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MICROBIOLOGY AS A TOOL FOR RESEARCH AND DEVELOPMENT-AN OVERVIEW

P. K. MAHESHWAR*

[1]Department of Microbiology, Yuvaraja's College University of Mysore, Mysore 570 005, Karnataka, India

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Abstract –Microbiology at present is one of the fast evolving disciplines in Biological Sciences. It includes studies on physiology, ecology, evolution and clinical / immunological aspects of microorganisms, including the benefit the society can achieve by exploiting the microorganisms. It is a huge employment generator, as well as the best area in biological sciences for research, all over the world. Microorganisms are of great importance to both humans and the ecosystem. Therefore, it should be a high priority to make use of the subject for the best output in research and also for the creation of employment. The present article enlightens the tremendous contribution of microbes and microbiology to the Man kind and environment. The article focuses mainly on the trends in microbiological research, industrial output, scope and future of microbiology on a global scale.

INTRODUCTION

Microbes are the most ancient living creatures and they had the plan *et al* for themselves initially, even after the advent of man they have been influencing Mankind both for good and bad since time immemorial. The astonishing truth about microorganisms is that, without the aid of microbes, other macro organisms like plants and animals, especially humans need to put extra effort for survival, because microbes are the key role players in maintaining many crucial activities on the earth. Microbe s are one of the essential components of the human body. The presence of Lactic acid bacilli in the gut is proven to be of immense help for humans as the lactic acid produced is known to avoid colon cancer (Zhang *et al*., 2013; Rowland, 2009) and they are also known to enhance resistance (Villena *et al*., 2014). Few enterobacteria synthesize Vitamin B and K for humans (Yoshida *et al*., 2011) which are sparingly available. The list of such beneficial activities is endless. Microbiology is the core contributor for the development of biotechnology as a subject. In fact, the origin of biotechnology was due to the invention of restriction enzyme in a bacterium *Escherichia coli* (Smith *et al*., 1970; Pingoud *et al*., 2014). Without these restriction enzymes, the biotechnology industry would certainly not have flourished. The article briefly focuses all the major research output associated with Microbiology. Further the article enlightens the tremendous contribution of microbes and microbiology to the Man kind and environment.

Microbes and Ecosystem

The simple decomposition of organic waste generated in millions of tons by human activity is taken care promptly by microbes, without which, we humans would make the entire earth a dustbin. The moment we throw a banana peel on the ground it is recognized by fungi and bacteria which initiate degradation, of course, with the help of sunlight and oxygen. The same technique is being applied in a large scale by many private companies which employ microbiologists to grow fungi like *Phanerochaete, Chrysosporium, Trichoderma, Aspergillus* (Kne•evic *et al*., 2013) and there is a wide range of bacteria *Pseudomonas* sp. *Azoarcus* sp. *Thauera* sp. *Paenibacillus* sp. , *Cohnella* sp. *Acinetobacter* sp. *Microbacterium* sp. which hasten the process of degradation of organic waste (Wang *et al*., 2013; Pollegionil *et al*., 2015). Soil microbes are responsible for many beneficiary activities in the ecosystem, such as dead matter degradation, the promotion of plant growth etc. Wild huge trees and 95% of the crop plants on earth depend on Mycorrhizal fungi for nutrient mobilization and nutrient cycling [Teste *et al*., 2014). They play a key role in recycling

***Corresponding author's email**: pmaheshwar@ycm.uni-mysore.ac.in

nitrogen (Mirza *et al.*, 2014), carbon and sulphur (Dutt *et al.*, 2014) and the degradation of pollutants and pesticides. Soil fungi are necessary for the production of many industrially important enzymes, antibiotics and other medicines.

Airborne bacteria indirectly contribute to weather changes and cloud formation across the world. There is an ongoing research to link the cloud formation and marine air- borne bacteria in altering the weather condition across the globe (Rodriguez *et al*., 2014; Smith, 2013).

One of the major contributions of bacteria for the survival of plant and animal life is nitrogen fixation. The biosphere is composed of 78% nitrogen, but most of it is not in a readily usable form. Nitrogen is used as one of the major components in the synthesis of DNA in all living creatures. Human beings and other animals depend on plants for nitrogen supplement to a major extent. Plants in turn need an obligate association of many free living bacteria (*Clostridium, Nitrosomans, Nitrosoccocus* etc.,) and symbiotic bacteria (*Rhizobium, bradyhizobia, Frankia* etc.). These bacteria convert nitrogen into easily absorbable form for the plants (Dodds, 2002). Theoretically if these bacteria are eradicated from the environment, the survival of any living organism is almost impossible and the situation could be a horrifying disaster. This explains the importance of microbiology. Now with the increase in urbanization, these soil bacteria are facing a lot of threat. Therefore some countries are favoring the process of bio-augmentation by cultivating the above mentioned bacteria in the laboratory and are trying to inoculate them back into the disturbed soil, to enhance the bacterial populations.

Microbiological research in plant pathology it self is a vast area where tremendous research ahs been done. The pathogenic fungi infecting staple crops like rice, wheat, maize and soybean has lead to identification of various toxigenic fungi which is detrimental to animals including human beings (Maheshwar *et al*., 2009; Duncan and Howard 2010; Wang *et al*., 2015). Viruses (Adkar-Purushothama *et al*., 2011) and Viroids (Singh *et al*., 2010) are some of the other pathogens of economically important plants which has raised lot of novel investigations in the field of agricultural microbiology.

Microbes in bioremediation

Bioremediation is a complex process, wherein biological degradation takes place by the cells of microorganisms which absorb pollutants (Singh, 2008). If they have specific enzymes, the degradation of pollutants and their corresponding metabolites will take place. Bioremediation of oil spill in the oceans by genetically modified bacteria *Pseudomonas putida* stands first among the highly appreciated microbe mediated bioremediation processes. Hydrocarbons present in the oil are used as a source of nutrients and energy for the growth of microorganisms. During this process, microorganisms decompose them to naphthenic acids, alcohols, phenols, hydro peroxides, carbonyl compounds, esters, and eventually to carbon dioxide and water. *P. putida* and *P. aeruginosa* are employed in degradation of huge oil spills (Shah, 2014).

Novel methods are being employed for the biodegradation of materials like Polyester polyurethane (PUR), a type of plastic widely used in industries which are hazardous to the environment. PUR has been shown to be susceptible to biodegradation by the enzymatic activity of both fungi and bacteria. Soil fungi comprise a majority of organisms screened for PUR degradation process. Fungi of the genera *Alternaria*, *Aspergillus*, *Phoma*, *Pennicilium* have shown promising results in PUR degradation (Zafar *et al*., 2014).

The number of new chemicals produced is on an increase daily by thousands and it is inevitable that many of these chemicals will reach the environment. Bacteria are constantly developing new catabolic pathways directed against these man made chemicals in order to either access sources of carbon, energy and nutrients or simply to detoxify them (Kolvenbach *et al*., 2014). Endosulfan (Kumar *et al*., 2008), Hexachlorocyclohexane (Lal *et al*., 2008), methyl parathion (Manoj *et al*.), are some of the major pesticides that are being cleaned up using bacteria. Therefore the role played by microorganisms in bioremediation is very much essential for a better ecosystem.

Major Industries associated with Microbiology

Food industry

Microbes are the main agents in breweries and food industries. Countries like Italy depend fully on the fermentation strains of yeast for their wine and breweries (*Sicarda et al.,* 2011). The major economy of Italy and France is brewery industry, which in turn is completely dependant on good strains of yeast. Italy and France produce and individually export more than 4.6 billion liters of wine per year,

making breweries the main source of income for these countries. Such a huge industry depends on the yeast *Saccharomyces cerevisiae.* Continuous culturing of pure strain of *S. cerevisiae* is the key for the survival of these industries. In breweries, microbiologists are employed to culture the best strain of *Saccharomyces* and also to maintain them without bacterial contamination. Other than yeast *Aspergillus* and *Penicillium* are the two major fungi that are associated with microbiology industry. Enzymes produced by *Aspergillus* spp. are used in textile, food and leather industry (Giardina and Sannia, 2015). Fungi like *Penicillium* are needed for the production of cheese (Nielsen, 2013).

Pharmaceutical industry

Pharmaceutical industries recruit microbiologists for the quality control of their products, which is a critical component in medicine. A simple disposable syringe needs a thorough examination by the microbiologist before packing; any error in the final product may be fatal. Probiotics is one of the major contributions of microbiology in the pharmaceutical field next to antibiotics. Probiotics are live microbial, dietary supplements that have a beneficial effect on the host. In addition, there are areas of medical use that have been proposed for future probiotic applications. There are also studies indicating that probiotics may be useful for prevention of respiratory infections in children, dental caries, irritable bowel syndrome, and inflammatory bowel disease. Areas of future interest for the application of probiotics include colon and bladder cancers, diabetes, and rheumatoid arthritis. The probiotics with the greatest number of proven benefits are bacteria *Lactobacillus rhamnosus* and yeast *Saccharomyces boulardii* (Goldin *et al*., 2014).

Antibiotics available in the market are based on the secondary metabolites produced by fungi and bacteria. *Penicillium* has contributed to the development of many penicillin derivatives and is one of the safe antibiotics available today (Wong *et al*., 2014). Streptomycin (Nelson *et al*., 2011), tetracycline (Zumla *et al*., 2013), Rifamycins (Sensi, 1983) are some other life saving antibiotics that are of microbial origin.

As nutraceuticals (products derived from food sources that are purported to provide extra health benefits, in addition to the basic nutritional value found in foods) (McClements *et al*., 2014), fungi especially mushroom offer a wide range of products which are directly related in providing food with medicinal qualities. Human body has antioxidant defense systems that are often insufficient to completely prevent the damage caused by oxidative stress. Thus, natural products such as mushrooms containing bioactive compounds can be used to help reduce such damage in the body (Giavasis, 2014; Finimundy *et al*., 2014). Products derived from cyanobacteria like *Spirulina* and other single cell proteins are slowly gaining the momentum as future foods (Idriss, 2014).

Microorganism in medicine

Microorganisms as such, offer a wide range of metabolites for the control of many diseases and ailments prevalent in the society. The fungi *Ganoderma lucidum* is one such mushroom with well-established medicinal properties. Lucidum extract has been shown to control *Plasmodium berghei* a rodent malarial parasite. The mechanism of action is on par with chemotherapy. The antimalarial activity of the extract was found to be suppressive, curative and also prophylactic. Serum aminotransferases (AST and ALT), alkaline phosphatase (ALP), and gamma glutamine transpeptidase (ã-GT) levels which get accumulated at high levels in the body were found to be significantly reduced, with a corresponding increase in the liver activity of mice treated with lucidum extract. The research in this area has given a silver line that it can also heal *Plasmodium* induced liver damage due to malarial infection (Oluba *et al*., 2012). The routine synthetic drug like chlorquinone protects against malaria, but it comes with all possible side effects; where as a compound from a microbe comes with bonus effect, wherein even the damaged liver cells may get healed. This shows the strength and benefits associated with the research in microbiology.

Mushrooms are credited with success against controlling cancer; they belong to the genus *Pleurotus, Agaricus, Ganoderma, Antrodia, Trametes, Cordyceps, Xerocomus, Calvatia, Schizophyllum, Flammulina, Suillus, Inonotus, Inocybe, Funlia, Lactarius, Albatrellus, Russula,* and *Fomes*. The anti-cancer compounds from these fungi play a crucial role as reactive oxygen species inducer in cancerous cells, mitotic kinase inhibitor, anti-mitotic, angiogenesis inhibitor, topoisomerase inhibitor, leading to apoptosis, and eventually inhibiting cancer proliferation (Patel *et al.,* 2012).

Extracts from the fungi *Agaricus blazei* have been reported to be medicinal and have been studied for their immune-stimulatory effects such as, the

induction of nitric oxide (NO) secretion and transcriptional up regulation of cytokines such as Inter Leukin-8, IL-6, IL1-b, IL2, and Tumour Necrisis Factor. These effects have been credited to the presence of high concentration of proteoglycans and b-glucans in *A. blazei*. This fungal metabolite is known to enhance the local and systemic inammation, up regulating pro-inammatory molecules, and enhancing leukocyte homing to atherosclerosis sites without affecting the lipoprotein prole, there by play a key role in controlling heart disease [*Juliana et al., 2012*].

Microbes are known to control viral replication also. Recent studies have determined the antiviral activity in the extracts from *Lentinula edodes* the replication of poliovirus type 1 (PV-1) and bovine herpes virus type 1 (BoHV-1) [Rincao *et al*., 2012], The compound extracted from *Lentinula* also suppressed the activity of HIV-1 reverse transcriptase. In combination with anti-retroviral drug 3'-azido-3'-deoxythymidine (AZT), lentinan suppressed the in-vitro expression of the surface antigens of HIV more efficiently compared to AZT monotherapy. It is also known to increase the *in vitro* antiretroviral effect on HIV replication.

Microbes in genetic engineering

Microbes are the inevitable components of genetic engineering. The list of microbes involved in genetic engineering is exhaustive. They are the major sources of restriction enzymes [*Roberts et al*., 2003], recombinant vaccines [Elizabeth *et al*., 2014] and production of hormones [*Maicas et al .,2013*]. Among these a significant application is in the production of Insulin. Insulin production is amongst the earliest contribution of biotechnology for pharmaceutical industry. Recombinant DNA technology is utilized to modify bacterium *Escherichia coli* to produce human insulin. Prior to the development of this technique, insulin was extracted from the pancreatic glands of cattle, pigs, and other farm animals. Animal-derived insulin [Ghazavi *et al*., 2011] produced a lot of allergic reactions in diabetic patients and also posed ethical issues. Therefore from 1990 onwards the insulin is being successfully produced by *E. coli* gene expression.

Microbial mining

Other than the medical applications, the exploitation of microbes has gained much importance in the recovery of minerals and petroleum products. Crude oil is one of the major sources of energy worldwide (Zhao *et al*., 2015) with the depletion of crude oil reserves and the subsequent increase in prices, the exploitation of oil resources in mature reservoirs is essential for meeting the future energy demands. This essentially requires the interference of certain bacterial species. As the conventional recovery methods currently used have become less efficient in meeting the needs, there is a continuous demand to develop a new technology which could help in the upgradation of heavy crude oil. Microbial enhanced oil recovery is an important tertiary oil recovery method which is cost-effective and an eco-friendly technology to retrieve the residual oil trapped in the reservoirs. The potential of microorganisms to degrade heavy crude oil to reduce viscosity is considered to be very effective in oil recovery. Relative studies suggest that thermophilic hydrocarbon degraders of *Bacillus*, *Thermus*, *Thermococcus*, and *Thermotoga* species occurring in natural high temperature or sulfur-rich environments are of special significance in oil recovery [Wang *et al*., 2006].

Future trends

Microbiology as a subject has exciting future trends in various branches of Science, with a positive effect on the society. Only a few prominent issues like contribution of microbiology in drug delivery, drug discovery and energy production are considered in this section. The future of this subject can be considered with the vision of the world's top one research Institute, National Aeronautics and Space Administration (NASA). NASA mainly concentrates on study factors such as infectious diseases, antibiotic resistance, and metabolic and genetic changes. The future trend of microbiology can be best understood if we look at the vision given by NASA- "NASA has a special focus on microbiology. Future research of NASA will focus on the microbiological implications of long-term space travel and habitation, with the International Space Station serving as one of the primary sites for further study"[http://www.nasa.gov/exploration/humanresearch/areas_study/environment/enviro_microbiology.html#.U8oKodLIuQE].With this strong message it is clear that NASA is planning to establish a microbiological laboratory in the International Space Station. Besides research and employability, microbiology can educate people and in turn the whole society, about the conservation of natural resources, public health and hygiene leading

to a healthy life style.

Drug delivery and Drug discovery

Drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals (Tiwari *et al*., 2012). The practice of drug delivery has changed dramatically in the last few decades and even greater changes are anticipated in the near future. One of the promising methods is the virus mediated drug delivery. Chemically synthesized drug carriers, exhibit certain drawbacks like Cytotoxicity, low water solubility, rapid clearance from circulation, and off-target side-effects which are some of the common errors in case of conventional small-molecule drugs. Viral nanoparticle assembly is another prevalent strategy in the field of non-polymeric nanocarriers for drug delivery. Virus-like particles (VLPs) take advan-tage of this highly evolved and efficient transfer strategy to deliver their cargos by mimicking the natural process of viruses. Current research into genetically engineered viral carriers only scratches the surface of potential applications (Shi *et al*., 2014).

Microbes play a key role in drug discovery research. Microbes have been very important in the production of natural drugs. Most important aspect is most of these drugs are patented and are already in the clinical trials. Of 23,000 active compounds from microorganisms, *i.e*., antimicrobials, antivirals, cytotoxic, and immunosuppressive compounds, 42 % are made by fungi and 32% by filamentous bacteria, the actinomycetes (Demain, 2014). Marine cyanobacteria produce many compounds with activities such as neurotoxic, antiproliferative, anticancer, and anti-infective. Production of protein encapsulated silver nanoparticles (AgNPs) assisted by marine actinomycetes strain has been investigated. The selected isolate identified as *Streptomyces parvulus* revealed antimicrobial property against gram negative as well as gram positive bacterial strains (Prakasham *et al*., 2014). Hence the research involving viruses and other microorganisms for drug delivery and drug discovery may be one of the upcoming research areas in microbiology.

Endophytic microbes for effective antibiotics

Endophytes refer to the microorganisms (mostly fungi and bacteria) colonising the intercellular regions of healthy plant tissues, whose presence is unobserved and asymptomatic (García *et al*., 2012). Antibiotics or hydrolytic enzymes can be released by the endophytes to prevent colonisation of other microbial plant pathogens (Hallmann *et al*., 2006), or prevent insects (Azevedo *et al*., 2000) and nematodes (Hallmann *et al*., 1997) from infecting plants. Endophytic microbes have been found to produce novel bioactive metabolites with wide-ranging medicinal applications such as antibiotics, immunosuppressants, antiparasitics, and anticancer agents. Therefore, it is hypothesised that endophytes could be useful sources of lead compounds in future drug discovery research. (Alvin *et al*., 2014). Even after a considerable number research work, few or no compounds have been released to the market and so this part of microbiology needs much research work in future.

Microbial Fuel Cell

One of the most challenging issues for any country is to tackle energy crisis. Energy consumption is on an increase as the world population is growing uncontrollably. Fossil fuels such as petroleum, coal, and natural gas have been the major resources for energy requirement. However, they are gradually being depleted because they are not renewable. Therefore, there is a great interest in exploring alternative energy sources to meet the growing demands of the society. One such alternative energy producer in the future can be the microbial fuel cell. Microbial fuel cells are bio-electrochemical systems that convert chemical energy into electrical energy from the respiratory metabolic pathway of electrochemically active bacteria (EAB) (Yuan *et al*., 2014). EABs that grow on anodes are mostly strict anaerobes like *Geobacter*, or facultative anaerobes like *Shewanella* (Bourdakos *et al*., 2014).

Microbial fuel cell research is a rapidly evolving field but it lacks established methods for the analysis of system performance. The construction and analysis of MFCs require knowledge of different scientific and engineering fields, ranging from microbiology and electrochemistry to materials and environmental engineering. Describing MFC systems therefore involves an understanding of these different Microbiological and Engineering principles in future.

Scope of Microbiology

The scope of any subject can be assessed by the associated research activity and the creation of employment, ultimately benefiting the society. Job creation is the fundamental priority for any country.

Microbiology offers promising technologies for employability. Microbiologists can be made employable if proper skill is imparted for students starting at the graduation level. United States one of the most advanced country, is making use of microbiologists offering a huge amount of salary. Further almost all states of US provide employment to microbiologists (Fig. 1), which itself projects the scope of microbiology.

In the United States of America, the data on the mean salary per annum and the state-wise microbiologists appointed in various Government, Public and private sectors is really encouraging. The employability data of a microbiologist in the US is shown in Table 1. Other than the government and the public sectors, even the private industries recruit microbiologists on top of any other subject. Table 2 provides the information regarding employability of microbiologists in top US Industries.

Taking into account the data of the US, other developing countries especially India should promote the subject. The younger generation should

Table 1. Annual wages for microbiologists in the top five industries in US

Sl. No.	Nature of Job	Salary per annum (in US Dollars)
1	Federal government, excluding postal service	$96,520
2	Pharmaceutical and medicine manufacturing	67,070
3	Research and development in the physical, engineering,and life sciences	62,920
4	State and local government, excluding education andhospitals	54,640
5	Colleges, universities, and professional schools; state	52,790

Source: U.S. Bureau of Labor Statistics, Occupational Employment Statistics

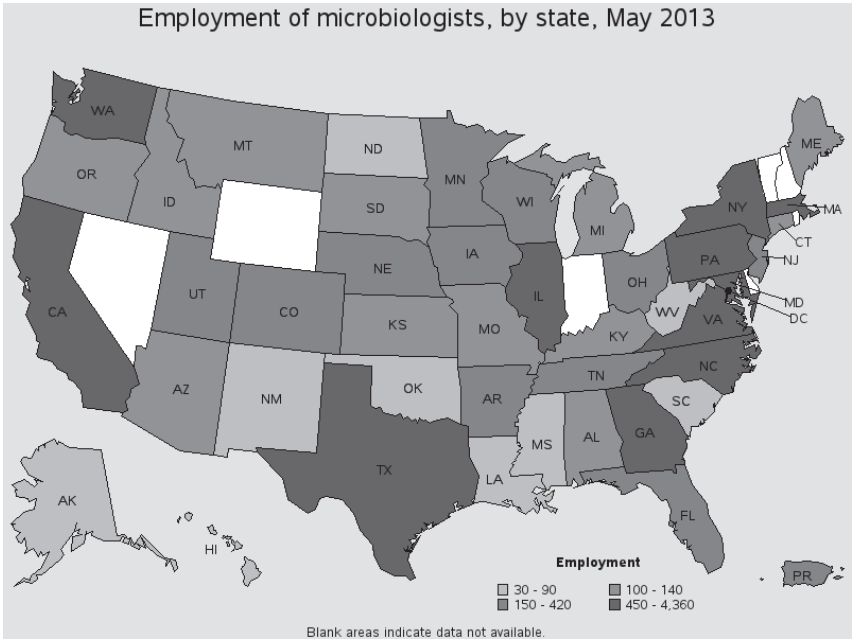

Fig. 1. Microbiology employment data in different regions/States of USA.

WA-Washington; MT-Montana; ND-North Dakota; MN-Minnesota; WI-Wisconsin; MI-Michigan; OH-Ohio; PA-Pennsylvania; NY- New York; ME-Maine; PA-Pennsylvania; OR-Oregon; ID-Idaho; SD-South Dakota; IA-Iowa; IL-Illinois; KY-Kentucky; WV-West Virginia; VA- Virginia; CA-California; UT-Utah; CO-Colorado; NE-Nebraska; KS-Kansas; MO-Missouri; NC-North Carolina; AZ- Arizona; NM-New Mexico; OK-Oklahoma; TX-Texas; AR- Arkansas; MS-Mississippi; AL-Alabama; GA-Georgia; SC-South Carolina; NC- North Carolina; FL-Florida; PR-Puerto Rico; AK-Alaska; HI-Hawaii; CT-Connecticut; NJ-New Jersey ;MD-Maryland.

(**Source:** U.S. Bureau of Labor Statistics, Occupational Employment Statistics)

Table 2. Top paying division of industries for Microbiologists in US

Sl. No.	Industry	Employment	Percent of industry employment	Hourly mean wage	Annual mean wage
1	Pharmaceutical and Medicine Manufacturing	4,850	1.75	$36.82	$76,580
2	Scientific Research and Development Services	5,060	0.80	$36.14	$75,170
3	Soap, Cleaning Compound, and Toilet Preparation Manufacturing	180	0.18	$32.64	$67,890
4	Pesticide, Fertilizer, and Other Agricultural Chemical Manufacturing	50	0.13	$34.37	$71,500
5	Federal Executive Branch (OES Designation)	2,490	0.12	$48.99	$101,900

Source: U.S. Bureau of Labor Statistics, Occupational Employment Statistics

be given the idea of the subject. Pre University education is considered as a major breakthrough in the career of a student and a majority of them are inclined towards professional degrees like medical and engineering subjects due to lack of knowledge in subjects such as microbiology. The employment and research opportunities provided by microbiology are quite appreciable.

CONCLUSION

The present article has put forth information on the amazing life of microorganisms and a useful insight into the research output, growth & the impact of microbiology at the international levels. The research and other aspects discussed in the present article are based on very few microorganisms identified till today. There is a huge estimate that 99 % of viruses and 90 % of the bacteria especially from soil need to be studied in order to exploit and control. Hence, there is a need for a high level exploration of microorganisms from various sources. The fact depicted in the article makes study of microbiology as the need of the hour. In the present scenario microbiology is a highly appreciated subject which has attracted huge number of students and research scholars, but taking into the account all the functions and importance of microbes presented in the article, the subject demands more input of human resources. Microorganisms are of great importance to both humans and the ecosystem. Therefore, it should be a high priority to establish the subject, make use of it for the best output in research and also for the creation of jobs. The knowledge of microbiology and manipulation of microbes in the future should be the key factor in the betterment of environment, agriculture and human health.

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