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The Importance of bioconversions of today

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Abstract

Recently increasing diseases, negative progress of human health, forced consumers to consume natural products. Natural products have been difficult and expensive to procure, as they are not as abundant as before, and as a result of increasing demand. In order to meet the increasing demand, mass production has started and different industrial products are put on the market. Most of these industrial products are treated with chemicals. Although products treated with chemicals have advantages such as cheap production, length of storage and ease of use, they may have harmful effects on health and increase the demand for natural products in consumers. Therefore, biotechnological methods have recently been considered as an alternative. It is known that biotechnological methods are widely used in food industry, health industry, leather and textile production, animal feed production. More innovative and effective products should be produced by focusing on each of these applications and utilizing the power of biology and technology sciences. In order to increase the applicability of biotechnology and biotechnological methods, which are popular in recent times, we need to understand and know biotechnology very well. In this review, bioconversion methods used in the production of some natural substances, which is one of the application fields of biotechnology, are discussed.

Key words: Biotechnology, bioconversions, natural products, biotechnological methods

Introduction

The first definition of biotechnology is the use of biological systems in technology and providing benefits. There are different definitions of biotechnology in the literature. Biotechnology; It is a combined application of biochemistry, microbiology and engineering sciences used to benefit from the technical application potential of cells, microorganisms and tissue cultures and various parts thereof (Çelik, 2009). According to Ayhan (2009); biotechnology is use of microorganisms such as bacteria and yeast, or biological materials such as enzymes to perform specific industrial production processes. It is defined as any technological application that uses biological systems, living organisms or derivatives thereof to make or modify products or processes for specific use, as approved by the United Nations Convention on Biological Diversity (CBD, 1992).

These applications are increasingly attract attention in various branches of science. The term biotechnology, whose practical and theoretical applications date back many years, is derived from the words biology and technology. The aim of biotechnology is to provide a better environment for people to live in better conditions. Hence; biotechnology using the biological systems, living organisms or their products, for the benefits of people and people around it to achieve positive results (Çelik, 2009). Biotechnology is divided into several subfields; blue biotechnology, red biotechnology, white biotechnology, green biotechnology and (Ayhan, 2009). Blue biotechnology is related to marine and aquatic applications of biotechnology. However, its use is relatively rare compared to other biotechnology areas.

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Green biotechnology, also known as agricultural biotechnology processes. It is a very important field of modern biotechnology. The main purpose of green biotechnology is to improve plants and to produce new products by implanting different genes into economically important plant species. This field consists of plant tissue culture, plant genetic engineering, plant molecular marker assisted breeding areas. For example, genetically modified organisms (GMOs) are directly related to this field. White biotechnology sometimes called gray biotechnology is connected with industry. White biotechnology uses biological organisms such as molds, yeasts, bacteria and enzymes to produce goods and services or parts of industry products. Some of the products of white technology are detergents, vitamins, antibiotics. Generally, the result of white biotechnology processes is saving of water, energy, chemical and waste reduction compared to traditional methods. The history of this area dates back to thousands of years, the history of wine, cheese, bread production. Red biotechnology is related with health care processes. It uses the human body's own tools and weapons in fighting a disease or illness as in the case of genetically modified yeasts and bacteria used for production of drugs that are hard to synthesize via classical methodologies. Red biotechnology plays a great role in traditional drug discovery and also in creating new possibilities for treatment, prevention and diagnosis by using new biotechnological methods. Biotechnology drugs account for about 20% of all market drugs (Ayhan, 2009; Bartoszek et al., 2006).

One of the most widely used applications in biotechnology is bioconversion. Bioconversion is the process by which microorganisms convert a compound into a different structurally similar compound (Tay, 2013). Bioconversion is the process by which microorganisms convert a compound into structurally another product (Wang Daniel et al., 1979). In other words, bioconversion; chemical transformations catalyzed by microorganisms (Ayhan, 2015). Such transformations are often called microbial transformations (Wang Daniel et al., 1979). Instead of using conventional chemical transformations, bioconversion (also called biotransformations) has been developed as an alternative (Ayhan, 2009). The earliest known example of bioconversion is the production of vinegar from ethanol by acetic acid bacteria (Wang Daniel et al., 1979; Walsh, 2001). Bioconversion processes generally occur in batch, continuous, or semi-continuous mode bioreactors. Furthermore, depending on the particular application, different types of bioreactors may be suitable. Generally a certain amount of moisture is needed for optimal microbial activity. To achieve maximum efficiency, it is necessary to optimize the biocatalyst and bioreactor configuration and operating conditions, such as residence time in continuous operation, pH or media composition (Kennes, 2018).

Some types of reactions that occur during microbial bioconversion are shown in Table 1. In most microbial bioconversion processes, two substrates are required. One is necessary for the growth of microorganisms; the other is substrate material that will undergo bioconversion. Since the substrate required for the growth of microorganisms can be afforded cheaply from natural sources, the cost is partially reduced (Walton et al., 2003; Waché et al., 2003; Ayhan, 2015).

Table 1. Some types of bioconversion reactions (Wang et al., 1979)

Hydroxylation	Esterification
Hydrolysis	Demethylation
Methylation	Hydration
Condensation	Amination
Decarboxylation	Phosphorylation
Amidation	Isomerization
Racemization	Reduction
Epoxidation	Acylation
Oxidation	Transglycosidation
Dehydration	Deamination
Halogenation	Epimerization
Cleavage of C – C bonds	

It is important to understand that metabolism and bioconversion are difference systems of molecular processing. Microbial metabolism consists of two main processes. The primary metabolism undertakes tasks related to cellular function, while the secondary metabolism uses pre-existing metabolic pathways to produce substances for adaption of the organism to the environment. Primary metabolism is associated with a number of factors. These are energy production, biomass production and basic cell components. Glycolysis and oxidative phosphorylation are examples of typical sets of reactions of primary metabolism (Bianchini et al., 2015; Keller et al., 2005; Brakhage, 2013). Bioconversion has several advantages over conventional chemical methods (Wang Daniel et al., 1979; Ayhan, 2015). These advantages: High substrate selectivity, specificity; organisms that catalyze biological transformations serve as stereospecific catalysts. For example, steroid bioconversions, which is so useful in providing new intermediates for chemical conversion to advanced steroidal drugs, has reached a final degree of specificity (Wang Daniel et al., 1979). High efficiency; high yields are generally obtained in bioconversion processes as seen in Table 2. Small amount of by-product formation. Easy isolation and purification of primary product, the product has many advantages such as being "natural'. The reaction conditions are mild. It therefore allows conversion of substances to low or high pH values or to heat. Reactions can occur even in cases where the reaction cannot normally begin due to insufficient activation energy in the molecule.

Table 2. Efficiency of Some Bioconversion Processes

Substrate	Product	Organism	Efficiency (%)
Glycerol	Dihydroxyacetone	*Gluconobacter suboxydans*	90
Glucose	5-Ketogluconic acid	*Gluconobacter suboxydans*	90
Glucose	Gluconic acid	*Aspergillus niger*	100
Maleic acid	Fumaric acid	*Alcaligenes faecalis*	98
Mannitol	Fructose	*Gluconobacter suboxydans*	95
Sorbitol	Sorbose	*Gluconobacter suboxydans*	98
Sorbitol	Fructose	*Bacillus fructosus*	90

Microbial Bioconversion Techniques

There are different microbial bioconversion techniques used in biotechnology (Ayhan, 2015).

Bioconversion with proliferating cells**:** After the cells are produced in an ideal medium and determined by tests, the substrate to be bioconverted is added to the medium.

Bioconversion with cells in static phase**:** Microorganism is produced in ideal medium and purified by filtration or centrifugation methods and then added to bioconversion medium.

Bioconversion with spores: Molds are produced under ideal conditions for spore formation and spores are separated from micelles and stored in the cold. These spores are utilized in the bioconversion process.

Bioconversion with fixed cells**:** Microorganisms are fixed in a polymer matrix (starch, polyacrylamide, cellulose, etc.) that allows the passage of product and substrate, or bound to a polymer. Immobilized cells can be removed and reused if necessary. This method is suitable for batch and continuous fermentation.

Important factors for bioconversion

In addition to the selection of the best microorganism and creation of optimum conditions, the following factors are important in the effective development of bioconversions. Some of these factors are listed below (Wang Daniel et al., 1979).

Regulation of enzyme synthesis; In order to produce cells of the best quality for a given bioconversion, the cells must have a maximum amount of the appropriate enzyme (s). Regulation of enzyme synthesis is very important for cell growth.

Mutation; Generally, the yield of a bioconversion can be mutatively markedly improved by the removal of enzymes catabolizing the desired product. For example; conversion of pentaerythritol to tris (hydroxymethyl) acetic acid using *Flavobacterium sp.*

Permeability; Some bioconversions are entirely dependent on changing the permeability of cell.

Avoidance of product inhibition; The product can inhibit bioconversion from time to time. This event is sometimes one of the major problems. The problem of product inhibition in the conversion of p-xylene to p-toluic and 2,3-dihydroxy-p-toluic acids, was solved by supplementation anion exchange resin to the broth.

Transformation of insoluble substrates; insolubility of some substrates causes difficulties in bioconversion processes. Nevertheless, even compounds that are not as soluble as steroids are sometimes easily converted. A variety of techniques are available to make insoluble substrates available, such as the use of finely divided suspensions, soluble complexes and esters (Wang Daniel et al., 1979). For example, use of the cycloborate complex of 16α-hydroxycortexolone, increases solubility of the steroid 20000 fold and significantly improves its bioconversion (Lee et al., 1971).

One of the most popular biotechnological applications in recent years is the production of aroma substances. Flavours and aromas are very important for the food, feed, cosmetic, chemical and medical industries.

For a long time, plants have been the main source of essential oils and flavours. However, low amounts of flavour components in plants making isolation difficult and the flavour products expensive. For this reason, most of the flavour compounds available on the market are now produced by chemical synthesis. More than 80% of the flavours used in the market are synthetic flavours today. The disadvantages of such chemical processes are the formation of undesirable racemic mixtures and the increasing drawbacks of the added chemicals. This has forced flavour companies to shift to the flavor components of biological origin, called natural or biological flavours. Currently the most promising possible alternatives for the production of flavouring compounds are biotechnological methods and the use of so-called ‘biocatalysts’ for plant cell and tissue cultures, microorganisms and enzymes their synthesis (Janssens et al., 1992; Yılmaztekin, 2008). In microbial bioconversion, aroma substances are produced by reactions such as dehydration, hydrolysis, oxidation, reduction in the precursor component. An example of aroma production by microbial bioconversion is the production of 2-phenylethanol (rose aroma) from L-phenylalanine by Saccharomyces cerevisiae (Figure 1) (Tay, 2013).

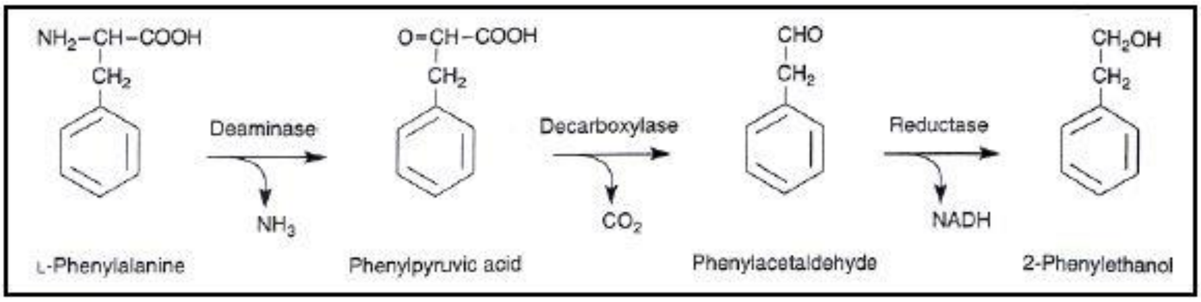

Figure 1. Bioproduction of 2-phenylethanol from L-phenylalanine by *Saccharomyces cerevisiae* (Vandamme, 2003)

Thanks to the advances in modern biotechnology, the production of aroma substances with the help of plant cell cultures, enzymes and microorganisms has become widespread. Two different methods are used in the production of aromatics by biotechnological methods. The first is the bioconversion of specific precursors to aroma compounds by microorganisms or enzymes, and the second is production by fermentation using carbon and nitrogen sources. While fermentation requires carbon and nitrogen sources, a suitable substrate is sufficient for microbial bioconversion. General characteristics of both methods are given in Table 3 (Yılmaztekin et al., 2008).

Table 3. General characteristics of fermentation and microbial bioconversion (Yılmaztekin et al., 2008)

Characteristics	Fermentation	Microbial Bioconversion
Microorganisms	Proliferating Cells	Cells in The Replication Phase and in The Stagnant Phase
Reaction	Complex Reactions	Simple Catalytic Reactions
Reaction Time	Long	Short
Substrate	Cheap Carbon and Nitrogen Sources	Specific
Product	Natural	Natural or Artificial
Product Quantity	Little	High
Product Purification	Difficult	Easy

Microbial flavoring volatile compounds are detected by various instrumentation such as gas chromatography (GC) and mass spectrometry (MS). Terpenes, benzaldehydes, lactones, pyrazines, esters are some of the important flavours components (Janssens et al., 1992; Yılmaztekin, 2008).

Terpenes

The most important components responsible for the characteristic odours of essential oils are usually terpenes (Janssens et al., 1992; Yılmaztekin, 2008). Isoprene units form terpenes. Terpenes may be in cyclic, open chain, saturated, unsaturated, oxidized form. Terpene producing microorganisms are ascomycetes and basidiomycetes fungi that can be found on rotting pinewood. For example, the genus Cerutcrcystis (Janssens et al., 1992; Yılmaztekin, 2008).

Lactones

Lactones are among the most commonly used flavoring agents, especially in foods and beverages. γ- and δ-lactones (4- and 5-alkanolides) are among the important lactones naturally present in fruits and in some fermented foods and are fragrant compounds. Lactones are related with buttery, coconut-like, fruity, sweet or nutty odours. These aroma compounds make them interesting food additives. The lactone cycle structure, length of the lateral carbon chain, presence of unsaturation etc. makes specific lactone flavor effective. They are usually produced chemically, but especially the production of optically active lactones by microorganisms can have several advantages over chemical synthesis. An example is the Trichoderma viride fungus that forms a strong coconut aroma on a simple soil environment (Janssens et al., 1992; Yılmaztekin, 2008).

Esters

Another group of particular importance among the flavours are esters. They form important aroma compounds of fruits in which they are present at very low (about between 1 and 100 ppm) concentrations. Long time ago, these compounds were synthetically produced, but it was also expected that these compounds could be synthesized by microorganisms. It is also well known that some lactic acid bacteria and *Pseudomonas* species produce ethyl butyrate and ethyl hexanoate and the formation of flavorless substances in pasteurized milk and cheese(Janssens et al., 1992; Yılmaztekin, 2008). Esters formed as a result of reactions between long chain acids and alcohols are used as additives in food, detergent, cosmetic and pharmaceutical industries. The products formed as a result of reactions between short chain acids and alcohols are important aroma substances. Many alcohol acetates are of commercial importance, of which ethyl acetate, isobutyl acetate and isoamyl acetate are used in the flavoring industry. The isoamyl acetate is especially consumed in the food industry thanks to its sharp banana aroma and its annual production is around 70 tons. The natural forms of esters are very expensive and difficult to obtain. As with other aroma products, those synthesized chemically are cheaper but are not preferred because they are not natural. It has been reported that it is possible to produce aroma esters with the help of lipases.

Various studies have been conducted on the production of free and immobilized lipases obtained from different sources in organic solvents (Janssens et al., 1992; Yılmaztekin, 2008; Güvenç et al., 2002).

Pyrazines

Normally pyrazines are a characteristic typical roasty or nutty aroma produced by Maillard reaction in baked meat products, roasted nuts, coffee and cocoa beans. Yet, the pyrazines were isolated from peas or vegetables that contain aroma called "green" (Janssens et al., 1992). Several microorganisms such as *Corynebacterium glutumicum*, which is a significant producer of tetramethylpyrazine, can also synthesize pyrazines. A fermentation time of about 5 days was required to achieve a concentration of 3 g/liter. Consumers who like nutty coffee, chocolate, bananas-like flavours can add pyrazines to their food to create these aromas. Furthermore, natural pyrazines may be a good alternative to the need for roasty flavours in food microwave processed where no browning reaction takes place (Janssens et al., 1992).

Benzaldehydes

Benzaldehyde is among the most important aromatic compounds. It was first synthesized by hydrolysis of benzalchloride in 1863 (Yılmaztekin, 2008). Today, benzaldehyde is obtained as a secondary product during the production of synthetic benzaldehyde phenol. Its annual production is about 7000 tons. Annual production of natural benzaldehyde is about 1/70 of this amount and about 80 tons is obtained from cinnamaldehyde. The remaining 20 tons can be obtained from apricot, peach, plum seeds and bitter almonds. Benzaldehyde produced by chemical synthesis is not considered to be natural under European Union Laws. They can produce benzaldehyde by fermentation and biotransformation of some decay molds (Yılmaztekin, 2008).

Another most popular biotechnological application in recent years is the production of enzymes. Enzymes are globular proteins that act as catalysts that speed up the rate of a reaction by lowering the energy of activation (Fernandes, 2018). Enzymes are considered as biological catalysts that have important function in metabolism of cell organism and biochemical reactions (Abada et al, 2017). Some enzymes require nonprotein chemical compound or metal ions cofactor or supporter molecules including metals such as Zn and Fe or small organic molecules such as vitamins that support the biological reactions for catalytic activity (Figure 2). Enzymes are classified according to different temperature ranges and pH ranges. Thermophilic, mesophilic and psychophilic according to temperature ranges; according to pH ranges, it is classified as acidophile, neutrophiel and alkalophile. The enzyme activity depends upon bind the reactants (substrates) capability to specific place called active side which specific for a certain substrate without any interference of others, and the enzyme converts substrates into a product.

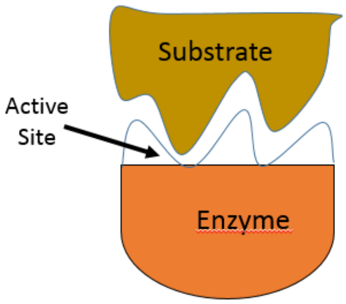

Figure 2. Enzyme structure

Table 4. Several enzymes with excellent value for industrial applications and commercial way

Enzyme Type	Sources	Extraction	Biotechnological use
Bacterial enzymes			
∞-Amylase	*Bacillus* sp.	Extracellular	Starch industry
β- Amylase	*Bacillus* sp.	Extracellular	Starch industry
Asparaginase	*E.coli*	Intracellular	Health industry
Glucose isomerase	*Bacillus* sp.	Intracellular	Fructose syrup
Penicillin amidase	*Bacillus* sp.	Extracellular	Pharmaceutical industry
Protease	*Bacillus* sp.	Extracellular	Detergent
Pullulanase	*Klebsiella*	Extracellular	Starch
Fungal enzymes			
α-Amylase	*Aspergillus*	Extracellular	Baking
Aminoacylase	*Aspergillus*	Intracellular	Pharmaceutical
Glucoamylase	*Aspergillus*	Extracellular	Starch
Catalase	*Aspergillus*	Intracellular	Food
Cellulase	*Trichoderma*	Extracellular	Waste
Dextranase	*Penicillium*	Extracellular	Food
Glucose oxidase	*Aspergillus*	Intracellular	Food
Lipase	*Rhizopus*	Extracellular	Food
Pectinase	*Aspergillus*	Extracellular	Drinks
Yeast enzymes			
Invertase	*Saccharomyces*	Intracellular/ Extracellular	Confectionery

Animals, microorganisms and plants are generally the source of biologically active enzymes. However, with the rapid development of biotechnology, microbial enzymes that are designed and produced using molecular techniques are preferred. These enzymes are suitable for many industrial applications and have high activity. In the present century, many studies have been conducted on the induction and characterization of small and large-scale microbial enzymes. Due to their ease of production, low cost, purification and their properties, many enzymes have been studied extensively. Table 4 shows several microbial enzymes with excellent value for industrial applications and commercial way.

Proteases are the most commercially viable hydrolytic enzymes that are synthesized by bacteria such as *Bacillus, Clostridium* and some fungi. Protease is one of the most commonly used enzymes for rennet as a produce of cheese and meat tenderization in food processing. In the classification of proteases, the properties such as pH, mode of action and structure of the active site are. The proteases produced from microorganisms may have acidophilic, neutral and alkalophilic properties according to their types (Abada et al, 2017; Fernandes, 2018). Xylanase means an enzyme complex that can completely hydrolyze xylan. The activity of xylanases is higher at 40-60 °C temperature conditions produced by many fungal genus *Trichoderma, Penicillium* and *Aspergillus*. The most common applications of xylanases in the field of biotechnology are applications such as clarifying fruit juice, production of fuels and increasing rumen digestion (Abada et al, 2017; Fernandes, 2018).

Conclusion

Agriculture and agriculture-based food industries are sectors that generate a high proportion of organic waste. At this level of perception, bio waste from agricultural and agricultural industries such as the beer industry is defined as sustainable resources rather than waste. Today, due to environmental pollution, waste of resources and decrease in raw material resources, recycling of industrial waste and by-products has become inevitable necessity. In particular, organic food industry wastes are a very important and rich source of raw materials and substrates for biotechnological processes due to the carbohydrates, nitrogen and minerals they contain. Moreover; recently, factors such as consumers' susceptibility to natural products and legal limitations have led to the production of natural substances and the development of new biotechnological methods. The use of these methods in the production of natural substances is cheaper than the cost of natural substances obtained from plants and animals. With the rapid and new developments in biotechnology, it is possible to increase the yield of biocatalysts used in the production of natural substances through researches. The continuation of these works, which play a role in the transition to industrial scale production, is extremely important both in terms of economic and natural products. As a result, this review emphasizes the current importance, status and the breadth application areas of biotechnology that widely used in food industry, health industry, leather and textile production, animal feed production. In addition, bioconversion methods, which are important applications of biotechnology, are discussed. It is expected that this study will contribute to the research and understanding of some methods of bioconversion, which is one of the most important fields of biotechnology.

Conflicts of Interest

The authors declare no conflict of interest.

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