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OVERVIEW OF THE IMPACTS OF MICROBIAL BIOTRANSFORMATION BIOPROCESSES – A REVIEW

Willian Ferreira da Luz
Bachelor of Biological Sciences, Institute of Biotechnology, Federal University of Catalão
Catalão – Goiás
http://lattes.cnpq.br/7733427200756887

Heliana Batista de Oliveira
Professor at the Department of Biological Sciences, Institute of Biotechnology, Federal University of Catalão
Catalão – Goiás
https://orcid.org/0000-0003-1099-1963

Jupyracyara Jandyra de Carvalho Barros
Professor at the Department of Biological Sciences, Institute of Biotechnology, Federal University of Catalão
Catalão – Goiás
http://lattes.cnpq.br/6606845827336525

Abstract: Human activities, in the most varied sectors of knowledge and technological production, have generated negative and positive impacts on the world stage. Current perspectives in the field of microbiology allow us to glimpse various alternatives for these issues in the applied biotechnologies, among which stands out the biotechnology of microbial biotransformation. The present study aims at the elaboration of a systematic literature review about microbiological events applied to different industrial sectors. For the organization of the data, queries were carried out in the online scientific databases Periodicals CAPES and SciELO, adopting the last 10 years as the period for collecting articles and analyzing the information. 22 files were found, however 8 articles were excluded, resulting in 14 articles for the literature review. In general, it was possible to show that the different articles portray that biotransformation is indeed a valuable strategy that can be applied in the environmental, laboratory and medicinal sectors, through simplified methodologies and with reduced costs, being evident in these events the application of fungi in the stages and processes of biotransformation in a comprehensive way in several areas of research.
Keywords: Biotransformation; bioprocesses; microbiology.

INTRODUCTION

Technological advances arising from modernization and innovations in the techniques used in various industrial and human activities have directly and indirectly impacted the planet, the activities performed by man, as well as the products obtained through these industrial activities. Such activities are capable of generating waste that accumulates in the environment, while at the same time enabling the improvement of products and/or by-products obtained throughout their production stages. This has led to the need for studies, research and the development of new techniques aimed at minimizing and maximizing the potential of these impacts, when negative and positive, respectively.

In this sense, current perspectives in the field of microbiologyallow us to glimpse in applied biotechnologies several alternatives for these questions. Among the available biotechnologies, the biotechnology of microbial biotransformation, also called microbial bioconversion, has proven to be a notorious alternative to be better studied and deepened (FRANCO et al., 2015).

Microbial biotransformation can be understood as a biotechnology based on the oxidation of organic compounds through biological routes, from micro-organisms or enzymes secreted by them (PINEDA et al., 2012; SILVA et al., 2012; OLIVEIRA et al., 2015). Demonstrating to be efficient in a wide range of research areas, according to what has been developed and reported in scientific productions.

The microbiological events of microbial bioconversion have been applied in areas such as food microbiology, and can be perceived as an alternative to increase the functional effect and bioavailability of compounds (SILVA et al., 2012), in environmental microbiology, as a mediating tool in reducing the concentrations of compounds harmful substances with marked difficulty of degradation present in the environment, such as chlorophenols, showing potential for the development of research related to bioremediation (LUCARINI; OLIVEIRA; GIANETTI, 2017), in clinical microbiology, presenting potential for differentiating pathogenic microorganisms in diagnoses (SOUZA; CORBELLINI, 2019), as well as in the agro-industrial context, participating as a biological route for the

synthesis of oxide nanomaterials, such as, for example,silica nanoparticles (PINEDA et al., 2012). The impacts of using this biotechnology can also be perceived in other areas of research, such as pharmacology, molecular biology and biochemistry.

It is worth mentioning that the importance of bioconversion, for issues that go beyond the laboratory and industrial scope, can be perceived in its effectiveness as an ecological measure in the control of environmental conditions (LUCARINI; OLIVEIRA; GIANETTI, 2017) or mitigating measure in issues of regional economic inequalities in the production processes of small and medium producers (FRANCO et al., 2015).

Given this scenario, the present work aimed to carry out a literature review to address and update perspectives on the surveys carried out within the theme "processes and techniques of biotechnology of microbial biotransformation" in the scientific production carried out between the years 2012 and 2021, in such a way that it can serve as support for future research focused on the field of microbiology with regard to microbial biotransformation.

METHODOLOGY

A systematic review of the literature was carried out through consultations with the collections of the online databases Periodicals CAPES and SciELO, aiming to update the information on the subject."processes and techniques of microbial biotransformation biotechnology" obtained between the years 2012 and 2021 of scientific production.

OBTAINING THE TOTAL FILES AVAILABLE

To collect the total number of files available during the study period, in both databases, the following search criteria were used: (i) search term: biotransformation; (ii) file type: article; (iii) availability: open access; (iv) publication date: 2012 to 2021; (v) language: Portuguese and English. Thus, a total of 46 files were found in the online database Periódicos CAPES and 7 files in the SciELO database.

PRELIMINARY SELECTION OF RELEVANT ARTICLES

For carrying out theFor the development of this study, 22 articles were filtered from the total amount of files available, according to the following filtering, selection and exclusion criteria: (i) the term "biotransformation" must necessarily be present in the keywords, title, abstract or subject of the article; (ii) articles that presented themselves as a literature review, both in their title and throughout their abstracts, were excluded from the study; (iii) verification of pertinence to the topic and research area of microbiology, carried out by reading the abstracts of each article; (iv); if the article appears in both languages selected for search, prefer the Portuguese language; (v) exclusion of articles that allow online reading only and do not have free access to their full PDF version.

FINAL SELECTION OF CONFIRMED RELEVANT ARTICLES

Of the 22 files filtered, 6 articles were present in both databases, 1 article was only read online and denied free access to the full PDF version, and 1 article mentioned being a literature review only in the presentation of objectives. Thus, 8 articles were excluded from the amount, totaling 14 articles to carry out the literature review.

Figure 1 shows the steps taken to obtain the articles, demonstrating the number of total bibliographies found in each online scientific database, according to the search and collection criteria, the number of articles

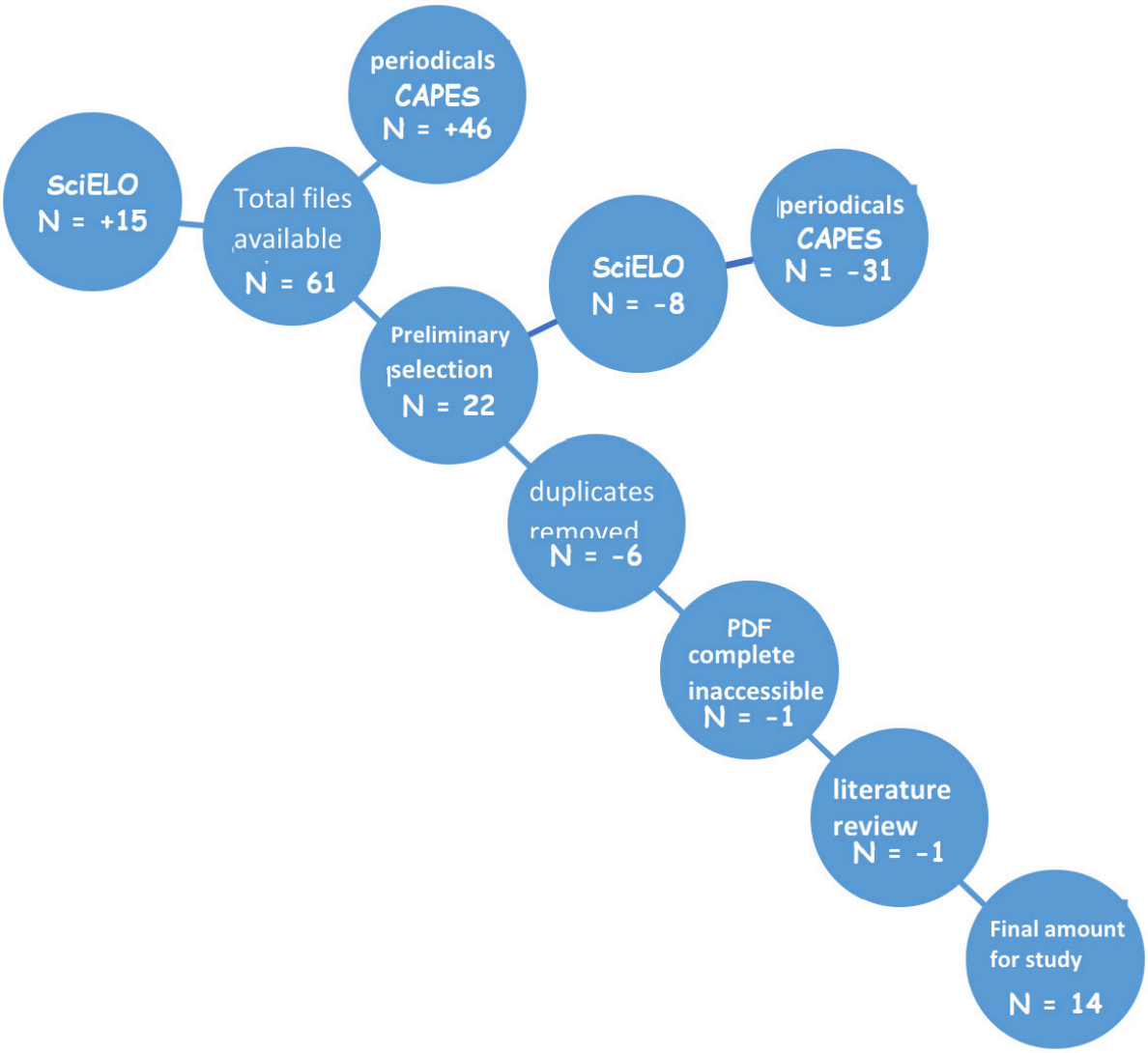

Figure 1 -Steps taken to obtain the articles selected for the study.

Source: Own authorship.

selected from the filtering criteria preliminary and the final number of articles obtained for the study, after applying the selection and exclusion criteria.

RESULTS AND DISCUSSIONS

GENERAL ASPECTS OF MICROBIAL BIOTRANSFORMATION APPROACHES

Microbial biotransformation can be understood as an important mediating toolfor numerous processes related to laboratory and industrial activities, with regard to processes (agricultural, pharmacological, textile), products obtained (food, biomolecules, drugs) and also to the results perceived in direct and indirect ways (solid waste, liquid effluents, suspended particles). Table 1 lists the areas of research related to the articles reviewed in this study.

Search area	Study proposal	Bibliography
genetics	Biochemical and genetic changes	Garcia and Martinez (2012)
Industry	Synthesis of oxide nanomaterials	Pineda et al. (2012)
Environment	Removal of compounds in liquid effluent	Lucarini, Oliveira and Gianetti (2017)
	decomposed bioreduction	Nascimento et al. (2013)
Foods	Optimize and produce fructooligosaccharides	Deffert et al. (2017)
	Protein and nutritional enrichment	Franco et al. (2015)
	Increased effectiveness of desired target effect	Silva et al. (2012)
Pharmacology	Obtaining drugs antiasthmatics	Ahmad et al. (2014)
	Obtaining drugs anthelmintics	Barth et al. (2015)
	Obtaining drugs antidepressants	Oliveira et al. (2015)
	Assessment of potential antimicrobial	Grabarczyk et al. (2013)
	monitoring of biomarkers	Machinski Junior et al. (2012)
Medicine	exams and diagnosis clinical	Souza and Coberllini (2019)
	Obtaining and evaluating of Phenolic Acid	Valente et al. (2013)

Table 1: Synthesis of areas of study and application of microbial bioconversion.

Source: Own authorship.

Agribusiness is an important human activity with regard to obtaining food. This activity releases toxic and recalcitrant components that accumulate in the environment, especially organochlorines (LUCARINI; OLIVEIRA; GIANETTI, 2017). In this context, chlorophenols become extremely worrying, since they are highly harmful and difficult to degrade, so that biotransformation processes have been shown to be an important tool capable of helping to reduce or minimize the amount of these components (LUCARINI; OLIVEIRA; GIANETTI, 2017), becoming a fundamental part with regard to the bioremediation of compounds.

The stages of food production are not limited to agricultural activities, but can also be understood in terms of improvement processes and laboratory analysis. Among these activities, one can observe the use of biotransformation in order to increase the effectiveness of compounds present in foods, as well as their bioavailability through the stabilization arising from the application of this biotechnology (SILVA et al., 2012). Not only food for humans has been contemplated with the innovations of this biotechnology, in the veterinary field, the protein enrichment of feeds has also been approached with biotransformation processes (FRANCO et al., 2015). Another activity has been laboratory analyzes to monitor metabolites,

originating from microorganisms, found in food,

The prebiotic market also demands the use of microbial biotransformation biotechnology to obtain food components that beneficially stimulate bacterial populations in the colon. This trend is due to the fact that consumers are more frequently looking for healthier and more nutritious food products. Thus, fructo-oligosaccharides stand out, compounds that can be catalyzed by various microorganisms and are capable of promoting improvements in health and well-being, stimulating desirable bacteria in the intestinal microbiota (DEFFERT et al., 2017).

Still in the laboratory context, in addition to the food area, this biotechnology has been explored in clinical and pharmacological issues, as a promising technique in the search for biological routes in the identification of pathogenic microorganisms in exams (SOUZA; COBERLLINI, 2019) or playing a role as a method of obtaining metabolites that may act as potential new drugs, such as, for example, in the biotransformation processes of antiasthmatic drugs (AHMAD et al., 2014), anthelmintics (BARTH et al., 2015), antidepressants (OLIVEIRA et al., 2015) al., 2015) or compounds with antimicrobial activity (GRABARCZYK et al., 2013). This biotechnology has also been linked to genetic and biochemical issues, evaluating the alterations that secondary metabolites, dispersed in the environment,

It must be mentioned that concomitant biotransformation has also been addressed at the intersection of activities in the food industry and industrial innovations. Used in modern chemistry as a tool capable of signaling biological routes for obtaining the most varied products, such as nanoparticles from waste from the agroindustry, reducing their quantities and promoting the obtaining of value-added products (PINEDA et al., 2012), or obtaining secondary metabolites with potential for medicine, agriculture or industry (VALENTE et al., 2013).

TECHNIQUES AND BIOPROCESSES

The biotransformation processes have taken placethrough the use, mainly, of fungal microorganisms (Table 2). Aspergillusniger are fungi that, through fermentation processes, can hydrolyze steroid compounds, transforming them into interesting metabolites for further studies (AHMAD et al., 2014). such as *Penicillium crustosum, Aspergillus fumigatus, Nigrospora sphaerica, Papulaspora immerse, Papulaspora immera Hotson and Mucor rouxii* demonstrate that microorganisms can be used as biocatalytic agents in obtaining new drugs (BARTH et al., 2015; OLIVEIRA et al., 2015).

Microorganism	Bibliography
Aspergillus fumigatus	Oliveira et al. (2015)
Aspergillus niger	Ahmad et al. (2014) Silva et al. (2012)
Acremonium sp	Grabarczyk et al. (2013)
Cunninghamella echinulata	Oliveira et al. (2015)
Cunninghamella elegans	Oliveira et al. (2015)
Cunninghamella japonica	Grabarczyk et al. (2013)
Cadida spp.	Souza and Coberllini (2019)
Fusarium avenaceum	Grabarczyk et al. (2013)
Fusarium Culmorum	Grabarczyk et al. (2013)

Fusarium oxysporum	Oliveira et al. (2015) Pineda et al. (2012)
Fusarium tricinctum	Grabarczyk et al. (2013)
Fusarium semitectum	Grabarczyk et al. (2013)
Fusarium solani	Grabarczyk et al. (2013)
Genus Aspergillus	Franco et al. (2015)
Mucor rouxii	Barth et al. (2015)
Nigrospora esphaerica	Barth et al. (2015) Oliveira et al. (2015)
Nigrospora oryzae	Grabarczyk et al. (2013)
Rizophus sp.	Franco et al. (2015)
Papulaspora immerse	Oliveira et al. (2015)
Papulaspora inmera hotson	Barth et al. (2015)
Penicillium crustosum	Oliveira et al. (2015) Valente et al. (2013)
Saccharomyces cerevisiae	Deffert et al. (2017) Nascimento et al. (2013)
Stemphylium botryosum	Grabarczyk et al. (2013)
Syncephalastrum cacemosum	Grabarczyk et al. (2013)

Table 2 -Fungal microorganisms addressed in the reviewed articles.

Source: Own authorship.

In the case of biomass, some species of filamentous fungi of the genera *Aspergillus* and *Rhizopus* are capable of increasing the protein content and producing proteins with specific catalytic activity with high digestibility and absence of toxic substances, proving to be promising microorganisms in this area (FRANCO et al, 2015).

Investigations based on biotransformations carried out by some fungal strains such as *Acremonium sp., Cunninghamella japonica, Nigrospora oryzae, Fusarium avenaceum, Fusarium culmorum, Fusarium tricinctum, Fusarium semitectum, Fusarium solani, Stemphylium botryosum*, and *Syncephalastrum racemosum* propose studies of metabolites with potential antimicrobial activity from the hydrolytic dehalogenation of some lactones (2tGRABARC, Y0BARC).

Endophytic microorganisms colonize the plant kingdom and are capable of secreting several bioactive metabolites, among which species of Penicillium fungi can stand out, producing mycophenolic acid (VALENTE et al., 2013). The antibiotic activity and successful administration as a pro-drug, after organ transplantation, as an immunosuppressant (VALENTE et al., 2013), demonstrate that the activities of mycophenolic acid imply the use of microbial biotransformation processes, also in the areas of medicine.

The application of microbial biotransformationmediated by fungi may encounter limitations in the processes involved in the technique, since the substance to be transformed can function as an inhibitor of fungal growth. Changes in the culture medium and/or in the carbon source can favor the process and/or reduce the number of secondary metabolites, thus reducing the number of interferences in the analysis (OLIVEIRA et al., 2015).

Other techniques may be the isolation of enzymes, capable of transforming compounds, such as lipases produced by Aspergillusniger (SILVA et. al, 2012) or the use of wild cultures of whole cells, such as Saccharomyces cerevisiae (DEFFERT et al., 2017). The demand for

cheaper alternatives may lead to the use of wild cultures with whole cells instead of using isolated enzymes (DEFFERT et al., 2017). The evaluation of the bioreduction potential of compounds by whole cells of different yeasts of Saccharomyces cerevisiae does not require the addition of cofactors for the maintenance of enzymatic activity during the biotransformation process (NASCIMENTO et al., 2013), corroborating the idea that the biotransformation systems that use whole cell cultures have greater advantages,

In view of in vivo biotransformation, in vitro microbial biotransformation is a cheap procedure, due to less complexity and strict control of the conditions involved in the process (OLIVEIRA et al., 2015). Although it is a technology that aims to simplify steps involved in the chemical synthesis of molecules, biotransformation may or may not be able to produce new compounds in significant quantities, being a technology that needs specific conditions (pH, temperature, availability of substrates, oxygen conditions, etc.) for the action of microorganisms, which cannot always be met.

Biotransformation has potential as a technique in clinical diagnosis, with regard to pathogenic microorganisms, through fluorescence methods capable of detecting resulting metabolites that require further investigation (SOUZA; COBERLLINI, 2019).

It is also revealed as a method for monitoring toxins from microorganisms in the environment and food, such as microcystins and aflatoxins, respectively, capable of triggering a series of health problems for organisms that accumulate their ingestion (GARCIA; MARTINEZ, 2012; MACHINSKI JUNIOR et al., 2012). Genetic and biochemical analyzes of the defense systems related to the activation of the biotransformation pathway, at the organ level, of fish that ingest, directly or indirectly, microcystins demonstrate a potential use of this biotechnology in the monitoring and investigation of biomarkers (GARCIA; MARTINEZ, 2012), at the same time

OUTLOOK

Biotransformation is used in the search for new metabolites that present greater efficiency in a certain effect of a previously known substance. These searches aim, in addition to increasing the effectiveness of a target effect, to improve aspects such as the therapeutic profile, safety and reduce the resistance of compounds (AHMAD et al., 2014).

This technology can act directly in health areas through the monitoring of biomarkers (GARCIA; MARTINEZ, 2012; MACHINSKI JUNIOR et al., 2012), promoting, to some extent, a potential mechanism for controlling the health safety of the environment, food and environments where human activities are carried out, such as hospitals.

The processes involving microbial biotransformation demonstrate the efficiency brought about by the use of this technology, both in time and quality, as well as in environmental issues. From a chemical point of view, processes that involve numerous steps for the chemical synthesis of new compounds can be reduced in number of steps, procedures, reagents and drastic conditions when using microbial biotransformation (BARTH et al., 2015). Thus, a reduction in the amount of hazardous substances involved or even their complete elimination from the synthesis processes of new metabolites can be observed, calling biotransformation green chemistry (AHMAD et al. 2014).

More simplified processes of microbial biotransformation can present considerable advantages both for the process itself, through the smaller number of variables that may interfere with the results and greater specificity and/or selectivity, and for the environment,

through mild and ecologically correct reactions (NASCIMENTO et al., 2013).

The use of this biotechnology can also minimize serious regional distortions in developing countries, such as Brazil. For example, in rural regions with arid and semi-arid ecological conditions, from the point of view of small and medium-sized cattle breeders, it becomes a viable alternative for obtaining forage with nutritional value, given the high prices of the concentrationscommercial and cereal grains for animal feed during periods of drought (FRANCO et al., 2015).

FINAL CONSIDERATIONS

The prospectsraised from the systematic literature review about microbial biotransformation, demonstrate that this is an important tool to guide and innovate research and applied methodologies in countless possibilities, highlighting the use, mainly, of fungi in the stages and processes of biotransformation in a comprehensive in several areas of research.

It was also possible to record that microbial bioconversion presents greater ecological adaptations, so that it can be considered a potential sustainable and innovative methodology for different areas of knowledge and technological development, since it can act as a tool in the processes of bioremediation, bioreduction and bioprocessing.

In fact, this biotechnology is an efficient methodology, being able to circumvent problems arising from its own technical limitations, such as controlling the conditions for bioprocesses to occur, oxygen concentration or pH changes, proving to be a trend in industrial and laboratory processes in the modern chemistry, supported by the various advantages that the methodology provides, making it possible to find several lines of research that support new studies that are necessary.

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