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Lorena de Oliveira Felipe, Ana Maria de Oliveira, Juliano Lemos Bicas

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BIOAROMAS – PERSPECTIVES FOR SUSTAINABLE DEVELOPMENT

Lorena de Oliveira Felipe[a], Ana Maria de Oliveira[a], Juliano Lemos Bicas[a,b]*

[a]Department of Chemistry, Biotechnology and Bioprocess Engineering. Alto Paraopeba Campus, Federal University of São João Del-Rei. Rod. MG443, Km 7. Fazenda do Cadete. Ouro Branco – MG, Brazil. 36420-000.

[b]Department of Food Science, School of Food Engineering, University of Campinas. Rua Monteiro Lobato, 80. Cidade Universitária. Campinas - SP, Brazil. 13083-862.

*corresponding author. E-mail: jlbicas@gmail.com; Phone: +55 19 3521 0065

ABSTRACT:

Background:

Aroma compounds can be produced using three main methods: chemical synthesis, extraction from nature, and biotechnological process (bioaromas). In the latter method, when compared with chemical synthesis and direct extraction from nature, the (bio)aroma compounds obtained present numerous advantages, in such a way that this approach meets two important demands of modern society: the first one refers to products obtained by biotechnological processes, which can be considered as natural, and the second one is related to the concept of sustainable development, since such production processes are aligned with the best practices in environmental preservation.

Scope and approach:

In this review we demonstrate that the technological development of the production of aroma compounds using microorganisms is effectively promising as a process that allows the inextricably approach of the three pillars of sustainability: environment, economics, and social aspects.

Key findings and conclusion:

This review shows that bioaroma production consists of renewable processes that employ mild conditions of operation, do not generate toxic waste, uses biodiversity rationally, and may also avail agro-industrial residues or by-products in a special way. Moreover, biological (e.g., antioxidant, anticancer, anti-inflammatory) activities attributed to some terpene biotransformation products are increasingly being reported, indicating that their applications may transcend food industry.

KEYWORDS: aroma, biotransformation, flavor, sustainability, terpenes

1. INTRODUCTION

Aroma compounds can be produced using three methods: (i) chemical synthesis, (ii) extraction from nature, and (iii) biotechnology. In the case of chemical synthesis, this method is marked by high yields and low cost. However, it generates low quality products. That is because, considering its low regio- and enantioselectivity, a mixture of products is obtained at the end of the process. In addition, aromas obtained using this method cannot be labeled as natural. Another questionable point about this method refers to the process parameters, which generally require a high energy cost (high pressures and temperatures), in addition to generating environmental liabilities (use of large volumes of organic solvents) (Akacha & Gargouri, 2014).

On the other hand, aroma compounds obtained by the method of direct extraction from nature or by biotechnology can be labeled as “natural”. Thus, products obtained using such processes have an undisputed marketing appeal. However, the method of direct extraction from nature is full of challenges, among which we can highlight: (i) seasonality (the availability of a product is related to certain periods of the year), (ii) ecological, social and political issues, and (iii) low yield, which results in a high price for the product. In the case of the last challenge, the vanilla essence produced from the orchid *Vanilla planifolia* illustrates this scenario. According to Gallage & Møller (2015), it is estimated that approximately 500 kg of pods of the aforementioned orchid are required for 1 kg of essence, in a process that takes more than twelve months.

Thus, the biotechnological production of aroma compounds outstands as a very promising option to overcome problems associated with these other methods of production. Among the main advantages of this method, we can highlight: (i) high enantioselectivity, which allows obtaining aromas of high optical purity, beneficially impacting sensory characteristics of the product; (ii) continuous production throughout the year and without seasonal interference; (iii) adoption of parameters of processes that are less stringent (thus reducing energy costs and the use of reagents harmful to the environment) (Berger, 2015); and, (iv) controllable and optimizable process conditions.

Therefore, the production of aroma compounds by biotechnology meets two major demands of modern society. The first one refers to the supply of natural products, meeting the expectations of consumers and contributing to a higher quality of the final product. The second one is related to the concept of sustainable development, since such production processes align the company with the best practices in environmental preservation, in addition to increasing the credibility of the consumer regarding such company (Manget & Münnich, 2009). This last aspect, in particular, deserves great prominence for being one of the most important topics in the modern world.

1.1 Sustainable development

The sustainable development concept was created from the need to combine industrial activities with the environment in a harmonious way. Therefore, it is a relatively new term that still finds barriers to its comprehensive understanding. That is because, often, sustainability is directly associated with the fulfillment of laws allowing only environmental protection (Cristina & Diana, 2014).

However, the creation of technologies that seek sustainable development must inextricably address three aspects that effectively provide the sustainability of this new process, namely: environmental, economic, and social aspects. In fact, the concept of sustainable development would be subjected to a considerable limitation if only the environmental aspect was necessary to the detriment of economic and social development (Ciegis, Ramanauskiene & Startiene, 2009).

Because of this, the triple bottom line was created (Figure 1), based on the inseparability of the aspects previously mentioned. Thus, a technology is only recognized as sustainable if it broadly and simultaneously meets the three pillars of that tripod (Gimenez, Sierra & Rodon, 2012). Several indexes have been proposed to measure sustainability. However, as it is a complex quantification due to the different aspects involved and the related contexts, each index has positive and negative points, being better shaped depending on the situation involved (Ciegis et al., 2009).

Figure 1

Currently, the trend of industrial processes – mainly chemical ones – is focused on the replacement of all or part of the procedure for new technologies that use microorganisms (bioprocess). This fact is widely justified based on the best interests of industries in offering products that are environmentally friendly, socially equitable, involving high added value and thus meeting marketing trends (Toldrá, 2015).

Therefore, the objective of this review is to demonstrate that technological development for the production of aromas using microorganisms is a promising idea from the point of view of the sustainable development, since it allows the inextricably approach of the three pillars of sustainability, each being detailed in the next sections.

2. ENVIRONMENTAL ASPECT

2.1. Operations conditions

Bioprocesses are used by mankind since ancient times, mainly in food and beverage production (Kwon, Nyakudya & Jeong, 2014). However, over the years, the use of microorganisms as biological factories for the production of various products went beyond the food sector and, currently, this tool is used in distinct areas such as environmental remediation, pharmaceutical industry, and others (Heux, Meynial-Salles, O'Donohue & Dumon, 2015). This fact clearly demonstrates the versatility, adaptability, and potential of using microorganisms in providing products with commercial interest. Moreover, industrial biotechnology might be advantageous in environmental terms, since they occur under mild conditions (process close to room temperature and atmospheric pressure) and there is a possible reduction in the volume of environmental liabilities (Boukroufa, Boutekedjiret, Petigny, Rakotomanomana & Chemat, 2014).

In the case of the aroma industry, the production process of vanillin is a good example to understand the reasons for the tendency to replace classical processes with biotechnological processes (Gallage & Møller, 2015).

Vanillin is one of the main aroma compounds in commercial terms, with annual demand of approximately 2.0×10^4 tons (Fache, Boutevin & Caillol, 2015). In the second half of the 19th century (1874-1875), the vanillin chemical synthesis was proposed from eugenol (clove essential oil) as a starting substrate. Subsequently, the chemical synthesis of that compound was made from the lignin present in black liquor, a residue of the pulp and paper industry. However, the production based on eugenol and black liquor as substrates for conversion were abandoned considering the volume of effluents with high polluting potential generated during the process. For example, to produce 1 kg of vanilla aroma, having lignin as a conversion substrate, the demand of the process is 160 kg of sodium hydroxide. Additionally, 150 kg of environmental liabilities are generated (Lampman et al., 1976). Hence, considering the significant demand for caustic soda and the consequent generation of liquid effluent, previously mentioned production routes have fallen almost into disuse. Thus, currently, the synthetic route preferably adopted for vanillin is made from the conversion of two substrates: guaiacol and *p*-cresol, both precursors derived from the petrochemical industry (Fache, Boutevin, & Caillol, 2015). The preference for this production method is due to the higher yield provided by the reactions, generating the least amount of effluents. Furthermore, when compared with the production method from lignin, it has lower economic cost (Hocking, 1997). These and other production processes for chemical synthesis are described in Table 1, in which we also present the operation parameters adopted in the chemical synthesis of two other commercially important aroma compounds: *γ*-decalactone and 2-phenylethanol. Comparatively, the production of these compounds may occur under milder conditions when using bioprocesses, such as the following examples:

i. *Streptomyces* sp. V-1, when cultivated at 30°C/120rpm in a culture medium (aqueous broth) supplemented with 45g/L ferulic acid and 8% macroporous adsorbent resin DM11 and pH 7.2, was able to produce 19.2 g/L vanillin after 55h (Xu et al., 2009);

ii. *Candida sorbophila*, when cultivated in a bioreactor containing 2L of culture medium (aqueous broth) supplemented with 400g ricinoleic acid and operated at 27°C, pH 6.0, aeration of 1L/min and 600 rpm, produced almost 50 g/L R-γ-decalactone (ee ≥99%) after 10 days of fermentation (Mitsuhashi & Imori, 2006);

iii. *Kluveromyces marxianus* CBS 600, when cultivated in a bioreactor containing a culture medium (aqueous broth) supplemented with 50g/L L-phenilalanine and polypropylene glycol 1200 and operated at 30°C, pH 5.0, aeration of 1-1.5vvm and 1,000 rpm, could produce 26.5 g/L 2-phenylethanol after 30h (Etschmann & Schrader, 2006).

Table 1

Therefore, the replacement of classical aroma production processes using biotechnology may be seen as a more environmentally friendly approach, since it minimizes the use of eventually toxic reagents and solvents, in addition to often employing weaker reactional conditions (temperature and pressure). Therefore, not only vanillin, but several other aroma compounds have had their production methods progressively replaced by microbial processes, and 22 biotechnology companies around the world already sell aromas of biotechnological origin (UBIC Consulting, 2014), such as the examples shown in Table 2. To illustrate this scenario, Figure 2 shows the increase in patent records, indicating a growing trend in the adoption of microbial processes for the aroma compounds production.

Figure 2

Table 2

In fact, many biotech companies are investing in synthetic biology to produce aroma compounds. Evolva, for instance, is currently producing biotech vanillin *de novo* from glucose using a modified yeast (*Schizosaccharomyces pombe*) (Hansen et al., 2009). Similarly, Amyris is using bioprocesses for the *de novo* synthesis of sesquiterpenes (Clearwood™ – patchouli – and Biofene™ – farnesene) with genetically modified *Saccharomyces cerevisiae* in large scale using sugarcane as substrate (Schalk & Deguerry, 2015; Renninger, Newman, Reiling, Regentin & Paddon, 2010). In the beginning of 2016, Ambrox® (amrboxide), produced by Firmenich using a similar approach (Schalk et al. 2012), was also announced to be in the market in the following months (Firmenich, 2016). These and other examples (Table 2) demonstrate that the production of flavor compounds using genetically modified organisms is already a commercial reality, and such strategy will be increasingly used in future.

However, despite the advantages inherent to the previously mentioned bioprocesses, it is necessary to consider factors that decrease their commercial competitiveness, including: (i) the energy cost spent in aerobic processes, (ii) the purification steps for the target product, (iii) the demand or the characteristics of the reagents used in the downstream step, and (iv) the yield of product that enables its economic viability (Najafpour, 2015). Moreover, the increasing use of genetically modified microorganisms for the production of “natural” bioflavors might have commercialization problems, as a reflex of legal and social constrains (i.e., consumer rejection), even though the regulations of use and labeling of genetically modified organisms are not applied to fermented ingredients, since the microorganism itself is not present in the final product (Hayden, 2014). As mentioned by Berger (2015), although the legal status of “natural” flavors derived from recombinant hosts is not clear, the flavor industry is being pressured by the depletion of petrochemicals.

Thus, considering the growing trend of replacement of classical processes for processes that uses biological catalysts, it is necessary to recognize the need for greater investment in the research and training of human resources (Woodley, Breuer & Mink, 2013). Specifically, higher yields and lower process costs can be achieved from the implementation of experimental planning tools to determine the optimum production conditions, with the use of strains resistant to process conditions, and appropriate systems to overcome problems related to toxicity and volatility of the substrate (Molina et al., 2013). Additionally, a detailed study on the parameters of scale-up and downstream steps of the target product is also necessary (Najafpour, 2015). In this context, multidisciplinarity is another point of great importance, since the understanding of satisfactory conditions to cultivate microorganisms requires knowledge on different areas such as engineering, microbiology, and biochemistry (Velayudhan, 2014).

2.2 Use of agro-industrial waste

Another significant point of interest for the use of microorganisms in the production of inputs for the industry is the growing trend to use alternative media for cultivation in bioprocesses (Wen, Liao, Liu & Chen, 2007). These alternative cultivation media are represented by by-products of low commercial value or waste originated from different industrial activities, mainly in the agricultural sector, which is characterized by the great generation of such waste (Table 3) (Madeira, Nakajima, Macedo & Macedo, 2014). This strategy has some advantages from the point of view of waste management, such as: (i) reduced financial expenditure for the suitability of environmental liabilities to current standards, and (ii) added value to what was considered as unusable (Mirabella, Castellani & Sala, 2014). In addition, the use of agro-industrial wastes and by-products as the culture medium of microorganisms represents a potential significant reduction in the costs of bioprocesses, given that the formulation of such medium can affect from 38 to 73% the total product cost (Stanburry, Whitaker & Hall, 1995).

Table 3

In this sense, there are several reports in the literature on the production of bioaromas using different agro-industrial wastes and by-products. Such studies have been especially focused on solid state fermentation (SSF), as in the following examples.

Christen, Meza & Revah (1997), using the fungus *Ceratocystis fimbriata*, have studied three different substrates: wheat bran, cassava bagasse, and sugarcane bagasse. By using such wastes, those authors have shown that the profile of volatile compounds obtained is closely linked to the type of substrate used and the supplementation available. Thus, the enrichment of sugarcane bagasse with 200 g L^{-1} of glucose culminated in the production of a fruity aroma, while the supplementation of this same substrate with leucine or valine produced volatile compounds with a sharp banana aroma. Differences in the volatile profile according to the supplementation of substrates were also observed in the study of Soares, Christen, Pandey & Soccol (2000), who have used coffee husks as solid support for fermentation by *C. fimbriata*. Supplementation with 20 and 35% of glucose resulted in a sharp pineapple aroma. On the other hand, the supplementation with 46% of glucose and 10mmol of leucine resulted in a strong banana aroma.

Years later, in studies with the same species (*C. fimbriata*), Rossi et al. (2009) investigated the influence of the supplementation of carbon sources (cane molasses and soybean), as well as the supplementation of nitrogen (urea or soybean meal), in the production yield of fruity aroma using citrus pulp as fermentation solid support. The best yield of volatile compounds – 99.60 μmol L^{-1} g^{-1} (120 h) – was achieved when the citrus pulp was supplemented with 25% of cane molasses, 50% of soybean meal, and mineral salt solution.

Larroche, Besson & Gros (1999) have also noted the importance of enriching the medium to increase the production of aroma compounds in solid state fermentation. Using crushed soybeans enriched with L-threonine and acetoin, they have achieved a yield of 2 g L^{-1} in the production of pyrazines (2,5-dimethylpyrazine and tetramethylpyrazine) by the bacterium *Bacillus subtillis* IFO 3013.

A similar conclusion was obtained by Fadel, Mahmoud, Asker & Lotfy (2015). These same authors used sugarcane bagasse as a carbon source for the fermentation with *Trichoderma viride* EMCC-107. The production of lactones was evidenced, in particular for 6-pentyl-α-pyrone (character impact compound of coconut), and their production reached 3.62 mg after five days of fermentation. Furthermore, with an established confidence level of 95%, it was possible to conclude that the yield in production and the increase in microbial biomass were directly related to the supplementation of sugarcane bagasse to the culture medium.

Aggelopoulos et al., (2014); Mantzouridou, Paraskevopoulou & Lalou (2015); Medeiros, Pandey, Freitas, Christen & Soccol (2000) and Rodríguez Madrera, Pando Bedriñana & Suárez Valles (2015) have investigated the use of yeasts in the production of volatiles from different agro-industrial wastes. In the case of Aggelopoulos et al. (2014), mixed agribusiness effluents (cheese whey, cane molasses, malt rootlets) were used as substrate of conversion for *Saccharomyces cerevisiae*, *Kluyveromyces marxianus*, and *kefir*. The best microbial fermentation yield was achieved using *kefir*, having been calculated a production of 4 kg of ε-pinene for each tonne of waste used.

Mantzouridou, Paraskevopoulou & Lalou (2015) have assessed the volatile production by *de novo* synthesis catalyzed by *Saccharomyces cerevisiae* having citrus pulp as solid support.

Among the volatile compounds identified as fermentation products after 72 hours, we can highlight: isoamyl acetate (48.7 mg kg^{-1}), ethyl dodecanoate (25.2 mg kg^{-1}), ethyl decanoate (9.3 mg kg^{-1}), ethyl octanoate (6.3 mg kg^{-1}), and phenyl ethyl acetate (4.5 mg kg^{-1}). The authors also have observed an intense production of ethyl hexanoate, whose maximum concentration was 154.2 mg kg^{-1} after 48 hours. The sum of the volatile esters production (≈ 250 mg kg^{-1}) showed that this production process is a viable way to add value to an agribusiness waste of *Citrus*.

On the other hand, Medeiros, Pandey, Freitas, Christen & Soccol (2000) have studied the influence of five agro-industrial wastes in the production of volatile compounds by *Kluyveromyces marxianus* using the response surface methodology. Cactus meal and cassava bagasse, both supplemented with 10% of glucose, were assessed as the most suitable substrates. Ethanol (418 µmol L^{-1}) and ethyl acetate (1395 µmol L^{-1}) were the major components obtained from cactus meal and cassava bagasse, respectively.

Finally, Rodríguez Madrera, Pando Bedriñana & Suárez Valles (2015) have tested the relationship between the production of volatile compounds and the microorganism used. Apple peel was used as solid support and four yeasts were used: *Saccharomyces cerevisiae* (obtained commercially) and three others isolated from cider (*S. cerevisiae*, *Hanseniaspora valbyensis*, and *H. uvarum*). Altogether, from the fermentation of the four strains, 132 volatiles were identified from different families, having been possible to conclude that the amount of volatiles produced is strain-dependent.

However, despite the clear advantages demonstrated by the use of agro-industrial wastes as a means of nontraditional cultivation for the production of bioaromas or for any other bioprocess, there are some challenges that permeate such application. Among them, we highlight the heterogeneity of such substrates and the possible need for pretreatments or supplementations. Additionally, there is a great challenge to be overcome in terms of downstream processing, which may entail additional costs, because the purification of products in these cases can be much more complex. For this reason, the value added in the final chain of product must justify adjustments in the use of this strategy.

Other issues that also deserve to have their economic viability assessed in the final cost of the by-product are: financial demands with the transport of such waste to the place where they will be reused, and the storage costs of these alternative cultivation means. Furthermore, we must think that the wide availability of a particular industrial waste is segregated to certain areas. In Brazil, for example, the availability of sugarcane bagasse is particularly abundant in the state of São Paulo; whey is mainly found in the state of Minas Gerais. Therefore, these logistical issues must be considered when studies on the added value of agro-industrial waste and by-products are proposed.

3. ECONOMICAL ASPECT

According to Leffingwell & Associates, the global sale of aromas and fragrances in 2014 was approximately US$ 24.9 billion, with expected growth rate from 5 to 6% per year. Regarding market segmentation, the American and European continents are responsible for more than half the consumption of the aromas and fragrances sold worldwide (UBIC Consulting, 2014). Despite this, Asia has emerged as a growing market. An example that illustrates this scenario is the increased market pressure for menthol (character impact compound of mint) in Asian countries, whose demand has increased at a rate of approximately two digits for years. This fact can be explained from the awareness of the benefits of the routine use of dentifrices by Chinese and Indians (McCoy, 2010).

Despite the clear economic potential of the aroma market, another interesting point about this sector is the ability to add value to commodities. Brazil, for example, has an important participation in the world market for the export of primary products. Among these products, we can highlight the significant production of oranges in Brazil (approximately 30% of the world production) (FAOSTAT, 2016), whose oil (annual production of 30,000 tonnes (Schwab, Fuchs & Huang, 2013)) contains >90% of the monoterpene *R*-(+)-limonene. This compound is commonly used in the synthesis of resins, adhesives, paints, solvents, cleaning products etc.

Similarly, pulp and paper industry generates 330,000 tonnes of the by-product turpentine (Schwab, Fuchs & Huang, 2013), whose composition presents large amounts of α-pinene, a bicyclic monoterpene that is very important as starting substrate in industrial syntheses (Surburg & Panten, 2006). However, such compounds are commonly underutilized in the formulation of low value-added products such as cleaning products in general, personal hygiene products, and solvents (Surburg & Panten, 2006).

Therefore, from an economic point of view, by-products of those commodities represent a promising alternative to stimulate the industry of aroma production. This is because the microbial biotransformation of *R*-(+)-limonene and α-pinene (Berger, 2015) is able to produce products with high added value, with a market value from 10 to 30 times higher than the starting substrate. Using the Molbase database (www.molbase.com) as reference, for example, it is possible to illustrate this scenario: while *R*-(+)-limonene has a reference price of US$34/L, its oxygenated counterparts, perillyl alcohol, carveol, and carvone present reference prices of US$405, US$529, and US$350, respectively. Similarly, the possible derivatives of α-pinene (reference price of US$64/L), i.e., myrtenal, myrtenol, verbenol, and verbenone, have reference prices of 913, 1939, 1926, and 906, respectively. Therefore, there is an important economic opportunity to be explored in the addition of value to commodities.

In recent years, a similar scenario has emerged with another commodity produced in Brazil. Currently, the company Amyris manufactures and markets *trans*-β-farnesene (Biofene®) to be used in the production of the so-called “sugarcane diesel”. Although there are no reports of the biotransformation of *trans*-β-farnesene in its pure form, a few reports describe fungi (*Aspergillus niger* and *Penicillium solitum*) as being capable of performing oxyfunctionalization of other farnesene isomers, obtaining aroma compounds with very peculiar sensory profile (Krings et al., 2006). Thus, trans-β-farnesene can be regarded as a great starting substrate for biotransformation studies, since, in addition to the possibility of producing new compounds with great interest to the aroma industry, there is still ample space for scientific and technological innovation, with the dissemination of novel research studies.

Therefore, it is important to emphasize that the economic aspect of any technology is closely tied to profit generation, market demand, and turnover of products. If this scenario is not widely covered, the new technology will, possibly, not be perpetuated. Thus, the creation of ideas (translated into patents, for example) does not necessarily mean that it will be immediately adopted by the business sector. Therefore, innovative processes should be firmly focused on the viability of an industrial scale from the bench scale (Shimasaki, 2014). That is why, when it comes to the production of bioaromas, it is essential that the economic part is profitably met, favoring the commercial feasibility and demand for these same products (Otte & Hauer, 2015).

The available data on the commercial values of aromas of biotechnological origin, compared with the natural and synthetic ones, indicate that this demand can be achieved. To illustrate this scenario, the prices of three different aroma compounds obtained by different methods are shown:

- **Vanillin**: synthetic = US$ 15; natural = US$ 1,200-4,000; “biotech” = US$ 1,000 (Gallage & Møller, 2015);
- **γ-Decalactone**: synthetic = US$ 150; natural = US$ 6,000; “biotech” = US$ 300 (Dubal, Tilkari, Momin & Borkar, 2008);
- **Ethyl butyrate**: synthetic = US$ 4; natural = US$ 5,000; “biotech” = US$ 180 (Dubal, Tilkari, Momin & Borkar, 2008);

In this way, it is possible to see clearly the production potential of the so-called “biotechnological” aromas. This is because aromas obtained by this method have a clear cost-benefit ratio. According to Janssens, de Pooter, Schamp & Vandamme (1992), aromas obtained from biotechnology have commercial competitiveness even when their market prices are 10 to 100 times higher than their synthetic analogues. In fact, flavor compounds biotechnologically produced (i.e., fermentations) might be labeled as “natural”, such as in EU and US legislations (Regulation (EC) no. 1334/2008; US Code of Federal Regulations, Title 21 Section 101.22). This is commercially interesting, since consumers tend to prefer foods formulated with “natural” components (Carocho, Morales & Ferreira, 2015). On the other hand, technology-based innovations, such as the use of irradiation and genetically modified organisms, might be rejected by consumers (Ronteltap, van Trijp, Renes & Frewer, 2007). In Brazil, for instance, a survey showed that one third of those interviewed considered that the consumption of transgenic food could be harmful (Folha de São Paulo, 2016). Therefore, from an economic point of view, the production of bioaromas is very promising in relation to the market acceptance of such products when we consider the commercial value and the benefit associated with their use in different sectors. However, as already mentioned in this text, it is important to recall the possible social issues and regulatory constrains that might come from the increased use of genetically modified organisms (Hayden, 2014).

4. SOCIAL ASPECT

4.1 BIOPROSPECTING

4.1.1 Rational exploration of the environment

Bioprospecting is an activity that consists in the investigation of the environment aiming at finding biological agents that could be used in the production of goods of commercial value (Artuso, 2002). These biological agents can be quite varied as well as the applicability found for each of them. Among the main ones, common agents explored by humanity since antiquity, we can mention plant extracts and biomolecules isolated from certain animals or microorganisms such as fungi and bacteria (Verpoorte, 2015).

According to Morales (2010), Brazil has approximately 70% of the world's species, integrating the group of seventeen countries considered as megadiverse (de Lima, Fortes-Dias, Carlini & Guimarães, 2010). Despite the Amazon presenting much of this heritage, biomes, such as the Brazilian Cerrado and Atlantic rainforest, have also been commonly pointed out as hotspots of significant value for the search for new genetic potentials that can be used in an industrial scale (Marchese, 2014). Therefore, considering this context, Brazil presents a huge window of possibilities for the bioprospecting of different biological resources (Adenle, Stevens & Bridgewater, 2015).

Hence, in general, bioprospecting activities are quite attractive according to the three main aspects that go beyond the contribution to innovation, namely: (i) appreciation of natural resources, (ii) access to associated traditional knowledge, and (iii) potential for contribution to the financial sustainability of certain localities. Thus, bioprospecting assumes an important value for the improvement of social conditions of a population, which presents natural resources as environmental heritage (Lewandowski, 2014).

Regarding social improvement, the appreciation of natural resources of a given region can clearly contribute to the increase in the quality of life of individuals who inhabit it (Sandifer, Sutton-Grier & Ward, 2015). This fact can be easily justified by: (i) preservation of green areas contributing to air quality, (ii) maintenance of water sources (lately considered as one of the most critical points of the indiscriminate environmental exploration), and, finally, (iii) preservation of endemic species (with concomitant reduction in the rate of extinction of species) that represent a wealth of expressive value because of the low probability of being found in other locations. Therefore, in this case, we can explore the environment, without, however, degrading it (Barrett & Lybbert, 2000).

Another point of great importance is the fact that bioprospecting is seen as an activity that values the traditional knowledge associated with the knowledge of the local population (Toledo, 2013). Therefore, it gives relevant value to learning linked to the experience of individuals who already enjoy the use of a certain biological potential for more noble uses such as the use of typical herbs for the production of infusions with medicinal properties, the manufacture of natural dye from the bark of trees, or the extraction of aromatic substances from the native flora (Cox & King, 2013).

In addition, access to the associated traditional knowledge often represents a clear positive impact on the financial sustainability of certain populations. This is enabled by sharing this knowledge for technological innovation and development of new products for commercial purposes. From this, the increase of the *per capita* income of low-income communities is possible with the creation of cooperatives and/or associations, which promotes the allocation of benefits from the exploration of natural resources of the place where this population lives (Weiss & Eisner, 1998).

Therefore, bioprospecting, despite the challenges permeating this activity, shows that the exploration of the biodiversity together with social development is possible, valuing popular knowledge, in addition to increasing the quality of life and the economic quality of these populations (Artuso, 2002).

4.1.2 Selection of strains

Among strategies, bioprospecting is used by some authors in an attempt to identify new strains of microorganisms for the production of bioaromas (van der Werf & de Bont, 1998). Particularly, soil samples have been frequently used for the prospection of microorganisms that are potential bio-transformers of terpene compounds. To illustrate this approach, some examples of microorganisms isolated from soil may be cited: *Bacillus fusiformis*, which was able to convert isoeugenol to vanillin (production of 8.10 g L^{-1} after 72 h) (Zhao, Sun, Zheng & He, 2006); *B. pumilus*, which was also able to convert isoeugenol to vanillin (production of 3.75 g L^{-1} after 150 h) (Hua et al., 2007); *Pseudomonas putida*, which was able to convert isoeugenol to vanillic acid (98% of molar conversion after 40 min) (Furukawa, Morita, Yoshida & Nagasawa, 2003); *Bacillus subtillis*, which was able to convert isoeugenol to vanillin (production of 0.9 g L^{-1} after 48 h) (Shimoni, Ravid & Shoham, 2000); and *Chrysosporium pannorum*, which was able to convert α-pinene to verbenone and verbenol (Trytek, Jedrzejewski & Fiedurek, 2015).

Other isolation and selection strategies, as further exemplified, can also be adopted, thus affirming the importance of prospection efforts in the biotechnological production of aromas.

Ferraz et al. (2015) have isolated *Penicillium crustosum* from a cheese sample. Lipase produced by said microorganism was immobilized in the fermentation system, being responsible for catalyzing the conversion of geraniol/propionic acid in geranyl propionate. The optimization of fermentation parameters showed that lipase produced by *Penicillium crustosum* has the potential to be widely applied in the production of geranyl propionate.

Pastore, Park & Min (1994), from samples of *beiju* (a typical food of the North/Northeast region of Brazil produced from cassava starch), have isolated eight different strains of *Neurospora* sp. identified as capable of producing pleasant fruity aromas.

Dai, Cheng, He & Xiu (2015) isolated a strain of *Bacillus subtilis* DL01 from marine sediment in China. The prospection of that bacteria was encouraging because of the tolerance shown on systems with low aeration rate (0.4 vvm) and high concentration of sugar (210 g L^{-1} of glucose) to produce acetoin (76 g L^{-1} / 1.0 g L^{-1} h^{-1}/ 60.9 g L^{-1} *d*-acetoin).

van der Werf, Keijzer & van der Schaft (2000), from sediment of the Rhine river, insulated *Xanthobacter* sp. C20 using cyclohexane as the sole source of carbon and energy. Such strain has proved to be able to quantitatively biotransform both enantiomers of limonene into limonene-8,9-epoxide (0.8 g L^{-1}). This study proved to be a novel one for describing a new metabolic pathway for limonene, which had not been described before.

Krings et al. (2006) have isolated a strain of *Aspergillus niger* from mango. This microorganism was able to biotransform α-farnesene into two main products: *p*-menth-1-en-3-[2-methyl-1,3-butadienil]-8-ol (aroma that refers to apricot) and 2,6,10-trimethyldodeca-2,7,9,11-tetraen-6-ol (citrus scent).

Rottava et al., 2010 and Bicas & Pastore (2007) have isolated strains from effluents of citrus industry as well as other samples (soil from the plantation of citrus, citrus fruits, and citrus leaves). Of the 405 strains isolated by Rottava et al. (2010), eight were able to bioconvert *R*-(+)-limonene and fifteen converted (−)-β-pinene, generating α-terpineol as a product in both cases. Bicas & Pastore (2007) have obtained 248 microorganisms, of which seventy were developed in medium containing limonene as the sole source of carbon.

However, as reported by Molina et al. (2013), there are several challenges to be overcome to enable the production of aromas by biotransformation, among them the high toxicity of both the substrate and the product and the low yields obtained. According to these authors, such difficulties can be overcome with a good work in the isolation and selection of strains as the studies mentioned above. This is justified by the constant difficulty of identifying microorganisms that are actually able to convert terpene substrates at economically viable concentrations. Moreover, bioprospecting shows itself as a key factor for detecting strains that convert substrates not yet explored to biotransformation processes, among them, the previously mentioned β-farnesene.

Finally, the search for new microbial "factories" is essential to reaffirm the enormous potential of the environment. This is because access to this biological richness has the clear ability of offering solutions to numerous demands in different bioprocesses.

4.2 BIOLOGICAL POTENTIAL OF BIOAROMAS

In this section, we will discuss potential applications of aroma compounds that can transcend food industry, reaching the pharmaceutical industry. For now, there is no reason to believe that these compounds will replace the traditional pharmaceuticals currently in use. However, we anticipate that this seething area of research might evolve in such a way that these compounds, in the future, might found use in medical applications rather than food, supposing that they might eventually have higher specificity and lower toxicity than conventional chemicals.

Used by traditional medicine, essential oils (rich in terpene compounds) are recognized for assisting in the treatment of different health problems. Among the applications widely described in the literature for them, we can mention anti-inflammatory, antispasmodic, anticancer, antimutagenic, antibacterial, antifungal, antiviral, and vermicide activities (de Sousa et al., 2015; Raut & Karuppayil, 2014).

Among the most promising terpenes for these applications, which are also important aroma compounds, we can mention limonene and its derivatives (Kaur & Kaur, 2015). Between the derivatives, we highlight: perillyl alcohol (Imamura et al., 2014), carvone (Carvalho & Fonseca, 2006), and α-terpineol (Pinto et al., 2014).

Regarding the anticancer activity associated with terpene compounds in particular, according to Crowell (1999), it can be explained by the following factors: (i) blocking effects (initiation phase), characterized by enzyme induction of phase I and phase II of the metabolism of xenobiotics, which is associated with the detoxification of the carcinogenic agent; and, (ii) suppressing effects (promotion phase), characterized by (ii.a) the inhibition of cell proliferation, induction of apoptosis or differentiation or by (ii.b) the inhibition of post-translational isoprenylation of cell growth regulatory proteins.

Additionally, considering the overall magnitude of oncogenic diseases, there is an increasing demand for new drugs that can help in the treatments of these disorders (Khazir, Mir, Pilcher, & Riley, 2014). Moreover, such a scenario is reinforced by data released on the World Cancer Report (2014) by the World Health Organization. According to this document, 14 million individuals were diagnosed with this disease in 2012. Of this amount, 8.2 million have died. Furthermore, estimates suggest that the number of cancer diagnoses may suffer an increase of 70% over the next two decades (López-Gómez, Malmierca, de Górgolas & Casado, 2013). Thus, considering the demands of attention of oncogenic diseases, different studies are described in the literature focused on the chemopreventive action of different terpene compounds (Bicas, Neri-Numa, Ruiz, de Carvalho & Pastore, 2011). Thus, next we consider some important studies explored in this and other areas.

4.2.1. Perillyl alcohol

In relation to *in vitro* studies, Sundin, Peffley, Gauthier & Hentosh (2012) have shown that perillyl alcohol, as well as rapamycin, presented chemopreventive activity for prostate cancer. Thus, after an incubation period between 1-16 h, perillyl alcohol was able to reduce the rate of activity of telomerase from 65 to 95%. The importance of this study lies in the fact that telomerase is one of the enzymes responsible for acting in the process of cell immortalization. In another study, Afshordel et al. (2015) have investigated the action of perillyl alcohol and lovastatin. The elucidation of the mechanism of action of both drugs demonstrated that they are able to affect the post-translational modification of isoprenoids (which are responsible for enabling the invasiveness, migration, and proliferation of brain gliomas). While lovastatin was able to suppress the substrates of the pathway, perillyl alcohol inhibited enzymes that catalyze the reactions of that pathway. In a research developed by Lebedeva et al. (2008), the synergy of perillyl alcohol was investigated with gene therapy as a tool for the chemoprevention of pancreatic cancer. On the other hand, Wagner, Huff, Rust, Kingsley & Plopper (2002) have found that the administration of perillyl alcohol presents significant potential as prophylactic therapy in the treatment of breast cancer. Its effects have been attributed to the intervention in the migration ability of tumor cells.

However, it is in *in vivo* studies that we can see that the biological potential of perillyl alcohol is really outstanding. Moreover, according to Chen, Fonseca & Schönthal (2015), the preliminary results obtained from clinical studies are significantly promising. In this context, a group led by researchers at the Fluminense Federal University and Federal University of Rio de Janeiro have conducted clinical assays on terminally ill patients with different malignant gliomas. The therapy adopted was based on the direct inhalation of 0.3% perillyl alcohol, four times a day. Results showed that such therapy was well tolerated and that some patients showed regression of the tumor (da Fonseca et al., 2008, 2006a; 2006b). Another pilot study, also conducted by the same team previously mentioned, has investigated the administration of perillyl alcohol in eight patients with pancreatic cancer (one of the most deadly forms of the disease). It was observed a reduction in the size of the tumor cell from the mechanism of cell apoptosis. Although a statistical significance was not demonstrated, patients had a higher survival rate of 84 days when compared with the control group (Matos et al., 2008).

In another study, Cho et al. (2014) have tested a new drug therapy for the treatment of brain gliomas resistant to temozolomide. This drug is a tumor agent widely used as reference therapy in the treatment of this type of neoplasia. Thus, the so-called NEO 212 (a conjugated drug of perillyl alcohol and temozolomide) was administered to mice and results were analyzed with 95% confidence ($p < 0.05$). Data analysis and tomography exams of the animals showed that NEO212 was effective in the regression of resistant tumors. Furthermore, this drug showed synergistic effect when compared with the separated administration of perillyl alcohol and temozolomide. Therefore, research studies highlighted here demonstrate the use of perillyl alcohol as a promising alternative in cases of failure of oncogenic treatments using conventional methods.

Additionally, administration of perillyl alcohol in other areas has also been extrapolated, as shown in the study of Tabassum et al. (2015). In this latter case, they have investigated the effect of therapy with perillyl alcohol on ischemia-reperfusion injuries (medical terminology applied to describe the changes that occur after a period of ischemia). Results showed that perillyl alcohol was critical to the mitigation of the oxidative stress and inflammatory processes. Mitigation of these processes gave a neuroprotective activity to that terpene.

4.2.2. Carvone

Carvone has demonstrated several applications from its biological potential (Carvalho & Fonseca, 2006). Thus, according to Patel & Thakkar (2014), in assays conducted *in vitro*, carvone was able to control the proliferation of breast cancer tumor cells by apoptosis. Results also showed that apoptosis was accompanied by the increase in the level of excretion of glutathione and reactive oxygen species (ROS). In an *in vivo* study, Vinothkumar et al. (2013) have shown that the administration of carvone proved to be effective in the chemoprevention of chemically induced colorectal cancer. The carvone dose of 10 mg kg^{-1} of body weight was satisfactory for reducing the rate of formation of polyps. The latter is generally deemed as responsible for the progression of intestinal neoplasms. According to studies developed by

Zheng, Kenney & Lam (1992), the anticarcinogenic effect of carvone is mainly associated with its ability in stimulating detoxifying enzymes, among which we can mention glutathione S-transferase.

Carvone has also been explored in other fields of study of science. Among these research studies, we can highlight the study developed by Karanisa, Akoumianakis, Alexopoulos & Karapanos (2015). These authors have verified the inhibition of post-harvest potato sprouting from the application of carvone in these vegetables instead of synthetic suppressors. Results showed that carvone was effective in promoting bud dormancy when the potatoes were stored at 10°C, even if for a long period. In another study, Holban et al. (2014) have investigated the potential of carvone as antimicrobial agent. This study has tested a bioactive system of conjugated nanoparticles of magnetite and carvone (Fe_3O_4@CAR). Results showed that the nanosystem was able to inhibit colonization and biofilm formation of *S. aureus* ATCC 25923 and *E. coli* ATCC 25922. In addition, *in vitro* tests showed that the nanostructured bioactive showed no cytotoxic effects on eukaryotic cells.

On the other hand, Peixoto et al. (2015) have studied the potential of carvone as a natural insecticide. This pilot study has aimed to study the toxicity of carvone against two species of insects: *Sitophilus zeamais* and *Tribolium castaneum*. These species are responsible for heavy losses in grain storage silos. Results were promising for the production of a natural insecticide from carvone as repellent. In the study case carried out by Souza, da Rocha, de Souza & Marçal (2013), it has been demonstrated that carvone has a powerful antispasmodic action, acting preferentially blocking calcium channels.

Finally, de Sousa, de Farias Nóbrega & de Almeida (2007) have studied the effect of two carvone enantiomers on the central nervous system. The *in vivo* study was conducted with mice. The LD_{50} (median lethal dose) was 484.2 mg kg^{-1} for (*S*)-(+)-carvone and 426.6 mg kg^{-1} for (*R*)-(−)-carvone. Both enantiomeric forms showed decreased brain activity. These effects were deducted by the reduced touch sensitivity and increased level of sedation and antinociception (described as the decrease in the capacity of pain perception). However, (*S*)-(+)-carvone applied at 200 mg kg^{-1} significantly increased the latency to seizure, while (*R*)-(−)-carvone did not.

4.2.3. Limonene

Among most recent studies with this monoterpene, we can highlight Zhang, Wang, Liu, Tang & Zhang (2014). Using cell strains of human gastric carcinoma, those authors have shown that, *in vitro*, the administration of limonene with barberine showed synergistic effect when compared with other drugs used alone. The scope of these results was assigned to the induction of apoptosis, increase in the production of reactive oxygen species, and cell cycle inhibition. In another study, Vandresen et al. (2014) have proposed the syntheses of a new drug and its respective derivatives containing limonene in their formulation. The formulations were tested against several types of tumor strains (gliomas, melanomas, leukemia etc.). Among the 22 derivatives prepared, 4-fluorobenzaldehyde proved to be especially selective for prostate tumor strains. On the other hand, 2-hydroxybenzaldehyde proved to be the most active compound, with potent antitumor activity against all cell strains tested.

In the case of Miller et al. (2013), an *in vivo* pilot study has been developed to investigate the bioactivity of limonene. The chemotherapeutic action of this terpene has been studied in a group of forty-three women diagnosed with breast cancer in the early stages of the disease. Despite early diagnosis, these women had surgical indication for organ extraction. Hence, two to six weeks before surgery, each of the patients ingested two grams of limonene per day. Histological analysis of breast tissue showed that limonene was able to homogeneously distribute itself in that organ. Although a control group was not adopted and the population sample adopted was reduced, it was still possible for the authors to conclude that cell proliferation was inhibited because of the subexpression of cyclin D1 (a cell cycle regulatory protein).

Later, a new study was developed by Miller et al. (2015). However, in this latter case, the sample population of women diagnosed with breast cancer and with surgical indication was equal to 39. To investigate the antitumor activity of limonene, the mapping of the metabolomic profile of the patients was used. The key changes identified were related, again, to the subexpression of cyclin D1. Other scientific studies have also contributed to elucidate the other applications of limonene such as illustrated in the sequence.

Bacanlı, Başaran & Başaran (2015), in experiments conducted *in vitro*, highlight the antioxidant action of limonene and narigin. Such potential is attributed to the protective effect against peroxide radicals. In addition, especially because of this antioxidant activity demonstrated by limonene, Bai, Zheng, Wang & Liu (2016) have carried out *in vitro* assays. Of such assays, limonene proved to be promising in the search for more effective therapies for the treatment of ocular degeneration associated with age such as cataracts. Antimicrobial activity of limonene has been investigated by Zahi, Liang & Yuan (2015). In this case, limonene was encapsulated in a nanoemulsion and tested against different microorganisms that cause foodborne illness. Damage to the integrity of the cells of such microorganisms was the main target of action of limonene.

Rossi et al. (2015) have conducted an *in vivo* pilot study on nine patients with psoriasis. Oral and/or topical administration of limonene was performed for 45 days. The good results obtained from both patient satisfaction and the reduction in the extent of the disease point out the need for extrapolation of this study to double blind assays. Tan, Chua, Ravishankar Ram & Kuppusamy (2015) have also signaled to limonene the potential to be used in the control of obesity and type 2 diabetes mellitus. This is because it stimulated the absorption of glycolysis and lipolysis. On the other hand, Hajagos-Tóth, Hódi, Seres & Gáspár (2015) have warned about the awareness of the use of medicinal herbs during pregnancy. That is because, often, this type of therapy deemed as natural seems to have a safe use. However, *in vitro* studies on the two enantiomers of limonene, demonstrated that it raises the rate of uterine contractility. Thus, these authors draw attention to the risk of the use of medicinal therapies, which can affect pregnant women with premature births.

4.2.4. α-Terpineol

In relation to the antitumor activity of α-terpineol, Hassan, Gali-Muhtasib, Göransson & Larsson (2010) have assessed the cytotoxicity of this terpene against cancer cells, *in vitro*. Results of the assays have shown that α-terpineol was able to reduce the expression of the nuclear transcription factor NF-κB. Thus, according to this interference, α-terpineol inhibited the proliferation of different cancer cell strains. However, carcinoma cells of the small cell lung cancer were those that showed greater sensitivity to the treatment. Bicas, Neri-Numa, Ruiz, de Carvalho & Pastore (2011) have also investigated the antioxidant and antiproliferative action of some bioaromas, *in vitro*. Results showed that, among the tested terpenes (limonene, perillyl alcohol, carvone, and a-terpineol), α-terpineol presented the best performance. In terms of antioxidant activity, α-terpineol presented results similar to BHA (butylated hydroxyanisole, a synthetic antioxidant). Additionally, such a compound presented a mechanism of inhibition of cell proliferation against six strains of different tumor cells. The most significant results were achieved with breast carcinoma and chronic myelogenous leukemia, with cytostatic effect (Total Growth Inhibition) for the concentrations of 181μM and 249μM, respectively. Because of this, *in vivo* studies have been encouraged to further this promising potential. Wu et al. (2014) have also developed an *in vitro* experiment with a liver tumor strain. The suppression of cell proliferation was mainly attributed to the triggering of mechanisms of apoptosis. However, γ-terpineol was used in this latter study.

Other research studies have pointed out other applications of α-terpineol. Prakash, Singh, Goni, Raina & Dubey (2015) have assessed the antimicrobial activity from the combination of Angelica essential oil, 2-phenyl ethanol, and α-terpineol in the proportion of 1:1:1. This compound has been tested against eight different moldy fungi responsible for the production of mycotoxins (responsible for the oxidative deterioration of nuts). Results showed that the inhibition of the synthesis of ergosterol in the fungal wall was the main target of the action of the proposed natural insecticide.

Held, Schieberle & Somoza (2007) have conducted *in vitro* studies with epithelial cells of the mouth. Results showed that α-terpineol suppressed the formation of IL-6, thus presenting anti-inflammatory activity. In another similar study, Nogueira, Aquino, Rossa Junior & Spolidorio (2014) have achieved a similar conclusion about the anti-inflammatory activity of α-terpineol. However, in this latter case, a reduction in the production of IL-10 and IL-1β, in addition to IL-6, was observed.

Mukherji & Prabhune (2015) have proposed the application of α-terpineol as the precursor for the synthesis of a glicomonoterpenol. This compound was obtained by the biotransformation promoted by *Candida bombicola* ATCC 22214 from a culture medium supplemented with linalool and α-terpineol. That glicomonoterpenol proved to be very efficient as antagonist of the quorum-sensing mechanism. The importance of this study focuses on the fact that, with the development of bacterial multidrug resistance to several drugs, the intervention in the quorum-sensing mechanism can be an alternative to solve such a problem.

In tests conducted *in vivo* by de Sousa, Quintans-Jr. & Almeida (2008), it has been shown that α-terpineol presented good results as an anticonvulsant agent. Activity in the central nervous system has also been demonstrated by Quintans-Júnior et al. (2011). In this case, the administration of α-terpineol (25, 50, and 100 mg kg^{-1}) in mice presented analgesic activity without apparent interference in the motor ability of those animals. On the other hand, Choi, Sim, Choi, Lee & Lee (2013) have conducted a study with mice, in which α-terpineol was orally administered for two weeks. After this period, the assessment of hepatocytes showed a steatosis result (fat accumulation in the liver). However, in this latter case, specifically, no studies have been developed on humans. On the other hand, as pointed out by Bhatia, McGinty, Foxenberg, Letizia & Api (2008), studies related to the toxicity of α-terpineol show that it presents oral toxicity of 4.3 g kg^{-1} in rodents and dermal toxicity above 3.0 g kg^{-1} in rabbits. In addition, there have been no reports in the literature about the carcinogenic potential presented by this terpene.

Despite the aforementioned research studies and the biological potential presented by the terpenes and their derivatives, reports on the activity of other derivatives of biotransformation of these compounds are still scarce in the literature, among which we can mention limonene-1,2-diol. Thus, we consider of utmost importance the exploration of these promising biological activities demonstrated by different terpene compounds.

5. FINAL REMARKS

The concept of sustainable development is a subject of extreme relevance in modern society. However, despite the trendiness of this subject, it is important to understand its systemic approach, the actual applicability of this concept, and the benefits obtained from such a practice. Especially when it comes to creating new technologies, clear perspectives must be well delineated in order to adapt innovative processes to new demands vividly discussed about sustainability. In this sense, the growing trend of replacement of classical processes for bioprocesses emerges as a promising opportunity to contemplate, at the same time, the three aspects of sustainability, i.e., social, economic, and environmental aspects. In our study, we suggest that this scenario is also applicable for the flavor industry, a point of view grounded in numbers.

Currently, the global market for fermentation-derived products worth $24.3 billion and it is expected to grow at a compound annual growth rate (CAGR) of 7.7% in the following years to reach a value of $35.1 billion by 2020 (PRNewswire, 2015). If we include the data for bioethanol, this market exceeds US$ 120 billion (Deloitte, 2014). Thus, considering that the greatest impact of white biotechnology may be on the fine chemicals segment (Europabio, 2003), the production of bioflavor not only has considerably increased in the last decades, but it is projected to have an increasing role in the food industry to supply the consumers' demand for more natural flavors, whose market (excluding seasonings and flavoring materials) is expected to grow with a CAGR of 9.1% (UBIC Consulting, 2014).

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TABLES

TABLE CAPTIONS:

Table 1 – Parameters of processes used by the chemical industry for the production of synthetic vanillin, *γ*-decalactone, and 2-phenylethanol.

Table 2 – Examples of commercially relevant processes for the biotechnological production of biotech aroma compounds (Gallage and Møller, 2015; Leffingwell & Leffingwell, 2015).

Table 3 – Annual generation of agro-industrial waste or by-products with potential application as nontraditional cultivation medium for biotechnological production of various bioaromas.

Table 1

Product	Conversion substrate	Reagents	Temperature (°C)	Ref*
Vanillin	Lignin	Sodium hydroxide/calcium hydroxide.	125-160	1
	p-cresol	Potassium hydroxide/sodium hydroxide/methanol	60	2
	Guaiacol	Formaldehyde	120-125	3
γ-decalactone	Gamma-bromocapric acid / 9-decen-1-oic acid	Sodium carbonate/ H_2SO_4 80%	90°C	4
2-phenylethanol	Friedel – Crafts Reaction of Benzene and Ethylene Oxide	aluminum chloride	10-15	5
	Hydrogenation of Styrene Oxide	Raney Nickel, sodium hydroxide	10-110	6

***References**: 1. Surburg & Panten (2006) and Harold & Tomlinson Jr (1937); 2. Surburg & Panten (2006) and Nishizawa, Hamada & Aratani (1984); 3. Surburg & Panten (2006) and Kamlet (1953); 4. Burdock, 2010; 5. Surburg & Panten (2006), Thomas, Nicholl & Bitler (1949); 6. Surburg & Panten (2006) and Wood (1971).

Table 2

Product	Company	Microorganism*	Substrate	Ref**
Vanillin	Evolva - IFF	GM *Schizosaccharomyces pombe*	Glucose	1
	Mane	GM *Streptomyces* strain	Eugenol	2
	Shanghai Apple	*Streptomyces* sp. V-1	Ferulic acid	3
	Solvay	*Streptomyces setonii*	Ferulic acid	4
	BASF	GM *Pseudomonas* strains	Ferulic acid	5
Patchouli	Amyris - Firmenich	GM *Saccharomyces cerevisiae*	sugarcane	6
Farnesene	Amyris	GM *S. cerevisiae*	sugarcane	7
Ambroxide	Firmenich	GM *Escherichia coli*	sugarcane	8
Nootkatone	Allylix (Evolva)	GM yeasts	Valencene	9

*GM: Genetically Modified. **References: 1. Hansen et al. (2009) and Hansen et al. (2014); 2. Lambert, Zucca & Mane (2013); 3. Xu et al. (2009); 4. Muheim, Müller, Münch & Wetl (2001); 5. Graf & Altenbuchner (2016); 6. Schalk & Deguerry (2015); 7. Renninger, Newman, Reiling, Regentin & Paddon (2010) and .Meadows et al. (2016); 8. Schalk et al. (2012); 9. Saran & Park (2016).

Table 3

Culture	**Volume of global annual generation (tonne)[1]**	**Type of agro-industrial waste generated**	**Estimated volume of waste (tonne)**	**Note**
Cassava	2.77×10^8	Manipueira (cassava wastewater)	2.7×10^9 m^3	2
		Cassava peel	1.48×10^6	2
Sugarcane	1.91×10^9	Sugarcane bagasse and trash	2.8×10^8	3
Apple	8.08×10^7	Apple pomace	2.0×10^7	4
Rice	7.41×10^8	Rice husk	1.5×10^8	5
Coffee	8.92×10^6	Coffee husk and pulp	3.6×10^6	6
Orange	7.14×10^7	Orange bagasse	2.7×10^7	7
Milk (cow)	6.36×10^8	Whey	4.07×10^7	8

[1] Data obtained from FAOSTAT (2016), for the global production of each of the products presented.

[2] Processing of 250-300 tonnes of cassava results in ≈ 2655 m3 (with 1% solids) of liquid effluent or manipueira. The processing of 250-300 tonnes of cassava tubers results in approximately 1.6 tonnes of solid peels and approximately 280 tonnes of bagasse with high moisture content (85%). Value calculated considering that all cassava produced is processed (Pandey et al., 2000).

[3] Source: del Río et al. (2015).

[4] The volume of apple pomace corresponds to 20-30% of the initial weight of the apple (Dhillon, Kaur & Brar, 2013). Value calculated considering that all apple produced is processed.

[5] The amount of rice husk corresponds to 20% of the total produced (Gul, Yousuf, Singh, Singh & Wani, 2015). Value calculated considering that all rice produced is processed.

[6] The amount of coffee husk and pulp corresponds to 30-50% of the weight of the total production (Oliveira & Franca, 2015). Value calculated considering that all coffee produced is processed.

[7] Peel, pulp, and seeds are ≈ 50% of the fruit (Macagnan et al., 2015). It was considered that ≈ 75% of the fruits produced are processed (Conceição, 1998).

[8] Source: Prazeres, Carvalho & Rivas (2012).

FIGURES

FIGURE CAPTIONS:

Figure 1 – Articulation of the triple bottom line that must be fully covered by a technology that seeks sustainable development. Adapted from: Sustainability – What do we mean?

Figure 2 – Patent search on the platform Google Patents for different periods and keywords: “vanillin and microbial process” (black), “2-phenylethanol and microbial process” (gray), “gamma-decalactone and microbial process” (white).

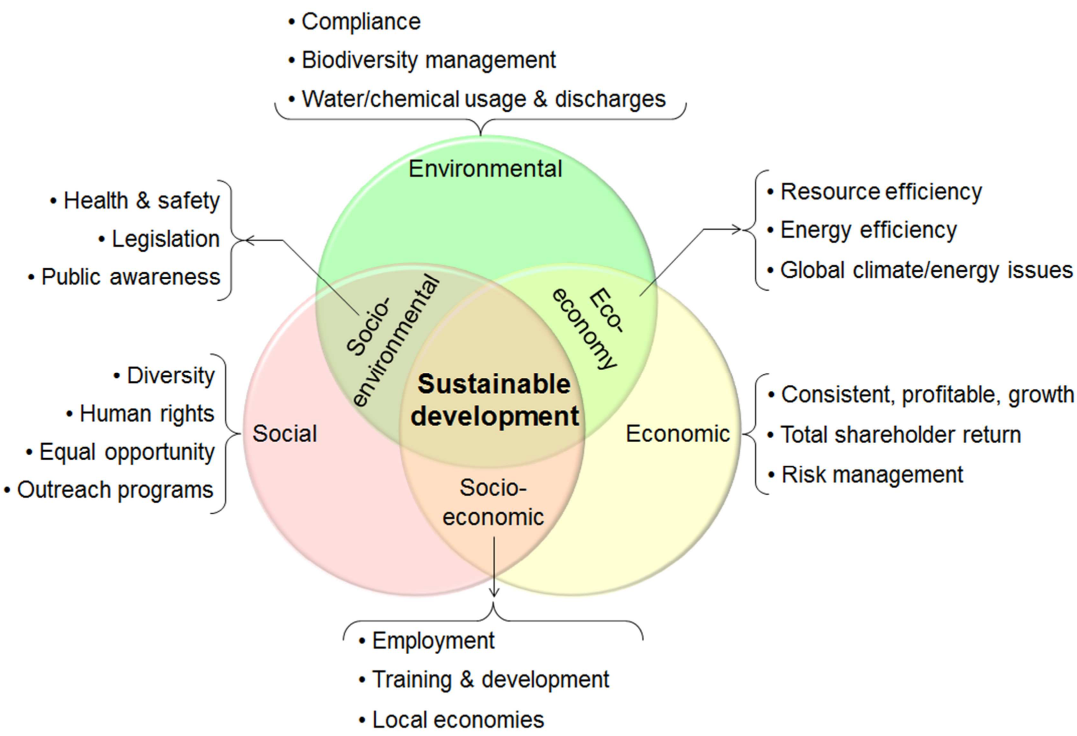
• Compliance
• Biodiversity management
• Water/chemical usage & discharges
Environmental
• Health & safety
• Legislation
• Public awareness
• Resource efficiency
• Energy efficiency
• Global climate/energy issues
Socio-environmental
Eco-economy
Sustainable development
• Diversity
• Human rights
• Equal opportunity
• Outreach programs
Social
Economic
• Consistent, profitable, growth
• Total shareholder return
• Risk management
Socio-economic
• Employment
• Training & development
• Local economies

Figure 1

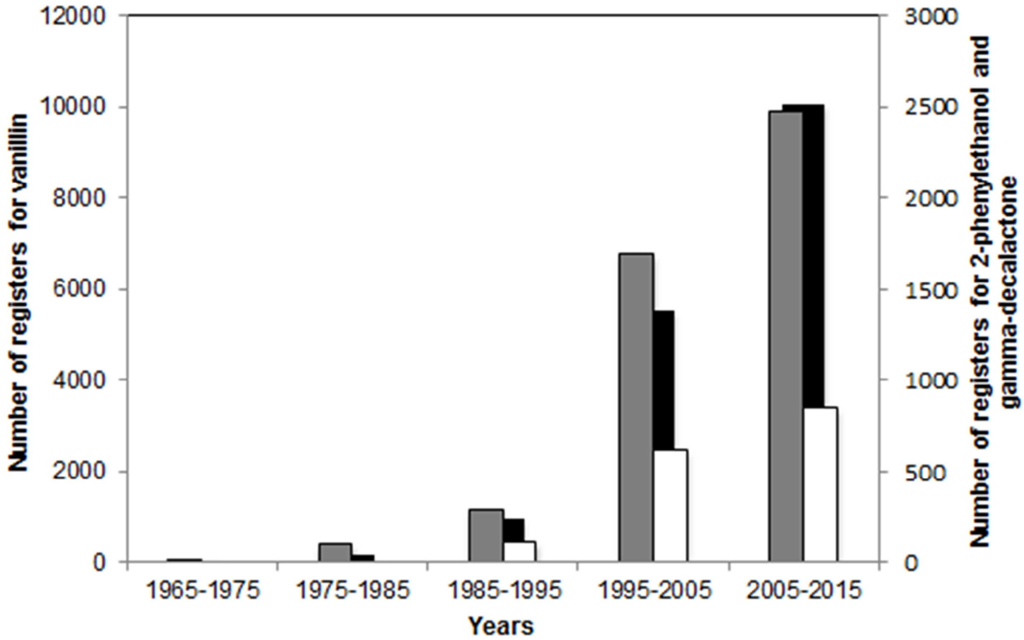
12000
10000
8000
6000
4000
2000
0
Number of registers for vanillin
3000
2500
2000
1500
1000
500
0
Number of registers for 2-phenylethanol and gamma-decalactone
1965-1975
1975-1985
1985-1995
1995-2005
2005-2015
Years

Figure 2

HIGHLIGHTS

- Bioaromas are natural aroma compounds biotechnologically produced;
- Bioaroma production is aligned with the three pillars of sustainability;
- Microbial aroma production is an environmentally friendly approach;
- There is an increasing market for natural aromas and bioaroma has competitive prices;
- Increasing reports show bioactivities of terpene biotransformation products.