oil as a substrate for the titrimetric analysis [68]. Rasmey et al. [69] measured the lipolytic activity of *Pseudomonas monteilli* 2403-KY120354 in a reaction mixture containing olive oil emulsion incubated at 37 °C for 1 h. Enzyme activity was terminated after addition of 20 mL acetone: ethanol mixture (1:1). The liberated free fatty acids were titrated against 0.1 M NaOH using phenolphthalein. One unit of lipase was defined as the amount of enzyme that liberated 1 μmol/min of fatty acids under standard assay conditions.

### Microbial lipase production

Microbial lipases are mostly extracellular in nature and are secreted in growth medium following utilization of the medium components by lipolytic microorganisms in the presence suitable inducer substrates under optimal fermentation conditions [14]. However, the synthesis of these biocatalysts varies based on appropriate selection of microbial strains, substrate type, and fermentation technology [6]. Microbial lipase production varies from a few hours to a few days during late

**Table 1** Some lipase-producing microorganisms and their sources

Microorganism	Source of isolation	Reference
<b>Bacteria</b>		
<i>Bacillus</i> sp.	Oil-contaminated soil	[39]
<i>Bacillus aryabhatai</i> SE3-PB	Lipid-rich wastewater from edible oil mill industry in Pietermaritzburg, South Africa	[14]
<i>Bacillus coagulans</i>	Soil from olive oil processing factory	[40]
<i>Bacillus</i> sp. L2	Hot spring, Perak, Malaysia	[41]
<i>Bacillus</i> sp. FH5	Tannery waste	[42]
<i>Bacillus coagulans</i> BTS-3	Kitchen waste	[43]
<i>Bacillus thermoleovorans</i> CCR11	“El Carrizal” hot springs, Veracruz, Mexico	[44]
<i>Bacillus pumilus</i> RK31	Oil-contaminated soil	[45]
<i>Acinetobacter</i> sp. AU07	Distillery unit	[13]
<i>Acinetobacter</i> sp.	Oil-contaminated soil, South Korea	[46]
<i>Acinetobacter haemolyticus</i> TA 106	Human skin	[47]
<i>Acinetobacter haemolyticus</i> NSO2-30	Olive pomace-soil mixture	[48]
<i>Enterobacter aerogenes</i> IABR-0785	Soil of IIT, Kharagpur	[49]
<i>Burkholderia</i> sp. HL-10	Lipid-contaminated soil	[15]
<i>Geobacillus thermoleovorans</i> YN	Desert soil sample	[50]
<i>Geobacillus</i> sp. ARM	Oil-contaminated soil, Selangor, Malaysia	[51]
<i>Geobacillus zalihae</i>	Palm oil effluent, Semenyih, Malaysia	[52]
<i>Pseudomonas</i> sp. BUP6	Rumen of Malabari goat	[16]
<i>Pseudomonas fluorescens</i> RB02-3	Pasteurized and raw milk	[53]
<i>Pseudomonas aeruginosa</i> KM110	Oil processing plant wastewater, Tehran, Iran	[54]
<i>Microbacterium</i> sp.	Pulp and paper mill effluent	[18]
<i>Staphylococcus aureus</i> NK-LB37	Oil-contaminated soil, Coimbatore, Tamilnadu	[17]
<i>Lactobacillus plantarum</i> DSMZ 12028	Dry fermented sausage	[19]
<i>Aeromonas</i> sp. S1	Soil and sludge in oil and grease chamber of dairy industry, New Delhi, India	[21]
<i>Arthrobacter</i> sp. BGCC#490	Oil-contaminated soil of automobile garage	[22]
<i>Stenotrophomonas maltophilia</i>	Soil sample	[23]
<i>Thermomyces lanuginosus</i>	Zoo waste and bird nest materials	[55]
<b>Fungi</b>		
<i>Aspergillus niger</i> DAOM	Dairy effluent	[29]
<i>Aspergillus tamarii</i> JGIF06	Rhizospheric soil, Bangalore, India	[56]
<i>Aspergillus terreus</i> NCF 4269.10	-	[57]
<i>Trametes hirsuta</i>	Chicken slaughterhouse effluent	[58]
<i>Hypocrea pseudokoningii</i>	Soil samples	[59]
<i>Geotrichum candidum</i>	Soil sample	[28]
<i>Fusarium</i> sp. ( <i>Gibberella fujikuroi</i> complex)	Decay plant matter in the Atlantic forest, São Paulo, Brazil	[27]
<i>Penicillium</i> sp. section <i>Gracilentia</i> CBMAI 1583	Atlantic rainforest soil	[30]
<i>Mucor geophyllus</i>	Soil sample	[26]
<i>Rhizopus chinensis</i> CCTCC M201021	Da Qu (Traditional leaven for production of Chinese liquor)	[25]
<b>Yeast</b>		
<i>Candida viswanathii</i>	-	[60]
<i>Candida guilliermondii</i>	Leaves of castor bean plant	[34]
<i>Rhodotorula mucilaginosa</i> MTCC 8737	Marine soil sample, Mangalore, India	[32]
<i>Aureobasidium pullulans</i> HN2.3	Sea saltern, Qingdao	[31]
<i>Cryptococcus</i> sp. MTCC 5455	Air	[35]
<i>Trichosporon coremiiforme</i>	Traditional tannery, Fez, Morocco	[33]

exponential or stationary growth phase [36, 70, 71]. The production of these biocatalysts occurs by submerged or solid state fermentation in a batch, repeated-batch, fed-batch, or continuous system [71]. However, submerged fermentation involving cultivation of microorganisms as a suspension in nutrient enriched broth is mostly preferred due to easily engineered process control and colossal amounts of extracellular enzyme released in the growth medium [72]. In addition, submerged fermentation permits higher homogeneity of the culture medium, easier lipase recovery from the fermentation medium, and eliminates production of undesirable metabolites [12, 14]. About 90% of industrial biocatalysts are produced by submerged fermentation [6].

## Influence of bioprocess parameters on microbial lipase production

Lipase production is greatly influenced by carbon and nitrogen sources, temperature, pH, presence of lipids, inorganic salts, dissolved oxygen concentration, incubation period, agitation speed etc. [12, 38, 72]. The various nutritional and physicochemical parameters affecting microbial lipase production are illustrated in Fig. 1 and discussed in details below:

### Carbon sources

Carbon sources represent the ultimate parameter that stimulates the growth of microorganisms for lipase production. However, among carbon sources, lipidic carbon sources play a vital role in lipase secretion since the enzymes are inducible in nature and are therefore generally produced in the presence of a lipid source including oils or other inducers (such as triacylglycerols, Tweens, hydrolysable esters, fatty acids, bile

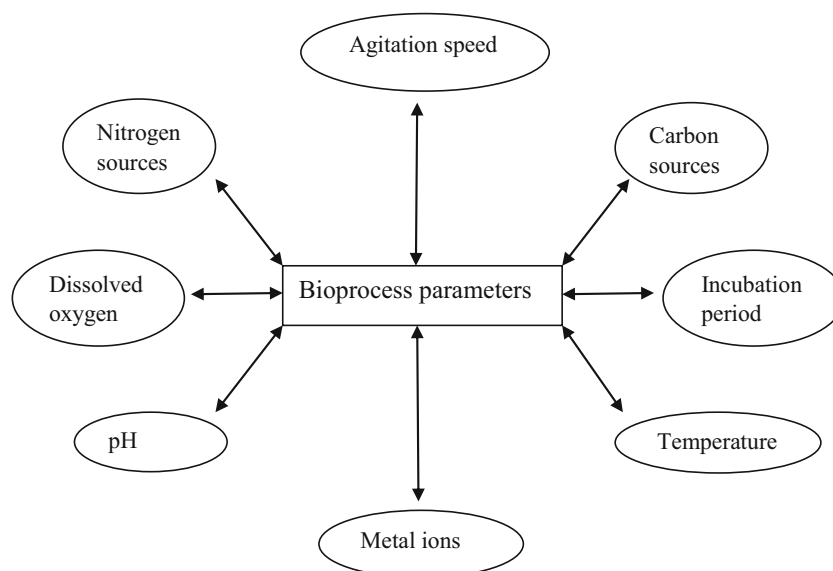
salts, glycerol) [36, 72]. For instance, lipase production by *Bacillus flexus* XJU-1 was stimulated by the presence of a surfactant (Tween-80), which favored the uptake of medium components and lipase release [73]. In addition, various oils such as coconut oil [74], olive oil [75], castor oil [13], cotton seed oil [73], soybean oil [76], sunflower oil [14], and neem oil [77] are used as inducers for lipase production. Lipases are produced with a low oil concentration (1–5%, v/v) [76]. When a large amount of oil is used, lipase secretion reduces due to limitation of oxygen transfer, which results in poor microbial growth [73].

In addition, other carbon sources including sugars, sugar alcohol, polysaccharides, whey, casamino acids, and other complexes influence lipase production [78, 79]. Mannitol was found as the best carbon source for lipase production by *Streptomyces griseochromogenes* [80]. In some cases, combination of carbohydrate and oil is used for maximum lipase secretion [81–83]. Furthermore, non-conventional carbon sources including whey, beef tallow, wool scour effluent, cheap agro-industrial wastes etc. are also incorporated in fermentation medium for lipase production [83–85].

### Nitrogen sources

The addition of nitrogen sources (organic or inorganic) in culture medium influences the amount of lipase yield by microorganisms [86]. Organic nitrogen sources including peptone, yeast extract, or a combination of these resulted in a significant lipase production by most microbial strains [54, 75, 87]. This is typical of optimum lipase production recorded in the presence of soybean meal and corn steep liquor as nitrogen sources by some microorganisms [83, 88–90]. On the other hand, inorganic nitrogen sources such as ammonium chloride, ammonium molybdate, and diammonium hydrogen

**Fig. 1** Schematic diagram depicting bioprocess parameters that influence microbial lipase production



phosphate are effective for maximum lipase production [91–93]. However, the preference of organic nitrogen sources by some lipase-producing microorganisms can be attributed to the presence of some minerals, vitamins, or other growth factors that they contain [73]. In some cases, inclusion of amino acids in the fermentation medium plays a significant role in microbial lipase production [94]. This is typical of phenylalanine found as a preferred nitrogen source for lipase production by *Streptomyces griseochromogenes* [80]. However, a higher nitrogen source concentration inhibits lipase production due to nitrogen metabolite repression [95].

### Physicochemical parameters

Physicochemical parameters including temperature, pH, metal ions, agitation speed, and incubation period play a crucial role in influencing the growth of microorganisms for lipase production. Microorganisms possess different optimum temperatures for maximum lipase yield. This usually correlates with peak growth temperatures of the organisms. For instance, optimum lipase production from *Aspergillus niger* (24 °C), *Bacillus* sp. SP5 (37 °C), *Bacillus aryabhatai* SE3-PB (40 °C), and *Bacillus* sp. RSJ1 (50 °C) was recorded at respective maximum growth temperatures [14, 96–98]. In addition, initial pH of fermentation media is vital, as this stimulates the growth of the organisms for the secretion of the biocatalyst. Usually, maximum lipase production by bacteria occurs at neutral or alkaline pH [3, 86, 99]. However, at nearly neutral and acidic pH, enhanced lipase secretion was recorded from most yeasts and fungi [30, 100].

Microorganisms are cultivated at varying incubation periods for optimal lipase yield. This is notable of increased lipase secretion at 12, 36, and 48 h by *Acinetobacter baylyi* G40, *Pseudomonas* sp. LSK 25, and *Arthrobacter* sp. BGCC#490, respectively [22, 101, 102]. Metal ions stimulate secretion of lipase by microorganisms. Divalent metal ions such as  $\text{Fe}^{2+}$ ,  $\text{Mg}^{2+}$ , and  $\text{Ca}^{2+}$  improved lipase production from *Bacillus subtilis* PCSIRNL-39, *Burkholderia* sp., and *Pseudomonas* sp. LSK 25 [91, 102–104]. Conversely, availability of metal ions can be inhibitory to microbial growth for lipase production. Agitation speed of fermentation medium is vital for microbial lipase production, as it enhances dissolved oxygen transfer rate and promotes dispersal of inducer oil micelles, thus permitting their contact into microorganisms [102, 105].

### Strategies for optimization of microbial lipase production

Optimization of appropriate bioprocess parameters is crucial for improvement in growth and metabolic activities of microorganisms [106]. In addition, exploration of optimal

conditions of the fermentation parameters is key for high lipase yields at lesser costs [14]. A traditional technique known as one variable-at-a-time (OVAT) approach involving change of one variable at a time while maintaining others at a constant level is commonly used to achieve these [107]. However, this method is not only time-consuming, laborious, and expensive, but also fails to depict interaction effects of the different variables tested, leading to misinterpretation of results [108]. In order to overcome these difficulties, statistical experimental designs have been recognized as a preferred method for lipase optimization studies [13, 14, 106, 109, 110] (Table 2). The significant variables influencing lipase production are usually selected with the aid of the Plackett-Burman design (PBD); the optimal conditions and interaction effects of these variables are deduced from the response surface methodology (RSM) or artificial neural network (ANN) [5, 112, 116, 120] (Table 2). The various experimental designs employed for lipase optimization are discussed in details below:

### Plackett-Burman design

Plackett-Burman design is employed for the screening of significant parameters from a large number of bioprocess parameters, and thus applicable in prelude studies involving selection of variables for further optimization studies [121, 122]. It comprises of two types of variables: real variables and dummy variables. Each variable is represented in two levels: high and low. PBD greatly lessens the overall number of experiments since only key variables that influence the synthesis of desired metabolite are selected [122, 123]. PBD is a dependable method for assessment of relative importance of bioprocess parameters for enhanced metabolite production by microorganisms [124–126].

### Response surface methodology

Response surface methodology is an assemblage of mathematical and statistical techniques for modelling and analysis in applications involving optimization of bioprocess parameters for enhanced yield of target metabolite (response) [14, 127]. RSM involves three basic steps: design of experiments for selection of significant parameters accompanied by path of steepest ascent/descent, and finally quadratic regression model is fitted and optimized with the aid of canonical regression method [122]. This approach permits building of models for precise approximation of true response function within a region around the optimum using bioprocess parameters as autonomous variables [107, 128]. RSM is a cost-effective approach applied in evaluating the interaction effects of fermentation variables. In addition, it results in improved productivity, lessens process changeability, and gives closer confirmation of predicted response to the experimental values [129]. Experimental designs such as central composite design



**Table 2** Improvements in lipase production from some microorganisms using statistical experimental designs

Microorganism	Design	Parameter optimized	Improvement yield	Reference
<i>Bacillus aryabhatai</i> SE3-PB	RSM	Temperature, agitation speed, pH, inducer oil concentration and inoculum volume	7.2-fold	[14]
<i>Burkholderia cepacia</i>	RSM	Glucose, palm oil, incubation time, inoculum density and agitation	4-fold	[111]
<i>Enterobacter aerogenes</i> IABR-0785	RSM	Temperature, oil concentration, inoculum volume, pH and incubation period	1.4-fold	[49]
<i>Geobacillus thermoleovorans</i> YN	RSM	Tween 80, olive oil, temperature and pH	4-fold	[50]
<i>Burkholderia</i> sp. HL-10	RSM	Olive oil, tryptone and Tween 80	3-fold	[15]
<i>Geobacillus</i> sp. ARM	RSM and ANN	Temperature, medium volume, inoculum size, agitation rate, incubation period and pH	4.7-fold	[51]
<i>Staphylococcus xylosus</i>	RSM and ANN	Temperature, pH, incubation period, inoculum size, and agitation speed	3.5-fold	[112]
<i>Alkalibacillus salilacus</i> SR-079 Halo	PBD and RSM	Olive oil, KH <sub>2</sub> PO <sub>4</sub> , NaCl, and glucose	4.9-fold	[113]
<i>Thalassospira permensis</i> M35-15	PBD and RSM	Glucose, peptone, yeast powder and olive oil emulsifier	1.85-fold	[114]
<i>Pseudomonas aeruginosa</i>	PBD and RSM	Gum arabic, MgSO <sub>4</sub> , tryptone, and yeast extract	5.58-fold	[115]
<i>Aspergillus niger</i> G783	RSM	Corn starch, soybean meal and soybean oil	16.4%	[116]
<i>Fusarium solani</i> SKWF7	RSM	Palm oil, (NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub> and CaCO <sub>3</sub>	1.7-fold	[117]
<i>Fusarium verticillioides</i>	RSM	KH <sub>2</sub> PO <sub>4</sub> , MgSO <sub>4</sub> , peptone and sunflower oil	2-fold	[118]
<i>Candida rugosa</i> NCIM 3462	PBD and RSM	Glucose, groundnut oil, peptone, (NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub> and FeCl <sub>3</sub> ·6H <sub>2</sub> O	1.64-fold	[119]
<i>Debaryomyces hansenii</i> YLL29	RSM	Glucose, olive oil and pH	2.28-fold	[109]

(CCD), Box-Behnken design (BBD), or Doehlert design are widely used in RSM to approximate a response function to experimental data that cannot be described by linear functions [130].

Response surface methodology in combination with PBD resulted in enhanced practicability of process scale-up and commercialization of lipase production from a multitude of bacteria, fungi, and yeasts [14]. Ruchi et al. [115] screened eleven media components (peptone, tryptone, NH<sub>4</sub>Cl, NaNO<sub>3</sub>, yeast extract, glucose, glycerol, xylose, gum arabic, MgSO<sub>4</sub>, and NaCl) for lipase production by *Pseudomonas aeruginosa* using PBD. The most significant parameters (gum arabic, MgSO<sub>4</sub>, tryptone, and yeast extract) were further optimized by RSM. Maximum lipase yield (5.58-fold) was recorded when tryptone, gum arabic, MgSO<sub>4</sub>, and yeast extract were utilized at concentrations of 1.01%, 0.02%, 0.10%,

and 0.02%, respectively. Similarly, the influence of ten medium components (peptone, glucose, NaCl, MgSO<sub>4</sub>·7H<sub>2</sub>O, FeSO<sub>4</sub>·7H<sub>2</sub>O, CaCl<sub>2</sub>, olive oil, KH<sub>2</sub>PO<sub>4</sub>, NH<sub>4</sub>Cl, and Na<sub>2</sub>HPO<sub>4</sub>) on lipase production by *Alkalibacillus salilacus* SR-079 Halo was studied using PBD [113]. Lipase production was maximally affected by olive oil, KH<sub>2</sub>PO<sub>4</sub>, NaCl, and glucose. Further optimization of the selected variables by RSM resulted in 4.9-fold enhancement in lipase production at optimal levels of glucose (1g/L), NaCl (4.18 mol/L), olive oil (2%), and KH<sub>2</sub>PO<sub>4</sub> (5 g/L).

In addition, cocktail of RSM and OVAT are employed for optimization of lipase production [106]. Papagora et al. [109] optimized lipase production from *Debaryomyces hansenii* YLL29 using RSM. The simple one-factor-at-a-time strategy showed that glucose, olive oil, and pH were the significant variables influencing lipase production. Further optimization

of the selected variables by RSM led to a 2.28-fold increase in lipase production at respective optimal levels of glucose (13.1 g/L), olive oil (19 g/L), and pH (6.4). Similarly, Lo et al. [15] employed RSM and OVAT for the optimization of extracellular lipase production by *Burkholderia* sp. HL-10. Preliminary studies by OVAT revealed that olive oil, tryptone, and Tween-80 exhibited significant effects on lipase production. Optimization by CCD resulted in almost 3-fold increase in maximum lipase production at respective optimum concentrations of olive oil (0.65%, v/v), tryptone (2.42%, w/v), and Tween-80 (0.15%, v/v).

## Potential biotechnological applications of microbial lipases

Microbial lipases constitute an important class of biotechnologically valuable enzymes, mainly due to their versatility in terms of enzymatic properties and substrate specificity. These features make lipases the enzyme of choice for various applications in food, detergent, leather, pharmaceutical, textile, cosmetics, and paper industries etc. (Fig. 2) [3, 131]. Some of the biotechnological applications of microbial lipases are illustrated in Table 3 and discussed in details below:

### Detergent industry

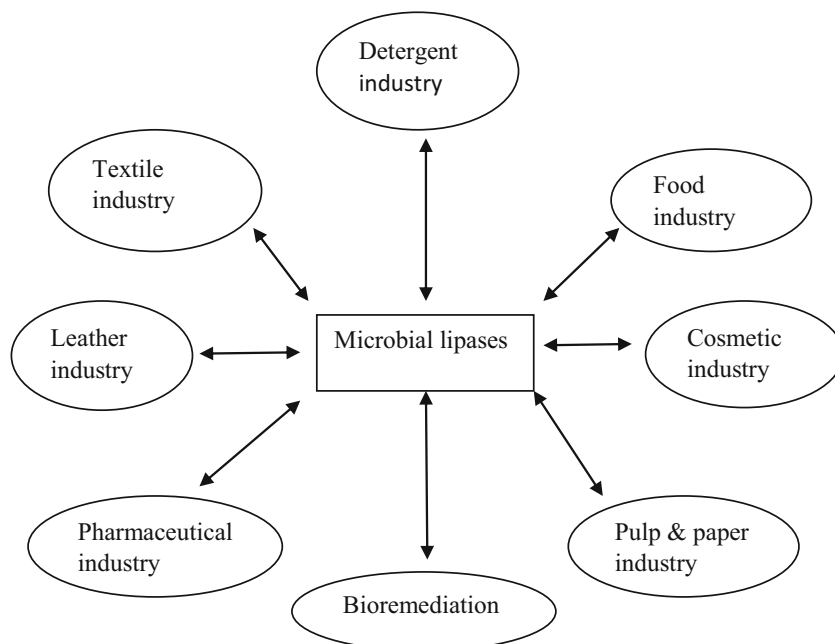
The most important and large-scale application of microbial lipases is their addition in detergent, used mainly in household and industrial laundry [132]. Lipases are employed in detergent formulations for the removal of oily stains on clothes,

thus reducing the need for the patronage of detrimental chemicals. In addition, they are eco-friendly without harmful residue and render no threat to aquatic life [3, 133]. Among the qualities of lipase as a suitable additive in detergents include broad substrate specificity, ability to withstand harsh washing conditions, and exhibit catalytic activity in the presence of various components of detergent formulations [72, 134]. Lipolase from *Thermomyces lanuginosus* represents the first industrial lipase to be introduced into detergent and was commercialized in 1988 by Novo Nordisk. Other lipases including Lumafast (*Pseudomonas mendocina*) and Lipomax (*Pseudomonas alcaligenes*) were commercialized by Genencor (now Du Pont) [11]. Recently, lipases from several microorganisms have been characterized as potent detergent additives [132, 135].

### Food industry

Fats and oils are vital constituents of foods; the nutritional and sensory values as well as physical properties of a triglyceride are greatly influenced by position of fatty acid in the glycerol backbone, the chain length of the fatty acid, and its degree of unsaturation etc. [136]. The modification of structure and composition of fats and oils is of great significance in food processing industries that require new economics and green technologies. Microbial lipases that are regiospecific and fatty acid specific are of enormous important for the production of many food products. For instance, lipase-catalyzed reactions can be used to modify and upgrade cheap oil into nutritionally important structured triacylglycerols such as cocoa butter substitutes, low calories triacylglycerols, and oleic acid enriched

**Fig. 2** Schematic illustration of potential biotechnological applications of microbial lipases



**Table 3** Some potential biotechnological applications of microbial lipases

Industry	Role	Product or application
Detergent	Removal of fat and oil stains on clothes	Clean fabrics
Pulp and paper	Elimination of pitch from pulp produced during paper-making processes	Paper with better quality
Pollution abatement	Hydrolysis and trans-esterification of oils and greases	Reduce organic pollutant load
Petroleum industry	Trans-esterification	Biodiesel
Leather	Removal of fats and greases from skins and hides	Cleaner finished products
Dairy foods	Hydrolysis of milk fat; cheese ripening; modification of butter, fat and cream	Flavoring agent in milk, cheese and butter
Beverages	Improved aroma	Alcoholic beverages, e.g. sake wine
Fats and oil industry	Hydrolysis, esterification and inter-esterification	Cocoa butter, margarine, fatty acids, glycerol, mono- and diglycerides
Bakery foods	Enhance flavor content; prolong shelf-life; improve texture and softness	Bread, rolls, pies, muffins, cookies, pastries
Meat and fish	Flavor development; fat removal	Meat and fish products
Food dressings	Quality improvement	Mayonnaise, dressing and whippings
Cosmetics	Esterification	Emulsifiers, moisturizers
Agrochemicals	Esterification, hydrolysis	Herbicides (such as phenoxypropionate)
Pharmaceuticals	Trans-esterification, Hydrolysis	Specialty lipids, digestive aids; intermediates used in the manufacture of medicines

oils [137]. Lipases have also been used in foods to modify flavor by synthesis of esters of short chain fatty acids and alcohol, which are known flavor and fragrance compounds [138]. In addition, lipases are used in the removal of fats from meat and fish products to produce lean meat. The fat is removed during processing of the fish meat by addition of lipases, a phenomenon known as bio-lipolysis [139]. Lipases also play a substantial role in the fermentative production of sausage and to determine change in long-chain fatty acid released during ripening [3]. Over decades, microbial lipases have been used for refining rice flavor, modifying soybean milk, improving aroma, and enhancing fermentation in apple wine [140].

### Cosmetics industry

Lipases are employed as a biocatalyst for the production of cosmetic products including isopropyl palmitate and 2-ethylhexyl palmitate, which are used as emollient in personal care products such as skin and sun-tan creams and bath oils [141]. In contrast to synthetic chemicals, the use of microbial lipases in cosmetics industries gives products of improved quality with minimum downstream processing. These include wax esters (esters of fatty acids and fatty alcohols) produced from catalytic reaction of lipase from *Candida cylindracea* and used in personal care products [142]. In addition, enzymatic production of water-soluble retinol derivatives from immobilized lipase has been reported [143]. Lipases are also

used in hair waving preparations and as a component of topical anti-obese creams or as oral administration [11].

### Pulp and paper industry

Microbial lipases are employed in pulp and paper industry for the removal of pitch (a hydrophobic component in wood), which creates severe problems in paper mill by producing gluey deposits in the paper machines and causes spots in the finished paper products [144]. This is achieved by hydrolyzing triglycerides in the pitch into monoglycerides, glycerol, and fatty acids, which are less sticky and highly hydrophilic [144, 145]. Thus, decreasing chemical consumption promote longevity of equipment and save energy and time [3]. The enzymatic pitch control technique involving the use of lipase has been a common practice for commercial paper making process [146]. These biocatalysts increase pulping rate and further enhance whiteness and strength of finished paper product [147].

### Bioremediation of oily wastewater

Lipids are noxious components of industrial and municipal wastewaters since they contribute greatly to the organic load of the wastewater and promote the growth of filamentous microorganisms [148]. Therefore, their transformation into innocuous products is imperative. The use of biocatalysts serves as a promising technology for the treatment of high



fat-containing wastewater [149]. An alternative to conventional approaches that is attracting growing interest is the use of enzymes, which significantly reduce the level of organic pollutants in the wastewater by means of enzymatic catalysis and enhance better performance of microbial community at the later stage of biological treatment process [149]. Application of lipases from different sources in the treatment of wastewater from lipid-processing factories, dairies, restaurants etc. offers a novel approach in enzyme biotechnology, thus making the wastewater acquiescent to conventional biological treatment [150]. The utilization of a solid enzymatic preparation from *Penicillium restrictum* for the treatment of dairy wastewater with high levels of oil and grease (O & G) has been reported [151]. Results obtained showed 13% higher chemical oxygen demand (COD) removal efficiency with 40% lower accumulation of O & G. In addition, enzymatic treatment of coconut mill effluent using lipase from *Staphylococcus pasteurii* COM-4A revealed COD and O & G removal efficiencies of 29% and 45%, respectively [150].

## Conclusions

Microbial lipases are produced by diverse groups of microorganisms including bacteria, fungi, and yeasts. The production of these biocatalysts is influenced by nutritional and physicochemical parameters. Optimization of fermentation parameters through statistical experimental designs is crucial in order to maintain a balance among various components for enhanced lipase production. Microbial lipases are employed in high demands for a variety of biotechnological applications in food, cosmetics, pulp and paper, and detergent industries as well as in environmental bioremediation.

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