Chapter

The Need to Use Microorganisms and Their Biosynthesized Bioactive Metabolites for Biological and Medical Activities

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Abstract

Some microorganisms (MOs) such as bacteria, fungi and aquatic creatures synthesize bioactive secondary metabolites synthesis that known as natural products. A series of landmark metabolomics studies by using mass spectrometry (MS) or nuclear magnetic resonance (NMR) analysis to identify potentially important microbial metabolites that derive from the intestine microbes. Vital roles for numerous microbial metabolic pathways in host physiology had been long established, such as in the synthesis of vitamin K and the synthesis of water-soluble B vitamins including biotin, folates, nicotinic acid, pyridoxine, riboflavin, cobalamin and panthotenic acid, the degradation of nutritional oxalates, and amendment of bile salts. These metabolites have biological and medical activities. The medical activities including antimicrobial, immunosuppressive, anticancer, and anti-inflammatory, antibiotic, antitumor, antioxidant activities, etc. Also biological activities derive from metabolites microbial transformation have effects on physiological processes such as gut and immune homeostasis, energy metabolism, vascular function, and neurological behavior such as short-chain fatty acids, trimethylamine N-oxide, tryptophan and tyrosine derivatives, and oxidized fatty acids. Using recombinant DNA technology synthesize a wide array of biopharmaceutical products, such as recombinant proteins, offering significant advances in treating a broad spectrum of medical. Such interventions will require modulating either bacterial species or the bacterial biosynthetic enzymes required to synthesis these metabolites.

Keywords: microorganism, metabolism, biosynthesis, metabolite, biological activities

1. Introduction

The biosynthesis process is multi-step for formation of organic compounds in a living microorganism by chemical energy (e.g. ATP). In biosynthesis, simple compounds or substrates by enzyme-catalyzed are modified, converted into other compounds, or joined together to form macromolecules [1]. Some important biological macromolecules include: proteins, which are composed of amino acid monomers joined via peptide bonds, and DNA molecules, which are composed of nucleotides joined via phosphodiester bonds [1].

Biosynthesis occurs due to a series of chemical reactions in which precursor compounds, catalytic enzymes, cofactors, and chemical energy are necessary for these reactions to take place. The biosynthetic processes responsible for the production can mentioned photosynthesis, lipogenesis, glycolysis, glyconeogenesis and Krebs cycle [2].

These biological processes result in the biosynthesis of intermediates which proceed towards manufacturing of secondary metabolites via alternate biosynthetic routes responsible for metabolite diversity in living organisms [3].

Metabolism is one of the biggest factors of inter-kingdom interactions along with the ones between microorganisms and their multicellular hosts. Ordinarily notion to fuel energy necessities and provide constructing blocks for biosynthetic pathways, metabolism is now liked for its position in imparting metabolites, small-molecule intermediates generated from metabolic techniques, to perform various regulatory features to mediate symbiotic relationships between microbes and their hosts [4].

Metabolite is divided into two main categories in living organisms: Primary and Secondary metabolite. Primary metabolites include biological molecules i.e., vitamins, amino acids, nucleosides, Organic acids, Acetone-butanol, Ethanol, Vitamins, fats, carbohydrates and proteins, essential for the survival and well-being of the organism and are produced to sustain cell growth. Secondary metabolites are compounds with varied and sophisticated chemical structures, produced by microorganisms after the rapid growth phase. These compounds are not essential for growth [5].

2. Microorganism metabolites

Microorganism such as bacteria and fungi are inhabitants of diverse habitats worldwide. Due to which, they have evolved to cope with adverse conditions [6]. The structurally diverse secondary metabolites produced by them possess biological activities such as antibiotic, antimicrobial, immunosuppressive, anticancer, and anti-inflammatory activities, many of which have been developed as treatments and have potential therapeutic applications for human diseases [6]. The produce secondary metabolites, also known as natural products. Aside from natural products, the recent development of recombinant DNA technology has sparked the development of a wide array of biopharmaceutical products, such as recombinant proteins, offering significant advances in treating a broad spectrum of medical illnesses and conditions [6, 7].

2.1 Characteristics of secondary metabolites

Secondary metabolites (SMs) are organic compounds with complex chemical structures and diverse physiological functions. Secondary metabolites include antibiotics, pigments, and other bioactive compounds (Bioactive word means Biologically Active). Many of these compounds have important agricultural and medical applications [8, 9].

Microorganisms are noted as a rich source of bioactive secondary metabolites and bioactive metabolites. Some of these bioactive metabolites, such as antibiotics, siderophores, immunosuppressants and degradative enzymes are also useful in medicine and biotechnology. These play a role in defense mechanisms against predators [8].

Many microorganisms synthesize secondary metabolite molecules that play essential ecological roles of their complex and heterogeneous microenvironments.

Commonly, the genes governing the biosynthesis of secondary metabolites are clustered collectively, and increasingly gene clusters accountable for the biosynthesis of secondary metabolites were located [10].

The provision of clusters has improved purposeful investigations of biosynthetic pathways of secondary metabolites. An intensive understanding of the enzymatic method is required for metabolic engineering to enhance manufacturing of secondary metabolites and for combinatorial biosynthesis to generate novel compounds or derivatives. Secondary metabolites are usually produced at some point of the desk bound section of growth in microorganisms [11].

2.1.1 Secondary metabolites have the subsequent traits

1) Secondary metabolites (SMs) may be produced only with the aid of a few microorganisms. 2) They will be inclined to be produced at the terminal of exponential growth or within the direction of substrate-restricted situations. 3) They're created from common metabolic intermediates but use specialized pathways encoded via a specific gene. Those products are not nessarary for the organism's very own growth, duplicate, and regular metabolism. 4) Secondary metabolites have uncommon chemical linkages, for instance, β-lactam rings, cyclic peptides, unsaturated linkage of polyacetylenes and polyenes, big macrolide rings, and so forth. 5) Increase situations, particularly the composition of the medium inside a fermentation machine, control the formation of secondary metabolites. 6) Those compositions are produced as a collection of carefully associated systems. 7) Secondary metabolic compositions can be overproduced [5].

2.2 Why secondary metabolites are produced by the organisms?

Secondary metabolites seem to act the organisms that produce them as (1) competitive tools used in opposition to different microorganisms, flora, bugs, and large animals; (2) sexual hormones; (3) agents of plant–microbe symbiosis and plant increase stimulation; (4) metallic transporting dealers; and (5) differentiation effectors [12]. Secondary metabolites have a first-rate impact at the fitness, nutrients, and economics of communities. Antibiotics are the most essential of the secondary metabolites. The alarming rise in emergence and occurrence of antibiotic resistance poses a primary danger to human healthcare. It is clean that novel antibiotics are urgently had to combat this trouble [12, 13].

Different secondary metabolites are insecticides, pesticides, pigments, xenobiotics, effectors of ecological competition and symbiosis, pheromones, enzyme inhibitors, immunomodulating factors, receptor antagonists and agonists, insecticides, antitumor agents, immunosuppressives, cholesterol-lowering factors, plant protectants, and growth promotants of animals and herbals. As a stop result, they have wonderful monetary significance [13].

3. Use tools to identify significance microbial metabolites

Intense interest in the intestine microbes over the past decade has led to understanding of diet–microbiota–host interactions suggests significant opportunities to create new therapeutic approaches, including selectively altering the microbial production of molecules to promote human health and prevent disease [14].

A sequence of landmark metabolomics research over the past decade have appreciably superior our know-how via the usage of mass spectrometry (MS) or nuclear magnetic resonance (NMR) evaluation to select out in all likelihood crucial

microbial metabolites that derive from the gut microbes, which might be enriched or depleted in diseased humans, or that can be used to are expecting physiological response to meals or different interventions [13].

Researchers have established a number of metabolites which can play essential roles in human fitness and ailment, together with short-chain fatty acids (SCFAs) and long-chain fatty acid metabolites which inclusives conjugated linoleic acid and 10-hydroxy-cis-12-octadecenoate, trimethylamine and trimethylamine N-oxide, tyrosine and phenylalanine metabolites collectively with hippuric acid, phenylacetylglycine, phenyl sulfate, paracresyl sulfate, phenylpropionylglycine, cinnamoylglycine and equol sulfate and tryptophan metabolites together with indole, indole-three- propionate and indoxyl-sulfate [13, 15].

A number of the metabolites diagnosed by manner of these research result from the transformation of unique nutritional components via pick out species of microbes that express the important enzymes to behave on these additives. For that reason, the variable presence of microbes using those eating regimen-established metabolic pathways can be key to knowledge the variable host reaction to particular nutritional components and susceptibility to illnessess [13].

lots work stays to completely symbolize the physiological results of those and the many other microbial metabolites that can be essential in human health [16].

Accordingly, it appears there may be a vast want for cautiously controlled research to decide the physiological outcomes of each recognized microbial metabolite and its particular mechanisms of action [16]. Moreover, so that you can fully take advantage of the capacity of the gut microbiota for disease prevention, we need a much more expertise of ways dietary additives and host genetics affect the manufacturing of numerous metabolites. The gut microbiota for human health, the remarkable progress of the last decade suggests that such approaches have significant potential to revolutionize therapeutic approaches to human disease [17].

4. Biosynthesis of vitamins by probiotic bacteria

The connection among vertabrates and the microbial cells that reside of their gastrointestinal tracts relies on a complicated molecular, with microbial metabolites acting as essential mediators of this a complex molecular. Important roles for numerous microbial metabolic pathways in host body structure were lengthy mounted, along side in the production of a few vitamins, the degradation of dietary oxalates, and change of bile salts [13].

Vitamins are crucial micronutrients which may be frequently precursors to enzymes, which all living cells require to carry out biochemical reactions. Since human body cannot synthesize many vitamins, simply so they want to be externally received [18]. The use of vitamins-generating microorganisms can be a natural and marketable approach to the usage of pseudo-vitamins which may be chemically produced, and could permit for the producing of foodstuffs with better levels of vitamins that could lessen unwanted facet outcomes. Probiotic bacteria, further to commensal microorganism observed inside the human intestine, consisting of Lactobacillus and Bifidobacterium, can de novo synthesize and supply nutrients to human body [18].

Within the human body, groups of the intestine microbiota are capable of synthesize vitamin K and the production of water-soluble B vitamins including cobalamin (vitamin B12), folate (vitamin B9), pyridoxine (vitamin B6), riboflavin (vitamin B2), and thiamine (vitamin B1). All of these vitamins are essential for the body and serve as a co-factor for the specific enzymes [19].

5. Using of microorganisms as valuable resource for healthy food

Microorganisms are taken into consideration a treasured resource for novel wholesome food ingredients and biologically lively compounds. Microorganisms have increasingly been used to synthesis value-added products with numerous functions inside the agricultural, foods and pharmaceutical industries [20].

These value-added compounds can also embody enzymes, prebiotics, fatty acid, antioxidants, proteins, polysaccharides, organic acids, and biofuels. For this reason, microbial biosynthesis offers a renewable, environmentally benign route, sustainable feedstocks and economically appealing alternatives [1].

Furthermore, the recent advancement in analytical measurement, such as chromatography, with a particular reference to ultrahigh-performance liquid chromatography (UHPLC) coupled with mass spectrometry (MS), allowed the simultaneous analysis of various compounds, with rapid and accurate results [21]. Functional foods and natural-health products comprise quite a wide range of food ingredients, with various bioactive compounds responsible for their activity in disease prevention and/or health promotion [22].

Prebiotics serve via various mechanisms, which includes producing vitamins, interacting with host immune structures, stopping pathogen adhesion to host cells, and affecting the morphological shape of the intestine, all of which likely act via the modulation of intestinal microbiota. A broad sort of dietary compounds may satisfy those criteria. so far, the maximum promising dietary fibers with promising prebiotic capabilities are nondigestible oligosaccharides containing 3–9 sugar monomers [15].

5.1 Fructooligosaccharides

Dietary carbohydrates especially Fructooligosaccharides are notably emerging as an important prebiotic due to their hypocaloric, bifidogenic, and noncariogenic functions. The possible health benefits associated with the consumption of Fructooligosaccharides has led to their increased acceptance as food ingredients and alternative sweeteners used in diabetic formulations [15].

5.2 Omega-3 PUFAs

There are numerous benefits of long-chain omega-3 PUFAs, particularly eicosapentaenoic acid (EPA, C20:5) and docosahexaenoic acid (DHA, C22:6), for human health. PUFAs, which are involved in many vital biological activities, such as inflammatory, immune, and cancer processes. In fact, PUFAs form a unique class of food constituents with numerous functions; they are considered food and nutritional products with specific health-promoting activities, modulating the risk of certain diseases [15].

PUFAs are fatty acids (FAs) are found in particular in fish, vegetable oils, inclusive of sunflower, flaxseed, soybean, rapeseed, and marine belongings. In latest many years, there has been interest within the utilization of microorganisms as ability promising producers of determined on PUFAs. But, the growth in PUFA call for and the decline in fish shares have stepped forward the attention paid to microorganisms, for the reason that microorganisms can be cultivated underneath managed conditions with immoderate growth rates and that additionally they do not compete for land for unique meals manufacturing. The principle microbial resources of PUFAs are marine algae, fungi, and microorganism [15, 23].

6. Microbial sources in recombinant drug discovery

An expansion of organisms, like bacteria, fungi, and plant produce secondary metabolites, called natural products. Natural merchandise are prolific sources and a revelation for numerous clinical factors with extensively divergent chemical structures and natural factors functions, at the side of antimicrobial, immunosuppressive, anticancer and anti-inflammatory features, many of that have been developed as remedies and feature functionality recuperation programs for human sicknesses [6, 12].

These structurally and chemically diverse molecules act as a remarkable class of therapeutics to heal various ailments. Aside from natural products, the recent development of recombinant DNA technology has sparked the development of a wide array of biopharmaceutical products, such as recombinant proteins, offering significant advances in treating a broad spectrum of medical illnesses and conditions [24].

6.1 Natural product from fungal sources

Fungi were used for a long time by humankind for plenty functions, inclusive of food manufacturing (beer, wine, leavened bread, soy substances and so on), remedies, and in regular existence. Loads of years ago, fungi were used to deal with intestinal illness. Since the producing of penicillin, which turn out to be isolated from the fungus Penicillium notatum, fungi had been a rich source of many recuperation factors. Fungi are a highrich supply of biologically energetic secondary metabolites [25].

Many healing factors, which includes cyclosporine and mycophenolic acid (immunosuppressive interest), fusidic acid and griseofulvin (antimicrobial interest), and exclusive novel semisynthetic antifungal pharmacy, in conjunction with anidulafungin and caspafungin, have been originated from fungal metabolites [6].

One of the most vital mediciene are statins, invlusive mevastatin from Penicillium citrinum and lovastatin from Aspergillus terreus. Statins as the most important member of antilipidemic medicienes for the remedy of cardiovascular ailments, also are derived from microbial resources. Fungal metabolites are not only crucial for treatment but additionally for plant safety. For example, the producing of strobilurins from Strobilurus species, precipitated compounds for artificial fungicides, which includes trifloxystrobin [25].

6.2 Natural product from bacteria sources

Almost three-quarters of microbial-produced bioactive compositons are from actinomycete bacteria. Extra than 500 species of streptomycetes that are the most extensively identified organization, generating extensive range of biologically energetic compositions. They will be gram-positive aerobic filamentous (regularly soil) bacteria. They often produce spores and are characterized by manner of the producing of geosmin, a risky metabolite that provide them “earthy” scent. The spore germination technique relies upon at the environmental conditions [25]. In everyday conditions, the germination of streptomycete spores starts off evolved by arthrospore (substrate mycelium), however inside the case of nutrient depletion, the increase starts with aerial mycelium. In one-of-a-kind phrases, underneath favorable conditions, a fully matured mycelia is produced. Beneath drastic conditions, alternatively, the aerial mycelium is subdivided with the resource of septa, then into spores, which in turn can, underneath sure conditions, germinate into mycelium [25–27].

Actinomycetes are recounted to provide diverse sorts of antibiotics, in particular, peptides/glycopeptides, angucyclinone, tetracyclines, phenazines, macrolides, anthraquinones, polyenes, anthracyclines, β-lactams, piercidins, octaketides, benzoxazolophenanthridines, heptadecaglycosides, and lactones [6].

6.2.1 Bioactive activities of natural products of bacterial sources

The secondary metabolites produce in actinomycetes is greatly affected by various fermentation parameters, such as nutrients availability, pH, aeration, temperature, mineral salts, heavy metals, precursors, inducers, and inhibitors, which often vary from organism to organism [28]. Streptomycetes are a rich source of many bioactive compounds. Most antifungals derived from streptomycetes tend to be macrolide polyene, such as nystatin, produced by streptomyces. About two-thirds of bioactive compounds are produced by this group, and they have many clinical efficacies against different kinds of organisms, such as bacteria, fungi, and parasites [29].

Further, antitumor features, such as aclacinomycin A, actinomycin D, bleomycin, daunorubicin, mithramycin, mitomycin C, and nogalamycin (synthesized with the aid of Streptomyces glalilaeus, Streptomyces antibioticus, Streptoverticillium verticillium, Streptomyces paecetius, Streptomyces argillaceus, Streptomyces lavendulae, and Streptomyces nogalater, respectively). These medications can act on DNA by using altering its function via mechanisms, including intercalation, cross-linking, DNA strand fracture, or interacting with DNA non-intercalatively [29].

7. Microbial metabolites for medical and anticancer activities

The search for novel microbial metabolites has shown Mevinolin, a potent cholesterol-lowering agent was isolated from Aspergillus terreus. Aspercilin was isolated from Aspergillus alliaceus. Later on, benzodiazepines were derived from aspercilin and used for curing anxiety or insomnia [30].

7.1 Fungal metabolites

Norsolorinic acid, isolated from Aspergillus spp. was reported to cause apoptosis in breast cancer (MCF-7) and human bladder cancer (T-24) cells [30, 31].

Extracts of Penicillium steckii and Aspergillus sydowii induced cytotoxicity in human cervical carcinoma cell line (HeLa). Whereas, extract of *Alternaria alternata* showed cytotoxic activity against *Staphylococcus aureus*, *Escherichia coli* and HeLa cells.

Similarly, ethanolic extracts of Fomitopsis pinicola induce cytotoxicity in various cancer cell lines including human hepatoma, colorectal, lung and breast cancer cells along with synergistic effects with cisplatin in vivo [6, 29].

Aspergillus parasiticus, a type of fungal endophytic, isolated from *Sequoia sempervirens* was reported to be a producer of sequoiatones A and B which showed moderate anticancer potential with the highest activity against breast cancer cell lines.

Torreyanic acid, isolated from endophytic fungi of *Torreya taxifolia* tree exhibited apoptotic activity in protein kinase C sensitive cancer cells [9]. Endophytic fungi, Taxomyces andreanae and Nodulisporium sylyiforme have been reported to produce taxol (an anticancer drug previously isolated from the pacific yew tree) [9].

Along with anticancer potential, this drug also exhibited antifungal activity against Pythium, Phytophthora and Aphanomyces spp. A novel polykedite,

5-hydroxyramulosin isolated from an endophytic fungus of Cinnamomum mollissimum showed both antifungal activities against Aspergillus niger and anticancer activity against murine leukemia cells [9].

7.2 Bacterial metabolites

Two bacterial strains, *Escherichia coli* and Bacillus subtilis are genetically more variable from each other than humans are from corns [9].

Nisin, a bacteriocin has been used as bio-preservative. Rapamycin, an antifungal agent was isolated from soil inhabiting Actinomycetes. It is also used for inhibiting organ rejection in transplant patients. Amrubicin hydrochloride, an anticancer compound was isolated from Streptomyces peucetius in 2002. A new class of antibiotics called Pumalicidins A, B, C, D, E, F and G were obtained from the culture broth of *Bacillus pumilus* [9, 31].

Homologs of Bacillomycin D, isolated from Bacillus subtillis (B38) were reported to have anti-oxidative and DNA protective activities. Additionally, Surfactin, produced by Bacillus subtilis CYS191, was reported to induce apoptosis in human breast cancer cells (MCF-7) by causing oxidative stress [9, 31]. Streptomyces hygroscopicus was identified as a producer of antifungal prenylated indole, galbonolides A and B, elaiophylin and its derivatives and herbimycins. Pterocidin, produced by endophytic Streptomyces hygroscopicus showed cytotoxic effects in human lung, ovarian, glioblastoma and melanoma cells [9].

There was an analogue of signal peptide 27 that produced by using *Streptococcus pneumoniae* has proven cytotoxicity in opposition to leukemia, gastric and breast cancer via cell permeabilization and induction of caspase-unbiased apoptosis [9]. Also any other anticancer peptide Entap (Enterococcal anti-proliferative peptide) remoted from Enterococcus spp. make induction of autophagous apoptosis and inhibits proliferation in numerous cancers [9].

8. Biosynthesis of nanoparticles by microorganisms

The improvement of eco-friendly technology in substances synthesis is of sizable significance to amplify their natural activities. In recent times, a selection of inorganic nanoparticles (NP) with properly-defined chemical shape, duration, and compunds had been synthesized by using of special microorganisms, and their capabilities in lots of cutting-edge methodological areas had been analyzed [32]. Elements that constitutive nanoparticles having one or greater dimensions of the order of 100 nm or a good deal less have attracted extremely good attention due to their uncommon and fascinating features, and applications tremendous over their bulk contrary numbers [32].

There are huge types of bodily, chemical, natural, and hybrid techniques available to synthesize awesome kinds of nanoparticles. Despite the fact that bodily and chemical techniques are extra famous inside the synthesis of nanoparticles, use of poisonous chemicals greatly limits their biomedical functions, especially in scientific fields [32].

Consequently, improvement of reliable, non-toxic and eco-friendly techniques for synthesis of nanoparticles is of utmost significance to expand their biomedical applications. One of the options to gather this motive is to use microorganisms to produce nanoparticles. These elements synthesized with the aid of manner of a biogenic enzymatic system are a long way superior, in several techniques, to those elements synthesized via chemical techniques [33].

Nanoparticles are produced whilst the microorganisms take target ions from their surroundings after which flip the metal ions into the detail metal via enzymes generated thru the cellular functions. It is able to be categorized into intracellular and extracellular synthesis in step with the area where nanoparticles are organized [33].

The intracellular system inclusives transporting ions into the microbial cellular to shape nanoparticles internal using enzymes. The extracellular synthesis of nanoparticles includes taking the metallic ions at the surface of the cells and reduction of ions the use of enzymes [32, 33].

8.1 Types of NPs

NPs are formed in two synthesized: metal and oxide by organisms. Metal nanoparticles such as gold (Au), silver (Ag), platinum (Pt), mercury (Cu), cadmium (Cd), selenium (Se), mercury (Hg) and chromium (Cr) are synthesized by microorganisms. Metal nanoparticles are usually spherical, flat and cube shapes, Pyramidal and Irregular polygonal. Their size of diameters range from 2 to 180 nm. The most important nanopatiticles are gold and silver. Gold nanoparticles are made by *Sargassum wightii* and Rhodococcus sp., Shewanella oneidensis, Plectonemaboryanum, *Plectonema boryanum* andYarrowia lipolytica, silver nanoparticles by Trichodermaide vir, Phaenerochate, chrysosporium and Bacillus lichformeniis [32–34].

The most important oxide nanoparticles include TiO_2, $BaTiO_3$, Sb_2O_3, $BaTiO_3$, ZrO_2, Fe_3O_4 and Fe_2O_3. Their size of diameters nanoparticles range from 3 to 80 nm. The size of these nanoparticles ranges from 3 to 80 nm and forms Rectangular, rhombic, hexagonal, Cubo-octahedral, Nanopowders, Wormhole-like, Bullet-shaped, Tetragonal, Spherical and Pseudohexagonal/irregular or rhombohedral is synthesized. These are by some bacterial and fungal microarchanis like Shewanella oneidensis, Lactobacillus sp.oxysporum, oxysporum, *Saccharomyces cerevisiae* and yeast cells are synthesized [32–34].

8.2 Utility of nanoparticles

Treatment using nanoparticles (nanomedicine) is a attractive and growing discipline to study with super potentialities possibilities for the improvement of the analysis and treatment of human illnesses. Dispersed nanoparticles are usually employed in nanobiomedicine as fluorescent natural, drug and gene delivery entrepreneurs, and in programs which include biodetection of pathogens, tissue engineering, tumor destruction through heating (hyperthermia), MRI comparison enhancement, and phagokinetic research [33].

The biosynthesized nanoparticles have been used in a variety of applications including drug carriers for targeted delivery, cancer treatment, gene therapy and DNA analysis, antibacterial agents, biosensors, enhancing reaction rates, separation science, and magnetic resonance imaging (MRI) [33]. Some of the purposes of using nanoparticles include drug delivery, antibacterial agent, biosensor, reaction rate enhancement agent and magnetic separation and detection. Here, we provide some examples to illustrate these applications [34].

8.2.1 Drug delivery

Magnetic nanoparticles like Fe3O4 and Fe2O3 are known to be biocompatible. They have been actively investigated for targeted cancer treatment (magnetic hyperthermia), stem cell sorting and manipulation, guided drug delivery, gene therapy and DNA analysis, and MRI [33].

8.2.2 Antibacterial agent

Silver nanoparticles (AgNPs) had been biosynthesized the use of fungus Trichoderma viride. These nanoparticles have been evaluated for their improved antimicrobial functions with numerous antibiotics towards gram-positive and gram-negative bacteria. The antibacterial functions of ampicillin, canamycin, erythromycin, and chloramphenicol had been elevated within the presence of silver nanoparticles (AgNPs) towards test traces [35].

The best improving effect changed into observed for ampicillin in opposition to take a look at lines. The end result confirmed that the aggregate of antibiotics with AgNPs has higher antimicrobial effects and provided beneficial insight into the development of latest antimicrobial dealers [35].

8.2.3 Biosensor

Nanoparticles possess interesting electronic and optical properties and can be used in biosensor applications. They are synthesized from spherical selenium nanoparticles by the Bacillus subtilis with diameters ranging. These sensors exhibited good electrocatalytic activity towards the reduction of H2O2 due to the good adhesive ability and biocompatibility of Se nanomaterials [36]. These H2O2 biosensors had high sensitivity and affinity for H2O2 with a detection limit of 8×10^{-8} M. The selenium (Se) nanomaterials-modified electrode will probably be promising for a wide range of applications related to the detection of H2O2 in food, pharmaceutical, clinical, industrial and environmental analyses [36].

8.2.4 Reaction rate enhancement agent

Magnetic nanoparticles have been used to improve the microbiological reaction rates.

In fact, magnetic nanoparticles were utilized not only for their catalytic function but also for their good ability to disperse i.e. use of the coated microbial cells of Pseudomonas delafieldii with magnetic Fe3O4 nanoparticles to fulfill desulfurization of dibenzothiophene. The high surface energies of nanoparticles resulted in their strong adsorption on the cells [36].

8.2.5 Magnetic separation and detection

Magnetic elements conjugated with organic molecules, that rectangular degree enticing substances for building assay structures, are deliberate to be used as a biological label [37]. Aggressive luminescence catalyst immunoassays utilizing antibodies immobilized onto microorganism magnetic elements had been evolved for the fast and sensitive detection of tiny molecules, like xenobiotics, hormone and cytotoxic detergents. The employment of magnetic particles as a solid-phase adsorbent is similar temperament for polymer extraction techniques because of they will be actually manipulated through smooth software of a magnet [37].

9. Conclusions

Microorganisms had been present in the world 4 billion years ago and have been evolving and increasing into new surroundings ever since, current anywhere. Their presence has driven the development of latest ecosystems, a number of which allowed the evolution of extra complex organisms. Issues about the supply

of healthy, secure meals for people have elevated research for the replacement of chemical substances with inexperienced biomaterials. Considered one of strategies of creating and processing renewable monomers and polymers are presently studied, thinking of their benefits and downsides. There is a need to supply a green substitute for foods, medicinal drug, and pharmaceutical packages. Microbial synthesis has attracted extremely good attention because of the ease of the process and transformation into critical primary and secondary metabolites. The function of natural merchandise in meals, medicine, remedy, and agriculture fields is extensively highlighted because of their chemical stability and biocompatibility. Microorganisms were employed in large-scale manufacturing of a diffusion of biochemicals, antibiotics, and inside the processing of meals and feeds.

It is increasingly possible to identify potential vitamin-producing strains and interpret the intertwined mechanisms for their biosynthesis, because of the expanding availability of genome sequences, which could be used to expand the vitamin-producing capacities of the human intestine. Probiotic bacteria, as well as commensal bacteria found in the human intestine, such as Lactobacillus and Bifidobacterium, can de novo synthesize and supply vitamins to human body.

The usage of vitamin-producing types supplied a brand new perspective at the precise makes use of probiotics. Many vitamin-producing bacteria overproduce B vitamins and K vitamin, that could allow them to organically enrich uncooked meals materials like soy, milk, meat, and greens with B vitamins, preventing the want for additives. Consequently, the meals enterprise ought to take benefit of those novel and efficient vitamin-producing types to feature nutritional value to fermented merchandise and economically viable. It's far an increasing number of feasible to identify capacity vitamin-producing types and interpret the intertwined mechanisms for their biosynthesis, due to the increasing availability of genome sequences, which will be used to increase the vitamin-generating capacities of the human intestine. Probiotic microorganism, in addition to commensal microorganism observed inside the human intestine, along with Lactobacillus and Bifidobacterium, can de novo synthesize and supply vitamins to human intestine. In human body, bacteria can produce vitamin K and most of the water-soluble B vitamins.

There were terrific trends in the field of microorganism synthesized nanoparticles and their functions over the past decade. Although an incredible deal work is wanted to enhance the overall performance of synthesis, the manipulate of particle duration and morphology. The biosynthesis of nanoparticles by using microbes is idea to be clean, safe, and environmentally appropriate "green chemistry" techniques. Biochemical, molecular and cellular mechanisms that mediate the synthesis of biological nanoparticles need to be studied in element to increase the rate of synthesis and to obtain favored duration and form of nanoparticles. In assessment with microorganism, fungi can produce big amounts of nanoparticles because they could secrete large quantities of proteins which directly translate to higher productivity of nanoparticles. The biogenic approach is further supported by way of the reality that most of the people of the bacteria inhabit ambient conditions of varying temperature, pH, and stress condition. With the present day development and the continued efforts in improving particle produce performance and exploring their biological and medical functions. We hope so, the implementation of these processes on a largescale and their commercial packages in medication and fitness care will take vicinity inside the coming years. It appears distinctly in all likelihood that future studies will become aware of many other disorder states in which intestine microbial metabolites are significantly enriched or depleted. It is far vital to keep in mind that by using the use of themselves such studies do no longer display causality.

Acronyms and abbreviations

NMR	nuclear magnetic resonance
MOs	microorganisms
SM	secondary metabolites
MS	mass spectrometry
NPs	nanoparticles
EPA	eicosapentaenoic acid
DHA	docosahexaenoic acid
ATP	adenosine triphosphatase
PUFAs	polyunsaturated fatty acids
DNA	deoxyribonucleic acid
MCF	cytotoxic cadmium chloride
FAs	fatty acids
UHPLC	ultrahigh-performance liquid chromatography
MRI	magnetic resonance imaging
Entap	enterococcal anti-proliferative peptide
Au	gold
Ag	silver
Pt	platinum
Cu	mercury
Cd	cadmium
Se	selenium
Cr	chromium
Hg	mercury
HeLa cell	Henrietta Lacks cell
AgNPs	silver nanoparticles
Fe3O4	magnetite
Fe2O3	maghemite
H2O2	Hydrogen peroxide

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References

[1] Abdel-Aziz S, Abo Elsoud M, H.Anise A: Handbook of **Food Biosynthesis** Microbial Biosynthesis: A Repertory of Vital Natural Products. 2017; 25 p. **DOI:**10.1016/B978-0-12-811372-1.00003-8

[2] Andryukov B, Mikhailov V, Besednova N: The biotechnological potential of secondary metabolites from marine macteria. FEBS Letters.2019; 7;176-192. DOI:10.3390/jmse7070176

[3] Mosunova O, Navarro-Muñoz J, Collemare J. The Biosynthesis of Fungal Secondary Metabolites: From Fundamentals to Biotechnological Applications. FEBS Letters. 2020; Encyclopedia of Mycology. DOI:10.1016/B978-0-12-809633-8.21072-8

[4] McCarville J,Chen G, Cuevas V, Troha K, Janelle S. Ayres: Microbiota Metabolites in Health and Disease. FEBS Letters. 2020; 38:147-70. DOI: 10.1146/annurev-immunol-071219-125715

[5] Nigam P, Singh A, , Lyngby, Denmark: Production of Secondary Metabolites – Fungi. FEBS Letters. 2014; 1319-1328

[6] Pham JV, Yilma MA, Feliz A, Majid MT, Maffetone N, Walker JR, Kim E, Cho HJ, Reynolds JM, Song MC, Park SR and Yoon YJ: A Review of the Microbial Production of Bioactive Natural Products and Biologics. FEBS Letters. 2019; DOI: 10.3389/fmicb.201901404

[7] Bachmann B, Van Lanen S, Baltz R. H: Microbial genome mining for accelerated natural products discovery: is a renaissance in the making J. Ind. Microbiol. Biotechnol. FEBS Letters .2014; 41:175-184. DOI: 10.1007/s10295-013-1389-9

[8] Guoqing T, HuaRong T: Biosynthesis and regulation of secondary metabolites in microorganisms. FEBS Letters.2013. 7: 581-583. DOI: 10.1007/s11427-013-4501-5

[9] Mushtaq S, Haider Abbasi B, Uzair B, Abbasi R: NATURAL PRODUCTS AS RESERVOIRS OF NOVEL THERAPEUTIC AGENTS. FEBS Letters. 2018; 17:420-451. DOI:10.17179/excli2018-1174

[10] Gutzeit H, Ludwig J: Handbook of Plant Natural Products Biosynthesis and Chemical Properties of Natural Substances in Plants. 1st ed. Wiley-VCH Verlag GmbH & Co. KGa. 2014; 1 p.

[11] Janardhan A, Praveen Kumar A, Viswanath B, Saigopal D, Narasimha G: Production of bioactive compounds by actinomycetes and their antioxidant properties. FEBS Letters.2014; DOI:10.1155/2014/217030

[12] Sanchez S, Demain A: Secondary Metabolites. FEBS Letters. 2011; 2: 155-167. DOI: 6/B978-0-444-64046-8.00012-4

[13] Zhang L, Davies S: Microbial metabolism of dietary components to bioactive metabolites: opportunities for new therapeutic Interventions. FEBS Letters. 2016; DOI: 10.1186/s13073-016-0296-x

[14] Dorrestei P, Mazmanian S, Knight R: Finding the Missing Links among Metabolites, Microbes, and the Host. FEBS Letters.2014; DOI: 10.1016/j.immuni.2014.05.015

[15] Sorour N, Tayel A, Abbas R, Abonama O: Handbook of Food Biosynthesis Microbial Biosynthesis of Health-Promoting Food Ingredients. 2017; 55 p. DOI:10.1016/B978-0-12-811372-1.00002-6

[16] Claus SP, Tsang TM, Wang Y, Cloarec O, Skordi E, Martin FP: Systemic multicompartmental effects of

the gut microbiome on mouse metabolic phenotypes. Mol Syst Biol. 2008;4:219. doi:10.1038/msb.2008.56.

[17] Marcobal A, Kashyap P, Nelson T, Aronov P, Donia M, Spormann A: A metabolomic view of how the human gut microbiota impacts the host metabolome using humanized and gnotobiotic mice. ISME J. 2013; 7:10. doi:10.1038/ismej.2013.89.

[18] LeBlanc JG, Laino JE, del Valle MJ, Vannini V, van Sinderen D, Taranto MP, de Valdez GF, de Giori GS, Sesma F. B-group vitamin production by lactic acid bacteria – current knowledge and potential applications. J Appl Microbiol. 2011;111:1297-1309. DOI: 10.1111/j.1365-2672.2011.05157.x

[19] Gu Q, Li P: Handbook of Intech Open. Biosynthesis of Vitamins by Probiotic Bacteria. FEBS Letters. 2016. DOI:10.5772/63117

[20] Verardo V , Gómez-Caravaca A.M, Tabanelli G: Bioactive Components in Fermented Foods and Food By-Products. FEBS Letters. 2020; DOI:10.3390/foods9020153

[21] Martinez K, Leone V, Chan E: Microbial Metabolites in Health and Disease: Navigating the Unknown in Search of Function. FEBS Letters. 2017;DOI: 10.1074/jbc.R116.752899

[22] Hernández-Almanza A, Muñiz-Márquez D, de la Rosa O, Navarro V, Martínez-Medina G, Rodríguez-Herrera R, Aguilar C: Handbook of **Food Biosynthesis**. *Microbial* Production of Bioactive Pigments, Oligosaccharides, and Peptides. FEBS Letters. 2017; **DOI:1016/ B978-0-12-811372-1.00004-X**

[23] Druart C, Neyrinck AM, Vlaeminck B, Fievez V, Cani PD, Delzenne NM: Role of the lower and upper intestine in the production and absorption of gut microbiota-derived PUFA metabolites. FEBS Letters. 2014;9(1), e87560. DOI: 10.1371/ journal.pone.0087560.

[24] Vrancken K , Anne J: Secretory production of recombinant proteins by Streptomyces. Future Microbiol. FEBS Letters .2009;4: 181-188. DOI: 10.2217/17460913.4.2.181

[25] Yun Lim F, Sanchez J, Wang C, Keller N: Toward Awakening Cryptic Secondary Metabolite Gene Clusters in Filamentous Fungi. FEBS Letters. 2012; 517: 303-324. DOI:10.1016/ B978-0-12-404634-4.00015-2

[26] Bumpus S, Evans B, Thomas P, Ntai I, Kelleher N: A proteomics approach to discovering natural products and their biosynthetic pathways. Nature Biotechnology. 2009; 27:951-956.DOI: 10.1038/nbt.1565

[27] Davies J: Specialized microbial metabolites: functions and Origins. FEBS Letters. 2013; 66: 361-364. DOI: 10.1038/ja.2013.61

[28] Nigam P, Singh A: Production of Secondary Metabolites – Fungi. FEBS Letters. 2014; pp 1319-1328. DOI: 10.1016/ B978-0-12-384730-0.00202-0

[29] Abdel-Razek A , El-Naggar M , Allam A, Morsy, Othman S: Microbial Natural Products in Drug Discovery. FEBS Letters.2020; 8: 470-489. DOI:10.3390/pr8040470

[30] Nataraj B, Ali S.A, Behare P, Yadav H: Postbiotics-parabiotics: the new horizons in microbial biotherapy and functional foods. FEBS Letters. 2020; 19:168-190. DOI: 10.1186/ s12934-020-01426-w

[31] Taghinasab M, Jabaji S: Cannabis microbiome and the role of Endophytes in modulating the production of secondary metabolites. FEBS Letters.2020; 8:355-371. DOI:10.3390/ microorganisms8030355

[32] Hulkoti N, Taranath T.C: Biosynthesis of nanoparticles using microbes. FEBS Letters. 2014; 121:474-483. DOI: 10.1016/j.colsurfb.2014.05.027

[33] Li X, Huizhong Xu, Chen Z-S, Chen G: Biosynthesis of nanoparticles by microorganisms and their applications. FEBS Letters.2011; doi:10.1155/2011/270974. DOI:10.1155/2011/270974

[34] Lef'evre C. T, Abreu F, Schmidt M: Moderately thermophilic magnetotactic bacteria from hot springs in Nevada. FEBS Letters.2010; 11: 3740-3743. DOI: 10.1128/AEM.03018-09

[35] Kalishwaralal K, Banumathi E, Pandian S. R: Silver nanoparticles inhibit VEGF induced cell proliferation and migration in bovine retinal endothelial cells. FEBS Letters. 2009; 73:51-57. DOI:10.1186/1477-3155-7-8

[36] Wang T, Yang L, Zhang B, Liu J: Extracellular biosynthesis and transformation of selenium nanoparticles and application in H2O2 biosensor. FEBS Letters.2010; 80: 94-102. DOI:10.1016/j.colsurfb.2010.05.041

[37] Xiang L, Wei J, Jianbo S, Guili W, Feng G, Ying L: Purified and sterilized magnetosomes from Magnetospirillum gryphiswaldense MSR-1 were not toxic to mouse fibroblasts in vitro. FEBS Letters. 2007; 45:75-81. DOI:10.1111/j.1472-765x.2007.02143.x