Novel Approaches in Drug Designing & Development

Juniper Publishers key to the Researchers

Mini Review
Volume 4 Issue 4 - January 2019
DOI: 10.19080/NAPDD.2019.04.555645

Nov Appro Drug Des Dev

Biotransformation: A One Pot Method of Novel Pharmacological Importance

Maria Yousuf[1]*, Khayala Mammadova[2] , Samira Baghirova[2] and Rana Rahimova[2]

[1]Dow College of Biotechnology, Dow University of Health Sciences, Karachi, Pakistan.

[2]*Azerbaijan Medical University Baku, Azerbaijan*

Received Date: December 28 , 2018; **Published Date:** January 16, 2019

***Corresponding author:** Dr. Maria Yousuf, e.mail: drmariayousuf@hotmail.com

Mini Review

Biotransformation is a process in which a substance (compound) is structurally transformed through enzymatic chemical reactions within a living system. such as nutrients, amino acids, toxins, and drugs in the body. It is also used to convert non-polar compounds into polar derivatives, therefore prevent from re-absorption in the renal tubules and excreted. Other definitions of biotransformation may include :

a. Chemical transformation of a substance which is mediated by the enzymes of cells from living organisms.

b. The use of living organisms to modify substances that are not normally used for growth [1].

c. The series of chemical reactions that occur in a compound, especially a drug, as a result of enzymatic or metabolic activities by a living organism [2].

d. Chemical alteration of a substance within the body by the action of enzymes [3].

Biotransformation processes are increasingly used in research laboratories, as well as in industry, because they can be conduct under mild and environmentally friendly conditions. Biotransformation reactions are stereospecific in nature, which are different from the conventional synthesis reactions by using traditional laboratory reagents. Biotransformation enzymes or drug-metabolizing enzymes plays an important role in the metabolism of foreign substances also known as xenobiotics. This may include drugs, chemical carcinogens, photochemicals, as well as endogenous compounds (e.g. steroid hormones). The metabolism of a drug or a toxin in a body is also an example of biotransformation. There are two main types of drug metabolism process:

a. Phase I drug metabolism in which polar functional groups (mainly OH, but also SH, NH2, COOH, etc), are add up to increase the polarity of metabolites.

b. Phase II drug metabolism in which conjugation reactions take place by the covalent attachment of small polar endogenous molecules, such as glucuronic acid, sulfate, or glycine to make it polar and water-soluble.

Biotransformation processes can be classified into three major types, which depend upon the enzymatic sources

a. Microbial transformation

b. Plant cell culture-based transformation

c. Animal cell culture-based transformation

Microbial transformation reactions generally include oxidation, reduction, hydrolysis, condensation, isomerization, formation of new C=C double bond, introduction of hetero functionalities, etc. Oxidation, isomerization, reduction, hydrolysis and condensation also have industrial applications, microbial transformation has several advantages over the conventional chemical synthesis methods, such as:

a. It required mild reaction conditions, therefore environmentally friendly.

b. Highly regioselective.

c. Highly stereo specific.

However, plant cell cultures also catalyze a vast variety of biochemical reactions for the production of specific secondary metabolites; its enzymes have great potential to transform cheap and plentiful substances such as industrial by products into valuable and expensive products. Plant bioconversion systems can also be used alone to produce novel chemicals, or in combination with organic synthesis [3-4]. Bioconversion of compounds by using animal cells is also important to produce metabolites, The cells are obtained surgically from the animal organs, then grows under suitable environmental conditions and used for biotransformation, usually liver cells are required for this purpose due to their ability to metabolize drugs upto a maximum level [5].

Fungi are the most effective microorganisms to be used in the biotransformation process. Various filamentous strains of

different cultures of fungi have been using for various regio-specific and stereo-specific chemical reactions. It is because of the similarity in metabolism process with humans, due to the presence of CYP450 enzyme system. Fungal biotransformations has been used to develop lead molecules with the potential to treat various disorders [6-8].

Drugs from Fungi in Market

Many of the fungal metabolites and biotransformed products have great medicinal importance. Some of the metabolites have been developed as pharmacologically active drugs. For instance antibiotics, including *β-lactam, cyclosporin, fusidic acid*, [9]. Although naturally occurring *penicillin* such as *penicillin G*, produced by *Penicillium chrysogenum* has a relatively narrow spectrum of biological activity, a wide range of other *penicillins* are produced by the chemical modifications of the natural *penicillin*. Modern *penicillins* are semi synthetic in nature, obtained initially from fermentation cultures, but then structurally altered for specific properties. Other drugs produced by fungi may include *griseofulvin*, isolated from *Penicillium griseofulvum*, statins (HMG-CoA reductase inhibitors). mevastatin is obtained from *Penicillium citrinum* while lovastatin from *Aspergillus terreus* and the oyster mushroom [10] (Figure 1).

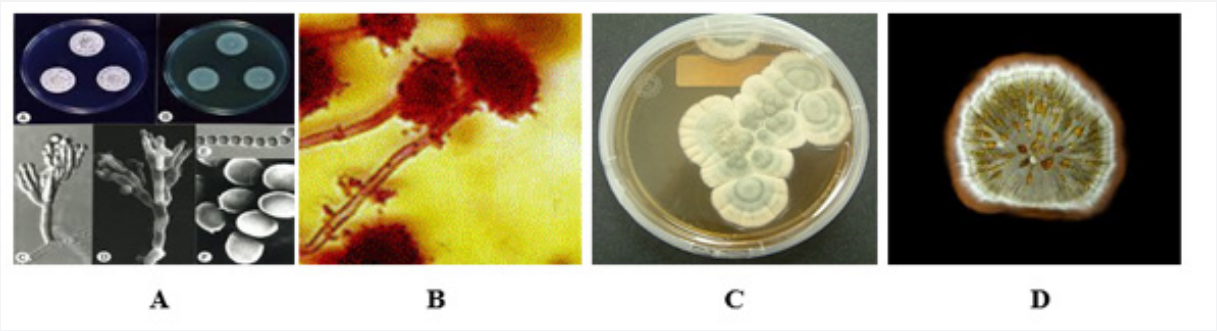

Figure 1: Fungi, mycelium and thallus like bodies: A. *Penicillium griseofulvum*, B. *Penicillium chrysogenum*,C. *Penicillium citrinum*, D. *Aspergillus terreus*.

Many of the fungal metabolites and biotransformed products have great medicinal importance. Some of the metabolites have been developed as pharmacologically active drugs. For instance antibiotics, including *β-lactam, cyclosporin, fusidic acid*, [9]. Although naturally occurring *penicillin* such as *penicillin G*, produced by *Penicillium chrysogenum* has a relatively narrow spectrum of biological activity, a wide range other *penicillins* are produced by the chemical modifications of the natural *penicillin*. Modern *penicillins* are semi synthetic in nature, obtained initially from fermentation cultures, but then structurally altered for specific properties. Other drugs produced by fungi may include *griseofulvin*, isolated from *Penicillium griseofulvum*, statins (HMG-CoA reductase inhibitors). mevastatin is obtained from *Penicillium citrinum* while lovastatin from *Aspergillus terreus* and the oyster mushroom [10].

In nature, antibiotics of fungal or bacterial origin plays a dual role, at high concentration they act as chemical defensive during competition with other microorganisms species-rich environments, such as the rhizosphere, while at low concentration they act as quorum-sensing molecules for intra- or inter-species signaling.

In the recent years, biotransformation has also been efficiently applicable to produce pharmaceutical lead compounds from natural products source. A wide variety of natural products, including aromatics, alkaloids, flavanoids, terpenoids, coumarins and steroids, can be biotransformed by using fungi, yeasts, bacteria, and plant cell cultures into therapeutically potent compounds. The biochemical reactions occurring in microorganisms and plant cells are typically regio-selective and stereo-selective, which are difficult to achieve by chemical methods, therefore, biotransformation has its own unique kind of importance to produce structurally novel and therapeutically potent compounds [11-16].

References

1. Prescott (2002) USGS Department of the Interior. Geological Survey, Science for a Changing World.
2. McGraw-Hill (2003) USGS Department of the Interior. Geological Survey.
3. Editors of the American Heritage Dictionaries (2000) U.S.G.S. Department of the Interior. Geological Survey.
4. Archana Giria VD (2001) Biotransformation using plant cells, organ cultures and enzyme systems: Current trends and future prospect. *Biotechnol Adv* 19: 175-199.
5. Fowler MW, Stafford AM (1992) Plant cell culture, process systems and product synthesis. In: Plant Biotechnology, Comprehensive biotechnology, second supplement, Pergamon Pres. *Oxford*, UK, p. 79-98.
6. Archana Giri, Vikas Dhingra CC, Ajay Singh, Owen P Ward, et al. (2001) Biotransformations using plant cells, organ cultures and enzyme systems: current trends and future prospects, *Biotechnology Advances* 19: 175-199.
7. Manzoni M, Rollini M (2002) Biosynthesis and biotechnological production of statins by filamentous fungi and application of these cholesterol-lowering drugs *Appl Microbiol Biotechnol* 58(5): 555-564.
8. Panke S, WM (2005) Advances in biocatalytic synthesis of pharmaceutical intermediates. *Curr Opin Chem Biol* 9: 188-194.

How to cite this article: Maria Yousuf, Khayala Mammadova. Biotransformation: A One Pot Method of Novel Pharmacological Importance. Nov Appro Drug Des Dev 2019; 4(4): 555645. DOI: 10.19080/NAPDD.2019.04.555645.

9. Huisman GW, GrayD (2002) Towards novel processes for the fine-chemical and pharmaceutical industries. *Curr Opin Biotechnol* 13: 352-358.

10. Straathof AJ, Panke S SA (2002) The production of fine chemicals by biotransformations. *Curr Opin Biotechnol* 13: 548-556.

11. Pan A, Lorenzotti S ZA (2008) Registered and investigational drugs for the treatment of methicillin-resistant Staphylococcus aureus infection. Recent Pat Antiinfect Drug Discov 3(1): 10-33.

12. Maria Yousuf , Saif ullah (2016) Biotransformation of Tolbutamide into 4′ Hydroxytolbutamide by Macrophomina Phaseolina and Plant cell culture, *International Journal of Advanced Research* 4(3): 218-225.

13. Lividans Ltd JH (2004) Future drug discovery, Lead expansion, metabolites and intermediates for future drug discovery. *Technol Serv* 1-2.

14. Liu, Ji Hua, Yu BY, (2010) Biotransformation of Bioactive Natural Products for Pharmaceutical Lead Compounds. *Curr Org Chem* 14(7): 1400-1406.

15. Syed Ghulam Musharraf , Arslan Ali, Naik Tameem Khan, Maria Yousuf, Muhammad Iqbal Choudhary, et al. (2013) Tandem mass spectrometry approach for the investigation of the steroidal metabolism: Structure-fragmentation relationship (SFR) in anabolic steroids and their metabolites by ESI-MS/MS analysis *Steroids* 78: 171-181.

16. Syed Adnan AliShah, Sadia Sultan, Normahanim Binti Hassan, Fauzia Khadija Binti Muhammad, Muhammad Afifi Bin Mohd Faridz, et al. (2013) Biotransformation of 17α-ethynyl substituted steroidal drugs with microbial and plant cell cultures: *A review Steroids* 78 (14): 1312-1324

DOI: 10.19080/NAPDD.2019.04.555645

How to cite this article: Maria Yousuf, Khayala Mammadova. Biotransformation: A One Pot Method of Novel Pharmacological Importance. Nov Appro Drug Des Dev 2019; 4(4): 555645. DOI: 10.19080/NAPDD.2019.04.555645.