Editorial

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Current Trends in Pharmaceutical Microbial Biotechnology for Sustainable Developments

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The biotechnological and microbiological aided pharmaceutical advances illustrate their application for the development and discovery of drugs. This fast growing field of science facilitates the rapid discovery of novel therapeutic drugs. The development of drugs based on bioformulations in the form of DNA vaccines, antibodies and nucleic acid products can be achieved through DNA manipulations and microbiological interventions. Pharmaceutical industries are making collaborations with scientists working on molecular biology and genetic engineering for the production of marketed bioformulations by utilization of biotechnological principles. The designing of more effective protein based drugs using RDT (Recombinant DNA technology) and Bioinformatics pave the novel ways for the drug discovery and development. The modern era of pharmaceuticals is based on the more effective and stable therapeutic proteins. Recent bioinformatics techniques like homology modeling and protein ligand docking facilitates the computer aided drug designing for the development of more effective protein based drugs. The recombinant DNA technology includes extensive microbiological expertise and is more favourable for the production of therapeutic proteins at large scale. The extraction of DNA of interest, application of cloning vector and transformation into suitable host bacterial cell to obtain proteins at large scale and in the pure form are very important aspects of pharmaceutical biotechnology.

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Microbes are the superabundant organism of secondary metabolites which have bought revolution in the pharmaceutical industries since 1950 to date. Over the past 50 years, antimicrobial activity of microbial metabolites were the solely interest and they were used to treat the various diseases caused by the microbes. Penicillin was the first and one of the most effective natural drug discoveries from *Penicillium*. This drug was discovered coincidently in mid-1940s by Fleming and colleagues and it provided the first effective treatments for the major plagues (Davies, 2013). Penicillin has opened floodgates for other natural metabolites since then and numerous microbial metabolites have been reported since for having antimicrobial activity. A secondary metabolite quellenin, which is an anti-saprolegniasis compound, was extracted from the deep sea fungus *Aspergillus* sp. (Takahashi *et al.*, 2018). In a report, the pharmaceutical compounds, 2,4-dihydroxy-2,5-dimethyl-3(2H)-furan-3-one, 5-hydroxymethylfurfural, heptose, triacetin, 2,3-dihydroxypropanal, pentadecane, and tetradecane were reported for having antimicrobial activity. These compounds were reported from endophytic fungi *Pestalotiopsis* sp. of *Cupressus torulosa* and they were having antimicrobial activity against human pathogens including *Bacillus subtilis, Escherichia coli, Staphylococcus aureus*, and *Salmonella typhimurium* (Sharma *et al.*, 2016). Bioactive compounds acropyrone, questinol, hydroxyemodin, citreoisocoumarin, and citreoisocoumarinol was found as important pharmaceutical compounds that have antimicrobial activity against *Aspergillus fumigatus, Bacillus subtilis, Candida albicans, Escherichia coli, Staphylococcus aureus*, and *Salmonella typhi* (Akpotu *et al.*, 2017). Violaceol I and II, the bioactive compounds of *Trichoderma polyalthiae*, was known for having antimicrobial activity against the pathogens of humans *Bacillus subtilis, B. cereus Candida albicans, Staphylococcus saprophyticus, S. aureus, Salmonella typhimurium*, and *Shigella sonnei* (Nuankeaw *et al.*, 2020).

Synthetic microbial biotechnology is an emerging field which merely focused on the engineering of the microbial system to enhance the activity and capabilities for the various applications. This field help in solving many human's problems by generating new potential therapeutics to augment traditional drug delivery method (MacDonald and Deans, 2016). The engineering of microbial cells to strain improvement, different tools are required such as microbial cell, genes, restriction enzymes, markers and vectors. Bacterial species *Escherichia coli* is most widely used organism in this particular field (Pandhal and Noirel, 2014). In a report, the most widely utilized strain of filamentous fungi, *Trichoderma reesei* RUT-C30 was genetically improved for the high cellulolytic production and depression of catabolite (Peterson and Nevalainen, 2012). In another report, manipulation of endogenous microbes of fish was done to improve the production of exogenous digestive enzymes and vitamins ti improve the fish health and its production (Dimitroglou *et al.*, 2011). The strain improvement of *Staphylococcus hominis* has also been done to protect the human skin as tropical therapy to kill the *S. aureus* which causes inflammation on the skin (Nakatsuji *et al.*, 2021).

Microbes are the tiny microscopic units of life that exist in nature and play a biological role in the Earth's microflora on their own. They have symbiotic interactions with the creatures present in their biological vicinity (Webster 2014). At the molecular level, microbial interactions with other organisms occur through the release of several molecules that are classified as bioactive substances (Braga *et al*., 2016). The bioactive compounds have been investigated by scientists and researchers for their use in therapeutics and pharmaceutical industries. Despite the fact that bioactive compounds are known for their therapeutic properties, it is important to create effective delivery techniques that allow bioactive molecules to reach the specified organ and perform their therapeutic function in the human body (Braga *et al*., 2016).

Medical drugs are essential requirement for all human being in their daily life. Chemically man-made drugs dominate our health care system due to low production costs and rapid commercialization. Secondary metabolites are organic substance that are largely involve in the healthcare activities as antimicrobial agents, antiparasitic agents, antitumor, enzyme inhibitors, and immunosuppressive (Demain, 1999). The basic component of secondary metabolites are alkaloids, phenolic acids, quinones, steroids, saponins, terpenoids, and tannins (Gupta *et al*., 2014). They are mostly employed in the biopharmaceutical business because of their ability to prevent infectious diseases in humans and animals, hence increasing life expectancy. Several marine bacteria and fungi have been recognized to produce secondary metabolites and bioactive compounds that have shown a therapeutic role (Debbab *et al.*, 2010). In this study, Romero *et al.*, (1997) reported *Micromonospora marina* isolated from marine corals that exhibited anticancerous properties. This strain produce thiocoraline as a metabolite that was showed anticancerous properties. In another study Sudharshana *et al.*, (2019) reported the endophytic fungus *Aspergillus flavus, Fusarium verticillioides* isolated from *Catharanthus roseus* leaves. These strains produce bioactive compound aflatoxin B1 (AFB1), fumonisin B1 (FB1) and have anti-microbial and anti-mycotoxigenic activities. Similarly, Niu *et al.*, (2019) reported the fungus of *Botryotinia fuckeliana* from sea water and produce diterpenoid, have antiallergic activity. The blue-green microalgae *Oscillatoria* sp. isolated from the marine water sample that produce Benzenemethanol which is a bioactive compound and have antibacterial activity (Bhuyar *et al.*, 2020). In another investigation, the bioactive compound like behenic acid, erucamide, palmitic acid, β-sitosterol, and phenylacetic acid were extracted from *Bacillus megaterium*. The palmitic acid has antibacterial activity against *Ralstonia solanacearum*, whereas behenic acid have antibacterial activity aginst *Agrobacterium tumefaciens*, and *Ralstonia solanacearum*,and β-sitosterol showed significant antimicrobial activity against *Ralstonia solanacearum*. In additional, phenylacetic acid has shown antimicrobial activity agianst *Agrobacterium tumefaciens, Erwinia carotovora,* and *Ralstonia solanacearum* (Xie *et al*., 2021).

Extremophiles are organisms that prefer to live in harsh environments. They often have unique survival mechanisms to cope with extremes in temperature, pH, salinity, pressure and aridity (Kohli *et al.,* 2020). Microbial communities i.e., archaic, bacterial and fungal under extremely adverse conditions have recently focused on applications in a variety of fields, including white and green biotechnology, medicine, food production and food processing industry (Yadav *et al.,* 2019). The biopharmaceutical industry has entered a new era, that of extremophilic microbial natural products. In the pharmaceutical industry, bacteria are used to make many antibiotics such as streptomycin from *Streptococcus*. Bacteria are also used for medically necessary investigations, such as bacteriorhodopsin, synthesis of chemicals drugs, chemical compounds and other compounds is the another important role in pharmaceutical industry. Currently, more than 120 microbial generated drugs are being used in clinical trials to suppress the immune response to infectious diseases, cancer and organ transplantation. Antibiotics such as penicillin, cephalosporin, streptomycin, and vancomycin, cancer treatments such as actinomycin and mitomycin, and immunosuppressant therapy such as cyclosporine are all examples of these widely used drugs. Today, pharmaceutical industries around the world (but especially in the United States and Japan) continue to rely on

extremophilic microbes as the most useful source for natural product medicines. Riboflavin and vitamin K are prepared through commercially using *Escherichia coli* bacteria. *E. coli* is also used to make D-amino acids like D-p-hydroxyphenyl-glycine, an important step in the production of the antibiotic amoxicillin.

Various studies have been conducted for extremophilic microbes that produce secondary metabolites and are used to make various antibiotics, in which *Emericellopsis alkalina* isolated from saline soils that have been produce lipopeptaibol emericellipsin A, which demonstrates promising antifungal activity against the yeast *Candida albicans* and *Aspergillus niger* (Rogozhin *et al.,* 2018). In another reports, *E. microspora* produced zervamicins (Ovchinnikova *et al.,* 2007), bergofungins A and B produced by *E. donezkii*, bergofungins C and D produced by *E. salmosynnemata* (Gessmann *et al.,* 2017; Berg *et al.,* 1996; Berg *et al.,* 1999), and heptaibin and emerimicines produced by *E. minima* (Ishiyama *et al.,* 2000). In another study, three thermoacidophilic Archaea *Thermoplasma acidophilum*, *Picrophilus torridus* and *P. oshimae* produced bioactive compound of glucoamylase (Serour and Antranikian 2002). Similarly, A new antibiotic, aristeromycin, produced by *Streptomyces citricolor* nov. sp., was isolated from the culture filtrate of a new streptomyces, aristeromycin was found to be effective against *Xanthomonas oryzae* and *Piricularia oryzae* (Kusaka *et al.,* 1968). *Streptomyces scopuliridis* isolated from deep-sea and produced desotamide B have antimicrobial activity against *Streptococcus aureus* and *S. pneumoniae* (Song *et al.,* 2014). In another study, reported *Aspergillus sydowii* isolated from deep-sea and produced asperentin (Wiese *et al.,* 2017). *Graphostroma* sp. isolated from deep-sea and produced guaianes compound, have anti-inflammatory activity (Niu *et al.,* 2018). Two new antibiotics abyssomicin and six known abyssomicin and proximicin these were extracted from marine bacterium isolated from sea sediments and identified as *Verrucosispora* sp. The new compound abyssomicin have antiviral activity against the influenza A virus (Zhang *et al.,* 2020).

Genetic engineering is an advanced technology that produces new pharmaceutical products including antibiotics, monoclonal antibodies, drugs, vaccines, hormones and recombinant proteins, which is used in the treatment of various diseases. It has provided a new way to create new products called recombinant DNA technology (Adrio and Demain 2010). Recombinant DNA (rDNA) technology (genetic, protein, and metabolic engineering) permits the manufacturing of a huge variety of peptides, proteins and biochemicals from naturally nonproducing cells. This era, now about 25 years old, is turning into one of the most important technologies evolved in the 20th century. Pharmaceutical products and commercial enzymes were the first biotech products in the world marketplace made via rDNA. Despite essential advances regarding rDNA applications in mammalian cells and yeasts, still represent attractive hosts for the manufacturing of heterologous proteins (Stryjewska *et al.,* 2013).

Omics approaches has given a wide range of research possibilities in the field of metabolic pathways disruption, gene and genome based studies along with proteomics enabled investigations. Genomics and proteomics study directly interpret and detect the level of various pathogenic micro-organisms present in a host. Technologies like Recombinant DNA and hybridoma explain better about biological functions and genetics that ultimately illuminate the causes of disease, changes in the drug responses along with discovery of novel pharmaceutical drugs. The biotechnology based techniques facilitates the cost effective drug development, improved medicinal agents and diagnostic kits. Moreover, genomics based therapeutic products are produced with more potential that is utilized in the clinical trials too (Sindelar, 2016). Genomics related investigations have impacted a lot on recent drug discovery projects. Nowadays the identification and validation of viable drug targets becomes more challenging which is analyzed more through genomics study (Yang *et al*., 2012). Furthermore, genomics technologies are more applicable in the treatment, detection, diagnosis of neglected and poorly treated diseases. Proteomics allow understanding new era of biomarker discovery and chemical proteomics by understanding the biological pathways.

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