Review Article

Bacteria: Salubrious Microbes

Mousumi Dutta*, Partha Sarathi Singha, Tushar Baran Mahata, Debarpita Bhattacharya, Amit Kumar Jana
Goverment General Degree College, Kharagpur-II, Ambegeria, Madpur, Paschim Medinipur- 721149, West Bengal, India.
***Corresponding author's E-mail:** duttamousumi10@gmail.com

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ABSTRACT

Bacteria are the most abundant form of life on the planet. They are found in most every environment, from Antarctic ice, to boiling hydrothermal vents, to inside your stomach. Most of these do not hurt us. Actually, many of these organisms are very important to our survival. Bacteria have lived in and on animals—constituting their microbiome—since multicellular life evolved about 1 billion years ago. Hosts derive many benefits from their bacterial guests. Bacteria have a bad reputation of causing disease but not all of them are bad, infact most of them do not cause any harm and are absolutely essential for life. It may be hard to believe but we actually harbour 100 trillion bacteria, most of which are found in the intestine. They are called Intestinal flora and weigh about 1.5-2 kg (as much as the liver). Scientists call them the "Forgotten Organ" because they influence our life, safeguard our health and shape our bodies. Besides, bad effects there are lots of beneficial utilities of bacteria for the society. And, the main focus of this review is to enlighten the beneficial utilities of bacteria as a whole.

Keywords: Bacteria, Beneficial effect, Harmful effect.

INTRODUCTION

In the 19th century, the Germ Theory was proposed by Louis Pasteur and Robert Koch where it was said that diseases were caused by germs. In 2001, first the term "gut microbiome" was coined by Joshua Lederburg. In time, this work is expected to shed new light a wide range of health conditions. Bacteria don't have proper nucleus within the cell but they have a systemic genetic material in the cell. They can exist everywhere in the environment.[1]

Beneficial effects of bacteria was explored first after the discovery of the two bacteria *Agrobacterium tumifaciens* and *Thermus aquatricus* which have causes a phase change in the research domain of molecular biology and biotechnology i.e. development of crown gall tumar and DNA amplification in PCR.[2] Eventually antiboitic discovery was the another impetus exploring the profuse role of bacteria in the field of research.

In this review the main objective is to unveil into the various beneficiary sides of the bacteria and its potential application in the field of research.

Decomposition of the dead matters/organic compounds

The nature continuously is getting rid of the dead matter through the decomposition by bacteria. The organic compounds are trapped in the dead matter are being recycled by bacteria because they use them as a source of nutrients. Normally other organisms can easily use these simpler forms of organic compounds/nutrients released from the dead matter by various bacteria.[3]

Nitrogen Fixation for availability to Plants

Atmospheric nitrogen is being converted to nitrates and nitrites by various bacterial species such as *Rhizobium sp.* and *Cyanobacteria sp.* via the process of nitrogen fixation, as a part of their metabolism.[4] This process makes the environmental nitrogen available to the plants. The bacteria live in the roots of some plants (leguminous plants) in the form of mutualistic association and become beneficial to the plant kingdom (Fig 1).[5]

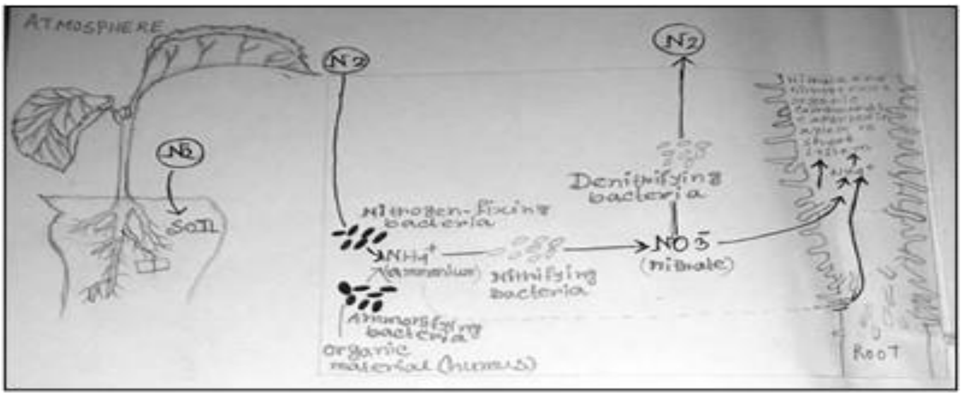

Figure 1: Schematic diagram of the process of nitrogen fixation.

Bioremediation

Bioremediation refers to the process of depletion/degradation of toxic compounds present in the natural environment by living organisms. Bacteria are one of the key players in Bioremediation.[6] For example, oil spills due to oil digging operations or accidents on oil transport channels in the ocean or on the soil, is highly determinant to the healthy environment. Bacteria like *Pseudomonas sp.* have been well known for the degradation of oil spills on oceans/soils (Fig. 2).

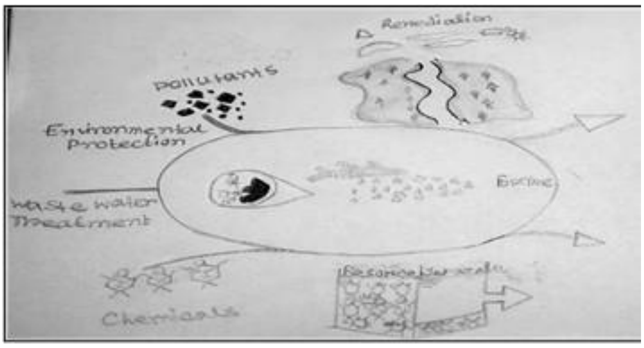

Figure 2: Schematic diagram of the process of bioremediation.

Bacteria in the improvement of host microbial community dynamics

The stability of host-associated microbiota is being increased by the administration of the probiotic. This administration also changes the network structure of correlations in microbial abundance, resulting in food microorganisms having a dominant influence on the operational taxonomical units (OTUs) associated with dolphin and non-dolphin sites. Environmentally derived exogenous bacteria can exert some influence on the dynamics of host microbiota; these differences are not as great as those resulting from direct stimulation with a completely foreign exogenous microbial source. It is important to state that changes in influence and stability statistics were observed, suggesting that many of the stability effects are driven by changes in rare species only.[7] This suggests that in host-associated systems, equilibrium is achieved in the presence of common microbial exposures, for example, those in the immediate usual environment. It also suggests that food and air, and hence, oral, gastrointestinal tract, and respiratory tract interactions, have the largest effect overall. Meanwhile, uncommon microbial exposures can have a profound impact on the stability and structure of microbial associations. The direct probiotic administration influences host microbial community dynamics and it has major implications for animal health and aquarium management practices. [7]

Bacteria as model organism

Perhaps even the first chemo-organoheterotroph had a similar mass composition as *E. coli*, providing the necessary to understand the evolution of modern bacteria.[8] Also called the “workhorse” of molecular biology for its fast growing rate in chemically defined media and extensive molecular tools available for different purposes, *E. coli* is considered the most important model organism of them all. For instances, cracking the genetic code,[9] unveiling the nature of DNA replication,[10] the groundbreaking advances on gene organization and regulation or as we love to call ‘the operon’,[11,12] important evidence for the basis of mutations and ultimately to the evolution of organisms,[13,14] and finally, the achievement of a genetically modified organism[15] that skyrocketed several applications of the enormous capacity for manipulating this organism, rendering *E. coli* as a key player in biotechnology.[16]

Phylogenetically, *E. coli* is a member of the Enterobacteriaceae and is closely related to pathogens such as *Salmonella*, *Klebsiella*, *Serratia*, and the infamous *Yersinia pestis*, which causes plague. Although *E. coli* is mostly harmless, pathogenicity islands have been identified and associated with pathogenesis in *E. coli* resulting in strains that colonize different tissues.[17]

The complete genome contains a single circular duplex molecule composed of 4,639,221 bp. Regarding its structure, protein-coding regions correspond to 87.8% of the genome, while 0.8% encodes for stable RNAs, and 0.7% consists of non-coding repeats. The remaining 11% encodes for regulatory and other functions. Nevertheless, nearly 34% (1431) proteins are considered orphan or without defined molecular function but in a recent study, it was demonstrated that by homology with distant phylogenetical relationships, they may play a role in defined molecular pathways or processes.[18] From the orphan set in *E. coli*, at least 446 contain some molecular signature that can assess their molecular role.

Lambda Redbased method have yielded a total of 4288 genes mutated without lethality (Keio collection), 303 genes were unable to be deleted, from which 37 are of unknown function.[19] This experimental evidence has pointed out one very important aspect of genome structure and function. Genome size increase is the result of horizontal gene transfer or DNA fragment retention that somehow is giving some beneficial features to recipient host, apparently an increase in fitness.[20]

Studies regarding genome size analyzed through deletions of specific genes or complete genomic regions have led on thinking about the minimal genome. In the case of *E. coli*, there are several pieces of evidence that points out that at least 23% of the genome can be eliminated gaining genomic stability and normal growth.[21] Also, eliminating insertion sequences can enhance the capacity of *E. coli* to synthesize proteins due to the decrease or insertions on plasmids and strains exhibit normal growth plus increased genome stability.[22] *E. coli* is an extensively studied organism; with all the cumulative data we can ensure that with all this knowledge, we can design tools.

Bacteria as biosensor

In biotechnology, biosensors are broadly defined as any device based on biological part, cell, tissue, or protein complex that are linked to a mechanical sensor or analytical receptor that provides a measurable signal proportional to the analyte in the reaction.[23,24] *E. coli*-based biosensors using plasmid or chromosomal constructs are useful for the detection of environmental traits or hazards or measuring cellular processes as any standard reporter system.[25,26,27]

In Figure 3, we depict the basic design for whole-cell biosensors and some applications. Plasmid vectors with all the possible modifications can lead to almost endless combinations. For practical applications, there are commercial vectors that can be used for such purposes or as mentioned in the previous sections, plasmid methods are powerful enough for fast and robust biosensor design.

In the literature, there are several reports where *E. coli*-based biosensors have been successful for detecting different traits: oxidants,[28,29] DNA damaging compounds,[30] membrane-damaging compounds,[31] protein-damaging compounds,[32] aromatic compounds,[33] xenobiotics,[34] antibiotic panels using reporter strains without antibiotic selection,[35] etc. The only limitation is the available sensor module and the design. The reporter protein is also important. Stability and reproducibility are two important aspects of biosensor design. In our experience, Green Fluorescent protein (GFP) protein is superior to luciferase, especially that we can detect GFP by various methods (we find flow cytometry, fluorometry, and confocal microscopy our top preferences) without cell lysis or substrate mixtures that are time-consuming.[36]

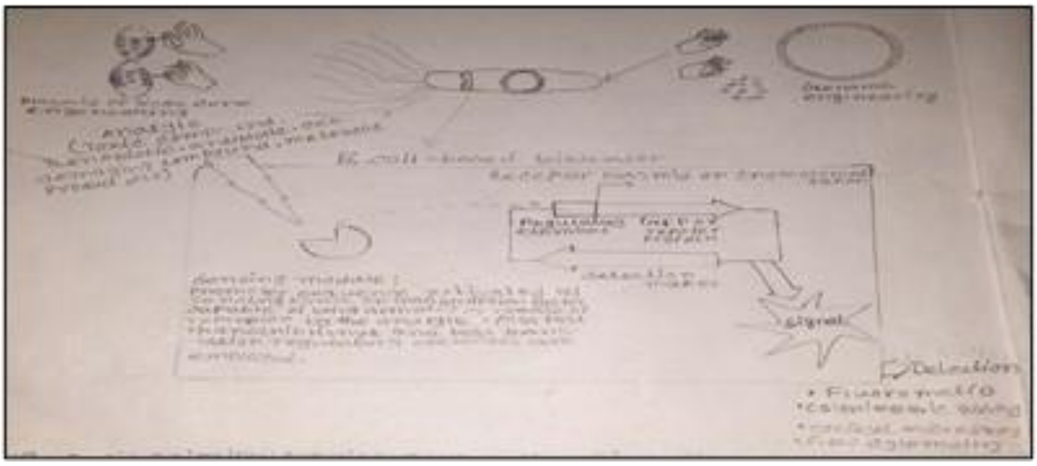

Figure 3: Schematic diagram of basic principles of biosensor design.

Bacteria as genetic equipment

Synthetic biology is a relatively new branch of molecular genetics that incorporate engineering principles for modifying several aspects of cell physiology, rewiring genetic circuits, creating novel circuits, and synthesizing custom-made DNA sequences and even genomes.[37] This particular branch of biology needs to be supported by an extensive knowledge of the organism that modifications or even whole genome synthesis is attempted, several novel tools for analyzing big datasets and molecular tools for that particular organism, for the generation of sequences and the computational design of DNA molecules, and a goal that can be achieved with the desired organism. *E. coli* along with *Saccharomyces cerevisiae* are the most studied and well-comprehended organisms in science, and diverse phenotypes have been identified that are helpful for bioengineering.[38] With all the technologies available, the advancement of using *E. coli* for biotechnological applications based on synthetic approaches have led to the development of strains capable of synthesizing several novel compounds.

Bacteria in biofuel production

Another relevant area was *E. coli* stepping in to biofuel production. The twentieth century is characterized by the human dependence on fossil fuels. They participate in a myriad of processes, and the demand is increasing. In order to alleviate the demand, scientists have turned to the development of novel technologies for biofuel production by the conversion of carbon sources into usable fuel. There are several reports where *E. coli* have been successfully engineered for the synthesis of branched-chain fatty acids or short-chain fatty acids that can ultimately lead to the mass production of fuel precursors or useful materials derived from oil.[39] Perhaps, the most promising future is a fully replicated fossil fuel, i.e., a mixture structurally and chemically identical to the fossil fuels that are currently under use, which is a mixture of aliphatic n- and iso-alkanes of various chain lengths.[40] Also, a more complete metabolic atlas of *E. coli* is needed, and recent efforts have mapped the metabolic flux from this bacterium further.[41]

Bacteria as biofertilizer

Plant growth-promoting rhizobacteria (PGPR) are naturally-occurring soil bacteria able to benefit plants by improving their productivity and immunity. These bacteria are associated with the rhizosphere, the part of soil under the influence of plant roots and their exudates. According to their interactions with plants, PGPR can be divided into symbiotic bacteria, which live inside plants and exchange metabolites with them directly, and free-living rhizobacteria, which live outside plant cells.[42] Several PGPR have been used worldwide as biofertilizers, contributing to increasing crop yields and soil fertility and hence with the potential to contribute to more sustainable agriculture and forestry. [43] According to Malusá and Vassilev,[44] a biofertilizer is "the formulated product containing one or more microorganisms that enhance the nutrient status (the growth and yield) of the plants by either replacing soil nutrients and/or by making nutrients more available to plants and/or by increasing plant access to nutrients".

Rhizobacteria can promote plant growth through a broad variety of mechanisms which can be grouped according to their mode of action in: (i) the synthesis of substances that can be assimilated directly by plants, (ii) the mobilization of nutrients, (iii) the induction of plant stress resistance and (iv) the prevention of plant diseases (Fig 4).

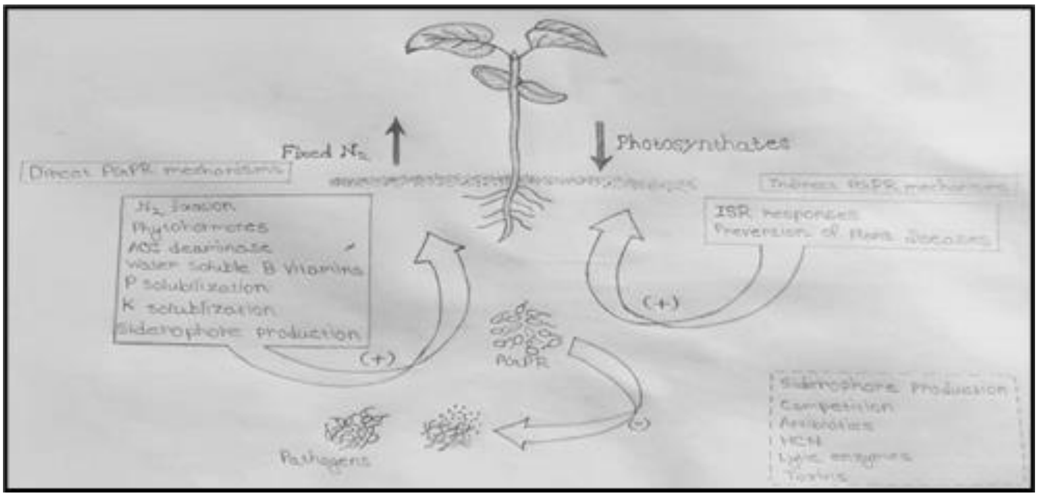

Figure 4: Schematic diagram of role of bacteria as biofertilizer.

The mechanisms of bacterial plant disease prevention may be direct, if pathogens are inhibited as a result from PGPR metabolism, or indirect, when the bacteria compete with the pathogens, reducing their ability to induce disease.[45] Some PGPR synthesize antibiotic substances, which inhibit the growth of some plants pathogens.[46] For instance, *Pseudomonas* sp. produces antibiotics that inhibit *Gaeumannomycesgraminis* var. tritici, the causal agent of take-all of wheat.[47] Most *Bacillus* sp. produce antibiotics those are active against Gram-positive and Gram-negative bacteria, as well as many pathogenic fungi.[48] *B. cereus* UW85 contributes to the biocontrol of alfalfa damping-off.[49] Cyanogenic compounds are nitrogen-containing compounds that have been shown to repel leaf-chewing herbivores.[50] Rhizobia-legume symbioses have been demonstrated to enhance the resistance of plants to herbivore attack. Presumably, additional nitrogen provided by the bacterium allows the plant to synthesize cyanogenic defense compounds.[51]

As long as the human population continues to increase the world will have to deal with an escalating demand for food. Consumers demand more and more organic food, and most countries have developing policies to reduce the use of chemical fertilizers. As a result, the commercialization and application of bacterial biofertilizers on agricultural fields or in arboriculture are increasing year by year.

Bacteria as biological control agent

Microbial biological control agents use a great variety of mechanisms to protect plants from pathogens. Important modes of action strengthen the resistance of the plant, e.g., induced resistance or priming, or modulate the local growth conditions for pathogen development, e.g., nutrient competition, but do not interfere directly with the pathogen. Hyperparasitism and secondary metabolites are directly affecting the targeted pathogen via highly regulated cascades of physiological events but not by a single constitutively produced metabolite. Secondary metabolites produced in vitro may have antimicrobial activity at high concentration but low amounts are produced in situ very locally during interaction and metabolites have short life spans, often with functions such as signalling, very different from antibiosis. During the cascades of events a range of different compounds with different modes of action are used to out the pathogen. Such events of signalling and interaction are common wherever microorganisms interact. The highly regulated in situ production of ubiquitous mechanisms commonly used in the microbial interplay makes the use of MBCAs a safe and sustainable technology. In situ produced compounds such as microbe-associated molecular patterns (MAMPs), enzymes or secondary metabolites are not relevant for risk assessments so that detailed toxicology and ecotoxicological studies of these compounds are not relevant, and should not be required. The fear of antimicrobial metabolites produced by microbial biological control agents (MBCAs) after their release is not based on real risks but fed by the wrong perception on how biocontrol acts if studied under *in vitro* conditions. If antimicrobial metabolites are the active ingredient in the formulation of the biocontrol product, risk assessment of such metabolites is relevant (Fig. 5).[52]

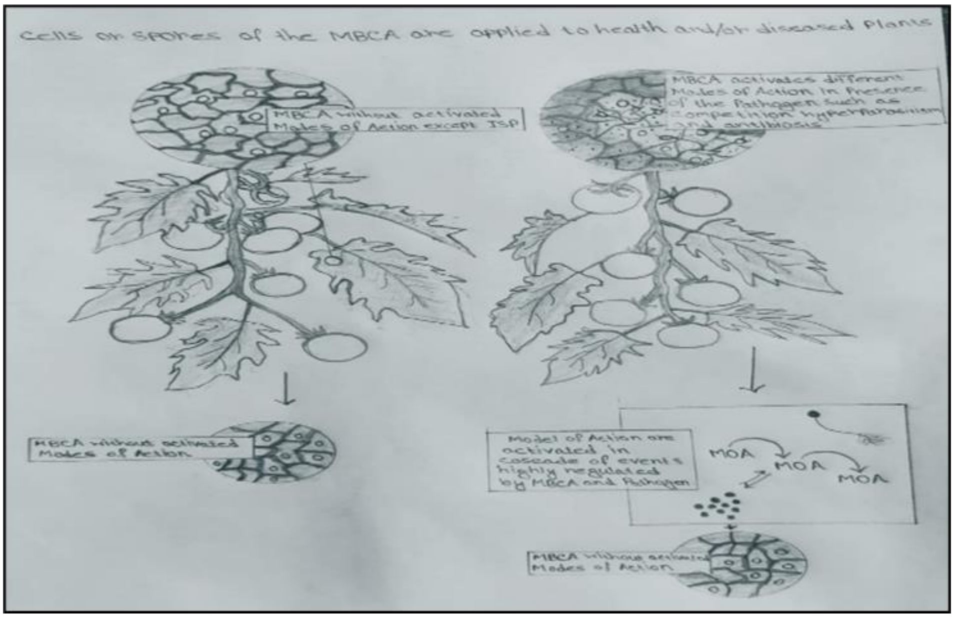

Figure 5: Schematic diagram of microbial biological control agent (MCA) temporally interacting *in situ* with the targeted pathogen activating different modes of action in cascades of events.

Bacteria as single-cell-protein

Protein can also be provided through the cultivation of various microbes and algae, preferably those which contain more than 30% protein in their biomass and which can provide a healthy balance of essential amino acids. Microbial protein is generally referred to as single cell protein (SCP), although some of the producing microbes, such as filamentous fungi or filamentous algae, may be multicellular. In addition to direct use as SCP, microbes contribute to protein demand when they are used to upgrade the protein content or quality of fermented foods.[53]

Bacteria also have a long history of use as SCP, particularly in animal feed. Some of the more commonly studied species have been reviewed by Anupama and Ravindra (2000).[54] Bacterial SCP generally contains 50–80% protein on a dry weight basis[54] and the essential amino acid content is expected to be comparable to or higher than the FAO recommendations.[55] Methionine content up to 3.0% has been reported, which is higher than that generally obtained in algal or fungal SCP.[56] Similar amino acid composition is observed with methanol or methane grown bacteria.[57] As with fungi, bacterial SCP has high nucleic acid content (8–12%), especially RNA, and thus requires processing prior to usage as food/feed.[58] In addition to protein and nucleic acid, bacterial SCP provides some lipid and vitamins from the B group. Imperial Chemical Industries developed a SCP (Pruteen) for animal feed from methanol, using the bacterium Methylophilus methylotrophus. Pruteen contained up to 70% protein and was used in pig feed.[59] Pruteen, however, could not compete with cheaper animal feeds that were available at the end of the 1970s and production was discontinued. Pruteen was produced from methanol, but methane is now gaining interest as a substrate for SCP. UniBio A/S (utilizing knowledge gained by Dansk BioProtein A/S) and Calysta Inc. have both developed fermentation technology to convert natural gas to animal feed protein by using methanotrophic bacteria. UniBio A/S uses a U-loop fermenter, to achieve a productivity of 4 kg m^{-3} h^{-1}, producing UniProteinR with 70% protein, which has been approved for use in animal feed. The U-loop fermenter is designed to enhance mass transfer rates of methane from the gas to the liquid phase, making more methane available for the bacteria.[60] Calysta Inc. opened a production facility for their product, FeedKindR, in the UK in 2016 and is partnering with Cargill to build a larger production facility in the U.S.A. FeedKindR, like UniProteinR, is used in animal feed. Methane is an interesting substrate, since it is a major by-product of cattle and pig farming,[61] as well as being available from biogas production (landfills, waste). Excess methane is currently flared. VTT Ltd. is investigating the reactor design and options for coupling farm methane generation with the production of microbial oil and feed protein from the methanotrophic bacteria *Methylococcus capsulatus* (group I), *Methylosinus trichosporium* (group II), and *Methylocystis parvus* (group II). As with SCP from fungi, other developments in the production of bacterial SCP focus on upgrading various waste substrates or valorisation of waste water treatment. Examples include the treatment of potato starch processing waste in a two-step process using *Aspergillus niger* to degrade fibresin the potato residue and *Bacillus licheniformis* to produce protein.[62] Economic analyses indicated that the process could address not only the pollution problem of the starch industry, but also the shortage of protein for animal feed in China.[62] Another example of simultaneous waste water management and

SCP production was reported by Kornochalert et al. (2014) for rubber sheet factory waste.[63] They demonstrated that the chemical oxygen demand, suspended solids and total sulphides in the waste water was reduced by the purple non-sulfur bacterium, *Rhodopseudomonas palustris*, to levels that met the guidelines for use as irrigation water in Thailand and that the biomass produced was suitable for SCP.[63] Soy-bean hull has been fermented with *B. subtilis* to improve its nutritional value as a feed for monogastric animals.[64] Kunasundari et al. (2013) describe a novel secondary product, co-produced with bacterial SCP. They cultivated Cupriavidus necator in a large scale to produce biomass high in both protein and polyhydroxyalkanoate (PHA).[65] This biomass was fed to rats. The feed was not only well-tolerated and safe for rats, but the rats also produced faecal pellets containing PHA granules, which enabled the purification of substantial amounts of PHA without use of strong solvents.[65]

Bacteria as biofilm

Biofilm formation enables single-cell organisms to assume a temporary multicellular lifestyle, in which "group behavior" facilitates survival in adverse environments. What was once defined as the formation of a community of microorganisms attached to a surface has come to be recognized as a complex developmental process that is multifaceted and dynamic in nature. The transition from planktonic growth to biofilm occurs in response to environmental changes, and involves multiple regulatory networks, which translate signals to concerted gene expression changes thereby mediating the spatial and temporal reorganization of the bacterial cell.[66,67] This cellular reprogramming alters the expression of surface molecules, nutrient utilization, and virulence factors and equips bacteria with an arsenal of properties that enable their survival in unfavourable conditions.[66]

Within the biofilm, bacteria are cocooned in a self-produced extracellular matrix, which accounts for ~90% of the biomass.[68] The matrix is composed of extracellular polymeric substances (EPS) that, along with carbohydrate-binding proteins,[69] pili, flagella, other adhesive fibers,[70] and extracellular DNA (eDNA),[71] act as a stabilizing scaffold for the three dimensional biofilm structure (Fig. 6).

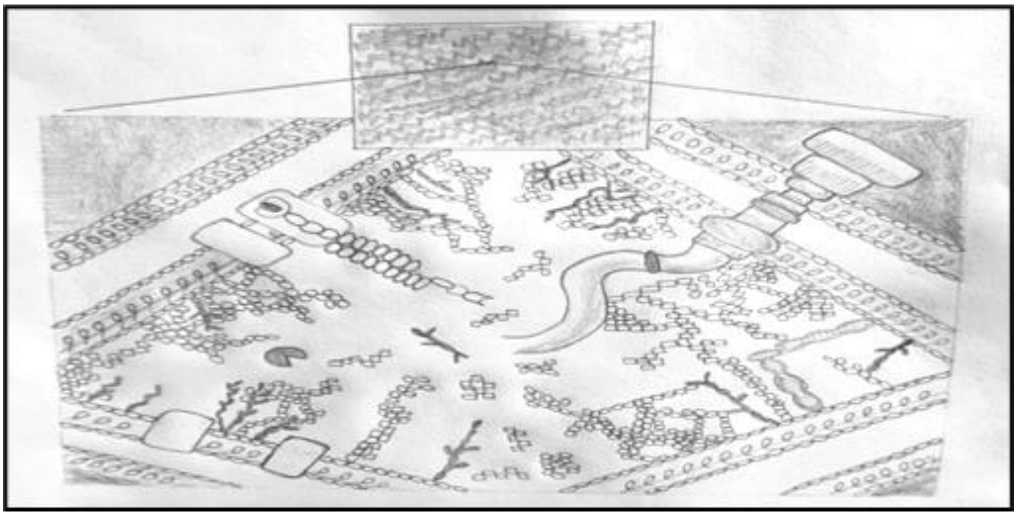

Figure 6: Schematic diagram of involvement of bacteria in the formation of biofilm.

P. aeruginosa, an important pathogen and avid biofilm former, also uses several attachment organelles to irreversibly adhere to a surface. Besides flagella, *P. aeruginosa* uses type IV pili-mediated twitching motility to wade through the liquid interface and contact the surface, maintain adherence, and move across the attachment plane.[72,73]

Biofilm formation enables bacterial pathogens to colonize a wide variety of host niches and persist in harsh environments, making their eradication particularly difficult. Biofilm characteristics determine whether, to what extent, and which antimicrobial treatments may be effective. The age and composition of the biofilm are the major factors influencing the susceptibility of the resident microorganisms. As the biofilm matures, increased EPS accumulation, combined with the nutrient and oxygen gradients that affect cell metabolism and growth rates, result in reduced entry and activity of antimicrobial agents making biofilm-forming pathogens progressively more resistant to antibiotic regimens. Thus, novel strategies, designed to block a specific biofilm step without killing the bacteria, such as the use of antiadhesion agents, or using natural, bacterially produced signals to promote bacterial dispersal, are exciting avenues for exploration and ultimately the development of fast-acting, potent, and bioavailable treatment strategies.

Bacteria as pesticide

The microbial pesticides come from naturally occurring or genetically altered bacteria. Microbial control agents can be effective and used as alternatives to chemical insecticides. A microbial toxin can be defined as a biological toxin material derived from a microorganism, such as a bacterium. Pathogenic effect of those microorganisms on the target pests are so species specific. The effect by microbial entomo-pathogens occurs by invasion through the integument or gut of the insect, followed by multiplication of the pathogen resulting in the death of the host, e.g., insects. Studies have demonstrated that the pathogens produce insecticidal toxin important in pathogenesis. Most of the toxins produced by microbial pathogens which have been identified are peptides, but they vary greatly in terms of structure, toxicity and specificity.[74]

These microbial pesticides offer an alternative to chemical insecticides with increased target specificity and ecological safety so that they are used either uniquely or in combination with other pest management programmes. One definition for integrated pest management (IPM) which is most relevant to this practice comes from Flint and van den Bosch [1981]: "It is an ecologically based pest control strategy that relies heavily on natural mortality factors and seeks out control tactics that disrupt these factors as little as possible. Ideally, an integrated pest management program considers all available pest control actions, including no action, and evaluates the potential interaction among various control tactics, cultural practices, weather, other pests, and the crop to be protected".[75] These microbials as biocontrol agents present u beneficence. They have efficiency and safety for humans and other non-target organisms. They leave less or no residue in food. They are ecologically safe, so that other natural enemies are free of their threatening, leading to preservation of other natural enemies, and increased biodiversity in managed ecosystem. So, microbial agents are highly specific against target pests so they facilitate the survival of beneficial insects in treated crops. This may be the main reason that microbial insecticides are being developed as biological control agents during the last three decades. Microorganism e.g., a bacterium, fungus, virus or protozoan as the active ingredient can control many different kinds of pests, although each separate active ingredient is relatively specific for its target pest. For example, there are fungi that control certain weeds, and other fungi that kill specific insects. One bacterial species like *Bacillus thuringiensis* may be more effective on *Aedes aegypti* while one another *B. sphaericus* strain can be effective on a different types of mosquito like *Culex quinquefasciatus.*[76]

Bacteria as water purifier

Bacteria were used to build filtering membranes. This type of membrane begins with feeding *Gluconacetobacter hansenii* bacteria a sugary substance so that they form cellulose nanofibers in water. Then graphene oxide (GO) flakes was incorporated into the bacterial nanocellulose while it was growing, essentially trapping GO in the membrane to make it stable and durable. After GO is incorporated, the membrane is treated with base solution to kill Gluconacetobacter. During this process, the oxygen groups of GO are eliminated, making it reduced GO. In the presence of sunlight the reduced GO flakes of membrane immediately generated heat, which is dissipated into the surrounding water and bacteria nanocellulose. Ironically, the membrane created from bacteria also can kill bacteria.

CONCLUSION

In this study the main focal theme was to establish the beneficial role that bacteria plays apart from harmful effects. Bacteria have several roles in different cellular process. Beside those bacteria have different types of utilisations which are helpful to the society. All the beneficial roles of bacteria has been summarised in the Fig. 7.

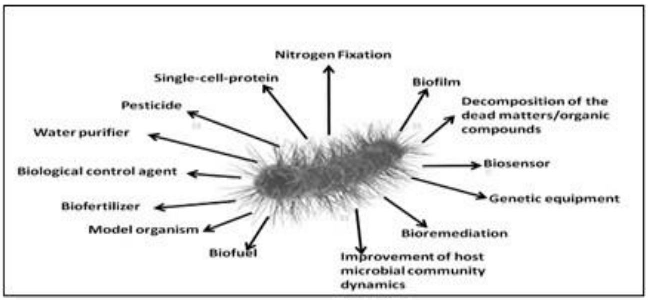

Figure 7: Summary of the beneficial utilities of bacteria.

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