Acta Scientific Microbiology (ISSN: 2581-3226)
Volume 8 Issue 3 March 2025

Systematic Review

A Systematic Review (Before 31 August 2024) on the Applications of *Yarrowia lipolytica*

Victor R Lukianto[1,2], Keng Yao Yeo[1,2], Madhunisha Arivazhagan[1,2], Ashmitha Senthilkumar[1,2], Tanisha Saisudhanbabu[1,2], Minh Anh Le[1,2], Travina BS Wong[1,2] and Maurice HT Ling[1,2,3]*

[1]*School of Life Sciences, Management Development Institute of Singapore, Singapore*

[2]*Department of Applied Sciences, Northumbria University, United Kingdom*

[3]*HOHY PTE LTD, Singapore*

***Corresponding Author:** Maurice HT Ling, School of Life Sciences, Management Development Institute of Singapore, Singapore.

DOI: 10.31080/ASMI.2025.08.1497

Received: February 06, 2025
Published: February 22, 2025

Abstract

Yarrowia lipolytica in both traditional and industrial processes due to its break down materials that are commonly found in the waste, and as a bio-factory for the production of target products such as biofuels. To date, no systematic review on the applications of *Y. lipolytica* has been published. Hence, we present a systematic review on the applications of *Y. lipolytica* using studies indexed in PubMed up to 31 August 2024. 40 out of original 59 articles were included. Three main themes were identified; namely, (i) Improving efficiency in industrial processes, (ii) Strain survey and (iii) Target products.

Keywords: Valorization; Biofactory; Waste Management; Lipids; Proteins; Fatty acids

Introduction

Yarrowia lipolytica is a yeast that has been widely studied for its ability to grow efficiently in a variety of environments and break down materials that are commonly found in the waste settings [1]. *Y. lipolytica* is also of interest due to its ability to use oils and fats as its sole carbon source [2,3]. They have also been found to be involved in certain traditional processes such as sausage making [4] and food fermentation [5]. *Y. lipolytica* has been found to be capable of producing target products of interest, and also in the breaking down of waste material. This has extended to the exploration of applying *Y. lipolytica* to different stages of waste management and the potential it has to produce biofuel from different phases of waste materials [1,6-20].

Systematic review is a good method for researchers to keep up with the various research effort [21]. In 2024, a systematic map [22] on the applications of *Y. lipolytica* [23] has been presented as poster in SynBioSG Conference 2024 by theming of articles in PubMed prior to 31 July 2023. No systematic review on applications of *Y. lipolytica* has been found in PubMed to date.

The purpose of this study aims to present a systematic review on the applications of *Y. lipolytica* using studies indexed in PubMed up to 31 August 2024. Of the 59 articles found through search, 40 were included, and three main themes were identified; namely, (i) Improving efficiency in industrial processes, (ii) Strain survey and (iii) Target products.

Methods

A PubMed search using the search term, "Yarrowia lipolytica" AND (valor* OR biofactory OR "bio-factory" OR "microbial factory"), was conducted. The date limit was set to 01 January 1000 (default start date) to 31 August 2024. The search URL was https://

pubmed.ncbi.nlm.nih.gov/?term="Yarrowia+lipolytica"+AND+(valor*+OR+biofactory+OR+"bio-factory"+OR+"microbial+factory")&filter=dates.1000/1/1-2024/8/31. Three exclusion criteria were used: (i) No full text availability, (ii) Article not written in English, and (iii) Non-primary literature.

Results and Discussion

59 articles were initially obtained from the search, and 40 articles were included in this review (Figure 1). From these 40 articles, three main themes were identified (Table 1); namely, (i) Improving efficiency in industrial processes, (ii) Strain survey and (iii) Target products.

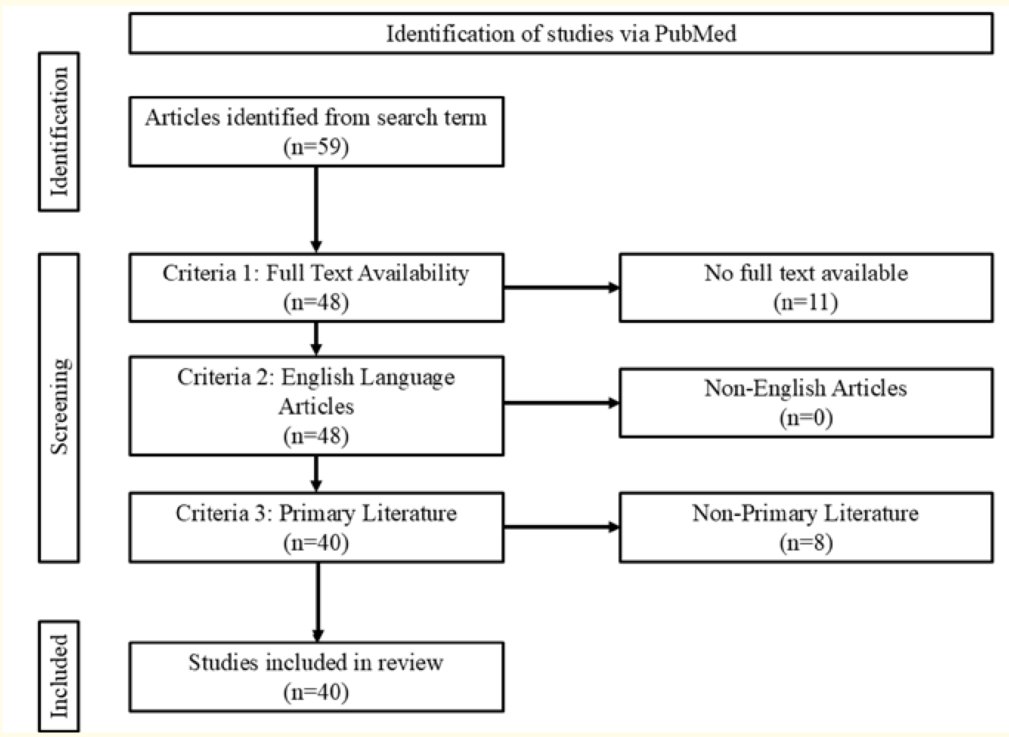

Figure 1: PRISMA Diagram [24,25].

Table 1: Theming of Included Studies.

Main Theme	Sub-Theme	Number of Articles
Improving efficiency in industrial processes	Genetic engineering	14 [3,12,17,19,26-35]
	Feedstock modifications	3 [3,36,37]
	Environmental parameters modifications	2 [38,39]
Strain survey	Viability for industrial processes	17 [2,6,8,12,18,19,27,32,36,40-47]
	Uses in traditional processes	2 [4,33]
	Food spoilage	4 [2,5,39,48]
Target Products	Lipids	9 [2,3,12,18,19,29,34,40,45]
	Proteins	2 [17,35]
	Fatty acids	3 [3,4,38]
	Other	30 [1,3,5,6,8,14,17,19,26-33,35-37,39,41-43,46,47,49-53]

Theme 1: Improving efficiency in industrial processes

Genetic engineering is generally conducted to either improve the product yield or to be able to survive in industrial environments. In some cases, *Y. lipolytica* was transformed in order to produce substances it is usually unable to [17,27,32]. In this situation, *Y. lipolytica* was picked as the organism for transformation because of its well-studied genetic lines and its adaptability to environmental stressors. Due to the increasing usage of *Y. lipolytica* as a bio-factory, there is also interest to enhance its production of target products, such as protein [35]. In relation to tolerance, *Y. lipolytica* was found to have inherent tolerance mechanisms to aromatic aldehydes [28]. This means that these mechanisms can be exploited and also enhanced to achieve tolerances as needed in any industrial setting. The development of higher tolerances to substances in the industrial setting is also an important field for research; they allow for better application of *Y. lipolytica* [26,29]; acetate is usually a toxic substrate for most microorganism, while adaptive tolerance to ferulic acid allows *Y. lipolytica* proves that mutated strains can be used for industrial applications. Other studies focused on the tolerance of *Y. lipolytica* to higher concentrations of feedstocks while maintaining or even improving its productivity under such conditions [12,30,34].

Research has been conducted into modifying the feedstock that *Y. lipolytica* has access to in order to manipulate the output of different target products. In some cases, this can result in an increase in the productivity in a bio-factory setting. Changing the base of the feedstock from glucose to oil increases its biomass yields and cell sizes; this however causes its protein content and enzyme abundance for product synthesisation to decrease significantly [3]. When comparing different strains of *Y. lipolytica*, it was also evident that different strains performed differently in its utilisation of glucose when the feedstock was modified [37]. A study also focused on getting the optimal ratio of feedstock composition to get the highest yield of erythritol [36].

By changing the temperature, pH and other variables in the bio-factory, the productivity of productivity of *Y. lipolytica* can be manipulated. Changes in the lipolytic activity of *Y. lipolytica* can be observed when these environmental parameters are tweaked [38]. This study also observed that *Y. lipolytica* strains coming from different environmental origins reacted differently to changes in their environment in the bio-factory setting [38]. Another study focused on the effect of the thermal history on the tolerance of *Y. lipolytica* to high pressure environments [39].

Theme 2: Strain survey

Research in this field focuses on the ability of different strains *Y. lipolytica* to produce target products and their adaptability to an industrial setting. While these strains can be engineered to survive better in an industrial setting as discussed in a previous point, it is important to survey if their native strains can be applied as they are [2,12,36,41,43,44]. These indicate that *Y. lipolytica* is a highly desirable microorganism as a bio-factory. In addition to this, proving that *Y. lipolytica* was able to not just break down, but also produce added-value products from waste (from food production and other applications) and industrial by-products opens many new avenues for the application of *Y. lipolytica* [6,8,12,18,42,44-46]. This also means that *Y. lipolytica* can be used in multiple phases of a bio-factory; production, followed by waste management, allowing for lesser wastage and higher yields for by products. It was also important to survey the ability of *Y. lipolytica* to grow on glycerol, which is the main by-product in the production of bio-diesel [41,43,47]; of particularly interest was whether waste water could be used as feedstock in combination with crude glycerol [45].

Finding the ways that *Y. lipolytica* might have been used in traditional processes, typically in the culinary field, can help to shine light on their capabilities. Processes involved with fermentation are also of particular interest as their environments can be potentially replicated in the industrial setting as a base point. *Y. lipolytica* was isolated from different sausages produced in Italy, and characterised for the lipolytic activity on pork fat [4]. These different yeasts were found to enhance the industrial process for the production of sausages. However, in another study, the usage of yeasts and its proteolytic activity on cheese ripening was characterised using Fourier transform infrared spectroscopy [33].

This research focuses on the presence of *Y. lipolytica* in various natural environments. This includes their presence and survivability in different urban environments, such as in a cold environment (the refrigerator). Surveying the characteristics of different strains of *Y. lipolytica* is an interest in the research field [2,48]. These environments included commercial chilled foods, lagoons, light butter and even irradiated poultry meat. The results from one study indicated that the strains were well adapted and featured characteristics that attributed to their success in their native habitats [2]. When compared with other yeasts, *Y. lipolytica* also exhibited the strongest proteolytic and lipolytic activities; both traits are desirable for the purpose of microbial factory [48]. Studies on strains of *Y. lipolytica* in comparison with other food spoilage yeast species helped to form a good survey into the growth conditions necessary for optimal growth [39]. Fermentation of okara (soybean residue) by *Y. lipolytica* was also studied and proved that it boosted the health benefit of the food [5].

Theme 3: Target products

Due to the ability of *Y. lipolytica* to accumulate lipids, these cellular products are often used for the measurement of different parameters [2,12,18,29,34,45]. In another case, the presence of lipids within the culture indicated that *Y. lipolytica* was capable of valorising the intended feedstock of interest [19]. A study conducted to investigate the capability of *Y. lipolytica* to valorise volatile fatty acids and glycerol to produce microbial lipids revealed that its usage to process these two industrial by-products was feasible [40]. Interestingly, the lipids found to have been produced by *Y. lipolytica* was found to be similar to that of vegetable oils, which is also of interest to the bio-industrial field.

Y. lipolytica also has the ability to produce proteins and recombinant protein products using carbon substrates. To that end, there has been interest in the usage of papaya fruit waste as a low-cost feedstock for the production of such target proteins and protein products [17]. Their ability to valorise the waste, including the juice and seeds of the papaya makes it an interesting subject for industrial usage. Further research to induce more optimal protein production in *Y. lipolytica* has also been conducted [35]; in this particular article, they focused on transformation to enhance protein expression.

In traditional processes such as food making, the lipolytic ability of *Y. lipolytica* is favoured for its major products: free fatty acids. This was apparent in the study conducted into the yeasts found in traditional sausage making processes [4]. There is also interest in the production of terpenoids and other fatty acids due to *Y. lipolytica*'s ability to produce these substances naturally and organically, in particular while growing on lipid-based waste products [3]. Fatty acids produced naturally by *Y. lipolytica* also served as a great method for measuring its activity when exposed to different environmental conditions and comparing their activity from different sources [38].

Biofuels and biomass as target products are of primary interest to researchers. Biomass can be loosely defined as just accumulated cell mass comprising of lipids and proteins; both of which *Y. lipolytica* accumulates well naturally [8]. These target products also serves as great indicators for their activity during research into the production of genetically engineered strains of *Y. lipolytica* [31]. Biomass was also used to measure the relative ability of *Y. lipolytica* to grow on media commonly found in the industry [26,41].

Sugars formed as a byproduct during the growth of *Y. lipolytica* was also used to measure their activity in different forms of media [28]. In the case of the fermentation of okara, sugars detected proved that *Y. lipolytica* was able to improve the digestibility and potential health benefits of okara [5]. Erythritol is another sugar that is of interest for production; this is due to its popularity as a noncariogenic sweetener [36].

Citric acid, which is another organic product of industrial interest, is a target product focused on by researchers. Global demand for citric acid has been on the rise [50] and the search for a method of production that is renewable places *Y. lipolytica* in a unique position.Their presence in a bio-factory setting proves that *Y. lipolytica* was able to produce citric acid in different environments [1]. Certain strains of *Y. lipolytica* have been shown to be able to produce citric acid in satisfiable amounts [50]. Curiously, it was also found that when *Y. lipolytica* was grown on glycerol, they produced citric acid instead of accumulating reserve lipids [42,47]; this opens up the avenue for the usage of *Y. lipolytica* to make use for crude glycerol formed as industrial by-product to produce even more citric acid, reducing further wastage.

The rest of the target products includes magnesium oxide [6], lanthanides [46] and mannitol [42,51]. Magnesium oxide nanoparticles was targeted to show that *Y. lipolytica* was capable of efficient dual valorisation of olive mill wastewater. The recovery of lanthanides from spent catalysts presents a renewable and sustainable method to optimise production. Mannitol is of interest in the medical community for its properties as a diuretic.

Conclusion

There is plenty of interest in *Y. lipolytica* as both a solution to waste management and also as bio-factories for the production of different natural products, including biofuel. At times, these interests also overlap and proves that *Y. lipolytica* is an excellent organism that is capable of doing both. Its ability to be easily enhanced to target specific products or increase production, and its tolerance to most extreme environments allows it to be quite viable for industrial processes. With time, there might be more research that goes into other interests for *Y. lipolytica*, such as using them in conjunction with other microorganisms for waste management, or comparing them to other yeasts as a bio-factory. Genetic engineering could also advance in that time, allowing *Y. lipolytica* to produce multiple target products at the same time.

Supplementary Materials

Supplementary materials for this study can be download from https://bit.ly/Ylipolytica_SR.

Conflict of Interest

The authors declare no conflict of interest.

Bibliography

1. Lanciotti R., *et al*. "Use of Yarrowia lipolytica strains for the treatment of olive mill wastewater". *Bioresource Technology* 96.3 (2005): 317-322.

2. Sinigaglia M., *et al*. "Biochemical and physiological characteristics of Yarrowia lipolytica strains in relation to isolation source. *Canadian Journal of Microbiology* 40.1 (1994): 54-59.

3. Worland AM., *et al*. "Analysis of Yarrowia lipolytica growth, catabolism, and terpenoid biosynthesis during utilization of lipid-derived feedstock". *Metabolic Engineering Communications* 11 (2020): e00130.

4. Gardini F., *et al*. "A survey of yeasts in traditional sausages of southern Italy". *FEMS Yeast Research* 1.2 (2001): 161-167.

5. Vong WC., *et al*. "Biotransformation with cellulase, hemicellulase and Yarrowia lipolytica boosts health benefits of okara". *Applied Microbiology and Biotechnology* 101.19 (2017): 7129-7140.

6. Hamimed S., *et al*. "Dual Valorization of Olive Mill Wastewater by Bio-Nanosynthesis of Magnesium Oxide and Yarrowia lipolytica Biomass Production". *Chemistry and Biodiversity* 17.3 (2020): e1900608.

7. Coleman SM., *et al*. "Evolving tolerance of Yarrowia lipolytica to hydrothermal liquefaction aqueous phase waste". *Applied Microbiology and Biotechnology* 107.5-6 (2023): 2011-2025.

8. Hamimed S., *et al*. "High-performance biological treatment of tuna wash processing wastewater using Yarrowia lipolytica". *Environmental Science and Pollution Research International* 28.2 (2021): 1545-1554.

9. Žganjar M., *et al*. "High-throughput screening of non-conventional yeasts for conversion of organic waste to microbial oils via carboxylate platform". *Scientific Reports* 14.1 (2024): 14233.

10. Kothri M., *et al*. "Microbial sources of polyunsaturated fatty acids (PUFAs) and the prospect of organic residues and wastes as growth media for PUFA-producing microorganisms". *FEMS Microbiology Letters* 367.5 (2020): fnaa028.

11. Gamraoui A., *et al*. "Musico-bioremediation of seafood canning wastewater by Yarrowia lipolytica". *World Journal of Microbiology and Biotechnology* 39.11 (2023): 303.

12. Katre G., *et al*. "Mutants of Yarrowia lipolytica NCIM 3589 grown on waste cooking oil as a biofactory for biodiesel production. *Microbial Cell Factories* 16.1 (2017): 176.

13. Do DTH., *et al*. "Organic Wastes as Feedstocks for Non-Conventional Yeast-Based Bioprocesses". *Microorganisms* 7.8 (2019): 229.

14. Fraga JL., *et al*. "Palm oil wastes as feedstock for lipase production by Yarrowia lipolytica and biocatalyst application/reuse". *3 Biotech* 11.4 (2021): 191.

15. Peterson EC., *et al*. "Single cell protein and oil production from solid cocoa fatty acid distillates co-fed ethanol". *Bioresource Technology* 387 (2023): 129630.

16. Wang S., *et al*. "Sustainable biosynthesis of squalene from waste cooking oil by the yeast Yarrowia lipolytica". *Metabolic Engineering Communications* 18 (2024): e00240.

17. Han Z., *et al*. "Valorization of papaya fruit waste through low-cost fractionation and microbial conversion of both juice and seed lipids". *RSC Advances* 8.49 (2018): 27963-27972.

18. Magdouli S., *et al*. "Valorization of raw glycerol and crustacean waste into value added products by Yarrowia lipolytica". *Bioresource Technology* 243 (2017): 57-68.

19. Cordova LT., *et al*. "Valorizing a hydrothermal liquefaction aqueous phase through co-production of chemicals and lipids using the oleaginous yeast Yarrowia lipolytica". *Bioresource Technology* 313 (2020): 123639.

20. Lopes M., *et al*. "Yarrowia lipolytica as a biorefinery platform for effluents and solid wastes valorization - challenges and opportunities". *Critical Reviews in Biotechnology* 42.2 (2022): 163-183.

21. Munn Z., *et al*. "Systematic Review or Scoping Review? Guidance for Authors When Choosing Between a Systematic or Scoping Review Approach". *BMC Medical Research Methodology* 18.1 (2018): 143.

22. Grant MJ and Booth A. "A Typology of Reviews: An Analysis of 14 Review Types and Associated Methodologies". *Health Information and Libraries Journal* 26.2 (2009): 91-108.

23. Ling MH., *et al*. "Yarrowia lipolytica as a Valorization Biofactory". *SynBioSG Conference 2024* (Matrix, Biopolis, Singapore) (2024).

24. Liberati A., *et al*. "The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies that Evaluate Health Care Interventions: Explanation and Elaboration". *PLoS Medicine* 6.7 (2009): e1000100.

25. Moher D., *et al*. "Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement". *PLoS Medicine* 6 (7 (2009): e1000097.

26. Wang Z., *et al*. "Adaptive laboratory evolution of Yarrowia lipolytica improves ferulic acid tolerance". *Applied Microbiology and Biotechnology* 105.4 (2021): 1745-1758.

27. Yu J., *et al*. "Bioengineering triacetic acid lactone production in Yarrowia lipolytica for pogostone synthesis". *Biotechnology and Bioengineering* 115.9 (2018): 2383-2388.

28. Zhou L., *et al*. "Combined adaptive evolution and transcriptomic profiles reveal aromatic aldehydes tolerance mechanisms in Yarrowia lipolytica". *Bioresource Technology* 329 (2021): 124910.

29. Narisetty V., *et al*. "Development of Hypertolerant Strain of Yarrowia lipolytica Accumulating Succinic Acid Using High Levels of Acetate". *ACS Sustainable Chemistry and Engineering* 10.33 (2022): 10858-10869.

30. Delfau-Bonnet G., *et al*. "Evaluation of the Potential of Lipid-Extracted Chlorella vulgaris Residue for Yarrowia lipolytica Growth at Different pH Levels". *Marine Drugs* 20.4 (2022): 264.

31. Georgiadis I., *et al*. "Identification and Construction of Strong Promoters in Yarrowia lipolytica Suitable for Glycerol-Based Bioprocesses". *Microorganisms* 11.5 (2023): 1152.

32. Shi X., *et al*. "Isopropanol biosynthesis from crude glycerol using fatty acid precursors via engineered oleaginous yeast Yarrowia lipolytica". *Microbial Cell Factories* 21.1 (2022): 168.

33. Lucia V., *et al*. "Use of Fourier transform infrared spectroscopy to evaluate the proteolytic activity of Yarrowia lipolytica and its contribution to cheese ripening. *International Journal of Food Microbiology* 69.1-2 (2001): 113-123.

34. Tsirigka A., *et al*. "Novel evolved Yarrowia lipolytica strains for enhanced growth and lipid content under high concentrations of crude glycerol". *Microbial Cell Factories* 22.1 (2023): 62.

35. Dulermo R., *et al*. "Using a vector pool containing variable-strength promoters to optimize protein production in Yarrowia lipolytica". *Microbial Cell Factories* 16.1 (2017): 31.

36. Rakicka M., *et al*. "An Effective Method of Continuous Production of Erythritol from Glycerol by Yarrowia lipolytica MK1". *Food Technology and Biotechnology* 55.1 (2017): 125-130.

37. Lubuta P., *et al*. "Investigating the Influence of Glycerol on the Utilization of Glucose in Yarrowia lipolytica Using RNA-Seq-Based Transcriptomics". *G3 (Bethesda, Md)* 9.12 (2019): 4059-4071.

38. Guerzoni ME., *et al*. "Variability of the lipolytic activity in Yarrowia lipolytica and its dependence on environmental conditions". *International Journal of Food Microbiology* 69.1-2 (2001): 79-89.

39. Lanciotti R., *et al*. "Effects of growth conditions on the resistance of some pathogenic and spoilage species to high pressure homogenization". *Letters in Applied Microbiology* 22.2 (1996): 165-168.

40. Fontanille P., *et al*. "Bioconversion of volatile fatty acids into lipids by the oleaginous yeast Yarrowia lipolytica". *Bioresource Technology* 114 (2012): 443-449.

41. Juszczyk P., *et al*. "Biomass production by novel strains of Yarrowia lipolytica using raw glycerol, derived from biodiesel production". *Bioresource Technology* 137 (2013): 124-131.

42. Papanikolaou S., *et al*. "Conversion of biodiesel-derived glycerol into biotechnological products of industrial significance by yeast and fungal strains". *Engineering in Life Sciences* 17.3 (2017): 262-281.

43. Filippousi R., *et al*. "Isolation, identification and screening of yeasts towards their ability to assimilate biodiesel-derived crude glycerol: microbial production of polyols, endopolysaccharides and lipid". *Journal of Applied Microbiology* 127.4 (2019): 1080-1100.

44. Louhasakul Y., *et al*. "Metagenomic insights into bioaugmentation and biovalorization of oily industrial wastes by lipolytic oleaginous yeast Yarrowia lipolytica during successive batch fermentation". *Biotechnology and Applied Biochemistry* 67.6 (2020): 1020-1029.

45. Sarris D., *et al*. "Production of Added-Value Chemical Compounds through Bioconversions of Olive-Mill Wastewaters Blended with Crude Glycerol by a Yarrowia lipolytica Strain". *Molecules (Basel, Switzerland)* 24.2 (2019): 222.

46. Azevedo DMF., *et al*. "Recovery of lanthanides from hydrocarbon cracking spent catalyst through chemical and biotechnological strategies". *Journal of Environmental Science and Health Part A, Toxic/Hazardous Substances and Environmental Engineering* 54.7 (2019): 686-693.

47. Papanikolaou S., *et al*. "Yarrowia lipolytica as a potential producer of citric acid from raw glycerol". *Journal of Applied Microbiology* 92.4 (2002): 737-744.

48. Guerzoni ME., *et al*. "Survey of the physiological properties of the most frequent yeasts associated with commercial chilled foods". *International Journal of Food Microbiology* 17.4 (1993): 329-341.

49. Vannini L., *et al*. "Evaluation of Fourier-transform infrared spectroscopy for data capture in predictive microbiology". *World Journal of Microbiology and Biotechnology* 12.1 (1996): 85-90.

50. Sarris D., *et al*. "Growth Response of Non-Conventional Yeasts on Sugar-Rich Media: Part 2: Citric Acid Production and Circular-Oriented Valorization of Glucose-Enriched Olive Mill Wastewaters Using Novel Yarrowia lipolytica Strains". *Microorganisms* 11.9 (2023): 2243.

51. Tomaszewska L., *et al*. "Production of erythritol and mannitol by Yarrowia lipolytica yeast in media containing glycerol". *Journal of Industrial Microbiology and Biotechnology* 39.9 (2012): 1333-1343.

52. Darvishi F., *et al*. "Production of Laccase by Recombinant Yarrowia lipolytica from Molasses: Bioprocess Development Using Statistical Modeling and Increase Productivity in Shake-Flask and Bioreactor Cultures". *Applied Biochemistry and Biotechnology* 181.3 (2017): 1228-1239.

53. Kubiak M., *et al*. "Thermal treatment improves a process of crude glycerol valorization for the production of a heterologous enzyme by Yarrowia lipolytica". *Biotechnology Reports (Amsterdam, Netherlands)* 31 (2021): e00648.