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OUR CORONA WARRIOR 🇮🇳

Working at Apollo hospital, Navi mumbai, completed 370 swab sample

ABINASH SAHOO

People from SLS Newsletter are privileged to honoring all the healthcare workers, volunteers, and frontline warriors for their dedication to fight pandemic. SLS Newsletter joint hands to eliminate and stop spreading by keep social distancing, wearing mask, and washing hands and protocol provided by the Ministry of Health, Govt of India. We also happy to announce and proud to mention that our students, Ms. Mrudula, Ms. Lakshmi Prasanna and Mr. Nagendra Atla (M.Sc. Microbiology) are involved in the corona sample collection and diagnosis of virus. To appreciate the braveness of these students, Microbiologist Society, India (MSI) honored them by posting their photos in MSI website under Corona Warriors section. We are also taking this opportunity to honor our own alumni here. We are proud of you for the frontline.

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Top 2% Scientist at SLS: Dr. P. Ashokkumar

Arshad Wahab and D. MubarakAli

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Stanford University of the United States of America has recently released a list of top 2% of the most cited scientists in diverse academic disciplines. A total number of ~160K professionals were enlisted from all over the world. Out of which approximately 1.5K scientists are Indians representing varied institutions. Prof. Ioannidis et al., compiled the list of scientists who were actively involved in research and assessments and analyzed the citations with a new set of parameters. This database included the top 2% of scientists of the world. The results so obtained have been segregated into 22 scientific areas and 176 sub areas recently published in the Journal PLOS Biology. Dr. P. Ashokkumar, Associate Professor in School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India is one of them who got enlisted at Sr. No. 85932 for his research accomplishment in the field of Cancer Biology. To celebrate his attainment, he was felicitated by Microbiologist Society, India. He keeps receiving wishes and honors from Vice chancellors, Registrar, Professors, Scientists, Students and industrialists for his deserving acknowledgement for his hard work and dedications towards his research.



❖ Mini Review

Pharmacological Potential of Astaxanthin

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Introduction

Astaxanthin is a pigment belongs to the family of xanthophyll, the oxygenated derivatives of carotenoids. It is ubiquitous in nature, found in marine environment such as microalgae, plankton, krill and sea food [1]. Astaxanthin is chemically 3, 3'-dihydroxy- β -carotene-4, 4'-dione which contain two terminal ring systems joined by a chain of conjugated double bonds or polyene system and are composed of carbon, hydrogen and oxygen. The polyene system gives these carotenoids their distinctive molecular structure, chemical properties, and light-absorption characteristics [2]. Astaxanthin has the molecular formula $C_{40}H_{52}O_4$. Its molar mass is 596.84 g/mol.

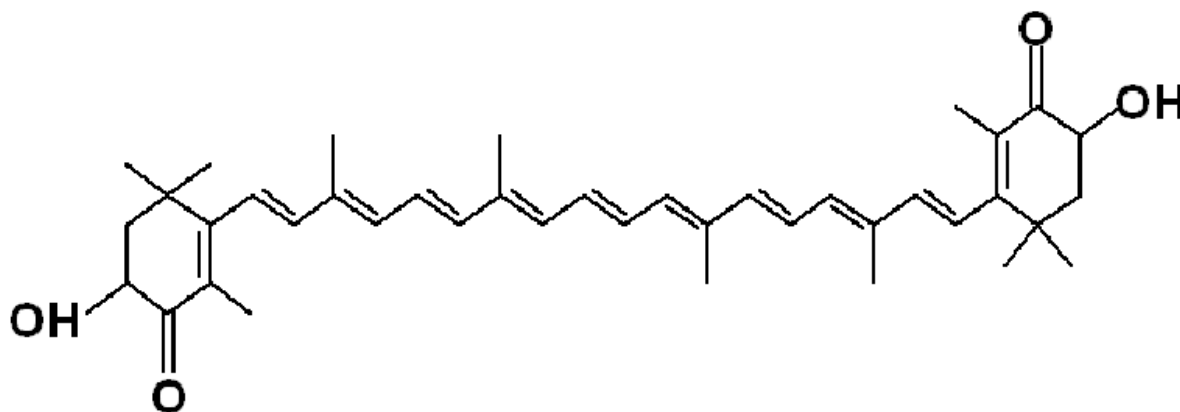


Fig. 1 Structure of Astaxanthin

Sources of Astaxanthin

Astaxanthin was found to be present in yeast, fungi, feathers of some birds including flamingos and quail, salmon, trout and crustaceans such as shrimp, crabs and lobster [3, 4]. The commercial astaxanthin is mainly isolated from *Haematococcus pluvialis* [5]. In addition, astaxanthin was also found to be present in several microorganisms such as *Chlorella zofingiensis*, and *Chlorococcum* sp., the red yeast *Phaffia rhodozyma*, and the marine bacterium *Agrobacterium aurantiacum* [6]. Astaxanthin is 10 times stronger than other carotenoids such as lutein, zeaxanthin, and β -carotene and 100 times stronger than α -tocopherol [7]. The use of astaxanthin as a nutritional supplement has been rapidly on the rise in foods, feeds, nutraceuticals and pharmaceuticals application.

Pharmaceutical Potential of Astaxanthin

Antioxidant activity

Powerful antioxidant activity of astaxanthin has been demonstrated in numerous studies showing the detrimental effects of free-radical-induced oxidative stress which have effective quenching effect against singlet oxygen, a powerful scavenging ability for lipid and free radicals and effectively breaks peroxide chain reactions. Astaxanthin had higher antioxidant activity when compared to various carotenoids such as lutein, lycopene, α -carotene and β -carotene [8]. The antioxidant properties of astaxanthin have a crucial role in numerous properties such as protection against UV-light photo oxidation, inflammation, cancer, ulcer's *Helicobacter pylori* infection, aging and age-related diseases or the promotion of the immune response, liver function and heart, eye, joint and prostate health [9].

Anti-inflammatory activity

Astaxanthin could exert its anti-inflammatory actions by inhibiting the expression of inducible nitric oxide synthase and cyclooxygenase-2 and the production of nitric oxide in lipopolysaccharide-stimulated BV2 microglial cells [10]. Astaxanthin due to its inhibitory action on the production of nitric oxide it has been implicated for the development of anti-inflammatory drugs for chronic inflammatory diseases such as sepsis, rheumatoid arthritis, atherosclerosis, inflammatory bowel disease, and brain inflammatory diseases [11].

Anticancer activity

Astaxanthin induces the inhibition of 5 α reductase enzyme which in turn restrain the growth of prostatic cancer cells. *In vitro* assay of astaxanthin effect was carried out using human cell line. The results show that Astaxanthin caused 98% inhibition of 5 α reductase, and a nine-day treatment of prostatic carcinoma cells with Astaxanthin produced a 38% decrease in growth [12]. Cancer metastasis can be inhibited by Astaxanthin, as well as certain intrinsic factors. Natural killer cells of the immune system are involved in anti-tumor activity and the inhibition of cancer. Dietary astaxanthin showed significant antitumor activity when compared to other carotenoids like canthaxanthin and β -carotene [13].

Antidiabetic activity

Astaxanthin could inhibit the nonenzymatic glycation and glycosylated protein/iron chelate-induced cytotoxicity in human umbilical-vein endothelial cells by preventing lipid and protein oxidation and increasing the activity of antioxidant enzymes *in vitro* [14]. The significant elevation in both glucose and insulin levels induced by a high fat plus high fructose diet in mice was abolished by astaxanthin supplementation, also indicating that astaxanthin could substantially improve insulin sensitivity [15].

Immunomodulatory

Enhanced antibody production and decreased humoral immune response in older animals after dietary supplementation of astaxanthin was reported [16, 17]. T and B cells were increased, DNA damage was low and C-reactive protein (CRP) was significantly lower in the astaxanthin supplemented group [18, 19].

Cardioprotective activity

Astaxanthin could increase heart mitochondrial membrane potential and contractility index dose dependently and tend to decrease plasma interleukin-1 α , tumor necrosis factor- α , and serum amyloid A concentrations and also reduced the wall/lumen ratio in coronary arteries and decreased elastin bands in the aorta [3, 20].

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RecA in Antibiotic Resistance Mechanism: Overview

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Abstract :-

Antibiotic resistance is one of the major challenges faced worldwide by modern medicine. It creates high economic drain in the healthcare sector. The rapid rate at which bacteria develop drug resistance is majorly due to mutations that arise during stress-induced DNA repair and also during the lateral transfer of genes between organisms, i.e. the SOS response, in which the bacterial RecA protein plays a key role. Inhibitors that can block the RecA protein and in turn block the antibiotic-induced activation of the SOS response could potentiate the effect of antibiotics on bacteria thus reducing its ability to develop antibiotic resistance mutations hence they can be used as an adjuvant to the existing antibiotic to slow down the emergence of antibiotic resistance in bacteria.

Introduction :-

Antibiotic resistance is one of the major challenges that is being faced worldwide by modern medicine. It creates high economic drain in the healthcare sector. **(1)**. For survival in various environmental conditions, bacterial cells have a repertoire of genes that they can express or silence according to their needs. Among this vast collection of genetically controlled networks, the SOS response is an inducible DNA repair system that allows bacteria to survive sudden increases in DNA damage and the key role in this process is played by the RecA protein.

RecA is a ubiquitous protein, which is conserved in almost all bacteria and organisms, including humans. The RecA present in bacteria which is essential for stress induced DNA repair and the lateral transfer of genes between organisms; SOS response, aids in

conferring mutations and results in development of drug resistance at rapid rate in bacteria **(2)** The SOS response is regulated by two key proteins- RecA and LexA. The RecA protein acts as inducer whereas the LexA protein acts as repressor of SOS genes.

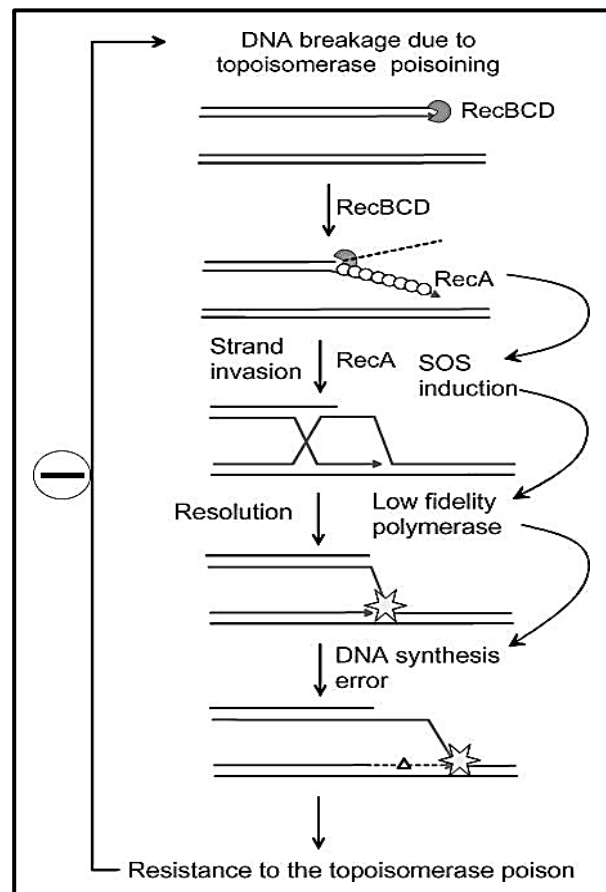


Fig. 1 A Model for SOS-Dependent Evolution to Antibiotic Resistance (2,4)

In absence of any stress, in normal conditions, the LexA repressor binds to the SOS box which is present in the promoter region of SOS genes and represses their expression. In case there is any stress and increased level of damage to the DNA, the RecA protein binds to the ssDNA and forms active nucleoprotein filament (NPF), this consists of multiple RecA monomers, ATP, and ssDNA. **(3)** The NPF has two major functions, it may either-

*Approach a homologous dsDNA sequence and catalyse the strand exchange which is an important step of homologous recombination or.

*It may promote self-cleavage of LexA protein thus inducing the SOS response.

In the PLOS Biology, June issue the Romesberg laboratory used a Murine infection Model to describe the role of SOS-Dependent Evolution in conferring Antibiotic Resistance to bacteria. Topoisomerase poisoning agents instigate DNA double-strand breaks. In turn RecBCD load RecA which induces the SOS response and initiates homologous recombination reaction which ends with a primer-template structure which the SOS-induced polymerases can access. These SOS-induced DNA polymerases that act at the replication forks have low fidelity and thus generate mutants some of which are resistant to ciprofloxacin. The mutant cell sub population that can resist the poisoning agent occupy the niche. **(2,4)** This study indicates that the SOS induction leads to the formation of resistant cells and suggest that blocking SOS induction which can be achieved by blocking its inducer RecA could be a general means to prevent the rapid evolution of bacteria to antibiotic resistance.

Additionally, RecA function is also essential for other aspects of pathogenicity which includes antibiotic-induced responses to ciprofloxacin and β -lactams, antigenic variations in Neisseriae, and induction of shiga toxin production.

Table1. Summary of experiments studying the inhibitors of RecA protein

Inhibitor	Model	Reference
Metal cations; zinc, copper, mercury	<i>Escherichia coli</i>	Lee et al. (5)
a-helical peptides	<i>Escherichia coli</i>	Cline et al. (6)
Curcumin	<i>Escherichia coli</i>	Bellio et al. (7)
Suramin	<i>Mycobacterium tuberculosis</i>	Nautiyal et al. (8)
Phthalocyanine tetra sulfonate	<i>Escherichia coli</i>	Alam et al. (9)
p-coumaric Acid	<i>Listeria monocytogenes</i>	Ojha et al. (10)

Inhibitors of RecA in antibiotic resistance mechanism:-

Mutations that arise due to stress induced DNA repair pathway; SOS response all require RecA protein. Thus, discovery of molecules that inhibit RecA are an important step in the development of inhibitors for the suppression of the evolution and transmission of antibiotic resistance. Various studies provoke the development of lead

compounds for inhibiting RecA-dependent processes leading to the development and transfer of antibiotic resistance.

Summary:

Through various research papers, the Role of RecA protein in inducing SOS response during stress leading to development of mutation and in turn development of antibiotic resistance in bacteria could be understood along with various compounds that inhibit RecA and thus help in reducing the emergence of antibiotic resistance.

Future perspectives:-

Recently discovered inhibitors of RecA protein like P-Coumaric acid which has already been found to be a good inhibitor of *Listeria monocytogenes* RecA experimentally could also be experimentally proven as potent inhibitor of RecA proteins of other pathogenic bacteria with further invitro and in vivo studies and can be used as adjuvant to specific antibiotics to improve their immune response.

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Cancer Drug Discovery and Design

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Introduction:

World's second most leading cause of mortality is due to cancer. As the number of cancer cases has surpassed all previous records the pharmaceutical industry has shown increased interest towards developing anticancer drugs and treatments for better therapeutic outcomes. Despite these efforts, cancer drug discovery remains a difficult area, with therapeutic advances failing to meet expectations in clinical trials. Clear understanding of physiopathology of the disease and engineering suitable molecular targets has emerged beneficial and provides the hope of creating more effective therapies. Based upon the exciting biological target's awareness novel drug composition are discovered and designed. Drug design, at its most basic level, entails creating molecules that are complementary in shape and charge to the molecular target with which they interact and bind. Preclinical studies on cell-based and animal models, as well as clinical trials on humans, are all part of drug production and discovery, which leads to regulatory approval. Several notable advancements have been developed to treat cancer, among which the most important is the invention of targeted therapies. computer modeling techniques and bioinformatics approaches has augmented the selectivity and efficacy of these oncologic treatment modalities. We can now comprehensively compile the genetic alterations in many human cancers at diagnosis and during treatment, thanks to recent transformative advances made by initiatives like The Cancer Genome Atlas and the International Cancer Genome Consortium. The importance of identifying the genetic makeup of individual tumors and developing tailored care plans to effectively treat patients is demonstrated by the complexity and interpatient variance of alterations exhibited by tumor cells. The application of combinational therapy is the future of tumor treatments.



Fig. 1 Steps involved in cancer drug discovery and design

Cancer drug discovery and design:

The first ever anticancer drug launched in 1949 was the mechlorethamine currently 150 anticancer drugs are being approved by the US Food and Drug Administration. Remarkable innovations such as the 4-amino-pteroylglutamic acid which is a folic acid antagonist are used to treat child leukemia have stimulated novel model in cancer therapy. Animal models are among the most powerful instruments in the arsenal of cancer researchers, but they have significant drawbacks. *in vivo* studies in xenograft models remain the foundation for preclinical drug discovery and development; specifically, they can be employed to evaluate the relationship between pharmacokinetic and pharmacodynamic measures of target regulation within a short period of time. Immune responses are being successfully studied using syngeneic mouse models. The use of patient-derived tumor xenograft (PDX) models developed by academic or commercial organizations is growing in popularity. As a result, data derived from the xenograft models provided should be viewed with caution before being administered into humans. The importance of specific target identification relies on validating the drug and its composition. *In vitro* and *in vivo* studies of RNA interference (RNAi) have been widely used to identify and confirm primary drivers of tumorigenesis and possible druggable targets for cancer therapy. Chemical probes which do not exactly mimic approved drugs are gaining awareness for this purpose. New targeted agents' mechanisms of action must be well-defined and validated both *in vitro* and *in vivo*, and plasma exposure in preclinical systems must be determined in order to ensure enhanced target engagement. Several oncology drugs currently in clinical trials are yet to be established as to how they function thus it is to be ensured

that only safer drugs are being developed and marketed which can be administered over a long period of time without jeopardizing patients' quality of life or causing harm to their wellbeing.

From commercially available oridonin, Wei Xiao, Huiming Hua, Jinyi Xu designed and synthesized a series of nine enmein-type ent-kaurane diterpenoid and furoxan-based nitric oxide (NO) donor hybrids. Their research into the antiproliferative properties of these hybrids led to the conclusion that these NO-donor/diterpenoid hybrids may be a fruitful way to explore new class of antitumor drugs. Feng Xu and colleagues used the hanging drop approach to test the anti-proliferative efficacy and cellular absorption of two promising anti-tumor drug candidates, evodiamine (EVO) and rutaecarpine, in 3D culture of MCF-7 and SMMC-7721 cells and suggested that it can support a new perspective on EVO and RUT's anti-tumor activity using 3D multicellular spheroids and cellular absorption using compound fluorescence, which could be useful for drug screening and cytotoxicity studies.

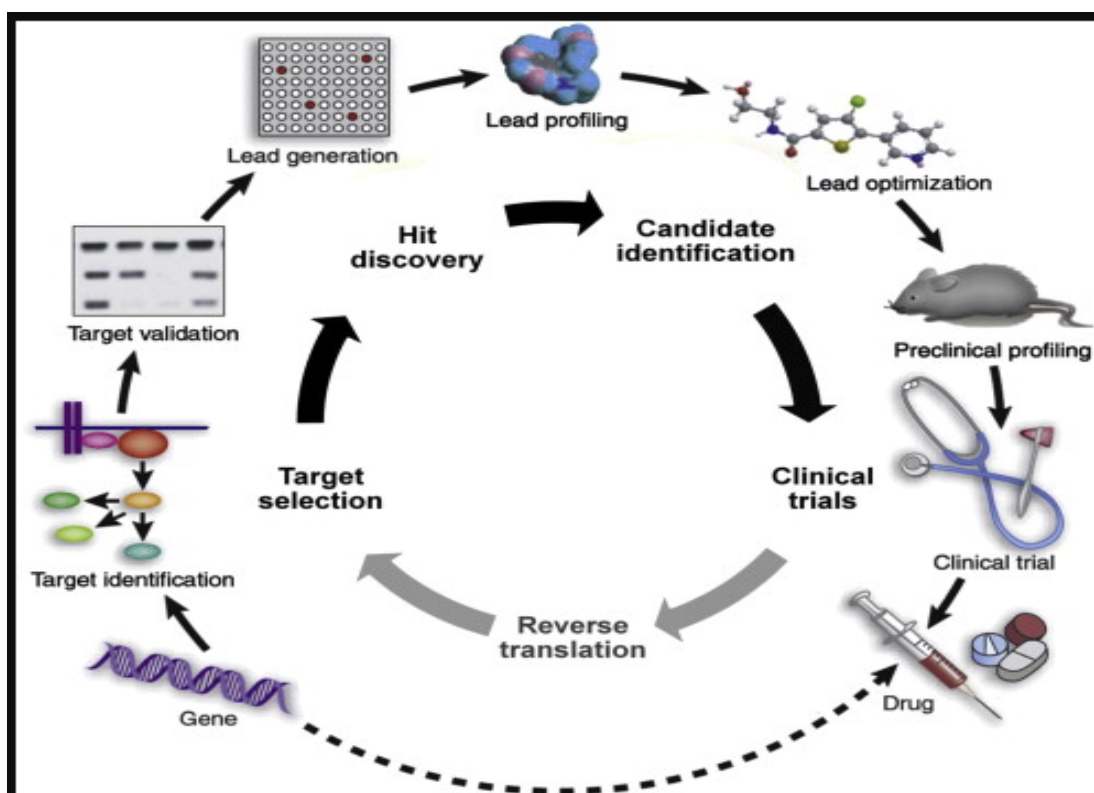


Fig. 2 Drug discovery and development: From gene to drug.

Summary:

Thus in vivo and in vitro studies accompanied with computational approaches, are continually improving the efficacy and efficiency of drug development processes, allowing for the selection of lead candidates with better prospects. the sectors of computer-aided drug discovery and development, drug design and synthesis approaches, in vitro and in vivo pharmacological and toxicological evaluations are rapidly improving and are becoming necessitated in the biological field.

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❖ Mini Review

Wastewater: Recycle and Reuse through Biotechnology

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Abstract:

Water is the basic thing that plays an important role in everybody's life. The main objective of this study is to show the importance of water in this modern world and role of biotechnology in water treatment. Recycling of polluted water is the main element to save our water resources. Biotechnology is a new system in this modern world that uses biological environment for the creation or modification of particular product. Also, it's a useful tool to deliver the improved products and processes for environmental sustainability.

Keywords: Water, Recycling, Biotechnology, Microbes, Pollutants

Introduction:

Without the contribution of hydrogen and oxygen in this world, life on earth would not have existed. Water is used by all living organisms, especially humans use it for drinking, washing, bathing and other industrial purposes. Earth is surrounded by 71% of water and it contains only 1.7% ground water which is pure water, that can be seen in river and lakes too. Pure water is essential for humans and other living beings even though there is no nutrition in water. Deaths in rural and developing nations increased in past few years due lack of pure water. Access to this pure water is improving day by day, but still millions of lives thriving for pure and safe water. Increase in the amounts of chemical industries and urbanization resulted in change in nature of underground pure water.

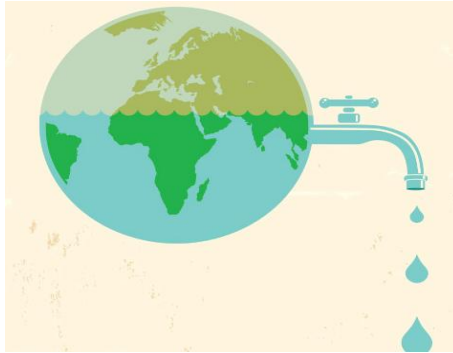


Fig. 1 Copyright: ©peangdao - stock.adobe.com

This will also result in microbiological contamination which allowed pathogenic microbes to penetrate into the ground water. Some bacteria like pseudomonas which has the ability to multiply rapidly in pure water, became a big threat to human lives and also resulted in various gastric diseases.

Biotechnology proved in generating enormous wealth and is able to influence various sectors of economy including healthcare and food processing. The main focus of biotechnology in water treatment is to completely remove or purify the contaminated water and to bring attraction of clean water towards public and environment. It finds the major application fields in treatment of waters using biological approaches.

Biotech promises a wide range of benefits to manage the waste water from industries economically and effectively around the world. Environmental biotech is one of the multidisciplinary unit of sciences and engineering to utilize the huge biochemical potential of microbes, plants for restoration and preservation of ecology.

Polluted water:

The main issue of water pollution or contamination happens because of irregular monitoring and improper recording of groundwater condition of industrial, domestic and agricultural lands. Improper monitoring facilities is one of the major reasons for cause of water pollution. There are thousands of toxic chemicals found in drinking

water supplies all around the world, they are relatively high in concentration which is hazard to human health.

Some pollutants are BOD (Biochemical Oxygen Demand), COD (Chemical Oxygen Demand), metals and other compounds. Most harmful chemical pollutants are heavy metals, arsenic, chlorides, cyanide, because of their high toxic level. Cadmium, zinc, lead, copper and chromium these are released by human activities or by natural calamities like earth's crust into the environment which is highly toxic heavy metals in nature.

Outcome of this polluted water:

- Polluted water in our society leads to the contribution of different types of cancers which can't be easy to get cured.
- Chemicals and heavy metals has the ability to cause birth defects by damaging the immune system of individuals.



Figure 2: copyright: shutterstock

Table 1: chemicals compounds and diseases caused by those compounds

Chemical compounds	Diseases
Nitrates	Blue baby syndrome
MPTP	Parkinsonism
Arsenic	Liver, nervous system damage & skin cancer
Pesticides	Nervous system damage & cancer

The four pillars for water treatment by biotechnology:

1. Nutrition in wastewater
2. Fouling of water treatment system
3. Energy production
4. Specific pollutants

Methods followed by Biotech/chemical industries for water treatment:

➤ **Basic methods:**

- 1) Activated sludge
- 2) Trickling filters
- 3) Oxidation ponds
- 4) Anaerobic treatment
- 5) Biofilters (sand, activated carbon, fabrics, membranes)
- 6) Reverse osmosis

These are the general systematic approaches followed by industries to purify the water.

➤ **Recycling of waste water:**

Recycling the water has the ability to minimize the diversion of fresh water from sensitive environment or ecosystem. It can reduce the discharge impure water to sensitive water bodies. It can able to reduce and prevent the pollution of pure water. Recycling of water takes huge amount of energy and it is a efficient process than other methods. Recycled water replaces the existence of drinking water for non-potable uses and it will be available at lower price compared to potable water.

➤ **Environmental biotechnology:**

The main objective of this concept is to use the living microorganism to transform the undesirable and harmful substances into non-toxic form. It works on the concept of engineering & scientific knowledge with the use of microbes & their secondary product to prevent pollution in water through biotreatment of solid & liquids, bioremediation, biomonitoring and finally treatment process.

Benefits of recycle & water treatment using biotechnology:

- It reduces the cost obtained from water treatment when comparing to conventional purification process.
- It reuses many
- resources that obtained in the systemic process like energy and salts.
- Reuse of phosphorous from wastewater as a fertilizer.
- Recombinant Microbes used in this treatment improves the
- quality of pure water for drinking.
- Recycled water can be used for non-potable purposes like agriculture, parks, golf
- court irrigation, constructions, industries and power plants.

Future of water:

Recycling of water technology proved to be a successful and effective in creating new and reliable water supply without any compromising in public health. Reuse of non-potable water widely accepted that it will continue to grow enormously.

The improvement in downstream flows of rivers resulting in 20% of reduction water demand through conservation and efficiency measures in both agriculture and urban, coupled with beneficial reuse of 90% of reclaimed water flows for non-potable uses. Using biotechnology as a remedy to treat water is not a new idea. Communities depended on natural sewage treatment by microbes over centuries. Recombinant DNA technology is now providing possible remedies to control water pollution and to improve bioremediation.

Conclusion:

Successful water recycling process have been developed in many nations. As water demand increases, the environmental needs will also grow randomly, recycling the waste water is going to play a important role in our overall water supply system. By working together to overcome the problem of water treatment and recycling, along with efficiency and conservation, can lead us to sustainably manage our vital water resources. Still there is much more to do for improving water recycling and technologically improve the water treatment in future. The world is getting threatened

by human activities day-by-day with usage of chemicals and non-renewable resources. If we can't able to stop polluting the nature's gift now, then there is no way to live a healthy life further.

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