

Emerging Trends in Discovery of Novel Bioactive Compounds of Microbial Origin

Iram Liaqat**Microbiology Lab, Department of Zoology, GC University, Pakistan****Corresponding author:** Iram Liaqat, Microbiology Lab, Department of Zoology, GC University, Pakistan

ARTICLE INFO

Received: 📅 April 21, 2021**Published:** 📅 April 29, 2021**Citation:** Iram Liaqat. Emerging Trends in Discovery of Novel Bioactive Compounds of Microbial Origin. Biomed J Sci & Tech Res 35(3)-2021. BJSTR. MS.ID.005701.

ABSTRACT

Advance studies interpret the values of microorganisms in the discovery of bioactive metabolites which eventually act as drugs to treat different infections, immune related diseases, and cancer. Bioactive compounds are actively conducive in the field of medicine and agriculture. Different bioactive metabolites have also been discovered from marine microorganisms which are useful in versatile biological activities acting as antitumor, antimicrobial, and anti-inflammatory agents. So, scientists, ecologists and chemists are increasing their attention to discover the new methods and techniques to extract advance type of bioactive compounds from microorganisms. The review described the main factors which contribute to the discovery of emerging trends for new bioactive metabolites disclosure. These include the assessment of biological activities of compounds (as effector of regulatory factors, lipid metabolism modulators, inhibitor of protein phosphorylation, agrochemicals, and anticancer compounds), discovery of new sources of microbes for active metabolites production, manipulation of genes in biotechnology screening systems and chemical modification. The incorporation of new methods for production of marine microbial metabolites are also given in which products from genomics, metagenomics, screening system, synthetic biology and combinatorial biosynthesis are included.

Introduction

Microorganisms are found in every environment and they have different abilities to interact with different organisms. They are numerous in their abundance so much that even a single spoonful of soil can contain millions of microbes in it. They may be pathogenic and non- pathogenic. The non- pathogenic microorganisms are huge in number and produce a variety of metabolites which are biologically active and have various applications in different fields. These biologically active compounds of microbes are called bioactive microbial metabolites. These metabolites are produced in minute amounts and have antibacterial, anti-microbial activities and other similar activities. The bioactive metabolites of microorganisms are now known to be very useful in the fields of medicine, biochemistry,

and agriculture etc. After the golden age of antibiotic discovery, it was thought that no more antibiotics can be discovered. But the number of antibiotics and bioactive compounds discovery has been increasing until today. The newly discovered antibiotics include monobactam, compactin, thienamycin, avermectin, tunicamycin, bialaphos, staurosporin and FK-506. Similarly, more than 100 bioactive compounds such as avermectin, rokitamycin, nanaomycin, tilmicosin etc., are also discovered in past 19 years. New trends are being developed in the field of finding new antibiotics and bioactive compounds. Some of the current trends are discussed in this review article. The study of these new trends and modern methodology will open new doors in the discovery of new microbial bioactive metabolites [1,2] (Figure 1).

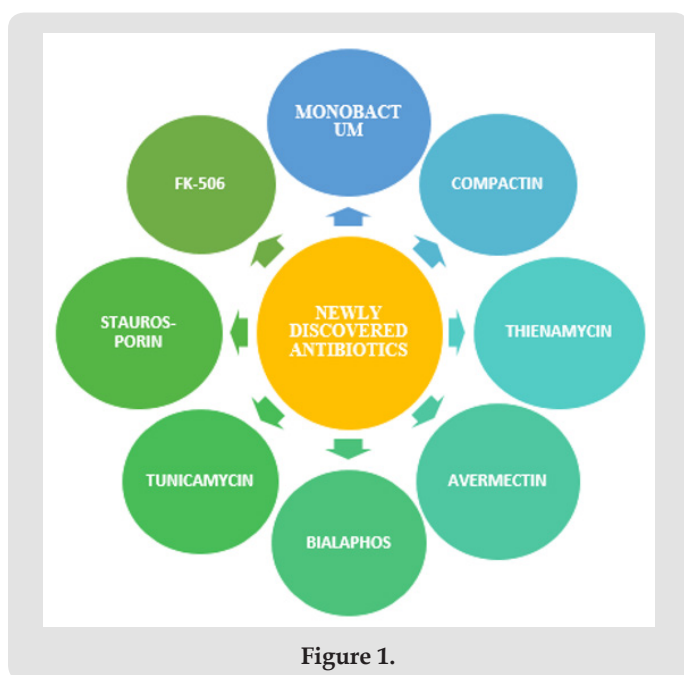


Figure 1.

Current Trends in the Studies of Microbial Bioactive Metabolites

New research in the discovery of bioactive metabolites produced from microorganisms has been continued because of their effective chemotherapeutic and long-lasting activities. There are numerous difficulties in the research methodologies but despite of these difficulties the number of new discoveries in bioactive compounds from microbes is increasing rapidly. The activities of bioactive compounds have been changed greatly in past decades and thus the methods to discover them are also changed. Some of the changes in their activities are given below:

- a) The bioactive compounds of non-antibiotic nature have increased in number.
- b) The antimicrobial agents have changed their target organisms from bacteria to different other microorganisms such as fungi, protozoa etc.
- c) The number of sources of microorganisms which produce bioactive metabolites has increased.
- d) The recombinant DNA technology is playing a vital role in the production of required microbial breeding and screening systems.
- e) There are discoveries in new biological activities of previously known antibiotics and their derivatives.

Evolution of Biological Activities

The most significant change is the increased number of active compounds of non-antibiotic nature. According to a report of a

database for bioactive microbial metabolites, the total number of reported bioactive compounds was 9046 until 1990. Of these 9046 active compounds, actinomycetes products were the sources for 67% of bioactive microbial metabolites. Before 1965 the research targets were antibiotics but after it the research work was shifted from the discovery of antibiotics to bioactive compounds. Until 1990 the percentage of discovered non-antibiotic bioactive compounds was 53%. But in recent 5 years most of the bioactive compounds have been discovered and are being utilized in various fields. These bioactive compounds include immune-modulators, enzyme inhibitors, and effectors of neurotransmission, receptor binding antagonists and many others. Ergot alkaloids were first bioactive microbial metabolites of non-antibiotic nature which were used in the field of clinical medicine. The second oldest type of microbial metabolites was Gibberellin. These Gibberellins also have non-antibiotic nature.

With the passage of time, it is also discovered that the activities of antibiotics are also changed. Such as the previously known target of antibiotics was only bacteria but now it targets other microorganisms also such as viruses, fungi, and protozoa. Antibiotics can also target certain invertebrates such as insects, nematodes and mites etc. Microbial bioactive metabolites show a variety of biological activities and this characteristic of these compounds have open new doors for the discovery of new compounds with new activities and uses. Some already discovered compounds are also under studies to determine their latent activities such as cyclosporin A. Cyclosporin A was discovered as antifungal antibiotic but after detailed studies it was reported as an effective immunosuppressant. And nowadays it has effective applications in transplantation. The latent activities of bioactive compounds and antibiotics can be made potentially more effective by modifying their chemical composition using various techniques.

Mechanism of Action of Bioactive Compounds

Insecticidal Activity: This antiseptic activity of the bioactive compounds was firstly discovered by Hamill from *B. bassiana* against salina, which was considered to be a model creature for study of pest control. Biologically active chemicals may not be used directly as an insecticide instead of insect repellent, for example entomopathogenic fungi can spread to bodies of insects and spread widely through insect movements. The entomo-pathogenic fungi can produce effective pest control even with the use of a small amount of entomopathogenic fungus particles. Careful examination of the production of bio-active compounds should be made sure that they will not rise above the limits.

Anti-Tumor Activity: Cytotoxicity of bioactive chemicals (Beauvericin) in human cells of leukemia has been reported repeatedly. Following figure shows the anti-tumor Beauvericin activities of leukemia cells of human.

Antibacterial Activity: The bio-active compounds have a strong anti-bacterial function against pathogenic bacteria of human, plants and animals, without any difference between Gram negative and Gram-positive bacteria. Some cells of the organelles or enzyme system may be the target of respiratory chemicals. Apart from its extensive anti-bacterial activity, the anti-fungal activity of bioactive compounds as a single agent is reported very rarely. Therefore, target of bioactive chemicals is different from fungi, bacteria and may include targets such as stem cell or ribosome. The activity of bio-active compounds should be investigated by bacteria which are resistant to drugs. Depending on the anti-bacterial activities of plant germs, compounds can be used to control the food borne diseases, to solve drug resistance issues, and to kill bacterial infections.

Antifungal Activity: The shortage of antifungal activities of bioactive compounds as a unit agent occurs because most of them are fungal products. There are some reports of anti-fungal activity of bioactive compounds in association with Miconazole or Ketoconazole. Bioactive chemicals when combined with ketoconazole have a significant antifungal effect against *Candida parapsilosis*, which can quickly cause high rates of mortality, especially in neo-nates. Both bioactive compounds and ketoconazole alone have little effects on *C. Parapsilosis*. If bioactive molecular mechanisms are similar to a cytotoxic mechanism in leukemia cells, this may indicate that fungi itself may block the unknown signal system until some other compound, such as ketoconazole, open the signaling system. This process of combining living organisms to other compounds provides a new option to develop and use the biological function of molecules.

Antiviral Activity: Bioactive compounds also possess antiviral activities. According to a study some bioactive compounds are most

effective inhibitors of cyclic hexadepsipeptides that inhibit enzyme HIV-1 integrase. But enniatin's have a relatively weaker function despite having the same structure, which means that activity of bioactive compounds is due to a major primary difference, N-methylation. Viral infection can lead to deadly diseases and epidemics and anti-viral activity of the biologically active compounds must be studied for effective clinical applications and sensitive viruses such as HBV etc.

Recent Discovery of Bioactive Compounds from Microbial Sources Via Screening Programs

A number of secondary metabolites or bioactive compounds has been isolated from microorganisms and tested to check their effects. Some more common isolated bioactive compounds are discussed below:

Discovery of Compounds Effective for Internal Regulatory Factors

Erythromycin, an antibiotic isolated from *Saccharopolyspora erythraea*, extensively used as chemotherapeutic agent. It protects from several bacterial infections particularly from those caused by mycoplasma species and β -lactamase releasing bacteria. Recent advances have been made in erythromycin function since 1984, one of which is its role in gastrointestinal contractions. Gastrointestinal contractions were observed in dog in an experiment during fasting state. It was observed contractions occurring in dog after every 100 minutes and lasts about 25 minutes, initially occur in gastric body. From there, they move to gastric antrum, then to duodenum and so on till ileum. Motilin is a gastrointestinal peptide hormone comprises of 22 amino acids control these inter digestive migrating contractions. Erythromycin is an agonist of motilin hormone. Structure of motilin is shown below (Figure 2).

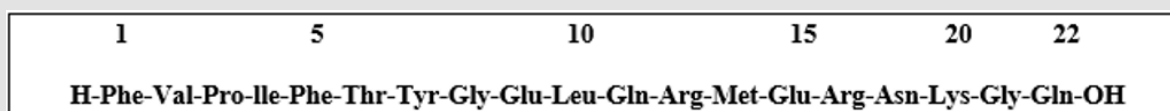


Figure 2.

Motilin Structure: It was found, contractions may induce by giving even 0.1 mg dose of erythromycin similar to natural contractions. About 250 erythromycin derivatives has been synthesized which has potential to induce gastrointestinal interactions and have reduced antimicrobial activity. Another important bioactive compound has been isolated from streptomyces lacta cystinaeus is lacta cystin which has function similar to neurotrophic factors (NFTs). These factors are very important for normal functioning of nervous system. They play roles like nerve cell protein from anoxia, regulate elongation of exons, etc. if NFTs are not available, the body may lead several diseases like Alzheimer's disorder. So an alternate compound lacta cystine with similar function to NFTs was isolated in order to cure neurological

disorders. There are several other compounds have been isolated, but they show some side effects like immunosuppressive effect caused by cyclosporine A. similarly herbimycin inhibit angiogenesis process.

Lipid Metabolism Modulators

Uniform lipid metabolism is important as it maintains balance between degradation and synthesis. Several problems may arise if this balance is not maintained, like it may result in hypercholesteremia which then led to disorders like diabetes, hypertension etc. to control such disorders lipid metabolism modulators play a significant role. Different fatty acid inhibitors have been discovered by screening of modulators. Examples of such inhibitors include, triacsin, 1233A, thiotetromycin etc.

Triacsin is an inhibitor isolated from *Streptomyces aureofaciens*, inhibits the working of acyl CO-A synthetase. This enzyme is important in conversion of long chain fatty acids to acyl CO-A which then convert into acetyl CO-A. In animals, major route to supply Acyl CO-A from long chain fatty acids is through CO-A synthetase. So, the major site where triacsin act to control lipid metabolism is this enzyme. Two kind of acyl CO-A synthetases (I and II) are found in fungus (*Candida sp.*). both have different role and presence as type 1 found in mitochondria and peroxisomes and functions in lipid biosynthesis while type II functions in catabolizing lipids and yielding of acyl CO-A. In contrast to animals, in *Candida sp.* Acyl CO-A may also generate through fatty acid synthase.

A screening method was performed to check the triacsin activity against acyl CO-A synthetase in *Candida sp.* Two mutant strains of *C. lipolytica* were taken. One was defective in acyl CO-A synthetase (strain L-7) and other one was lack in fatty acid synthase (A-1) s. Both strains were grown on two media, carbon source provided by adding fatty acid. After some time, strains were assessed. It was examined that *Streptomyces sp.* showed inhibitory action against A-1 but no action against L-7 strain. This examination showed presence of synthetase inhibitors in cultured broth. Triacsin also work as inhibitors against the formation of Arachidonoyl CO-A in mouse cells.

Other lipid metabolism modulators have also been identified from several microorganisms. For instance, 1233A is an inhibitor against HMG-CO synthase. Similarly, Purpactin inhibits the working of acyl-CoA cholesterol transferase. This enzyme is responsible for cholesterol accumulation and formation which results in several disorders like atherogenesis and hypertension etc. purpactin inhibitor is effect to cure such diseases [3-5].

Inhibitory Compounds Against Protein Phosphorylation

Phosphorylation of protein, carried out by protein kinases and phosphatases, impart a serious effect on normal functioning of organs sometimes. Some processes like cell growth, its motility and differentiation, metabolism and neurological functions may be affected by protein phosphorylation. As protein kinase is responsible for this mainly, so it is the main target for inhibitors, to prevent coagulation, asthma and hypertension etc. Several inhibitors against protein phosphorylation have been isolated from microorganisms like staurosporin inhibitor isolated from *Saccharothrix sp.* by screening methods. Staurosporine provides a number of pharmacological activities as it is a potent, competitive inhibitor against kinase C. however, it shows nonspecific against kinase A and B. it has also been observed that staurosporin works in relaxing rabbit aortic strips (agonists contract them).

Another inhibitor against tyrosine kinase which is also isolated from *Streptomyces sp.* is herbimycin (A, B and C). It has been found that herbimycin A works effectively in conversion of transformed cells caused by kinases to normal state. Erbstatin is another

important product which acts as inhibitor against tyrosine kinase. As protein phosphorylation may also occur due to phosphatases. Two important inhibitors of phosphatases are Okadaic acid and tautomycin. Both are significant in studying protein phosphorylation mechanism and its role in signal transduction, carcinogenesis as well as in drug development.

Bioactive Compounds Against Cancer

In order to control bacterial, fungal and viral infections, discovery of excellent chemotherapeutic agents is still a need. Now a days, cancer is going out of our control due to lack of proper therapeutic agents. However, efforts are continuous for discovery of new compounds against cancer and bacterial therapeutics. Two important compounds which work against biosynthesis of yeast mannan, include pradimicins and benanomycins. Other compounds belonging to anticancer family are Calcheamicins and dinemicins, which are produced from strains of actinomycete. These two compounds possess a diyne moiety which enhances their anticancer activity. another anticancer compound showing immuno- modulating activity is spergalin. However, in addition to above discussed compounds, eight new bioactive compounds against cancer have been isolated. Three of them are discussed below.

Kazusamycin, an anticancer compound had been isolated from *Streptomyces sp.* by fermentation of broth. Two forms of this compound (A and B) were isolated. The characteristic property of this compound is to possess long chain of fatty acids along with gamma-lactone terminal ring. This compound work effectively (showing cytotoxic activity) against leukemia cells when carried invitro. During in vivo, giving broad antitumor spectrum. Another bioactive compound isolated from extracts of mycelia (*Streptomyces Sp.*) was phenanzinomycin. It appeared as dark blue color. The main property of this compound which was observed was its in-vitro cytotoxic activity against the HeLa-S3 cells. in-vivo, it showed anticancer property for S180 tumor. The third bioactive compound isolated from *Streptomyces sp.* broth was furaquinocins (A and B). these two compounds have same molecular formula, but structure is different (isomer of each other). Five units of acetone, two of mevalonate and from methionine (two units) makeup the carbon Skelton of furaquinocins.

Production of Bioactive Compounds by using Novel Sources of Microbes

The major and most significant sources for the production of bioactive compounds are the various strains of *Streptomyces* as well as some Actin-omycelates genera. Actinomycetes also provide a large number of metabolites like *Streptomyces*. Other microorganisms such as bacteria and fungi can also be used significantly for the production of bioactive compounds. The search for the production of metabolites has been sponsored among bacteria by the innovation of monobactams that are manufactured

by different strains of eubacteria. Recent strategies for separation of various microbes involve morphological as well as functional separation of unusual microbial culture of *Streptomyces* while non-*Streptomyces* culture can be exploited as well. Marine microbes can be used as a sample by isolating various microorganisms as well. This strategy is enhancing as it provides novel metabolites along with the structures of metabolites.

Recombinant DNA Technology

Various applications of this approach for the study of bioactive compounds can be categorized in two groups. In the first category, the metabolites are engineered genetically for following purposes.

- a) Hybrid molecules production.
- b) Increased concentrations by using the influences of gene dosage.
- c) Production of beneficial compounds through gene activation as well as deactivation.
- d) Study of metabolic reactions.

The second category includes the genetic manipulation of microbes as well as cells of animals and plants for following purposes:

- a) Manufacturing of biological compounds that are involved in bioactive metabolites screening.
- b) Study of mechanism of action or resistance of metabolites.

Advanced applications of this approach involve the plant's breeding that has the potential to resist herbicide, as well as the engineering of proteins i.e., glycoconjugates. Other compounds that are manufactured from this approach include recombinant vaccines, anti-sense fragments of RNA as well as nor-erythromycin etc.

Production of Marine Microbial Natural Products

There is a significant need of innovative antibiotics to cope with various diseases along with resistant disease-causing microorganisms that have become a major threat for the health of community. In order to discover various diseases plants, animals as well as certain strains of microorganisms have been used. However, due to recent increase in the diseases there is a critical need to produce novel antibiotics. Current strategies involve the use of marine samples to produce innovative bioactive compounds. Some of the most significant and widely used approaches for the discovery or production of bioactive compounds are discussed here:

Production of Bioactive Compounds by Meta-Genomics

Meta-genomics is the widely used and significant approach that enables the researchers to access the genetic material of microbes directly, without cultured them in laboratory through the isolation

of environmental DNA of microbes. By using this approach, various bioactive compounds have been discovered along with their distinctive configurations that include violacein, terragins as well as turbomycins. The shortcomings or disadvantages of this approach involve incompetence of effective achievement of integral portion of gene as well as incompatibility of certain expressive components in their respective host.

Marine Microbial Bioactive Compounds Through Combinatorial Biosynthesis

The production of derivatives through chemical synthesis became very difficult due to the complex structure of natural products. To gain the chemical diversity of these natural products, combinatorial biosynthesis technique is used. In this method the genes of biosynthetic cluster of natural products are manipulated. In this way altered form of structures are formed which cannot be obtained by other methods. So, it plays an important role in drug production programs. The natural products obtained through marine microorganisms have unique compounds as halogenase and novel enzymes.

The combinatorial biosynthesis is also responsible to produce unnatural products by biosynthetic gene's heterologous expression. For example, a compound known as Salinosporamide A is synthesized. Halogenation of adenosyl-l-methionine takes place which produce 5'-fluoro-5'-deoxyadenosine by nucleophilic substitution. By adding this compound to mutant of *S. tropica* and a new altered compound formed known as fluorosalinosporamide. The combinatorial biosynthesis can also generate unnatural derivatives of salinosporamide including antiprotealide by certain modifications in the proteasome inhibitors. There is also a limitation in the use of combinatorial biosynthesis with its importance that the derived compounds have less productivity than parent compounds. And there is no collection of modified compounds which may be improved in coming days.

Different Microbial Bioactive Compounds Through Synthetic Biology

There are large number of very effective technologies have developed which elucidate the structure and activity of many natural products. The diversity in structure can give a pool of drugs but due to their high cost of production, they are not reachable to ordinary people. The discovery of synthetic biology has led to the production of compounds. It can assemble in the host microbes the artificial and natural biosynthetic pathways by gene manipulation techniques like multiplex automated genome engineering and synthetic protein scaffolds. It can give valuable microbial bioactive compounds which we can estimate by its yield of erythromycin precursor, amorphadiene as the precursor of artemisinin and taxadiene which is precursor of taxol. The biosynthesis of natural products is similar in marine and terrestrial microbes but microorganisms of marine such as cyanobacteria, actinomycete

and symbiotic fungi are more important to obtain heterologous expression. One of the most important biological chassis are genome minimized (less essential part of DNA is removed) microorganisms. All these processes including heterologous gene expression of natural products are helpful to elucidate gene clusters and their role. The biosynthetic clusters of griseorhodin encodes the oxidoreductases which are functionally diverse, polyaromatic tridecaketide's oxidative modification is done by them. Another very important compound known as eptidemannamide is a cyclic peptide which is developed by the *E. coli*. There should be focusing on new methods in synthetic biology which will trigger a new era in the development of marine microbial natural products.

Production of Bioactive Compounds by Pathway Engineering

For increased production of biologics, the technology of pathway engineering can also be applied by using the process of gene deletion, repetition of gene expression and by introducing the new genes in the native host. For instance, in *S. coelicolor* the production of actinorhodin can be enhanced 20 times by the overexpression of some tandem replicas of actinorhodin gene clusters. In addition, the production of validomycin A can also be 34% increased by the overexpression of some tandem replicas of Validomycin A gene clusters in the strain of *S. hygroscopicus*. Gene deletion is also useful for the elimination of competing pathways that siphon off the useful precursor metabolites. These competing pathways may also contribute to use of those resources of cells that are required for the improvement of product yields of interest. For improved secretion productivity and capability of natural products, similar technologies or approaches have been applied. The research reveals, by deleting the certain genome that are associated with fission, may also increase hGH secretion i.e., human growth hormones that are protease sensitive.

Production of Bioactive Compounds by Precursor Supply Engineering

Precursor molecule supply is the increase in the accessibility of the metabolites that are necessary or important for the synthesis of biologics. These primary metabolites are obtained from primary metabolism and have an important and effective role in the production of microbial products. By the manipulation of enzymes or metabolic pathways that are involved in the supply of precursor molecule, enhanced supply of precursor molecule can be achieved. For instance, the most widely used biosynthetic precursors for the synthesis of polyketides are methylmalonyl-CoA and Malonyl-CoA and these are available metabolically as well. Study demonstrates that the precursor molecule for the synthesis of FK506 is the methylmalonyl-CoA. The methylmalonyl-CoA concentration can be increased by the supply of methyl oleate that will ultimately lead to an enhanced production of FK506 i.e., 2.5 times more formation in microbial species *S. clavuligerus*.

This technique is majorly utilized to produce biologics of different classes successfully. This technique can be successfully applied in the heterologous host when the native host cannot be modified genetically, or it may be slow growing. For instance, in *E. coli*, the production of yersiniabactin was enhanced up to 175mg/L by introducing the cysteine molecules to the *E. coli* culture. This technology is also applied for enhanced production of natural products that is achieved by reducing by products formation that are not required. In *E. coli*, for example, acetate production i.e., a by-product is the primary hindrance in recombinant protein production. This by-product is formed during the process of aerobic fermentation by the excessive flux of carbon. The accumulation of this by-product i.e., acetate hampers the formation of recombinant protein and the growth of the cell even if it is present in minute concentration. In *E. coli*, to enhance the production of recombinant protein as well as in order to reduce the formation of acetate, various approaches of engineering technology have focused on [6-9].

Conclusion

Advancement in new methodologies for bioactive compound's discovery has proved beneficial in the treatment of various diseases. Screening programs and gene manipulation methods help in isolation of secondary metabolites which play significant roles in pharmaceutical industry. Compounds effective in gastrointestinal contractions, several lipid modulators, inhibitors against protein phosphorylation and a number of anticancer bioactive compounds have been isolated from different microbial sources via screening programs. Overall, the natural compounds that are of microbial origin have an integral and diverse role in the lives of human beings. Thus, the production and discovery of novel bioactive metabolites are of great importance and their production is offering a major challenge to the scientists as well. There are various approaches available to discover innovative natural compounds as well as catalysts that are microbial in origin. The production of bioactive compounds can be improved in the coming years by the development of advanced strategies or trends that may include single cell technology, eDNA direct sequencing, synthetic biology as well as meta-proteomic. With the development and advancement of NGS technologies that are easily accessible, bioinformatics tools and other emerging approaches, the discovery of novel biologics could be facilitated.

Moreover, a very important basis of drug expansion is the natural compound. To produce new biological compounds, a lot of plants, bacteria as well as marine animals have been investigated. But this approach is not sufficient for the discovery of new biologics, specifically marine plants that are endophytes. Due to the mistreatment of antibiotics, many microbial strains have developed the resistance against many drugs. That is why, the production of novel drugs is highly demanding. There is also needed to do

research in the chemistry of natural products as for the treatment of cancerous organs or tissues, chemotherapy has done. It is believed that in the coming decade, novel microbial metabolites can be discovered by coupling both conventional as well as advanced technologies.

Conflict of Interest

Nil.

References

1. Roberto Mazzoli, Katharina Riedel, Enrica Pessione (2017) Editorial: Bioactive Compounds from Microbes. *Frontiers in Microbiology* 8: 1-10.
2. Omura S (1992) Trends in the search for bioactive microbial metabolites. *Journal of Industrial Microbiology* 10(3-4): 135-156.
3. Irma ES, Luis JV (2012) Bioactive Compounds from Bacteria Associated to Marine Algae.
4. Olga NS, Sergey BZ (2019) Novel bioactive natural products from bacteria via bioprospecting, genome mining and metabolic engineering. *Microb Biotechnol* 12(5): 828-844.
5. Rocha-Martin J, Harrington C, Dobson A, OGara F (2014) Emerging Strategies and Integrated Systems Microbiology Technologies for Biodiscovery of Marine Bioactive Compounds. *Marine Drugs* 12(6): 3516-3559.
6. (2017) Bioactive Compound - an overview | ScienceDirect Topics.
7. Shukla R (2015) Studies on Bioactive Compounds from Different Microorganisms. *International Journal of Scientific & Engineering Research* 6(6).
8. Sekurova ON, Schneider O, Zotchev SB (2019) Novel bioactive natural products from bacteria via bioprospecting, genome mining and metabolic engineering. *Microbial Biotechnology* 12(5): 828-844.
9. Iwai Y, Takahashi Y (1992) Selection of Microbial Sources of Bioactive Compounds. *The Search for Bioactive Compounds from Microorganisms*: 281-302.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2021.35.005701

Iram Liaqat. Biomed J Sci & Tech Res



This work is licensed under Creative Commons Attribution 4.0 License

Submission Link: <https://biomedres.us/submit-manuscript.php>



Assets of Publishing with us

- Global archiving of articles
- Immediate, unrestricted online access
- Rigorous Peer Review Process
- Authors Retain Copyrights
- Unique DOI for all articles

<https://biomedres.us/>