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RESEARCH ARTICLE

MICROBIAL TRANSFORMATIONS: SESQUITERPENES FUNCIONALIZATION BY PHYTOPATHOGENIC FUNGI

***Bustos Crescentino, D. and Bustos, D. A.**

Basic Sciences Institute, National University of Saint John, Saint John, (Argentine)

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ABSTRACT

Biotransformation processes are defined as the use of complete biological systems or its parts to make structural funcionalizations to xenobiotics compounds. Microbial transformations are characterized by versatility, efficiency, regioselectivity, chemoselectivity and enantioselectivity of the enzymatic processes involved. In a single process one or more products can be obtained and they occur under mild conditions considered environmentally friendly and can be placed in the field of white biotechnology and green chemistry. The microorganisms are capable of transforming a wide variety of organic compounds, in especial phytopatogenic fungi are an interesting group because of the large number of genera and species that form and the variety of enzymatic processes that can be achieved by them. In this article, it is described the biotransformation of many sesquiterpenes by different fungal species applied towards the obtaining of derivatives. The transformation of these compounds can result in compounds with enhanced biological activities with potential applications in various industrial sectors such as the pharmaceutical, agricultural, food, etc.

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INTRODUCTION

Throughout the history of mankind, microorganisms have been of enormous social and economic importance. Without even being aware of its existence, from early history man was using them in the production of foods and beverages. The Sumerians and Babylonians practiced brewing 6000 BC, references to wine making can be found in the book of Genesis and the Egyptians used yeast to make bread (Liese y col., 2006). The history of microbial transformation is closely associated with the production of vinegar dating from around 2000 BC.

The production of vinegar is perhaps the oldest and best known example of microbial oxidation, which can illustrate some of the most important events in the field of live cell biotransformations (Liese y col., 2006). But it was only in 1894 when Pasteur perceived the role of microorganisms in the acidification. During the latter part of the nineteenth century Bertrand began a systematic approach to microbial transformations since the turn of the century had found the following reactions: *Oxidation*: ethanol to acetic, glucose to gluconic acid; *Reduction*: malic acid to succinic acid, fructose to mannitol; *Hydrolysis*: tannins to gallic acid, di- and tri-saccharides to the constituent monosaccharides; *Resolution of racemic mixtures* of: tartaric acid (the famous experiments of Pasteur), lactic acid, mandelic acid and gliceric acid. Several transformations were soon added, and thus observations of Mamoli and Vercellone in 1937 of yeast during fermentation could reduce 17-keto steroids to 17β-hydroxysteroid, led 15 years later to one of the most important applications of biotransformations, the production of steroid hormones (Bu´Lock y Kristiansen, 1991). In the last decade, biotransformation have received increasing interest and currently has become one of the most promising areas of scientific research, because of their possible application in the production of raw materials and products useful in various industrial processes and in such important sectors such as pharmaceuticals, chemicals, food and agriculture; hence significant investments in the world for its development (Velasco *et al*., 2009). Biotransformation processes are defined as the use of complete biological systems (higher organisms, microorganisms, plants, algae, etc.) or its parts (organs, cells or enzymes) to make structural modifications to exogenous compounds (Correa Navarro, 2009). Biotransformation are characterized by versatility, efficiency, regioselectivity, chemo selectivity and enantioselectivity of the enzymatic processes

****Corresponding author: Bustos Crescentino, D.,***
Basic Sciences Institute, National University of Saint John, Saint John, (Argentine).

involved; further, the metabolism of substrates undergoing biotransformation occurs under mild conditions and with low power consumption; reagents and solvents that are regularly used in these processes have low toxicity and therefore are considered environmentally friendly and can be placed in the field of white biotechnology and green chemistry (Velasco *et al.,* 2010). The products obtained by biotransformation processes are considered natural which gives them an added value with respect to their synthetic counterparts, especially when added as raw materials for food or health care (Velasco *et al.,* 2010). Furthermore, by biotransformation they can be obtained in a single process one or more products, which otherwise requires several steps using classic synthesis methodologies (Castellanos, 2007). The microorganisms are capable of transforming a wide variety of organic compounds such as terpenes, hydrocarbons, alkaloids, steroids, antibiotics and amino acids in their metabolites. Many compounds with therapeutic properties of industrial interest were obtained by microbial transformation (Choudhary y col., 2004). Among the great diversity of organisms that are used in biotransformation, phytopatogenic fungi are an interesting group because of the large number of genera and species that form and the variety of enzymatic processes that can be achieved by them (Correa Navarro, 2009). This work can be considered as a review regarding the advantages and applications of microbial transformations using phytopathogenic fungi, which may involve processes in one step to obtain the desired product working under mild conditions. Also the goal of this work was to show background of diverse types of reactions that can be performed by fungi in different sesquiterpenes to get a wide range of derivatives.

Advantages of biotransformation processes

Biotransformations are becoming increasingly in an important tool in the structural modification and in the study of metabolism of natural or synthetic organic compounds (Li y col., 2006).

Compared to conventional methods of chemistry

- The reactions are not only regio and stereospecific, but can also be obtained enantiospecífics chiral products from racemic mixtures.
- In most cases, no specific protection of functional groups of the substrate is required.
- Some processes are more economical and products are obtained more directly than in the analogous chemical processes.
- The reasons governing regiospecificity differ from those which control chemical processes; therefore biotransformation can be obtained on not chemically reactive centers.

Considering the environmental conditions

- Working conditions in biotransformation processes are in biological environmental conditions.
- The reactions usually occur under cleaner conditions for the environment.
- Unwanted side and secondary reactions products can be avoided (Carballeira y col., 2009).

- *As for costs:*
- Some processes are more economical and products are obtained more directly than in the analogous chemical processes.
- The "microbial models of mammalian metabolism" can reduce the number of animals used, beneficial from an economic and humanitarian viewpoint.

The most immediate application of biotransformation is to obtain chiral compounds and synthons applicable to the asymmetric synthesis of commercially important molecules such as drugs, pharmaceutical intermediates, food additives, agrochemicals, among others (Correa Navarro, 2009). Many biotransformations have been reported in the literature. Several have been successfully applied on a preparative and industrial scale even as an alternative to pure chemical methods or even as the only access to certain useful products. Biotransformation technology has proven to be a useful additional tool in organic synthesis (Leuenberger, 1990). The most immediate application of biotransformation is to obtain chiral compounds and synthons applicable to the asymmetric synthesis of commercially important molecules such as drugs, pharmaceutical intermediates, food additives, agrochemicals, among others (Correa Navarro, 2009).

Advantages of microbial cells

Microbial cells, plants or animals can provide enzymes for transformation, but microorganisms outweigh the cells of plants and animals in several aspects. The high ratio surface-volume confers rapid growth and high speed metabolism, leading to the efficient conversion of substrates added (Bu´Lock y Kristiansen, 1991). Another great advantage is that, microbial cells are easier to develop in a culture medium. This is in part a reflection of the combination of a thin and resistant cell wall, giving microbial cells a high mechanical strength. This makes them more resistant than the cells of animals and plants to different rigorous cultivation techniques. In addition, the range of substrates that can be metabolized by microbial cells is more extensive (Roberts y col., 1995). There are basically two strategies to perform biotransformation, by using pure enzymes or partially pure enzymes isolated at the laboratory or purchased from a commercial dealer, or using whole cells (Leuenberger, 1990). Pure enzymes are rare and have high economic value, reason why there is a strong preference for full biological systems with a faster growth and the formation of multi-enzyme systems (Correa Navarro, 2009). Microorganisms also serve as a source of enzymes for use in analytical systems and microbial transformations play an important role in metabolism studies to clinical assessments of drugs must accompany. The "microbial models" are useful to predict, and sometimes necessary to prepare, metabolites derived from drugs administered to animals and humans (Bu´Lock y Kristiansen, 1991). The approval and use of drugs in humans require rigorous studies to establish its safety and efficacy. The evaluation of both safety and efficacy of any drug takes knowledge about drug metabolism. Understanding drug metabolism plays an important role in the development of new drugs which can then be evaluated to determine their biological, pharmacological and toxicological activities. Metabolism involves a series of enzymatic transformations leading to the chemical alteration of a compound that is, the

conversion thereof into compounds useful for the body (anabolism) or to hydrophilic polar metabolites to be easily excreted from the body compared to lipophilic substances (catabolism). The use of microorganisms as models of metabolism of mammals is well documented. Therefore, microorganisms can be used as factories to produce metabolic compounds, which by synthetic routes results in tedious and costly processes (Swathi *et al*., 2012). Is then that the "microbial models of mammalian metabolism" can be defined as the use of microorganisms (bacteria, yeasts and fungi) to facilitate the study of biotransformation of xenobiotics in mammals including man (Kouzi, 1991). In 1974, Smith and Rosazza first introduced the concept of using microorganisms as "Microbial Models of Mammalian Metabolism". While conducting the microbial hydroxylation of aromatic substrates, they noticed similarity between microbial metabolites and those obtained from mammalian systems. Ferris *et al*. (1973) used the fungus *Cunninghamella bainieri* to metabolize aromatic compounds and to obtain a number of metabolites similar to those detected in mammalian systems. They suggested that fungi exhibited "monooxygenases" with similar activity to liver microsomes. Therefore, the assumption behind the concept of microbial model, introduced by Smith and Rosazza is the fact that fungi and mammals are both eukaryotes and possibly share very similar enzymatic machinery for most physiological functions. Therefore, it is expected that the result of xenobiotic metabolism in many other biochemical processes is very similar in both fungal and mammalian systems (Abourashed Swathi *et al*., 1999). Microbial metabolisms show distinct advantages that make them attractive in case of being used as predictive models for in vitro studies of initial metabolism. The major advantages are: a) easy experimental design b) can produce significant amounts of metabolites by up-scale bioconversions to determine the structure and carry out biological tests c) the ability of microbial systems offer simple bioconversion steps d) reduce costs on mammalian systems. In addition, the number of animals required for research evaluation of metabolic profiling of xenobiotics can be significantly reduced when microorganisms are used as predictive models (Kouzi, 1991).

Microbial hydroxylation

As mentioned above, an advantage of biocatalysis is the functionalization of carbon atoms not chemically reactive. The functionalization by oxidation of such non-reactive carbon atoms, which is often a key step in organic synthesis, using the traditional method is fraught with many disadvantages, oxidants based on toxic metals, unwanted side reactions, and many difficulties to carry out in a regio and stereoselective manner. Many of these disadvantages can be avoided by using biological methods, particularly in cases where stereoselectivity is required (Dalton, 1980; Schewe Swathi *et al*., 2011). Particularly, hydroxylation of hydrocarbons is one of the most useful biotransformations, in general, the relative reactivity of carbon atoms in the microbial hydroxylation follows the primary> tertiary> secondary order (Mansuy, 1990; Faber, 1997). Practically any unreacted carbon can be hydroxylated by a microorganism (Abraham, 1994; Gouiric Swathi *et al*., 2004; Allendes Swathi *et al*., 2011). When a compound is incubated with microorganisms, it can be inserted a hydroxyl group at a site that is inaccessible to other functions. This ability of microorganisms to hydroxylate compounds on "chemically inactive" sites is a very useful synthetic tool. For these transformations the intact organism is usually used, because many of the enzymes systems involved are attached to the membrane and are consequently difficult to obtain stable in isolation. The microbiological hydroxylation of a large number of substances has been examined using a variety of organisms. The microbiological hydroxylation charge lies in the fact that attack sites are often different from those where chemical reactions occur and, therefore, some may be considered as chemically remote (Musharraf, 2004). Monooxygenase is the enzyme responsible for the microbiological hydroxylation and transfer of an oxygen atom into the organic substrate (Musharraf, 2004). Monooxygenase systems use not only cytochrome P450, but also require a source of electrons from usually NADPH (Musharraf, 2004). The use of biotransformations with whole cells, represents a great advantage considering the cost involved in the regeneration of cofactors (Goretti *et al.,* 2009). This functionalization can be accomplished, for example, by using phytopathogenic fungi because their enzymatic machinery involves enzymes similar to cytochrome P450 monooxygenases, which are also found in humans and other mammals' enzymes (Rojas *et al*., 2001; Leak *et al.,* 2009).

The role of cytochrome P450 in biotransformation

One of the biggest battles in nature is that observed between plants and phytopathogenic fungi; they constitute a large group of microbes that usually resides on the outside of plants and are one of the main goals of the defense system of plants. To combat these fungi, plants generate a large number of compounds such as terpenes, flavonoids and alkaloids, known as phytoalexins. These products of the secondary metabolism of plants are almost always produced in response to infection (Ribera and Zuñiga, 2012). Is to say that, phytoalexins are antibiotics; secondary metabolites of low molecular weight produced by plants in response to microbial attack. Some pathogens respond against these substances of defense to prevent harmful effects through biochemical reactions called as detoxification reactions (Farooq y Tahara, 1999). Most phytoalexins and related compounds are hydrophobic, and they are metabolized by the phytopathogenic fungi to hydrophilic compounds through the introduction of hydroxyl group/s, by oxygenation, hydration, reduction or rupture of carbonyl group. Hydrophilic metabolites can, therefore, be stored in vacuoles and excreted; and this process is similar to mammalian xenobiotic oxidation by cytochrome (P-450) monooxygenase (Farooq y Tahara, 1999). Filamentous fungi have developed an extraordinary capacity to adapt to the changing environment, largely due to enzymatic defense systems that protect them from toxic exogenous xenobiotic compounds. Thus, filamentous fungi play a crucial role in the degradation and mineralization of a diverse array of environmental pollutants, and in catalyzing important reactions for biotechnological production (Črešnar and Petrič, 2011). Xenobiotics (chemicals that are not part of the normal composition of the human body) are not used as nutrients, which are not incorporated into the biochemical pathways of intermediary metabolism and are not degraded by these metabolic pathways.

Table 1. Examples of sesquiterpenes transformations using fungi whole cells of phytopathogenic fungi

Compounds	Microorganisms	Results	Publication
Sesquiterpenes			
(-)-Ambroxide	*Cephalosporium aphidicola*	3β and 6β hydroxy derivatives oxidation of the heterocycle to lactone	Hanson & Truneh, 1996
	Fusarium lini	Mono, di and tri hydroxylated metabolites in position 1α; 3α; 6α and 11α	Choudhary *et al*., 2004
	Rhizopus stolonifer	3β and 6β hydroxy derivatives	
	Cunninghamella elegans	Ambrox-3-one and sclareolide	
	Actinidia deliciosa	Dihydroxylations in positions 1α,6β and 1α,3β	Nasib *et al*., 2006
	Alternaria alternata	3β hydroxy derivative	Allendes *et al*., 2011
	Cunninghamella sp.	1β hydroxy derivative	
	Macrophomina phaseolina	3β; 6β; 1α,3β hydroxy derivatives	Musharaff y col., 2012
Sclareolide	*Cephalosporium aphidicola*[1]	3β and 6β hydroxy derivatives	Hanson & Truneh, 1996
	Aspergillus niger[2]		Cano *et al*., 2011
	Cunninghamella blackesleeana[3]		
	Beauveria bassiana[4]	1-ketosclareolide (1,2,3)	
	Rhizopus oligosporus[5]	3-ketosclareolide (1,3,5,6,7,8)	
	Mucor miehei[6]	3β hydroxy derivative (1,2,3,4,5,6,7,8)	
	Rhizopus nigricans[7]	3α,6β hydroxy derivative (1,7,8)	
	Fusarium moliniforme[8]	C-15 hydroxy derivative (1)	
Curdione	*Mucor spinosus*	2β and C-11 hydroxy derivatives Epoxidations 1β,10α and 1α,10β	Xiao-chi Ma *et al*., 2006
Curcumenol	*Mucor polymorphosporus*	Hydroxylations in positions 2,7,10,11,12,15 Oxidation in position C6-C7 Degradation and rearrangment reactions to generate a ring-contracted metabolite	Li-Xia Chen *et al*., 2015
5α-hydroxy-14-eudesm-11-en-3-one	*Rhizopus nigricans* *Cunninghamella elegans* *Mucor plumbeus*	Hydroxylations in C-6 and C-11 The 11-hydroxylated compounds can be chemically transformed into α-agarofuran	Alarcón *et al*., 2007
(+)-nootkatona	*Fusarium culmorum*	An hydroxylated compound on C-11 and C-12	Gliszczynska *et al*., 2011
Ciclonerodiol	*Penicillium* sp.	new glycosidic metabolite	Li *et al*., 2007
4β-hydroxyeudesmane-1,6-dione	*Gliocladium roseum* *Exserohilum halodes*	7α-hydroxylated, 7α,11- and 1α,8α-dihydroxylated derivatives Reduction of the keto group at C-1	García-Granados *et al*., 2001
Cadina-4,10(15)-dien-3-one		Hydroxylations in C-12 and C-14	Collins *et al*., 2002
Aromadendr-1(10)-en-9-one (squamulosone)	*Mucor plumbeus*	Was converted to the novel 2α,13-dihydroxy derivative with four other metabolites	
Cadina-4,10(15)-dien-3-one 3α-hydroxycadina-4,10(15)-diene	*Curvularia lunata*	3α-hydroxy; 4S-3α-hydroxy and 12-hydroxy derivatives (4S)-1α,3α-dihydroxy; 3α,14-dihydroxy and 3α,12-dihydroxy derivatives	Collins and Reese 2002
(+)-cedrol		3β; 3α hydroxyl derivatives Dehydration at the C-8 position	Miyazawa *et al*., 1995
β-selinene	*Glomerella cingulata*	Oxidized at the double bond of the isopropenyl group and hydroxylation in C-1	Miyazawa *et al*., 1997
(+)-γ-gurjunene		Oxididation at the double bond of the isopropenyl and oxidation at the C-10 position	Miyazawa *et al*., 1998
Isoprobotryan-9α-ol	*Botrytis cinerea*	12-, 14- and 15-hydroxyderivatives	Aleu *et al*., 2002
(+)-1(10)-aristolene	*Mucor* sp. *Chlorella fusca* var. *vacuolata*	Introduction of oxygen function into the cyclohexane ring	Furusawa *et al*., 2006
	Aspergillus niger	Oxidation of one methyl of the 1,1-dimethyl group on the cyclopropane ring of aristolanes and 2,3-secoaromadendrane to give C-12 primary alcohol and C-12 carboxylic acid	
(-)-α-bisabolol	*Bipolaris sorokiniana*	Oxidation of the double bond of the branched chain 4,5-epoxidation	Limberger *et al*., 2003
Cedrol	*Mucor plumbeus*	3α, 8β; 3β,8β; 2α,8β; 8β,12 dihydroxy derivatives 3β,8β,10 trihydroxy derivative	Fraga *et al*., 1996
	Curvularia lunata	3α; 3β; 12 hydroxy derivatives	Collins and Reese, 2001
Squamulosone	*Curvularia lunata*	2α; 2β; 13, 14; 2β, 13; 13,14 hydroxy derivatives 10α-hydroxy with epoxidation in C1-C2	Collins *et al*., 2001
Patchulol	*Botrytis cinerea*	(5*R)*-5-hydroxy; (7*S*)-7-hydroxy; (8*R*)-8-hydroxy; (8*S*)-8-hydroxy; (9*R*)-9-hydroxy; (3*R*)-3-hydroxy; 13-hydroxy; (2*S*)-2,14-dihydroxy derivatives	Aleu *et al*., 2001
Ginsenol		9β; 8β; 10β; 6α hydroxyl derivatives; 9-oxo and 8-oxo	
Cedrol		3β; 12; 3α; 2α; 4α; 10β hydroxyl derivatives	
Sesquiterpenes lactones			

Continue……..

Santonina	*Botrytis cinerea*	11β hydroxy derivative	Farooq & Tahara 2000
	Rhizopus stolonifer	3,4-epoxidation Reduction in position C4-C5	Ata & Nachtigall, 2004
	Cunninghamella bainieri	Reduction in position C1-C2	
	Mucor plumbeus	11β-13-dihydroxy	Lamm *et al*., 2009
	Whetzelinia sclerotiorum	Oxidation in position C6-C7	
	Aspergillus niger	Oxidation and ring B opening	
	Absidia coerulea	11β and 8α hydroxy derivatives	Yang *et al*., 2006
	Cunninchamella sp.	8β hydroxy derivative	Bustos *et al*., 2012
	Aspergillus parasiticus	3,4-epoxidation Reduction in position C4-C5 Reduction in position C1-C2	Siddhardha *et al*., 2012
Achalensolide	*Penicillium* sp. *Rhizopus* sp.	Reduction of the exocyclic double bond of the lactone	Bustos *et al*., 2014
Zaluzanina-D	*Fusarium equiseti* *Fusarium oxysporum*	Reduction of the exocyclic double bond of the lactone	Krishna *et al*., 2003
Partenolido	*Rhizopus nigricans*	Reduction of the exocyclic double bond of the lactone	Galal *et al*., 1999
(+)-Costunolide		Reduction of the exocyclic double bond of the lactone Ring closure and cyclization of double bonds	Barrero *et al*., 1999
	Cunninghamella echinulata	Hydroxylations in C-1 y C-4	
(+)-Cnicin		Hydroxylations in C-8 y C-15	
(+)-Dehydrocostuslactone		Reduction of the exocyclic double bond of the lactone	
(+)-Lychnopholide		isomerization of C8 radical	
Onopordopicrin	*Aspergillus niger*	11α and 11β dihydro derivatives 3β–hydroxy-11β and 14-hydroxy-11β dihydro derivatives	Esmaeili *et al*., 2012

It is generally lipophilic nature of compounds so they can relatively easily cross biological membranes, enter into cells and bind to cell structures with lipophilic character. At the same time, its removal from the body is difficult, since excretion of non-volatile compounds is via aqueous fluid nature, primarily urine (Donato Martin, 2006). In this situation, living organisms have developed alternative metabolic systems to accelerate the elimination of these compounds. There is series into enzymes not integrated into the pathways of energy metabolism or intermediary of body and whose substrates are xenobiotics. Its function is to convert xenobiotics into polar compounds soluble in water to be excreted more easily (Donato Martin, 2006). The enzymatic assembly are subjected to xenobiotics in the body, which generally tend neutralization and removal processes are known as biotransformation reactions or xenobiotic metabolism. Traditionally, these processes have been grouped into two phases or stages. In *phase 1* xenobiotics are modified by oxidation reactions, reduction or hydrolysis and converted into more water-soluble products by the appearance of new functional groups of polar character (hydroxyl, amino, carboxyl). In *phase 2* xenobiotics, or the metabolites produced by the reactions of *phase 1*, are combined with endogenous molecules of polar character to form conjugates products which are rapidly excreted (Donato Martin, 2006). The P450 system has a huge functional versatility that is reflected in the variety of processes that can catalyze such as the high number of substrates that can metabolize. This broad substrate specificity is due to the existence of multiple forms of the enzyme, each of which is adapted to the metabolism of groups of compounds structurally related (Donato Martin, 2006). Given the background in literature, the P450s have a great versatility in its ability to recognize substrates of different size and character, and their ability to perform a wide range of different chemical transformations on these substrates (Munro *et al.,* 2013).

Microbial transformation of sesquiterpenes

Sesquiterpenes, together with monoterpenes, are the main constituents of essential oils (those of citrus fruits, herbs and spices). Essential oils are, among others, in special glandular cells on the leaf surface and have numerous ecological functions in the plant kingdom, such as act as allelopathic agents, repellents or attractants in interactions plant-plant, or plant-pathogen/ herbivore. Other functions are the defense and wound healing of some species of pine or increasing the thermotolerance in plants. The families of plants particularly rich in essential oils include the *Apiaceae, Asteraceae, Labiatae, Myrtaceae, Pinaceae, Rosaceae* and *Rutaceae* (Harborne, 1998). As monoterpenes, sesquiterpenes whose structure is based on the union of three isoprene units; chemically they are grouped in different groups according to the basic carbon skeleton. Among the most common they are acyclic as farnesol, monocyclic as γ-bisabolene or bicyclic as the β-selinene and carotol (Harborne, 1998). Within this group we can also find the sesquiterpene lactones. These are a large group of compounds with more than 1400 different structures and are characteristics in the Asteraceae family, which are about 90% of known structures. Outside it, they have also been isolated in some genera of *Apiaceae, Magnoliaceae* and *Lauraceae,* and even in some liverworts and mushrooms (Llorens Molina *et al*., 2008). Many sesquiterpene lactones have biological activity that makes them interesting for various purposes. Several sesquiterpene lactones produced by plants of the genus *Artemisia* have fungicidal properties, herbicidal, insecticidal or antimicrobial, and could be a good source of new plant protection products (Llorens Molina *et al*., 2008). To sesquiterpene lactones have also been associated biological activities such as: cytotoxic, anti-inflammatory, antitumor, antibacterial, anti dermatitis in humans, and inhibiting plant growth (Martinez, 2001), whereby the biotransformation of these compounds can result in derivatives with enhanced biological activities. In the following table (Table 1) it can be seen a summary of some sesquiterpenes and sesquiterpene lactones using various fungal species as a source of enzymes for bioconversion. It can be seen that in most of these work in biotransformations of different compounds, the two main objectives are to obtain derivatives with increased biological activity and secondly predict xenobiotic metabolism in mammals. Table 1

Conclusion

It have been highlighted in this work the advantages and applications of biotransformations, as well as the use of whole cells of phytopathogenic fungi constituting a simple, economical and clean method for modifying structurally organic compounds. It attempts to summarize a variety of different types of reactions of bioconversions of sesquiterpenes and sesquiterpenes lactones using fungi, giving a broad overview to select a proper microorganism to efficiently and selectively convert different substrates into desired derivatives.

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