



## Review

# Microbial Based ‘Cradle-to-Cradle’ Approach to Attain Sustainable Development Goals of Food and Water Security, Good Health and Well Being without Crossing the Planetary Boundaries

Simrat Kaur<sup>\*</sup> , Fatema Diwan, Brad Reddersen

Climate Survival Solutions India Pvt. Ltd., India  
E-mail: [kaursimrat.drl@gmail.com](mailto:kaursimrat.drl@gmail.com)

**Received:** 6 October 2022; **Revised:** 1 December 2022; **Accepted:** 8 December 2022

**Abstract:** Our planet is facing a wide range of inevitable and unprecedented changes such as, the water and food scarcity to the natural calamities, namely flooding, droughts and rising sea levels. All these global challenges had been addressed through the Sustainable Development Goals (SDGs) drafted by the general assembly of the United Nations. In light of the current population growth, it is difficult to attain the sustainable development using conventional and non-renewable natural resources by remaining within the planetary boundaries of Earth. In order to maintain the environment and ecological integrity, the utilization of renewable living natural resources such as microbes become inevitable. Due to their roles in geo physio-chemical processes and bioenergy transformations, microbes allow ‘cradle-to-cradle’ model of development using wastewater as a renewable resource. The circular wastewater economy is the sole sustainable method to achieve the SDGs of providing clean water and the sanitation to address the issue of water insecurity. The review presents an inter-connected overview on the roles and functions performed by the prokaryotic (bacteria) and eukaryotic (algae and fungi) microorganisms, which are crucial for attaining the environment sustainability within the planetary boundaries. Apart from the environmental roles of microbes, the review also highlights the importance of human-microbe interactions (gut microbiome) and edible microbial species (algae and fungi) which are essential for developing sustainable future alternatives to human nutrition, well being and prevention of diseases.

**Keywords:** algae, bacteria, bioenergy, microbiome, sanitation, sustainability, wastewater

## 1. Introduction

The United Nations Sustainable Development Goals are crucial for the future existence of life on Earth, as these are aimed at resolving the global crisis that the planet is currently facing. The major crisis that relate to every being on planet are rising global temperatures, and water and food shortages. Subsequently are the driving factors for the health and wellness of the beings. Thus, holistic approaches must be taken to avoid the phenomenally catastrophic destruction of the planet. The rising global temperatures and declining water resources are two interconnected factors that have wide impacts on socio-political and economic sectors of the world.

Food security and nutrition are fundamental and principal human rights. However, these civil rights have been

critically endangered by the global drivers such as increasing war and political conflicts, climate change, natural calamities, destitutions, social inequalities, economic diminution, and pandemic diseases. The main factors to ensure global food security are the definitive sources to obtain quality food and the unperturbed access to the resources for food production and purchasing. The agriculture-led economic growth tackles both food security and poverty; however, due to high demands for water and fertilizers, the steady and fast growth in agriculture and related sectors (livestock and fisheries) demand holistic and sustainable development model.

The major challenges involved in meeting the demands for the resources in the agriculture sector are the abrupt supplies of fertilizers, water scarcity and climate change. The use of conventional synthetic fertilizers in extensive agriculture all over the world will become a major limiting factor in attaining the sustainable food, oil, and fodder crops. The chemical pollution arising from these fertilizers further elevate water scarcity which limit the agriculture productivity and consequently leading to food insecurity. As animal and aquaculture feed are derived from conventional agriculture; the livestock and fisheries are also burdened with fertilizers related environmental issues.

Due to high costs and inefficient management, countries of the African, South American and Eastern Europe are suffering from high phosphorous depletion rates which would ultimately impact agricultural soils worldwide [1]. The slow geophysical phenomenon of rock weathering and the anthropogenic inputs of inorganic fertilizers are the main contributors towards the replenishment of phosphorous depletion in the agricultural soils. Phosphate fertilizers are obtained from the Phosphate Rocks (PR) reserves and approximately 70% of the PR reserves are found in Morocco and Western Sahara followed by the US and China [2].

In addition to the depleting geological P reserves, the inefficient usage in crop fields is leading to increasing agriculture run-off discharges into the inland and coastal water bodies causing eutrophication. In addition, the mining and processing of PR, release by-products such as phosphogypsum and heavy metals toxic waste containing cadmium and uranium causing both air and water pollution [2]. The regions of the world such as the US-mid west, Western Europe, the Ganges Valley and East Asia have high P application rates in their agricultural fields; and thus, will transgress into the biogeochemical Planetary Boundary for P in a zone of high risk [3]. Tackling the P losses associated with the cradle-to-grave supply chains could best be achieved, by improving the efficiency of fertilization and recovery of P from the wastewaters, which also subsequently ensures food security, sustainability, and establishment of circular economy.

In this paper, we have described the biological measures to overcome the consequences of transgressing phosphate usage in agriculture for ensuring food security and conservation of freshwater quality. Various types of microorganisms play influential roles in enhancing the bio-availability of phosphorous in agriculture fields which simultaneously reduce the fertilizer inputs to the soils and increase the crop yields. The most economical and environmental friendly approach to restore the phosphorous from wastewater is, through the systematical utilization of microorganisms including bacteria, fungi and algae. The wastewater treatment integrated with enhanced nutrient recovery and production of renewable energy such as biogas is the most sustainable model which ensures food-water-energy security. Efficiently treated wastewaters using a diverse array of microorganisms tackle the major environmental issue of freshwater eutrophication.

The biologically treated wastewater effluents resourced for irrigation usage become a win-win approach towards achieving sustainable development goal of food security without burdening the depleting groundwater aquifers. In addition, the high quality standards of the treated wastewater post nutrient recovery and advanced treatment processes also address the sanitation issue that has direct influence on human health and well being. From ecological perspective, the interactions of microorganisms are not restricted to other microorganisms and plants but human well being is also dependent on various types of microorganisms such as gut microbiome and the edible ones like algae and fungi. Certain useful microbes, which establish symbiotic associations within the human body play influential roles in their nutrition and disease prevention.

## **2. Sustainable development goals and planetary boundaries**

The United Nation General Assembly drafted a set of 17 global Sustainable Development Goals (SDGs) in 2015 and laid a policy framework [4] for the period of 2015-2030 as a Network of Targets [5]. According to the critiques, the

SDGs are unenforceable as countries have to create national or regional plans for execution. The social, economic and environmental are among the most important pillars of SDGs; however, to achieve the global sustainable development, the focus for developed nations should be more on their social and environmental policies whereas the developing countries need to improve their social and economic policies [6]. These measures are a must to attain zero poverty, global sustainability, equity in the utilization of natural resources and eradication of world hunger. The fundamental causes of poverty, depletion of natural resources, food insecurity and global malnutrition are extremely complex as these are linked to political interferences and economic policies. Eradication of these problems cannot be attained merely by increasing the inputs as the planet Earth has sufficient yet exhaustible natural resources such as fossil fuels, inorganic nutrients and freshwater.

This brings the focus on planetary boundaries, a concept which was first introduced in 2009 and is defined as the safe operation of human activities within certain environmental limits, else the Earth system is at the risk of destabilization [3]. Although, this concept of boundaries for the planetary resources has become popular now, but the idea originated way back in the 1970s when factors namely population, agriculture production, natural resources, industrial production and pollution were considered as ultimate limits to growth on this planet [7].

The biggest challenge for humanity today, is to fulfill the basic demands for the high quality life for more than 7 billion people through sustainable use of available natural resources, without crossing the planetary boundaries [8]. In other words, sustainability is directly linked with planetary processes within the defined boundaries. There is growing scientific consensus about the environmental threats including climate change, water and food shortages and other depleting resources; yet anthropogenic actions are defying the safe operating limits of environmental sustainability. The social and economic development based on the construction of new materials is clearly unsustainable. However, the growth has to be continued; as well as service based business models which take the circular economy approach of reuse and recycling are the need of the hour [9].

Food and water insecurities are the critical issues for both humans and the environment. Many components considered under the planetary boundaries concept come under the biogeochemical group including the nitrogen and phosphorous cycles, freshwater use and land system change, which are the direct threats to food and water security on a global scale. The disruption of these processes would paralyze the survival of humans and other life forms. The two most crucial and urgent limits to agricultural food production are arable land and the availability of freshwater; with limits of water shortages be reaching earlier than land in many parts of the world [7].

The sustainable usage of natural resources in order to uncross the planetary boundaries, is only possible when every sector pertaining to economic development adopts the approach of circular use of resources. The main aspect of circular economic development is waste management using technological improvements for an efficient resource recovery and re-utilization. In the proceeding sections, we will discuss the practical roles of various types of microorganisms in wastewater management for resource and green energy recovery.

### **3. Addressing nutrient depletion and food insecurity through soil microbes**

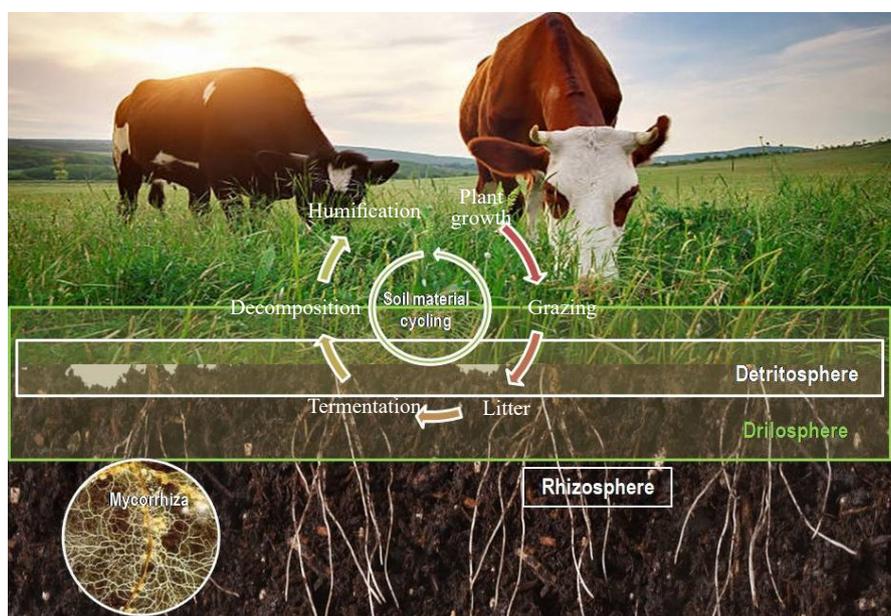
The benefits of healthy soil, which hosts a quarter of the planet's biodiversity include food production, combat of climate change, and filtering and storing water. As vital biotic components of the soil ecosystems, the microbial mitigation is one of the most important adaptation methods against the climate change [10]. The high population density and diversity of soil microbes preserved in viable state in the natural banks of peatlands and paleosols for thousands of years influence the global carbon and nitrogen biogeochemical cycles which are being destroyed under land use changes [11].

The diversity of Environmentally Relevant Microorganisms (ERMs) includes both prokaryotes and eukaryotes namely the bacteria, fungi, viruses, yeast, algae and actinomycetes. The ERMs play active roles in mitigating the impacts of environmental challenges [12] such as persistent droughts, torrential rains, flooding, heat waves and frost, the major factors affecting agri-productivities resulting into the food shortages. The domesticated mono-cultivated agricrops lack the ubiquity and rich genetic diversity of soil microorganisms that would allow crops to show tolerance to abiotic extremities [13].

The establishment of plant communities whether in the agriculture crop fields or in a natural ecosystem, depends

solely on the quality and physio-chemical properties of the soil. As an integral part of agriculture, soil act as a primary source of food nutrition. Soil is a complex mixture of all three states of matter such as liquid, gases, minerals, organic matter and living beings including microorganisms, worms, and insects. The living organisms names cyanobacteria, lichens, fungi and mosses which live on the surface and inside the soil forms the soil biocrusts [14] or biological soil crusts [15]. The microbes involved in the soil formation respond to the environmental fluctuations at the interface within minutes by changing their phenotypes by switching on and off their gene transcription [15].

Microorganisms play an essential role in soil genesis through the release of metabolic byproducts such as organic acids that dissolve rock during the weathering process [16]. A rich diversity of soil microorganisms take part in the biogeochemical cycling of macronutrients names carbon, nitrogen, sulphur and iron through decomposition, hums formation and mineralization of dead and decaying flora and fauna residues (Figure 1). These entire biogeochemical processes take place in different spheres of the soil namely, the rhizosphere, drilosphere and the detritosphere within it [16].



**Figure 1.** Soil material cycling involves different biogeochemical processes taking place in different soil spheres

The free living soil microbes as well as those associated with plant roots perform important biotransformations associated with nitrogen and phosphorous nutrient availability for plant growth [17]. Soil bacteria and fungi biotransform the natural and synthetic compounds which are used as fertilizers for crop production. For example, the compound struvite ( $MgNH_4PO_4 \cdot 6H_2O$ ), commonly found in bird droppings, fish bones and human kidney stones is a potential P fertilizer source, which if not biotransformed may cause sanitation problems by blocking the sewage pipeline system [18].

Microbes improve soil fertility by mobilizing the elemental P, both bacteria and fungi play critical role in P biotransformation and degradation of environmental pollutants such as, the P-based surfactants. The untreated runoff of synthetic fertilizers and pollutants, which cause eutrophication in water bodies, also lead to the irreversible loss of non-renewable phosphorous resources (Table 1).

### 3.1 Improving phosphate efficiency to enhance crop yields

The intensive farming practices involving the overuse of synthetic fertilizers and high tillage of soil prevail in many countries such as South Asia and Brazil. Although, extensive agriculture support high food crop and livestock

production; it is the leading cause of soil degradation and soil erosion. The underutilized fertilizers and chemicals by the crops are lost as P loadings from agriculture to freshwaters [19]; the consequence of which is described in the next section. The physio-chemical disturbances in agricultural soil are not only detrimental for the environment but also cause loss of soil biodiversity including useful microbes. Therefore, soil management is of utmost importance to ensure both food security and water conservation. The holistic approach by which the soil can maintain its integrity and remain productive enough to meet the growing global food demands by enhancing the nutrient efficiency of soil through gradual replacement of synthetic fertilizers with biofertilizers.

**Table 1.** List of important bacterial and fungal species which show P biotransformation capabilities

Soil microorganism (B, bacteria; F, fungi)	Element	Mechanism of biotransformation	References
<i>Pseudomonas</i> (B)	P	Inorganic P solubilization by secretion of organic acids	[20]
<i>Bacillus</i> (B)	P	Inorganic P solubilization by secretion of organic acids	[16]
<i>Erwinia</i> (B)	P	Secretion of organic acids	[21]
<i>Azotobacter</i> (B)	P	Secretion of organic acids	[21]
<i>Pantoea anantisi</i> , <i>Bacillus thuringiensis</i> (B)	P	Solubilization of inorganic P compounds in soils through pH reduction	[22]
<i>Enterobacter</i> sp. (B)	P	Solubilize and release through secretion of acids and enzymes	[23]
<i>Aspergillus niger</i> (F)	Mn, La, U, P, Al, Ti, Fe	Colonize, penetrate, solubilize and precipitate minerals through excretion of metabolites such as H <sup>+</sup> , oxalic acid, citric acid	[18]
<i>Pseudomonas butanovora</i> , <i>P. oleovorans</i> , <i>P. fluorescens</i> (B)	Pollutant degradation of polyfluoroalkyl phosphates and fluorotelomer alcohol		[24]
<i>Aspergillus sydowii</i> (F)	Triphenyl phosphate degradation	Biotransformation occurs through hydrolysis, hydroxylation, methylation and sulfonation	[25]

Synthetic P fertilizers may also contain toxic elements such as fluorine, lead, cadmium, arsenic, mercury, chromium and radium and in alkaline soils with high calcium carbonate minerals, the efficiency of P uptake by plants is compromised [26]. Therefore toxic heavy metal stabilization and immobilization are essential to prevent their uptake by food crops and cereals. In this regard, the Phosphate Solubilizing Microorganisms (PSMs) including bacteria and fungi play a key role in soil bioremediation process, which simultaneously improves P efficiency. For example, the rhizospheric and endophytic bacteria increase the P efficiency of wheat cultivars by enhancing the root and shoot growth leading to high grain yield [26]. Similarly, the phosphate solubilizing fungus *Penicillium oxalicum* improves the growth of wheat and maize fertilized with rock phosphate in alkaline soils [27]. Thus, the phosphate solubilizing microorganisms contribute to plant nutrition by transforming insoluble forms of P present in rock phosphates to accessible soluble form that are can readily be taken up by the staple food crops such as corn, rice, wheat and sorghum [28].

In addition to the cereals crops, the PSMs bacterium *Pseudomonas putida* improves the rhizobium-legume efficiencies between *Bradyrhizobium japonicum* and *Sinorhizobium meliloti* and alfalfa and soybean respectively [29]. Apart from the PSMs, the arbuscular mycorrhizal fungi *Glomus mosseae* improve the phosphorous efficiency of paddy crop, thereby improving the rice production [30]. Although PSMs prove beneficial in improving the productivities of various crops under different soil regimes and act as biofertiliser; these microorganisms also play a role in the biogeochemical P cycle through processes such as dissolution-precipitation, sorption-desorption, and weathering [31].

### ***3.2 Crossing of planetary boundary for P cycling***

As an irreplaceable and limiting nutrient, the P usage under industrialized agriculture set up had crossed 90% of the planetary boundary a decade ago [32]. The unidirectional flow of phosphorous to the inland water bodies driven by imprudent applications for agriculture and aquaculture production is causing the proliferation of toxic blooms and impedes global P cycling. The high deposition of phosphorous at the water interface and in the sediments of the aquaculture lakes occurs due to the decomposition of organic matter, which includes dead phytoplankton and fish debris, leading to permanent burial [33]. The unrestricted P loadings in the freshwater bodies from wastewater changing the habitat conditions, and favor the dominance of opportunistic species, adapted to high nutrient loadings and low oxygen content. The high primary productivities in the surface waters consequently lead to continuous mineralization of degradable organic matter, creating O<sub>2</sub> depletion at the sediment-water interface. This phenomenon further enhance eutrophication as O<sub>2</sub> hypoxia trigger the release of orthophosphate from the internal P loadings [34]. In addition, the anoxic conditions cause the reduction and dissolution of iron oxide, which release additional P and Fe (II) from the sediments [33]. The internal P loadings in aquatic lakes change the dynamics of P cycling which is influenced more by the climate change than the anthropogenic activities that reduces the mobility of phosphorous, particularly in alpine lakes [35]. The increasing temperatures enhanced microbial activity and mineralization of organic matter leading to the migration of sediment Fe/Al/Ca-P [33]. The reduced water quality due to mobile P pool in lakes and inland water bodies, which are important drinking water resources also suffer from delays in the mitigation of eutrophication and toxic blooms. The internal P release degrade lentic habitats by turning macrophytes-dominated clean water ecosystem into turbid water with proliferated growth of invasive blooms [35].

Therefore, the restoration of P from the polluted freshwater bodies is necessary to mitigate various environmental challenges such as invasion of toxic species, change in prey-predator dynamics, water scarcity and to overcome depleting P reserves.

### ***3.3 Impacts of P depletion on food-water-renewable energy***

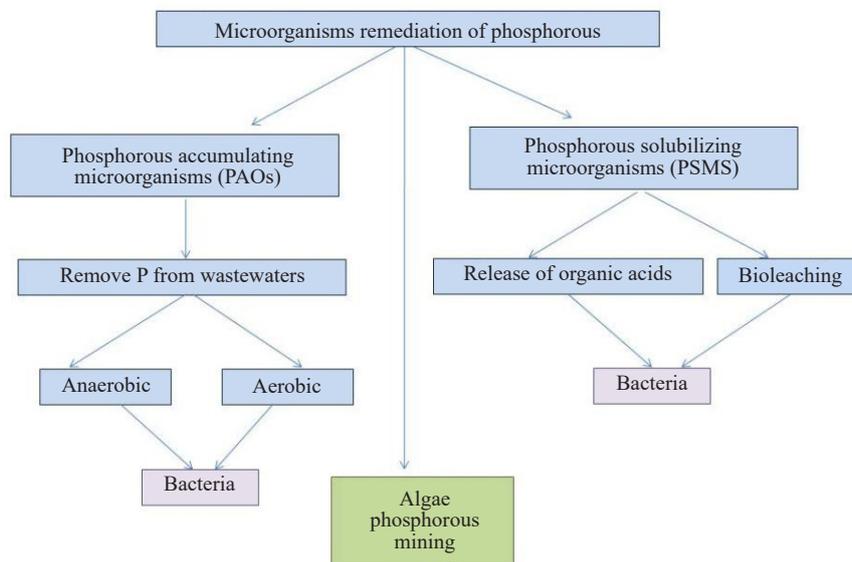
The perturbations in P biogeochemical cycling due to excessive internal loadings, eutrophication and climate change are accumulatively causing the depletion of P reserves which is subsequently leading to global hikes in the cost of fertilizers. As P is the second greatest used nutrient element worldwide for food production, the high costs of fertilizers directly affects the availability and affordability of food supply [36]. Apart from the worldwide shortages of fertilizers, the fresh water resource required for the irrigation of intensive food and feedstock crops are also under the threats of extinction due to excessive nutrient loadings as discussed in the previous section. The changing land use pattern to expand the agriculture set up, cause the destruction of biodiversity. These are other planetary boundaries that humanity is crossing which will have dreadful consequences. The perennial ecosystems are being replaced with fields to undertake the industrial production of monoculture biofuels crops such as sugarcane and corn to meet the global demand for the fossil fuel alternatives. In addition to the nutrients, the intensive agriculture practices also require great inputs of freshwater which is competing with the domestic and industrial demands. The polluted waters are neither suitable for domestic or industrial usage nor for the generation of hydroelectric energy. Therefore, P plays a pivotal role in the food-water-energy security nexus [37]. Apart from freshwaters, the marine or sea ecosystems are also endangered due to the release of internal phosphorous under anoxic conditions, for example the Baltic Sea, Gulf of Mexico, Maowei Sea [38].

### ***3.4 Microbial remediation and recovery of phosphorous***

Different methods to improve the water quality by restoration of P include chemical inactivation and artificial oxygenation to retain P and sediment removal. The major drawbacks of geoengineering (artificial oxygenation) and chemistry (use of metal oxides/hydroxides as adsorbents) are that these are more expensive and may cause the release of toxic substances to surface waters; thereby raising additional environmental concerns [39]. The inadequacies of these technologies to sustain the excess P in both inland and coastal waters is an urgent call for adopting bio-based strategies using microorganisms, microalgae, seaweeds and plants, which are cost effective with low environmental risks [38].

The wastewaters and aquatic sediments (inland and coastal) are two main reservoirs of waste and used phosphorous containing compounds including agriculture and aquaculture fertilizers, and industrial and household P-based synthetic

products. The microbial diversity, particularly of bacteria and microalgae play an influential roles in mitigating this unidirectional loss of phosphorous by restoration and recovery of phosphorous through both ex-situ and in-situ approaches (Figure 2).



**Figure 2.** Phosphorous mining using different types of microorganisms from wastewaters and sediments. Source of information [38]

To overcome the P depletion crisis, it is inevitable to integrate the removal process with recovery and reuse in the form of biofertilizers. The phosphorous or polyphosphate accumulating organisms commonly used in Enhanced Biological Phosphorous Removal (EBPR) for the treatments of various types of wastewaters best representative working units for simultaneously achieving removal and reuse [40]. The EBPR is a cyclic anaerobic and aerobic process by which the different forms of phosphorous accumulating bacteria affluently take up inorganic P in excess of their metabolic needs and store it as poly-phosphate [41]. The common sewage bacteria found in activated sludge and are used for wastewater treatment for EBPR called *Candidatus accumulibacter* can accumulate large amounts of intracellular poly-phosphate [41]. The Polyphosphate Accumulating Organisms (PAOs) utilize aerobically stored poly-P to support their metabolic uptake of carbon under anaerobic conditions such as *Tetrasphaera* spp., *Pseudomonas* and *Microtholunatus phosphovorius* [42]. The P accumulating capabilities of PAOs is much higher than heterotrophic microbes and therefore, EBPR-integrated wastewater treatment plants can remove up to 85% P from the influent streams [43].

The activated sludge carrying poly-P containing microbes is partly circulated back to the anaerobic process for metabolic C uptake by the PAOs and the remaining sludge is most often used as fertilizer or is incinerated. Alternatively, the poly-P rich sludge can be treated with organic reagents such as trichloroacetic acid to precipitate out the phosphate residues from the microbial biomass. Due to their thermally stability, the another method to obtain crude form of poly-P in different chain lengths is high temperature calcinations [40].

Sewage sludge ash is being considered as a secondary source of phosphorous; however, it contains toxic levels of heavy metals. The sulfur-oxidizing bacteria which are also known as bioleaching bacteria create acidic conditions suitable for phosphate dissolution along with heavy metals which are subsequently separated through electrodialysis to obtain phosphorous [44].

### 3.5 Algae-based nutrient recovery from wastewaters

Algal-based waste water treatment specifically involves the removal of both phosphorous and nitrogen along with elimination of coliform bacteria, heavy metals, and xenobiotic compounds and lowering the chemical and biological

oxidation demand. The principle underlying the treatment of wastewater by microalgae incorporates the removal of contaminants by accumulating them or utilizing them in their cells. The add-on advantages of using microalgae for nutrient recovery from wastewater are reduction in sludge formation, no aeration required, reduction in greenhouse gases such as methane and CO<sub>2</sub> and instead it captures the atmospheric CO<sub>2</sub> for intracellular production of biomass suitable for bio-fuels, bio-polymers, bio-fertilizers, paints, dyes, and colorants. Algae biomass derived from the upstream waste water recycling and nutrients recovery process is a rich source of various nutrients such as proteins, sugars, oils and essential nutrients. The biomass paste rich in proteins has a desirable amino acid composition and is therefore a suitable feed for both aquaculture and animal farms. Thus, algae make an ideal alternative to P rich synthetic aquaculture fertilizers that are massively contributing to the internal P loadings in the marine sediments. The usage of microalgae in WWT plants has two main aims: (1) the direct uptake or transformation of water contaminants, and/or (2) improving the purification performance of bacterial systems (microalgae-bacteria aggregates) by providing additional oxygen from photosynthesis (symbiotic co-cultures), thus reducing the total energy costs of direct (gassing performance) or indirect (stirring performance) oxygen supply [45].

The microalga *Chlorella sorokiniana* cultivated in anaerobically treated blackwater with different N:P ratios of 15,17, 20, 23 and 26 show retention time of 10 days for complete assimilation of both the nutrients [46]. The nutrient rich biomass of microalgae is efficiently used in the form of biofertilizer [47]. The hydrochar made from microalgae *Chlorella vulgaris* and *Microcystis* sp. grown in wastewater from poultry farms lead to slow and persistent release of P which enhanced the P-use efficiency in wheat crop. Therefore, charring in algal fertilizers simultaneously substitute mineral P fertilizer and improve the phosphate use efficiency in food crops [48].

## 4. Resource recovery from decentralized wastewater treatment for clean water-energy

By transitioning from pollutant removal toward resource recovery, the wastewater is no more considered as waste stream but as a renewable resource. By establishing more circular resource flows, wastewaters can contribute to sustainable development in food, water and power sectors. The redesigning of wastewater treatment plants from mere treatment facilities into water resource factories is an emerging opportunity for establishing circular economies. Most water management utilities still focus on wastewater collection and treatment rather than resource recovery. Thus, there is a need for water management utilities across the globe to strategically plan the transition from treatment toward resource recovery via decentralized treatment systems. The principal component of wastewater is water which is around 99% and the remaining 1% accounts for the suspended, colloidal and dissolved solids. The wastewater, particularly the domestic and agriculture is rich in phosphorous which would be exhausted in less than 100 years. Therefore, P must be recycled and recovered from the wastewaters.

### 4.1 Wastewater transformations to renewable energy

As opposed to the current linear economy which can better be described as cradle-to-grave, the cradle-to-grave approach for resource recovery from sewage could tackle water scarcity problems and meet our pressing water needs without amplifying the carbon footprints. The biological interventions using diversity of bacteria and algae help to achieve accessibility to potable water and carbon-neutral energy. These are the best contenders for attaining sustainable development goals by establishing a circular bio-economy. The use of prokaryotic and eukaryotic microorganisms and their consortia provide potential benefits of improving nutrient recovery efficiencies with simultaneous production of biomass rich in revenue generating bio-products. The potential benefits of biomass production, nutrient recovery, renewable biofuel generation and fixation of atmospheric CO<sub>2</sub> are a win-win situation in sustainable economic development.

The prokaryotic life forms such as anaerobic bacteria treat wastewater to generate bio energy in the form of biogas via the process of anaerobic digestion. Biogas is generated by the anaerobic digestion of organic matter such as sewage sludge, animals, and municipal waste. Biogas forms a vital source of energy in heat and electricity generation along with being the worthiest renewable source of energy globally. It comprises of methane (55-60%), carbon dioxide (35-40%), hydrogen (2-7%) hydrogen sulphide (2%), ammonia (0-0.05 %) and nitrogen (0-2%). The methane undergoes a scrubbing process to remove other gases to obtain pure methane. This methane gas then passes through a fuel cell

to produce electricity and is also used as a source of energy for heating purposes. The production of biogas from the wastewater fills in the gap created between the demand and supply of electricity due to water shortages in the power sector.

Microbial driven approach for the direct generation of electricity using wastewater through the use of ‘Microbial Fuel Cell’ (MFC) serve as an innovative technique to offset the pressure on the energy grid. Technically, the MFC comprises of anode (in an anaerobic environment) and cathode (in the aerobic environment) separated by a cationic selective membrane which are linked together with an external conductor through a load. The input of organic fuel, i.e. the wastewater into the anodic chamber (comprising of microbes) results in oxidation of the substrate by microbes to generate ATP that fuels the cellular machinery forming electrons, protons, and carbon dioxide as the by-products. The electrons produced pass from the anode to the cathode through an external load connection, generating an electric current. At the same time, the protons migrate to the cathode chamber from the anode chamber freely through the protonic selective membrane separating the two chambers. The sediment microbial fuel cell is also promising in immobilizing phosphate for mitigation of P pollution in lakes [34].

#### **4.2 Circular wastewater bio-economy**

As an obligation towards the goal SDG 6, in the 2030 sustainable development agenda of the United Nations, countries must reduce their grey water footprint to ensure potable water and sanitation. An alternative approach is to develop biorefinery that converts waste water to economically valuable resources and support various sectors of the economy. From the biotechnological perspective, various types of micro and macro organisms such as bacteria, fungi, algae and plants are exploited in the biological water reclamation processes with co-production of renewable bioenergy and bioproducts. The conversion of the organic and inorganic nutrients present in wastewater, into the renewable and utilisable form of biomass present the best option for a circular economy in which the raw materials and final products are obtained from within the same process cycle.

When exploited sustainably, biomass is a renewable resource and effectively processing each of its constituents individually to produce different kinds of products is defined as a biorefinery. When the biomass is derived via water treatment and reclamation process plant, it is called wastewater biorefinery. Important considerations during the setting up of wastewater biorefinery include the composition and complexities of the wastewater and the market assessment for the co-products recovered from the refinery [49]. For example, the baker’s yeast wastewater or the vinasse has a very high Chemical Oxygen Demand (COD) of 29,000 mg/l with acidic pH of 4-5 is a cost-effective substrate for fermentation growth of the protein rich filamentous fungi which is subsequently grown with suitable bacteria for further breakdown of organic nutrients via anaerobic digestion. Thus with a two step wastewater biorefinery process, the chemical oxygen demand is lowered with co-production of protein rich biomass and methane rich biogas [50].

In comparison to other micro and macro organisms, the microalgae presents unique characteristics such as a) their abilities to drive nutrition via photo-, hetero- and mixo-trophically b) pollutant scavenging c) CO<sub>2</sub> assimilation and sequestration d) synergistic growth with bacteria e) production of numerous bioproducts. Due to these advantages, microalgae can be simultaneously exploited for treating wastewater from industries, agriculture and municipalities along with the co-production of industrial products. On the other hand, the commercial production or microalgae farming have several constraints such as high production cost, nutrient requirement which has high environment footprint, water scarcity and need for phosphorous which is a non-renewable resource [51]. Therefore, wastewater becomes a necessity for sustainable and economical farming of microalgae. Thus, the ‘marriage’ of microalgae and wastewater treatment is inevitable.

### **5. Microbial influence on human health and well-being**

The presence of microbes in the human body has always been associated with the cause of disease; however, several microbes residing in the human body impart beneficial effects. Microorganism readily colonizes surfaces of human bodies such as skin, oral cavity, and respiratory tract, urogenital and gastrointestinal tract. When these microbes establish symbiotic associations with their human host, they are referred to as “ Microbiota” or “Microflora” [52]. The human gut houses the largest accumulation of microbial flora, comprising of 10-100 trillion cells [53],

which are mutually and intrinsically associated with the gut's environment. These interactions aid in developmental, immunological, physiological and nutritional functions, which impact the overall health and disease manifestation in the host [54]. The human gut microbiota comprising of the bacteria, bacteriophages, viruses, fungi, protozoa, and the archaea greatly influence the human health. The bacterial cells remarkably exceed the human cells numbers (10-40 trillion cells) [55] by 3 to 10 times [56]. Viruses may actually outnumber bacterial cells, while fungi are present in the least amounts. The microbial cells account for 1-3% of human body mass [57].

The gut harbours most of the microbiota cumulatively present in the human body. The members of the microbiota largely fall under three major domains of life on planet Earth - Bacteria, Archaea and Eukarya. The 90% of the bacteria fall under two major phylotypes - the *Bacteroidetes* and the *Firmicutes* [52]. Major bacterial phyla, which inhabit the gut ecosystem include *Actinobacteria*, *Bacteroidetes*, *Cyanobacteria*, *Firmicutes*, *Fusobacteria*, *Lentisphaerae*, *Proteobacteria*, *Spirochetes*, TM7, *Verrucomicrobia* and *Euryarchaeota* [52]. The variation in the gut microbiota along the different anatomical sections of the Gastro Intestinal (GI) tract is as mentioned:

- Stomach - *Lactobacillaceae*, *Veilonellaceae*, *Helicobacterceae*.
- Small Intestine - *Bacillaceae*, *Streptococcaceae*, *Actinomycinaeae*, *Corynebacteriaceae*, *Veilonellaceae*.
- Large Intestine - *Lachnospiraceae*, *Bacteroidaceae*, *Prevotellaceae*, *Clostridium*, *Lactobacillaceae*, *Enterococcaceae*, *Bacteroidaceae*, *Bifidobacterium*, *Streptococcaceae*, *Enterobacteriaceae*, *Enterococcaceae*, *Clostridium*, *Lactobacillaceae*, *Ruminococcaceae* [52].

The establishment of the gut microbiota starts *in utero* or immediately after the birth and the composition drastically changes to match the adult-like composition as early as 2-3 years of age [58]. However, once established the microbiota tend to be relatively stable over time, but is distinct for different individuals. These differences in microbial composition are attributed to genetic, physiological, and psychological factors. However, each person has a few standard GI microbiota [59].

### 5.1 The functionality of gut microbiota

The gut microbiota offers a large array of benefits to humans. The microbial richness and diversity of a healthy gut microbiota enhance several metabolic pathways, offers resistance to infection and inflammation, retards the growth of the tumour cells, protects against autoimmunity, and improves endocrine signalling and brain functioning [60]. The microbiota potentially carries out these functions by the secretion of factors that influences intestinal permeability, the mucus layer, innate and adaptive immunity and neurotransmission. Likewise, the gut microbiota provides nourishment to the intestine membrane by the generation of Short-Chain Fatty Acids (SCFAs), which plays a vital role in energy production, and epigenetics, and possess anti-inflammatory effects inside the body [59]. Furthermore, the gut microbiota plays a significant role in nutrient and drug metabolism, regulating the strength of the gut mucosal barrier and protecting against invading pathogens [61].

### 5.2 Factors altering the gut microbiota and its impact on human health

The human gut microbiota fluctuates with age, diet and antibiotic exposure. The endogenous microbiota drastically deviates during infancy and old age, when the immune system is unstable, indicating that microbiota holds an important spot in determining the immunity of an individual. For example, the mode of delivery of an infant majorly determines the composition of the microbiota. The vaginally delivered infants acquires mother's vaginal microbiota, while the infant born through C-section acquires the microbiota from the environment and the mother's skin [62]. The microbial composition of an infant delivered through different modes is as mentioned.

- Natural birth - *Lactobacillus*, *Prevotella*, and *Sneathia* [63], *Bifidobacterium longum* and *Bifidobacterium catenulatum* [64], *Escherichia coli*, *Staphylococcus*, *Bacteroides fragilis* and *Streptococcus* [62].
- Birth through C-section - *Staphylococcus*, *Corynebacterium*, *Propionibacterium* spp. [63]. It is noteworthy, that the intestinal microbial diversity of vaginally delivered infants, is much higher than the infant born through C-section procedure [64].

The microbial community of the vaginally delivered infant remains much more stable (up to 2 months) than the infant delivered through the C-section [65]. The manifestation of immune diseases such as asthma, allergy, inflammatory bowel disease, and type 1 diabetes is also observed to be higher in the Cesarean births [66].

It has been observed that the gut microbiota of old age people is quite different in composition when compared to a healthy adult, which could be attributed to the alteration in the lifestyle and dietary patterns, compromised immune system, recurring infections, hospitalization, medication, and reduction in overall functionality [67]. The gut microbiota of the elderly population illustrates a significant decrease in the bacterial diversity involving a drastic shift of dominant species, a steep decline of good microbes and an increase of facultative anaerobes [68]. The short chain fatty acids (SCFAs), primary metabolite of the gut microbial community decrease in the elderly population, which are responsive towards regulating glucose homeostasis, appetite energy intake, neuronal activity and inflammatory response [69]. Similarly, in several metabolic diseases such as obesity, obesity-related disease - Nonalcoholic Fatty Liver Disease (NAFLD), type 2 diabetes [70], cardiovascular diseases [71] as well as in cognitive well-being [72], the SCFAs play a central role. The altered microbial composition in the elderly population has been repeatedly linked with frailty [73].

Diet plays the most crucial role in determining the composition of the gut microbiota. The diet influences the gut microbiota as early as the infant stage. A striking difference is observed in the breastfed and formula-fed infants. *Escherichia coli*, *Bacteroides*, and *Clostridium difficile* largely colonize the gut of formula-fed infants as compared to breastfed infants [74], while breastfed infants comprise a more complex diversity of *Bifidobacterium* as compared to the formula-fed infants [75]. One of the fermentative products of *Bifidobacterium* is SCFAs which impart several health benefits to the infant as discussed above. However, these differences almost coincide during the weaning period. The microbial community predominately comprises of *Bifidobacterium*, *Clostridium coccoides*, and *Bacteroides* after weaning [76]. Likewise, maintaining a healthy gut microbiota during pregnancy could also influence the composition of the milk microbiota and proves to be beneficial for the newborn. Therefore, the procedure of child birth as well as the neonatal dietary patterns play significant role in determining the composition of gut microbiota through the early age of humans.

The gut microbial composition of vegetarians/vegans and omnivores/non-vegetarians also illustrates a prominent difference. Plant-based diet possesses the potential of promoting the colonization of diverse microbial communities which are responsible for regulating BMI, obesity, and arterial stiffness [77]. A plant-based diet demonstrates a higher abundance of *Bacteroidetes* and lower numbers of Firmicutes regulating obesity. An obese person comprises a lower ratio of *Bacteroidetes*:*Firmicutes*. Similarly, *Prevotella*, a genus of *Bacteroidetes* phyla appears to be significantly diverse in the vegan diet. Some of the mice studies suggests links of *Prevotellain* enhancing glucose metabolism by improving glycogen storage in the body [78]. The *Bacteroides* forms one of the major constituents of the gut microbiota of vegetarians/vegans. These *Bacteroides*, ferment the dietary carbohydrates into the volatile fatty acids that are reabsorbed by the host intestine and suffice the daily energy requirements of the host [79]. Long-term consumption of fruits and vegetables seems to have an association with the abundance of *Ruminococcus*, which positively influence the BMI, lowering of the endotoxemia and the arterial stiffness, as well as reduces the risk of cardiovascular diseases [80]. Compared to an omnivorous diet, the vegan diet has a larger amount of dietary fibers which promotes the growth of more beneficial microbes. The higher content of polyphenol in vegan diets increase the abundance of *Bifidobacterium* and *Lactobacillus* which are beneficial for promoting the cardiovascular health and anti-inflammatory response [81].

Antibiotics act as the major destroyer of the healthy gut microbiota, resulting in both long-term and short-term consequences. The intense complexity and interdependency of microbial diversity and host metabolism, play a vital role in maintaining the normal functioning and development of the body, as well as in maturing the adaptive immune response. However, the antibiotic exposure, significantly reduces the gut microbial diversity and richness; thereby, altering the metabolic activities. Overuse of antibiotics promotes the development of the antibiotic-resistant organism (pathogenic species), which could likely cause short-term impacts, such as antibiotic-associated diarrhea and recurring infection of *Clostridioides difficile* [82]. The long-term impact of gut microbiota alteration involves the development of allergic conditions, namely - asthma or food allergies and obesity [83].

Several studies link the early childhood exposure to antibiotics to various gastrointestinal, immunologic and neurocognitive disorders. The renewal of the healthy gut microbiota in children destructed due to antibiotic exposure appears to occur approximately after 1 month [84]. Similarly, in adults, a combined course of meropenem, gentamicin and vancomycin leads to an increase in *Enterobacteriaceae* communities, while significantly reducing the *Bifidobacterium* and butyrate-producing species [85]. The consequences of higher levels of *Enterobacteriaceae* include the dysbiosis associated with Inflammatory Bowel Disease (IBD) pathogenesis and development [86]. Additionally, the reduction in the butyrate-producing species leads to a sharp decrease in the anti-inflammatory activity of the gut [87]. In

adults, the restoration of the normal gut microbiota reverts within 1.5 months [85].

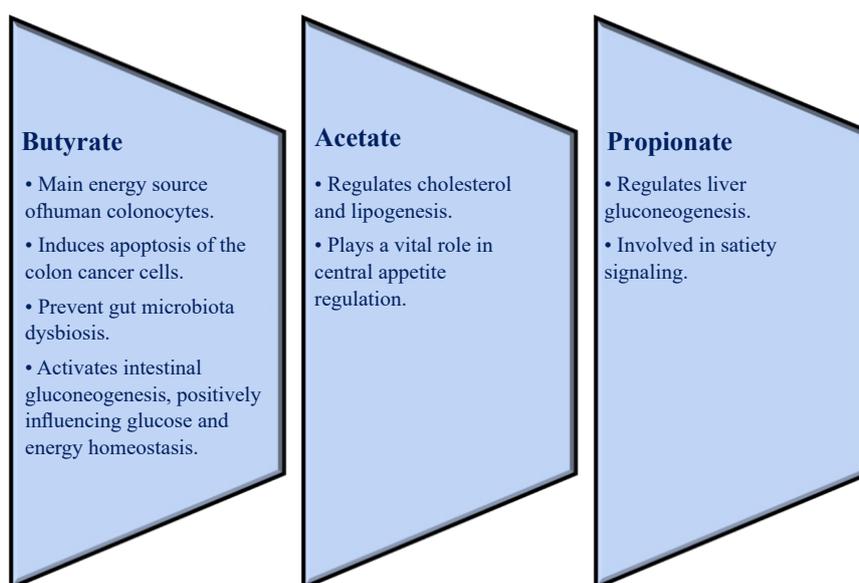
Certain antibiotics such as ampicillin, sulbactam and cefazolin, not only disrupt the gut microbial ecology but also impact the production of strong metabolites such as acetyl phosphate and acetyl-coA, that have several cellular functions [88]. The antibiotic Clindamycin, leads to the active destruction of anaerobic gut microbes, which are crucial in maintaining a healthy gut. Consequently, leading to the pseudomembranous colitis, that manifests into the abdominal pain, tenderness, cramps, diarrhea and other associated symptoms [88].

The reduction of microbial diversity post-antibiotic exposure, not only reduce the number of bacteria but also diminishes its diversity. Thus, with the decrease in the antibiotic susceptible microbes, the resistant microbes flourish. The antibiotic-resistant infections necessitate the utilization of second and third-line treatments which could largely cause side effects such as organ failure which requires a prolonged care and recovery. In conclusion, the synthetic compounds such as antibiotics are detrimental to both, human and the environment health. By altering the endogenous microbial populations, antibiotic resistance affect human health; similarly, overuse of these compounds in food production (livestock, aquaculture) seemingly impact the quality of produce and destroy the biodiversity in the natural environment.

## 6. Gut microbiome promote health by reducing disease manifestation

The global malnutrition is the core challenge associated with human health and well being. The lack of adequate amounts of nutrients is one of the global health issue. Food shortages in poor countries due to war and other socio-political factors affect, populations, particularly children and women who tend to be immobile, and therefore suffer extreme malnutrition. In contrast, the malnourished people in rich countries suffer from ill-nourishment due to high consumption of industrially produced or processed food commodities. The raw materials for industrially produced food, originates in intensive agriculture farms, that demand high inputs of resources including water, land and synthetic fertilizers. The food grown and produced through conventional method is neither sustainable nor healthy, as they are laden with many synthetic compounds, which alter the human-microbiome associations within the body and manifest many metabolic disorders including diabetes and obesity.

The primary microbial metabolites released in human gut are SCFAs such as acetate, butyrate and propionate (Figure 3). Trial studies have demonstrated link between microbial metabolites and the lower incidence of diet-associated obesity.



**Figure 3.** Beneficial roles of small chain fatty acids released by microbial community in the human gut [89]

Most of the studies illustrate dysbiosis and characteristically low microbial diversity in obese individuals [89]. Gut microbiota dysbiosis encourages diet-induced obesity and other related metabolic complication by a variety of mechanisms including immune dysregulation, changed energy regulation, altered gut hormone regulation and pro-inflammatory processes [90]. The administration of beneficial strains of *Lactobacillus*, is linked with the decrease in the amount of weight gained due to the consumption of a high-fat diet, fat accumulation, and metabolic disturbance associated with diet-induced obesity [91]. Similarly, consumption of the fermented milk, rich in *Lactobacillus rhamnosus* NCDC 17, significantly reduce the body weight, epididymal fat mass, fasting blood glucose levels and serum insulin levels in mice fed with a fat-rich diet [92]. Apart from beneficial bacteria, the consumption of yeasts (*Saccharomyces boulardii*), promote healthy gut microbiota such as the *Bacteroidetes* and simultaneously decrease the *Firmicutes*, resulting in a steep decline in host adiposity and circulating inflammatory markers [93].

The gut microbial enzymes also have interesting roles during the bile acid metabolism such as, producing unconjugated and secondary bile acids that serve as signalling molecules and metabolic controllers of the important host pathways [94]. Besides producing SCFAs, the gut microbial community appears to control the Lipopolysaccharide (LPS) levels which are involved in the development of diabetes [95]. The intake of dietary fibres increase the diversity and stability of gut microbiota, which generate more SCFAs. These SCFAs regulate the mechanism of glucose homeostasis, and are therefore crucial for preventing the diabetes in host [96]. Similarly, intake of high-fibre food, increases the abundance of *Bacteroidetes*, *Actinobacteria*, and decreases the *Firmicutes: Bacteroidetes* ratios, which are be responsible for SCFAs production, and regulation of gene expression related to the glycan and lipids metabolism [97].

Furthermore, a low-fat diet has been associated with the expanded numbers of *Bacteroidetes* and low numbers of *Firmicutes*, which prevents the development of Insulin resistance and type 2 diabetes. Increased in the abundance of *Bifidobacteria* and *Bacteroidetes* improve glucose tolerance, stimulate the secretion of GLP-1 (Glycogen-like peptide) from L-cells and reduce the low-grade inflammation and oxidative stress [97].

The high abundance of *Bifidobacterium* spp. in humans resulted in improved glucose tolerance, enhanced mucosal membrane function and normalized inflammatory tone associated with diabetes. Thus, diet and gut microbiota plays significant roles in the prevention of the chronic diseases such as diabetes [98].

Apart from metabolic disorders, the microbes also influence the hypersensitive immune responses such as allergies. Allergies occur when the host immune system reacts to a foreign substance, such as pollen, molds, animal dander, insect venoms and certain foods. Most food allergies are associated with the composition of gut microbiota which is established during the infancy. The early colonization of healthy gut microbiota in new born translates to a lower risk of developing allergies in later years of life. The higher gut richness and lower ratio of *Enterobacteriaceae* to *Bacteroidaceae* ratio (at 3 months) is associated with the low to negligible food sensitization at age one and vice versa [99]. A substantial increase in *Leuconostocaceae* families and a decrease in *Streptococcaceae*, *Lachnospiraceae* genera, occurred in non-egg-allergic children as compared to egg-allergic children, characterized by intestinal dysbiosis [99]. Similarly, the milk-allergic children had a higher abundance of *Lachnospiraceae* and *Ruminococcaceae*. Thus the gut microbiota varies largely among the allergic and non-allergic populations and is associated with allergic responses.

In addition to the physical health, the healthy gut microbiota is also linked to healthy mental health and normal functioning of the central nervous system. The gut microbiota releases several hormones, neurotransmitters and immunological factors, which are involved in signals to transmission the brain. Recently, there has been an exponential rise in the studies recognizing the part of the Brain-Gut-Microbiota axis (BGM axis) in the stages of neurodevelopment. The intestinal microbiota plays a significant role in neurodevelopment and was effectively studied by performing experiments on germ-free mice. The experiment on germ-free mice illustrated an increase in exploration activity and a decrease in the levels of anxiety in mice with healthy guts [59].

Another method illustrating the role of gut microbiota in brain development involves the colonization of an expecting GF mouse with a strain of a specific bacterium and observing the development of the nervous system of the infant. Through the use of this model, pregnant GF mice were colonized with an infant's microbiota which showed poor growth. The decrease in the expression of neuronal nuclei (marker for neuronal structure development) showed in this study indicate uneven development of the nervous system [100].

A recent research [101] illustrated the association of gut microbiota with COVID-19 disease manifestation. The gut microbiota appears to be significantly altered in the COVID-19 patient, as compared to COVID-19 negative patients. Various gut microbial communities known for immunomodulatory potentials such as *Faecalibacterium prausnitzii*,

*Eubacterium rectale* and *bifidobacterial* were in decreased abundance in the COVID-19 patients. This altered composition demonstrate a link with disease severity, with respect to elevated concentrations of inflammatory cytokines and blood markers [101]. Furthermore, the gut microbial dysbiosis post-COVID-19 infections, could form persistent symptoms, representing the need to further understand the role of gut microbiota, and gut microbial modulation during the inflammation and COVID-19 infections.

## 7. Sustainable and alternative foods to attain better health

The sustainable nutrition security will continue to be a pressing national issue for low-income countries. For instance, in India where more than 70% of population is protein deficient due to their dietary habits and religious choices, it is necessary to develop the alternate and non-conventional protein sources. This is particularly important during the pandemic times for the urban populations, where sedentary lifestyles and new norms on ‘work from home’ are impacting their muscle health. Another alarming reason, that global population will be deficient in protein and other minerals, is the alarming increase in atmospheric CO<sub>2</sub> and global warming. These are influencing both macro and micro-level climatic changes across the living planet which have severe direct and indirect consequences on our health and immune response to various ongoing and upcoming pandemic diseases. As the deficiencies of various micronutrients such as iron, vitamin A, iodine and Zn inflict global populations due to poor and constricted diets [102]. The elevated CO<sub>2</sub> levels will further reduce the content of proteins and several minerals such as zinc (Zn) and iron (Fe) in the foliar and edible tissues of the major cereal crops [103]. Under the future climate change scenerios, the growing need for climate proof and nutritional alternatives to the conventional food is not only relevant but has become a necessity.

Microorganisms including algae and fungi provide various forms of nutrients and health promoting benefits in the form of single-cell proteins. These do not rely on arable land; can be grown indoors, both autotrophically and heterotrophically and in saline waters. Their rich abundance and diversity, for example conservative estimate of the total number of fungal species residing on the planet comes approximately near to 1.5 million [104] is useful and renewable natural resource which must be tapped. Although in the form of molds, certain types of fungi do harm the food and agriculture sector and could cause several infectious diseases in humans and animals; these heterotrophic microbes have several health benefits (Figure 4) which need to be considered.

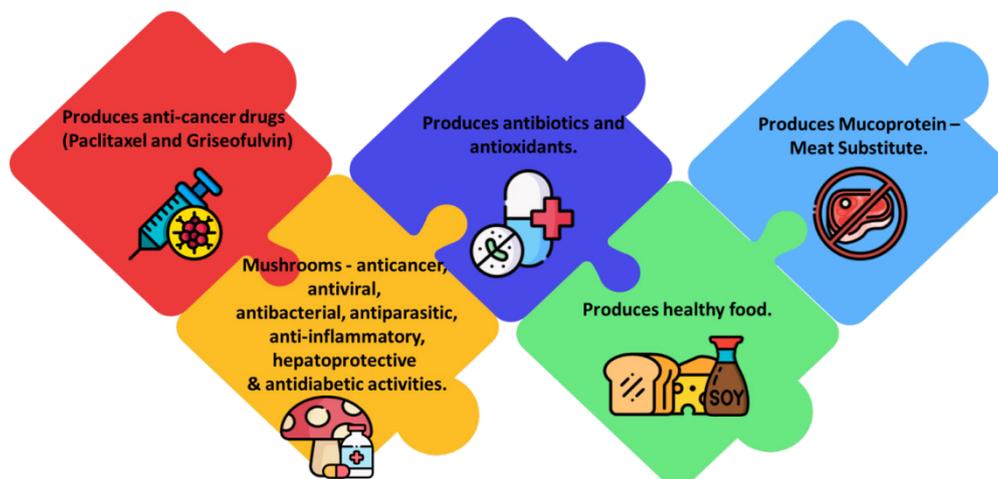


Figure 4. Health benefits of Fungi (Illustration by author after [105] and [106])

Another unconventional and sustainable dietary protein source is algae, which provide omega fatty acids, vitamins, anti-oxidants and various other bio active compounds. Apart from the nutritional benefits, compounds sourced from alga have therapeutic properties as well. The bioactive secondary metabolites derived from algae such as cyanobacteria

(Spirulina) can activate our immune response and alleviate RNA virus induced oxidative stress [107]. Spirulina derived nutraceuticals have been well explored in clinical studies and reported to boost our innate and adaptive immunity; therefore, it can act as potential therapeutic against the deadly viral infections including the COVID-19 [108].

Algae had been an integral part of complementary food solutions for the humans. Microalgae species namely *Spirulina*, *Chlorella*, *Dunaliella*, *Haematococcus*, *Schizochytrium*, *Porphyridium cruentum*, *Phaeodactylum tricornutum* and *Cryptocodinium cohnii* are useful source of protein, omega-3 fatty acids, vitamins and antioxidant compounds. These have been categorized as 'Generally Regarded as Safe' (GRAS) species and have been exploited as novel and functional foods in the global market. The Chlorella whole microalgal protein has also got approval from the Food and Drug Administration (FDA). These microbial options offer climate proof, less resource intensive and sustainable nutrition source for the growing malnourished populations worldwide, without compromising the environmental integrity; and therefore, within the safe planetary boundaries.

## 8. Conclusions

The world is facing acute food shortages and the planet is running out of the freshwater due to melting of glaciers and intrusions of sea water into the inland freshwater aquifers. Food insecurity is interconnected with other phenomena such as high calories uptake, nutrient deficiencies, inequity in distribution, food wastage, poverty, loss of biodiversity, crossing planetary boundaries and capitalism. To attain food security, it must be produced in sustainable manner which should protect both humans and natural resources from deficiencies and depletion. As nutrition is fundamental right for all living creatures, the production of food for humans should not completely rely on the use of toxic fertilizers which is the leading cause of destruction of both soil and water by impacting its biodiversity which is another planetary boundary that is being transgressed. Climate crises and conflicts have aggravated the food crisis globally as its production is dependent on fossil fuels. Strategically, the world is living in the era of socio-political conflicts which further is an important threat to the global food security particularly in the poor and developing nations where the hunger and malnutrition is an existing issue. Anthropogenic exploitation of environmental resources is reaching beyond the limits of Earth's carrying capacity and we have already overstepped some planetary boundaries namely biogeochemical flows for nitrogen and phosphorous, lost natural genetic diversity, land-system change and climate change (including ocean acidification) which have caused unacceptable environment consequences. Microorganisms are the greatest renewable resources which perform numerous ecological functions including conversion of wastewater into biorefinery, decontamination of hazardous wastes and positively impacting crop yields. Being the progenitors of life on our planet, microorganisms are irreplaceable and are indispensable for sustenance of future lives on Earth.

## Conflicts of interest

The authors declare they have no competing interests.

## References

- [1] Alewell C, Ringeval B, Ballabio C, Robinson DA, Panagos P, Borrelli P. Global phosphorus shortage will be aggravated by soil erosion. *Nature Communications*. 2020; 11(1): 4546.
- [2] Nedelciu CE, Ragnarsdottir KV, Schlyter P, Stjernquist I. Global phosphorus supply chain dynamics: Assessing regional impact to 2050. *Global Food Security*. 2020; 26: 100426.
- [3] Steffen W, Richardson K, Rockström J, Cornell SE, Fetzer I, Bennett EM, et al. Planetary boundaries: Guiding human development on a changing planet. *Science*. 2015; 347(6223): 1259855.
- [4] Hák T, Janoušková S, Moldan B. Sustainable development goals: A need for relevant indicators. *Ecological Indicators*. 2016; 60: 565-573.
- [5] Blanc DL. Towards integration at last? The sustainable development goals as a network of targets. *Sustainable Development*. 2015; 23(3): 176-187.

- [6] Swain RB. A Critical analysis of the sustainable development goals. In: Leal Filho W (ed.) *Handbook of Sustainability Science and Research*. Cham: Springer International Publishing; 2018. p. 341-355. Available from: doi: 10.1007/978-3-319-63007-6\_20.
- [7] Meadows D, Meadows D, Randers J, Behrens IIIW. *The Limits to Growth*. New York: Universe Books; 1972.
- [8] O'Neill DW, Fanning AL, Lamb WF, Steinberger JK. A good life for all within planetary boundaries. *Nature Sustainability*. 2018; 1(2): 88-95.
- [9] Wijkman A, Rockström J. *Bankrupting Nature: Denying Our Planetary Boundaries*. 2012. Available from: doi: 10.4324/9780203107980.
- [10] Dastagir MR. Role of microorganisms in managing climate change impacts. *Microbial Interventions in Agriculture and Environment*. 2019; 3: 1-16. Available from: doi: 10.1007/978-981-32-9084-6\_1.
- [11] Dobrovol'skaya TG, Zvyagintsev DG, Chernov IYu, Golovchenko AV, Zenova GM, Lysak LV, et al. The role of microorganisms in the ecological functions of soils. *Eurasian Soil Science*. 2015; 48(9): 959-967.
- [12] Malaviya P, Sharma R, Sharma S, Pant D. *Role of Microorganisms in Environmental Remediation and Resource Recovery through Microbe-Based Technologies Having Major Potentials*. John Wiley & Sons Ltd.; 2022. p. 247-264. Available from: doi: 10.1002/9781119762621.ch20.
- [13] Grover M, Ali SkZ, Sandhya V, Rasul A, Venkateswarlu B. Role of microorganisms in adaptation of agriculture crops to abiotic stresses. *World Journal of Microbiology and Biotechnology*. 2011; 27(5): 1231-1240.
- [14] Gholamhosseinian A, Sepehr A, Asgari Lajayer B, Delangiz N, Astatkie T. Biological soil crusts to keep soil alive, rehabilitate degraded soil, and develop soil habitats. In: *Microbial Polymers*. Singapore: Springer; 2021. p. 289-309. Available from: doi: 10.1007/978-981-16-0045-6\_13.
- [15] Schulz S, Brankatschk R, Dümig A, Kögel-Knabner I, Schloter M, Zeyer J. The role of microorganisms at different stages of ecosystem development for soil formation. *Biogeosciences*. 2013; 10(6): 3983-3996.
- [16] Kaviya N, Upadhayay VK, Singh J, Khan A, Panwar M, Singh AV. Role of microorganisms in soil genesis and functions. In: Varma A, Choudhary D. (eds.) *Mycorrhizosphere and Pedogenesis*. Singapore: Springer; 2019. p. 25-52. Available from: doi: 10.1007/978-981-13-6480-8\_2.
- [17] Prakash O, Sharma R, Rahi P, Karthikeyan N. Role of microorganisms in plant nutrition and health. In: Rakshit A, Singh HB, Sen A. (eds.) *Nutrient Use Efficiency: from Basics to Advances*. New Delhi: Springer India; 2015. p. 125-161. Available from: doi: 10.1007/978-81-322-2169-2\_9.
- [18] Suyamud B, Ferrier J, Csetenyi L, Inthorn D, Gadd GM. Biotransformation of struvite by *Aspergillus niger*: phosphate release and magnesium biomineralization as glushinskite. *Environmental Microbiology*. 2020; 22(4): 1588-1602.
- [19] Qian T, Lu D, Soh YNA, Webster RD, Zhou Y. Biotransformation of phosphorus in enhanced biological phosphorus removal sludge biochar. *Water Research*. 2020; 169: 115255.
- [20] Teodosieva R, Bojinova D, Nedialkova K. Rock phosphate solubilization by soil bacteria. *Journal of the University of Chemical Technology and Metallurgy*. 2006; 41: 297-302.
- [21] Liu X, Chen C, Wang J, Zou S, Long X. Phosphorus solubilizing bacteria *Bacillus thuringiensis* and *Pantoea ananatis* simultaneously promote soil inorganic phosphate dissolution and soil Pb immobilization. *Rhizosphere*. 2021; 20: 100448.
- [22] Lai W, Wu Y, Zhang C, Dilinuer Y, Pasang L, Lu Y, et al. Combination of biochar and phosphorus solubilizing bacteria to improve the stable form of toxic metal minerals and microbial abundance in lead/cadmium-contaminated soil. *Agronomy*. 2022; 12(5): 1003.
- [23] Lewis M, Kim MH, Liu EJ, Wang N, Chu KH. Biotransformation of 6:2 polyfluoroalkyl phosphates (6:2 PAPs): Effects of degradative bacteria and co-substrates. *Journal of Hazardous Materials*. 2016; 320: 479-486.
- [24] Feng M, Zhou J, Yu X, Mao W, Guo Y, Wang H. Insights into biodegradation mechanisms of triphenyl phosphate by a novel fungal isolate and its potential in bioremediation of contaminated river sediment. *Journal of Hazardous Materials*. 2022; 424: 127545.
- [25] Kopittke PM, Menzies NW, Dalal RC, McKenna BA, Husted S, Wang P, et al. The role of soil in defining planetary boundaries and the safe operating space for humanity. *Environment International*. 2021; 146: 106245.
- [26] Emami S, Alikhani HA, Pourbabaee AA, Etesami H, Motasharezadeh B, Sarmadian F. Consortium of endophyte and rhizosphere phosphate solubilizing bacteria improves phosphorous use efficiency in wheat cultivars in phosphorus deficient soils. *Rhizosphere*. 2020; 14: 100196.
- [27] Singh H, Reddy MS. Effect of inoculation with phosphate solubilizing fungus on growth and nutrient uptake of wheat and maize plants fertilized with rock phosphate in alkaline soils. *European Journal of Soil Biology*. 2011; 47(1): 30-34.

- [28] Duarte N de F, Oliveira Paiva CA, Pagano MC, Correa EJA. Chapter 15-Phosphate solubilization by microorganisms. *New and Future Developments in Microbial Biotechnology and Bioengineering*. 2022; 257-282. Available from: doi: 10.1016/B978-0-323-85163-3.00019-3.
- [29] Rosas SB, Andrés JA, Rovera M, Correa NS. Phosphate-solubilizing *Pseudomonas putida* can influence the rhizobia-legume symbiosis. *Soil Biology and Biochemistry*. 2006; 38(12): 3502-3505.
- [30] Zhang S, Wang L, Ma F, Zhang X, Fu D. Arbuscular mycorrhiza improved phosphorus efficiency in paddy fields. *Ecological Engineering*. 2016; 95: 64-72.
- [31] Tian J, Ge F, Zhang D, Deng S, Liu X. Roles of phosphate solubilizing microorganisms from managing soil phosphorus deficiency to mediating biogeochemical P cycle. *Biology*. 2021; 10(2): 158.
- [32] Carpenter SR, Bennett EM. Reconsideration of the planetary boundary for phosphorus. *Environmental Research Letters*. 2011; 6(1): 014009.
- [33] Li Y, Wang L, Yan Z, Chao C, Yu H, Yu D, et al. Effectiveness of dredging on internal phosphorus loading in a typical aquacultural lake. *Science of The Total Environment*. 2020; 744: 140883.
- [34] Haxthausen KA, Lu X, Zhang Y, Gosewinkel U, Petersen DG, Marzocchi U, et al. Novel method to immobilize phosphate in lakes using sediment microbial fuel cells. *Water Research*. 2021; 198: 117108.
- [35] Ren Z, He J, Cheng Q, Ding S, Liu W, Duan P, et al. Climate change prior to human activity reduces the immobility of phosphorus in eutrophic alpine lake. *Journal of Cleaner Production*. 2022; 335: 130364.
- [36] Harseim L, Sprecher B, Zengerling C. Phosphorus governance within planetary boundaries: The potential of strategic local resource planning in the hague and delfland, the Netherlands. *Sustainability*. 2021; 13(19): 10801.
- [37] Jarvie HP, Sharpley AN, Flaten D, Kleinman PJA, Jenkins A, Simmons T. The pivotal role of phosphorus in a resilient water-energy-food security nexus. *Journal of Environmental Quality*. 2015; 44(4): 1049-1062.
- [38] Cakmak EK, Hartl M, Kisser J, Cetecioglu Z. Phosphorus mining from eutrophic marine environment towards a blue economy: The role of bio-based applications. *Water Research*. 2022; 219: 118505.
- [39] Kiani M, Tammeorg P, Niemistö J, Simojoki A, Tammeorg O. Internal phosphorus loading in a small shallow Lake: Response after sediment removal. *Science of The Total Environment*. 2020; 725: 138279.
- [40] Chu W, Shi Y, Zhang L. Recovery of phosphorus in wastewater in the form of polyphosphates: A review. *Processes*. 2022; 10(1): 144.
- [41] He S, McMahon KD. Microbiology of 'Candidatus Accumulibacter' in activated sludge. *Microbial Biotechnology*. 2011; 4(5): 603-619.
- [42] Stokholm-Bjerregaard M, McIlroy SJ, Nierychlo M, Karst SM, Albertsen M, Nielsen PH. A critical assessment of the microorganisms proposed to be important to enhanced biological phosphorus removal in full-scale wastewater treatment systems. *Frontiers in Microbiology*. 2017; 8. Available from: doi: 10.3389/fmicb.2017.00718.
- [43] Zhang C, Guisasola A, Baeza JA. A review on the integration of mainstream P-recovery strategies with enhanced biological phosphorus removal. *Water Research*. 2022; 212: 118102.
- [44] Semerci N, Kunt B, Calli B. Phosphorus recovery from sewage sludge ash with bioleaching and electro dialysis. *International Biodeterioration & Biodegradation*. 2019; 144: 104739.
- [45] Quijano G, Arcila JS, Buitrón G. Microalgal-bacterial aggregates: Applications and perspectives for wastewater treatment. *Biotechnology Advances*. 2017; 35(6): 772-781.
- [46] Fernandes TV, Suárez-Muñoz M, Trebuch LM, Verbraak PJ, Van de Waal DB. Toward an ecologically optimized N:P recovery from wastewater by microalgae. *Frontiers in Microbiology*. 2017; 8: 1742. Available from: doi: 10.3389/fmicb.2017.01742.
- [47] Singh D, Nedbal L, Ebenhöf O. Modelling phosphorus uptake in microalgae. *Biochemical Society Transactions*. 2018; 46(2): 483-490.
- [48] Chu Q, Lyu T, Xue L, Yang L, Feng Y, Sha Z, et al. Hydrothermal carbonization of microalgae for phosphorus recycling from wastewater to crop-soil systems as slow-release fertilizers. *Journal of Cleaner Production*. 2021; 283: 124627.
- [49] Kusch-Brandt S, Alsheyab MAT. Wastewater refinery: Producing multiple valuable outputs from wastewater. *J*. 2021; 4(1): 51-61.
- [50] Sajad Hashemi S, Karimi K, Taherzadeh MJ. Integrated process for protein, pigments, and biogas production from baker's yeast wastewater using filamentous fungi. *Bioresource Technology*. 2021; 337: 125356.
- [51] Delrue F, Álvarez-Díaz PD, Fon-Sing S, Fleury G, Sassi JF. The environmental biorefinery: Using microalgae to remediate wastewater, a win-win paradigm. *Energies*. 2016; 9(3): 132.
- [52] Kovatcheva-Datchary P, Tremaroli V, Bäckhed F. The gut microbiota. In: *The Prokaryotes*. 2013. p. 3-24.
- [53] Ursell LK, Metcalf JL, Parfrey LW, Knight R. Defining the human microbiome. *Nutrition Reviews*. 2012; 70(Suppl

1): S38-44.

- [54] Drasar B, Hill M. The metabolic activities of the gut bacteria. *Human Intestinal Flora*. 1974; 26-35.
- [55] Bianconi E, Piovesan A, Facchin F, Beraudi A, Casadei R, Frabetti F, et al. An estimation of the number of cells in the human body. *Annals of Human Biology*. 2013; 40(6): 463-471.
- [56] Conrad R, Vlassov A. The human microbiota: Composition, functions, and therapeutic potential. *Medical Science Review*. 2015; 2: 92-103.
- [57] MacDougall R. NIH Human Microbiome Project defines normal bacterial makeup of the body. *National Institutes of Health*. 2012.
- [58] Akagawa S, Akagawa Y, Yamanouchi S, Kimata T, Tsuji S, Kaneko K. Development of the gut microbiota and dysbiosis in children. *Bioscience of Microbiota Food and Health*. 2021; 40(1): 12-18.
- [59] Sayyed RZ, Khan M. *Microbiome-Gut-Brain Axis: Implications on Health*. Singapore: Springer Nature Singapore; 2022.
- [60] Hollister EB, Gao C, Versalovic J. Compositional and functional features of the gastrointestinal microbiome and their effects on human health. *Gastroenterology*. 2014; 146(6): 1449-1458.
- [61] Jandhyala SM, Talukdar R, Subramanyam C, Vuyyuru H, Sasikala M, Reddy DN. Role of the normal gut microbiota. *World Journal of Gastroenterology*. 2015; 21(29): 8787-8803.
- [62] Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GAD, Gasbarrini A, et al. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. *Microorganisms*. 2019; 7(1): 14.
- [63] Dominguez-Bello MG, Costello EK, Contreras M, Magris M, Hidalgo G, Fierer N, et al. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proceedings of the National Academy of Sciences*. 2010; 107(26): 11971-11975.
- [64] Biasucci G, Benenati B, Morelli L, Bessi E, Boehm G. Cesarean delivery may affect the early biodiversity of intestinal bacteria. *Journal of Nutrition*. 2008; 138(9): 1796S-1800S.
- [65] Reyman M, van Houten MA, van Baarle D, Bosch AATM, Man WH, Chu MLJN, et al. Impact of delivery mode-associated gut microbiota dynamics on health in the first year of life. *Nature Communications*. 2019; 10(1): 4997.
- [66] Sevelsted A, Stokholm J, Bønnelykke K, Bisgaard H. Cesarean section and chronic immune disorders. *Pediatrics*. 2015; 135(1): e92-e98.
- [67] Nagpal R, Mainali R, Ahmadi S, Wang S, Singh R, Kavanagh K, et al. Gut microbiome and aging: Physiological and mechanistic insights. *Nutrition and Healthy Aging*. 2018; 4(4): 267-285.
- [68] Salazar N, Valdés-Varela L, González S, Gueimonde M, de los Reyes-Gavilán CG. Nutrition and the gut microbiome in the elderly. *Gut Microbes*. 2016; 8(2): 82-97.
- [69] Morrison DJ, Preston T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes*. 2016; 7(3): 189-200.
- [70] Canfora EE, Meex RCR, Venema K, Blaak EE. Gut microbial metabolites in obesity, NAFLD and T2DM. *Nature Reviews Endocrinology*. 2019; 15(5): 261-273.
- [71] Chambers ES, Preston T, Frost G, Morrison DJ. Role of gut microbiota-generated short-chain fatty acids in metabolic and cardiovascular health. *Current Nutrition Reports*. 2018; 7(4): 198-206.
- [72] Dalile B, Van Oudenhove L, Vervliet B, Verbeke K. The role of short-chain fatty acids in microbiota-gut-brain communication. *Nature Reviews Gastroenterology Hepatology*. 2019; 16(8): 461-478.
- [73] Claesson MJ, Jeffery IB, Conde S, Power SE, O'Connor EM, Cusack S, et al. Gut microbiota composition correlates with diet and health in the elderly. *Nature*. 2012; 488(7410): 178-184.
- [74] Penders J, Thijs C, Vink C, Stelma FF, Snijders B, Kummeling I, et al. Factors influencing the composition of the intestinal microbiota in early infancy. *Pediatrics*. 2006; 118(2): 511-521.
- [75] Roger LC, Costabile A, Holland DT, Hoyles L, McCartney AL. Examination of faecal Bifidobacterium populations in breast- and formula-fed infants during the first 18 months of life. *Microbiology*. 2010; 156(11): 3329-3341.
- [76] Fallani M, Amarri S, Uusijarvi A, Adam R, Khanna S, Aguilera M, et al. Determinants of the human infant intestinal microbiota after the introduction of first complementary foods in infant samples from five European centres. *Microbiology*. 2011; 157(5): 1385-1392.
- [77] Tomova A, Bukovsky I, Rembert E, Yonas W, Alwarith J, Barnard ND, et al. The effects of vegetarian and vegan diets on gut microbiota. *Frontiers in Nutrition*. 2019; 6: 47.
- [78] Kovatcheva-Datchary P, Nilsson A, Akrami R, Lee YS, De Vadder F, Arora T, et al. Dietary Fiber-Induced Improvement in Glucose Metabolism Is Associated with Increased Abundance of Prevotella. *Cell Metabolism*. 2015; 22(6): 971-982.

- [79] Lora H, Midtvedt T, Gordon J. How host-microbial interactions shape the nutrient environment of the mammalian intestine. *Annual Review of Nutrition*. 2002; 22(1): 283-307.
- [80] Menni C, Lin C, Cecelja M, Mangino M, Matey-Hernandez ML, Keehn L, et al. Gut microbial diversity is associated with lower arterial stiffness in women. *European Heart Journal*. 2018; 39(25): 2390-2397.
- [81] Losno EA, Sieferle K, Perez-Cueto FJA, Ritz C. Vegan diet and the gut microbiota composition in healthy adults. *Nutrients*. 2021; 13(7): 2402.
- [82] Ramirez J, Guarner F, Bustos FL, Maruy A, Sdepanian VL, Cohen H. Antibiotics as major disruptors of gut microbiota. *Frontiers in Cellular and Infection Microbiology*. 2020; 10: 572912.
- [83] Konstantinidis T, Tsigalou C, Karvelas A, Stavropoulou E, Voidarou C, Bezirtzoglou E. Effects of antibiotics upon the gut microbiome: A review of the literature. *Biomedicines*. 2020; 8(11): 502.
- [84] Yassour M, Vatanen T, Siljander H, Hämäläinen AM, Härkönen T, Ryhänen SJ, et al. Natural history of the infant gut microbiome and impact of antibiotic treatment on bacterial strain diversity and stability. *Science Translational Medicine*. 2016; 8(343): 343ra81. Available from: doi: 10.1126/scitranslmed.aad0917.
- [85] Palleja A, Mikkelsen KH, Forslund SK, Kashani A, Allin KH, Nielsen T, et al. Recovery of gut microbiota of healthy adults following antibiotic exposure. *Nature Microbiology*. 2018; 3(11): 1255-1265.
- [86] Baldelli V, Scaldaferrì F, Putignani L, Del Chierico F. The role of enterobacteriaceae in gut microbiota dysbiosis in inflammatory bowel diseases. *Microorganisms*. 2021; 9(4): 697.
- [87] Takahashi K, Nishida A, Fujimoto T, Fujii M, Shioya M, Imaeda H, et al. Reduced abundance of butyrate-producing bacteria species in the fecal microbial community in crohn's disease. *Digestion*. 2016; 93(1): 59-65.
- [88] Yang L, Bajinka O, Jarju PO, Tan Y, Taal AM, Ozdemir G. The varying effects of antibiotics on gut microbiota. *AMB Express*. 2021; 11(1): 116.
- [89] Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. *BMJ*. 2018; 361: k2179.
- [90] Baothman OA, Zamzami MA, Taher I, Abubaker J, Abu-Farha M. The role of gut microbiota in the development of obesity and diabetes. *Lipids in Health and Disease*. 2016; 15(1): 108.
- [91] Yoo SR, Kim YJ, Park DY, Jung UJ, Jeon SM, Ahn YT, et al. Probiotics *L. plantarum* and *L. curvatus* in combination alter hepatic lipid metabolism and suppress diet-induced obesity. *Obesity*. 2013; 21(12): 2571-2578.
- [92] Pothuraju R, Sharma RK, Chagalamarri J, Kavadi PK, Jangra S. Influence of milk fermented with *Lactobacillus rhamnosus* NCDC 17 alone and in combination with herbal ingredients on diet induced adiposity and related gene expression in C57BL/6J mice. *Food & Function*. 2015; 6(11): 3576-3584.
- [93] Davis CD. The gut microbiome and its role in obesity. *Nutr Today*. 2016; 51(4): 167-174.
- [94] Long SL, Gahan CGM, Joyce SA. Interactions between gut bacteria and bile in health and disease. *Molecular Aspects of Medicine*. 2017; 56: 54-65.
- [95] Cani PD, Delzenne NM. The role of the gut microbiota in energy metabolism and metabolic disease. *Current Pharmaceutical Design*. 2009; 15(13): 1546-1558.
- [96] Gholizadeh P, Mahallei M, Pormohammad A, Varshochi M, Ganbarov K, Zeinalzadeh E, et al. Microbial balance in the intestinal microbiota and its association with diabetes, obesity and allergic disease. *Microbial Pathogenesis*. 2019; 127: 48-55.
- [97] Sharma BR, Jaiswal S, Ravindra PV. Modulation of gut microbiota by bioactive compounds for prevention and management of type 2 diabetes. *Biomedicine & Pharmacotherapy*. 2022; 152: 113148.
- [98] Wu X, Ma C, Han L, Nawaz M, Gao F, Zhang X, et al. Molecular characterisation of the faecal microbiota in patients with type II diabetes. *Current Microbiology*. 2010; 61(1): 69-78.
- [99] Han P, Gu JQ, Li LS, Wang XY, Wang HT, Wang Y, et al. The association between intestinal bacteria and allergic diseases-cause or consequence? *Frontiers in Cellular and Infection Microbiology*. 2021; 11: 650893.
- [100] Lu J, Claud EC. Connection between gut microbiome and brain development in preterm infants. *Developmental Psychobiology*. 2019; 61(5): 739-751.
- [101] Yeoh YK, Zuo T, Lui GCY, Zhang F, Liu Q, Li AY, et al. Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19. *Gut*. 2021; 70(4): 698-706.
- [102] Müller O, Krawinkel M. Malnutrition and health in developing countries. *Canadian Medical Association Journal*. 2005; 173(3): 279-286.
- [103] Courtney P. Leisner. Review: Climate change impacts on food security- focus on perennial cropping systems and nutritional value. *Plant Science*. 2020; 293: 110412.
- [104] Hawksworth DL. The magnitude of fungal diversity: the 1.5 million species estimate revisited. *Mycological Research*. 2001; 105(12): 1422-1432.

- [105]Mohmand AQK, Kousar MW, Zafar H, Bukhari KT, Khan MZ. Medical importance of fungi with special emphasis on mushrooms. *Isra Medical Journal*. 2011; 3(1): 7.
- [106]Ślusarczyk J, Adamska E, Czerwik-Marcinkowska J. Fungi and algae as sources of medicinal and other biologically active compounds: A review. *Nutrients*. 2021; 13(9): 3178.
- [107]McCarty MF, DiNicolantonio JJ. Nutraceuticals have potential for boosting the type 1 interferon response to RNA viruses including influenza and coronavirus. *Progress in Cardiovascular Diseases*. 2020; 63(3): 383-385.
- [108]Ratha SK, Renuka N, Rawat I, Bux F. Prospective options of algae-derived nutraceuticals as supplements to combat COVID-19 and human coronavirus diseases. *Nutrition*. 2021; 83: 111089.