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Bacillus thurengiensis: Biotechnologocal applications and potentials

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Abstract
Bacillus thuringiensis is a gram-positive bacterium, which produces crystalline parasporic proteins during the sporulation process and is known as an important microbial insecticide, which plays an important role in combating agricultural pests. Biological control of insecticide-resistant Anopheles mosquitoes with the help of *Bt* in medicine is very effective in controlling malaria. *Bt* is biologically active against parasites and the deltatoxin of this bacterium can be used to treat leishmaniasis infections or to treat ascariasis caused by ascariasis parasitic worms due to its cytosidal effects against *leishmania* parasite promastigotes. In addition to Cry crystalline proteins, *Bt* is able to produce paraspores, which, unlike the first group, have no insecticidal properties and have anti-cancer effects in humans. The protein / glycoprotein surface layer in this bacterium can be widely used in nanobiotechnology. It is also important in the bioremediation of contaminated environments due to the biological absorption of heavy metals (copper, manganese, cadmium, nickel) which are soluble in industrial effluents and have a high durability in nature and a high tendency to accumulate in the tissues of living organisms. Biodegradation of biological wastes such as ethidium bromide and methylene blue, pharmaceutical effluents such as ibuprofen, synthetic pesticide residues such as halothane, malathion, as well as biodegradation of light petroleum polymers from the sea surface and biodegradable biomass biomass biomass Other applications of this bacterium and also having different enzymes such as: lipase, alpha-amylase, creatinase, protease and cellulase can be used in food, cosmetics, detergents, paper production, biogas production and medicine. Simultaneous production of several widely used types of polyhydroxyalkanoate by *Bt* strains as environmentally friendly microbial biopolymers to replace petroleum-derived plastics is another application of this microorganism. *B*t can help us fight antibiotic resistance by producing bacteriocin and antimicrobial peptides. *B*t plays an important role in creating microbial pathways for the

production of silver nanoparticles for antimicrobial applications and nanobiological insecticides.

Keywords*:* *Bacillus thurengiensis* applications, Crystalin proteins, Biotechnology

Introduction:

Bacillus thuringiensis (Bt) is a gram-positive and optional anaerobic endophosphate bacillus, used as a biological insecticide in agriculture due to the production of protein toxins during sporulation, and has many advantages, including a specific effect on pests, no adverse effects on humans. The environment and non-target insects are less expensive, and easier to use than chemicals (Du and Nickerson 1996). This bacterium is able to produce different types of toxins (exotoxins and endotoxins). Delta endotoxins are protein crystals of two different groups with different insecticidal mechanisms (Mizuki et al, 2000). The first group is delta endotoxins, Cry proteins (derived from the word crystal), and the other group are Cyt proteins with cell lysis ability (Ammons et al, 2009). The genes that encode Cry / Cyt proteins are activated during sporulation and production It is controlled by RNA polymerase, which is synthesized specifically during spore formation. Crystals Cry proteins have different shapes but are usually in the form of a polygonal pyramid (Nair et al, 2018). After being released from the spores, these crystals aggregate to form larger parasporal wind crystals, the insect-killing toxin. Cry proteins have very specific chemical properties, including high molecular weight, resistance to proteolysis, and solubility at alkaline pH. These toxins are located on the spore surface and are protected by the exosporium (Du and Nickerson, 1996) .The Nomenclature Committee now classifies Bt toxin Cry proteins into 73 categories (Cry1-Cry73). (Höfte and Whiteley, 1989). Cry toxins are inactivated as protoxins and after activation due to alkaline conditions of insect intestines and host protease activity, they react with specific receptors located on the surface of intestinal epithelial cells, forming a pre-porous oligomeric structure and eventually creating a hole in the cell membrane. And become insect death (Curtis, 1984). Human and animal safety against these products is due to the fact that the intestinal conditions of humans and animals are very acidic and unfavorable for these toxins, because pH causes denaturation of the protein solution of insecticide crystals and prepares them for hydrolysis by intestinal protease. سازد. Poisoned insects may perish rapidly or, due to blood poisoning, stop feeding and die within 2 to 3 days (Yezza et al, 2006). In contrast, Cyt toxins react directly with membrane lipids and attach to them. Cyt proteins also exhibit general cytolytic activity in vitro and often have specific insecticidal activity on Diptera in vivo. Cyt proteins are also classified into 3 families (Cyt1, Cyt2 and Cyt3) (Palma et al, 2014). Exotoxins produced by different strains of Bt include alpha exotoxins, beta exotoxins, gamma exotoxins, Vip toxins, and Sip toxins (Zhong et al, 2000). In addition to insects, alpha exotoxins are toxic to mice and other vertebrates. Beta-exotoxins, which are produced in some strains of this bacterium, are heat-resistant and have widespread adverse effects on mammals, including humans, and their presence in commercial products is prohibited (Palma et al, 2014). Gamma exotoxins are not toxic to insects. In the vegetative phase, some Bt strains are able to secrete proteins with insecticidal properties into the culture medium. This increases the host range of this bacterium. These proteins are grouped into: Vegetative insecticidal proteins (or VIP for short) and Secreted insecticidal protein (SIP). Previously, VIP proteins were in 3 families (VIP1, VIP2, VIP3) and recently a fourth family has been added to them. VIP1 and VIP2 together form a highly toxic unit of two units against the pests of the order Coleoptera and the sucker pest of the plant sap called Aphis gossypii (cotton aphid) of the order Hemiptera. VIP3 proteins act individually, not in pairs, against a wide range of species of the order Lepidoptera. Insecticidal properties (activity and host range) of VIP4 protein are not yet known. Phylogenetically, however, it is closely related to VIP1 proteins. The SIP protein is the first and only member of the Bt secretion family of proteins and is toxic to Coleoptera larvae, killing some species and inhibiting growth for others. In addition to these protein groups, Bt also produces other proteins that are expected to be toxic based on their sequence and conserved regions. But few studies have been done on them. Bacillus thuringiensis has a surface layer S with symmetry P2, the outer surface of which is smooth and the inner surface is wavy (Shipp et al, 1998) and is morphologically very similar to pure parasporal crystals. This layer is produced during the bacterial growth phase (Spence et al, 2019). Due to the unique traits of this bacterium, including the production of various metabolites, it has great potential for application in various fields of biotechnology, and our aim in this review article is to focus on the applied aspects of Bt in various fields of biotechnology.

Bacillus thuringiensis in medicine:

Bt can be important in medicine in many ways.

Characteristics of Anopheles mosquitoes: Malaria is a monotonous disease that affects more than 3 billion people worldwide and kills more than 3 million people a year. It is the most important human parasitic disease with many complications. Is. About 45% of the population of the eastern Mediterranean region (which also includes Iran) is at risk for Vivax and Falciparum malaria (Alonso et al, 2005). Female Anopheles mosquitoes are carriers of the transmission of infection among humans. This disease can have fatal consequences if not taken care of in time. Iran is located in the temperate region of the northern and eastern Mediterranean and has a diverse climate in the endemic region of the global malaria distribution map. Reports show that malaria has been prevalent in Iran since ancient times and therefore this disease has long been considered as one of the native infectious diseases in Iran by health policy makers (Srivastava et al, 2003). Today, malaria is considered as one of the main threats to human health due to climate change and the emergence of resistant species of its carrier Anopheles mosquitoes due to the widespread use of chemical insecticides and the destructive environmental effects of these toxins. Therefore, efforts are being made to adopt biocontrol methods as an efficient and nature-friendly alternative. In the meantime, special attention has been paid to mosquito-repellent bacteria, especially Bacillus thuringiensis and its cry protein toxins due to the unique benefits and characteristics of this group (Walker and Moreira, 2011). However, so far different approaches to prevention, treatment and prevention Malaria transmission has been used, the lack of effective vaccine and the lack of design and discovery of anti-malarial drug has made the destruction and control of disease-carrying mosquitoes one of the most effective, efficient and major approaches.The mosquito-specificity of Cry4A (Poncet et al, 1995), Cry4B, Cry11B, (Rosso and Delecluse, 1997) Cry19A, Cry24Ca and Cry39A (Ito et al, 2002) against the order Diptera has been identified.

Antifungal characteristics of Bacillus thuringiensis in medicine and phytotherapy:

Bacillus thuringiensis can have anti-nematode properties for several reasons:

1. Having the enzyme metalloproteinase that causes digestion of digestive tissue
2. Delta endotoxin, which by pore-forming mechanism causes lysis of cells in the gastrointestinal wall
3- Exotoxin which due to its analogy with nucleotides and inhibition of RNA-pol enzyme causes damage to gastrointestinal wall cells
4. Bacterial chitinase enzyme is involved in digestion of digestive tissue and body wall (Jouzani et al, 2017)

One of the most important nematodes in the field of botany are nodule-forming nematodes in plant roots that cause damage to agricultural products, especially in developing countries, and due to high reproduction, wide host range and wide geographical distribution, one of the most difficult plant nematodes. In terms of control (Ravari and Moghaddam, 2015). Crystalline proteins from the Cry5, Cry6, Cry12, Cry13, Cry14, Cry14, Cry21, and Cry55 families have a nematode effect on Wangli larvae (Bravo et al, 2013) and the production of AMPs (antimicrobial peptides) to win larval competition and co-phenol oxidase activity. Cry3Aa protein will be effective in larvae for which Bt dose is non-lethal (Yang et al, 2019). Ascaris worm is also one of the main nematodes in causing chronic infections in humans and pigs and produces toxic secretions in the intestine and due to their large number. They cause obstruction (Urbon et al, 2013). Cry5B crystal has a very good potential for poisoning adult ascaris larvae and worms (Charuchaibovorn et al, 2019) and its efficacy in the treatment of ascaris infection in invino conditions in pigs has been studied.

Insecticide characteristics against human and animal infecting mites:

In tropical and subtropical regions, there are human and animal infecting mites that cause diseases such as: Babesia, anaplasmosis. These mites are controlled with the help of chemical products, however, these parasites are resistant to almost all used organophosphatic insecticides, pyrethroids and amides and should be used in high doses or in a mixture of several products (Miller et al. 2006). These practices increase costs and pollute the environment. An alternative method is biological control.

Increased toxicity of crystalline proteins by the effect of S-layer and VIP proteins of Bacillus thuringiensis on Ripicephalus microplus mite (causing disease in livestock) has been investigated. The importance of this type of protein is due to its expression in the bacterial vegetative phase The fermentation process will be suitable, if in 2019 in Korea with the help of Gp543 Bacillus thuringiensis strain the production of high-performance S-layer in industrial fermentation medium has been done, which its toxicity has been done in vivo and in vitro on adult Ripcephalus microplus mite (Lormendez et al, 2019). .

Toxicity to Leishmania tropica and Major:

The anti-leishmaniasis effects of Bt crystalline toxin on Leishmania tropica and Leishmania major have been studied. Leishmaniasis is an infectious disease caused by a forced intracellular parasitic parasite belonging to the genus Leishmania. Soil is transferred to matter. This disease, which is seen in cutaneous, cutaneous, mucosal and visceral forms, is endemic in 88 countries of the world, including Iran. In 2008, Hanan et al. Found that the deltatoxin Bacillus thuringiensis was effective against Leishmania major promastigotes (El-sadwy et al, 2008). Fereydoni et al. In a study conducted in 2018 on the anti-leishmaniasis effect of Crys crystalline toxin Cry1 35sb isolate of Bacillus thuringiensis on Leishmania tropica, it was found that the best lethal effect (40%) of this strain at a concentration of 1-10 mg / ml Liters and the cytopathic effects of promastigotes treated with crystalline toxin are short and swollen due to the possible effects of cytokine proteins on the cell membrane and the cytoplasm of Leishmania proteins in promastigotes. The toxin of this bacterium destroys the connection between the parasite classes and appears as a decrease in cell volume, loss of the parasite shape and finally its disintegration (Feridoni et al, 2018).

On the other hand, antimicrobial peptides have recently received a lot of attention due to their rapid action, wide range of activity and low probability of resistance, but due to their poor penetration into pathogen-infected cells, their use in the treatment of infections. Intracellular is challenged. Cry3Aa protein crystals formed within Bt are readily and specifically absorbed by infected macrophages, and thus cry3Aa crystals can be an effective carrier of antimicrobial peptides (Amp) for the treatment of intracellular infections, including leishmaniasis. In a study conducted in 2019, Cry3A Bacillus thuringiensis crystalline protein was used to increase the uptake of an anti-leishmaniasis peptide called Dermaseptin S1 (DS1). And reduced toxicity to host macrophage cells (Khan et al, 2016). Therefore, Bt toxins can be used as anti-leishmaniasis agents or carriers to better treat leishmaniasis.

Bt can also be important in medicine due to the production of antimicrobial peptides. Bacteriocins are small peptides (between 12 and 70 amino acids) produced by bacteria that exert inhibitory activity against gram-positive and gram-negative bacteria and fungi (Dobson et al, 2012). Bacillus thuringiensis produce large amounts of metabolites, which have biocidal and antagonistic activities. In addition to the widespread production of insect-resistant proteins Cry, Vip, and Cyt, and biocidal paraspores against a variety of cancer cells, they also synthesize compounds with antimicrobial activity, including bacteriocins. The production of many bacteriocins has been reported by Bacillus thuringiensis, which can be seen in the table below:

Table 1 - Bacillus thuringiensis bacteriocins with biological activity against gram-positive and gram-negative bacteria and fungi: (Salazar-Marroquín et al, 2016)

	Gram positive	Gram nagative	fungi
Thuricin	*Bacillus megaterium, B. cereus, Bacillus polymyxa, Bacillus sphaericus, Corynebacterium xerosis, S. aureus, E. epidermidis, L. monocytogenes*	*Enterobacter cloacae, Pseudomona srynigae. S. enterica ser. Cholerae*	
Thuricin S	*L. monocytogenes, B. cereus, Bt, B. subtilis, B. megaterium, Pediococcus acidolacticis, Streptococcus thermophiles*	*Enterobacter cloacae, Pseudomona srynigae. S. enterica ser. Cholerae*	

Thuricin Bn1	*B. cereus, Lactococcus lactis,* *L. monocytogenes*	*Paucimonas lemoignei, Pseudomonas savastanoi*	
Thurincin H	*B. cereus, B. subtilis, B.megaterium,L.monocytogenes, L. innocua, L.ivanovii, S. aureus, Carnobacterim psicola, Geobacillus stearothermophillus*		
Bacthuricin F4	*B. cereus, B. subtilis, Bacillus licheniformis, S. aureus, Brevibacterium flavum*	*K. pneumonia*	
Thuricin 17	*B. cereus*	*E. coli MM294*	
Entomocin 110	*B. cereus, Bacillus coagulans, B. megaterium, Bacillus mycoides, Bacillus pseudomycoides, Lactococcus lactics, L.monocytogenes, Paenibacillus larvae Paenibacillus polymyxa*	*P. aeruginosa*	
Tochicin	*B. cereus, Leuconostoc mesenteroides*		
Bacthuricin F103	*B. cereus, B. subtilis, B. licheniformis,* *L. monocytogenes*	*A.tumefaciens*	
Thuricin 7	*B. cereus, B. subtilis, B. pseudomycoides* *B. mycoides, Staphylococcus pyogenes,* *L. monocytogenes, B. weihenstephanensis*	*A.tumefaciens*	
Entomocin 9	*B. cereus, B. pseudomycoides, B. mycoides,* *B. weihenstephanensis, Lactobacillus sp. Lactococcus lactics, L. monocytogenes*	*P. aeruginosa*	*Aspergillus nidulans, Fusarium graminis*
Morricin 269 Kurstacin 287 Kenyacin 404 Entomocin 420 Tolworthcin 524	*B. cereus, B. weihenstephanensis, C. difficile, Listeria innocua, S. aureus,* *S. pyogenes, Enterococcus faecium*	*V. cholerae, Shigella flexneri, Salmonella sp., E. coli, K. pneumoniae, Enterobacter cloacae, Proteus vulgaris*	*Rizophus sp., Fusarium oxysporum, Mucor rouxii IM80, Trichoderma sp SH1., Trichoderma sp. SD3*

Thuricin CD	*B. cereus, Bacillus firmus, B. mycoides, C. difficile, C. tyrobutyricum, Clostridium lithuseburense, Clostridium indolis, Clostridium perfringens, Listeria monocytogenes, Li. innocua, Lactobacillus fermentum, La. johnsonii, La. crispatus, Lactococcus lactis*		
Thuricin 439	*B. cereus, Li. innocua 4202*		

The emergence of drug-resistant bacteria encourages us to search for and develop new antimicrobial agents. High-potential Bacillus thuringiensis bacteriocins can be a good alternative in controlling food, environmental and medical pathogens (Salazar-Marroqouin et al, 2016).

Cytosidal characteristics of Bacillus thuringiensis:

Nowadays, due to the fact that current treatments for cancer are expensive and most treatments either usually do not respond to the patient or cause harmful effects again in patients, scientists and specialists turn their attention to drugs and extracted metabolites. Driven from natural materials. One of the things that has been done in this field and is still being studied is the use of crystalline proteins of the bacterium Bacillus thuringiensis, which is not pathogenic to humans. Recent research shows that this toxin has anticancer and stimulatory effects on the immune system, and global efforts to detect Bt isolates with unique anti-cancer properties are increasing (Ammons, 2002). Many strains of Bacillus thuringiensis have no insecticides, but can have cytosidal effects and are more prevalent than Bacillus thuringiensis insecticides (Johnson et al, 1998). In 1999, for the first time, the Japanese scientist Mizuki isolated strains of Bacillus thuringiensis with a non-hemolytic toxin and cytosidal properties against human cancer cells. In 2006, Saito et al reported that crystal protein had strong cytosidal activity against human blood cell lines. This toxin binds to the surface of susceptible cancer cells but does not bind to healthy cells (Katayama et al, 2007). Because of their selective effect against cancer cells in humans rather than normal cells, a number of these proteins and their mechanism of action in selectively killing human cancer cells have been extensively studied. The abundance of these bacilli in nature and their selective effect have made them potential candidates for cancer treatment. However, the literature on the effectiveness of these proteins in living tissue is very rare, as different species of Bacillus thuringiensis have different cytotoxic proteins with a wide range. They produce different anti-cancer effects and mechanisms of action, further investigation and their effects on living tissues are necessary to be used in human samples (Akiba et al, 2009).

Parasporin (PS):

Parasporins are a group of non-insecticidal crystalline proteins produced by Bt strains and have anticancer activity in vitro. The protein is cytolysin and has a specific locus on the surface of specific cells and induces cell death in cells. Induces cancer (Biazar et al, 2016). These proteins show their cytosidal activity when digested by the protease enzyme. Currently, these proteins are classified into 4 families: PS1, PS2, PS3 and PS4. The level of activity and spectrum of cell killing of these 4 families are different (Akiba et al, 2009).

The mechanism of action of these toxins in killing cancer cells has been investigated (Ohba et al, 2009). Katayama et al. Have shown that the cytotoxin PS1, unlike its insecticide Cry proteins, is not able to perforate membranes. This toxin rapidly increases intracellular calcium ion concentrations within 1 to 3 minutes without altering plasma membrane permeability and ultimately killing The cell becomes apoptotic. While other cry proteins with anti-cancer properties, PS2, unlike the first type, increase the permeability of plasma membranes in sensitive cancer cells and thus exert their cell killing effect. PS2 does not perforate the mitochondrial membrane and reticulum of the endoplasmic reticulum. The first step is the specific binding of the toxin to the receptor protein, which is located in the lipid layer of the cell plasma membrane. The PS2 oligomer then forms in the plasma membrane, leading to perforation and cell lysis. For other parasporins (PS3 and PS4), little is known about their mechanism of action (Katayama et al, 2007). Due to the convergence effect of drugs and toxins, even bacteria, spores or toxins can be used as suitable vectors to transfer therapeutic compounds to the tumor. Cyt1A protein is a cytotoxic protein in Bacillus thuringiensis israelinesis that is produced by the cyt gene during the sporulation phase. By moving 5 amino acids in this crystalline protein Cyt1A, we can see an increase in toxicity to lung epithelial cancer cells in 2017. S-Layer protein of Bacillus thuringiensis has been identified with toxic activity against MDA-MB-231 breast cancer cells (Nair et al, 2018).

In addition to the direct effect of Bacillus thuringiensis crystal toxin on cancer cells, the effect of cytosidal-specific Cry1 toxin on breast cancer cell line on stimulating the production of two cytokines, interleukin-2 and interleukin-5, has also been evaluated as an immune-stimulating toxin. Identified and increased the production of cytokine interleukin-2 and stopped the stimulation of inhibitory cytokine interleukin-5 (Rubio et al, 2017). Interleukin-2 is a cytokine therapy and belongs to the family of cytokines associated with T cell growth factors (Soleimani et al, 2018). This cytokine is also used in the treatment of kidney and intestinal cancer and has anti-angiogenic and anti-inflammatory effects (Dranoff, 2004). Interleukin-5 is an inhibitory cytokine that suppresses the activity of anti-tumor cytokines (Pak et al, 2015).

The use of immunotherapy in the treatment of cancer is one of the studied methods, which is effective in strengthening the immune system. Strengthening the immune system reduces the growth and prevents the spread of cancer cells. Current treatments for cancer are mostly done with drugs that kill cancer cells or prevent them from dividing, these treatments have many side effects on healthy cells, and as a result, treatment is associated with morbidity and mortality. Immunotherapy is the most specific anti-cancer treatment and therefore, it is important to use the best immunotherapy methods to fight cancer. Due to the characteristics of Bacillus thuringiensis toxin and the spread of cancer in the world, as well as the tendency for bio-risk and low-risk treatments, with further study on this toxin, it can be recommended as an immunotherapy drug in the treatment of cancer.

The role of Bacillus thuringiensis in solving environmental problems:

Heavy metals, laboratory chemical, agricultural and pharmaceutical wastes, and hydrocarbon pollutants can cause major environmental problems and affect human and animal health. Water pollution with heavy metals is one of the environmental challenges. Bt strains are able to remove these metals from water. There have been reports of removal of copper and manganese, mercury, cadmium, chromium and nickel by Bt strains (Vijayaraghavan and Yun, 2008). Industries such as mining, chemical fertilizer production, paper and pesticide production, tanning, and battery manufacturing are among the most important producers of heavy metals. The presence of these metals as soluble in the effluents and effluents of these industries due to their long shelf life in nature and also a great tendency to accumulate in the tissues of living organisms are very undesirable and cause a variety of disabilities and diseases. Bacillus thuringiensis CASKS3 is isolated from mangrove beaches in southeastern India and used for biological adsorption of mercury (Saranya et al, 2019). Biological uptake of heavy metals: cadmium, chromium, copper and nickel from industrial effluents of northern India by OSM29 strain Bacillus thuringiensis, at appropriate temperature and pH (Oves et al 2013).

Chemical wastes of laboratory, pharmaceutical, agricultural, etc. origin can also have destructive effects on the environment.

Ethidium bromide In biological laboratories, ethidium bromide has been used as a probe to detect nucleic acids with UV light, which is a potent carcinogen and mutagen. PSU9 strain of Bacillus thuringiensis isolated from soil is capable of degrading ethidium bromide (Sukhumungoon et al, 2013).

Methylene blue, a water-soluble powder, is most commonly used as an oxidation and reduction detector in chemical laboratories. In addition, it is used today in pharmacy to prepare drugs and in dentistry to detect microbial plaque and in aquariums to prevent fish eggs from being contaminated by bacteria and fungi, and all of these methods can be spread to the environment. This pollutant affects the physical and chemical properties of water resources and is one of the substances that should be completely removed in industrial effluents, because its small amount also has a significant impact on the natural ecosystem. Methylene blue is removed by Bacillus thuringiensis 016 in two steps:

1. Rapid uptake of methylene blue by Bacillus thuringiensis 016 through electrostatic attraction or group chelating activity

2. Degradation of time on methylene blue by Bacillus thuringiensis 016 through enzymes dependent on or coupled with bacterial metabolic process (Chen et al, 2015).

Ibuprofen is one of the most important environmental pollutants, although it is considered as one of the drugs with high removal efficiency, its metabolites are still found in the effluent of biological wastewater treatment system. In addition, contaminants containing drugs are often associated with other compounds such as heavy metals and aromatic compounds that affect their decomposition. Despite the toxic effects of mercury, copper, cadmium, cobalt, and chromium, the new non-destructive pathway of ibuprofen was performed by Bacillus thuringiensis (2015b) B1, and research has shown that ibuprofen is decomposed in the presence of phenol, benzoate, and 2-chlorophenol and simultaneously degraded by phenol. Benzoate has also been made. In this reaction, the hydroxybuprofen intermediate compound changes the rate of the degradation process. Degradation of ibuprofen is easier and faster as a result of interaction with the surface of bacterial cells (Marchlewicz et al, 2017).

C-halotrine is a potent synthetic pyrethroid insecticide analogous to naturally occurring pyrethrins. When pesticides are used in concentrated plants, they kill some of the beneficial organisms in the ecosystem, such as ladybugs. In organisms such as humans, pesticides tend to alter normal metabolism and physiology, and in the long run may cause poisoning, neural deformities at birth, disorders of the nervous, cardiovascular, and digestive systems (Izah, 2017). For the first time in 2015, a new strain of Bacillus thuringiensis called ZS-19 was isolated in China, which completely decomposed C-halothrin in at least 72 hours. In addition, this strain was involved in the efficient degradation of a wide range of pyridoids such as fenpropatrin, deltamethrin, betasipermethrin, syflotrin, and biphthenetine.

Malathion is also one of the organophosphorus toxins (derived from phosphoric acid) with dangerous ecotoxicological and health effects on a variety of organisms, including birds (Khosrow et al, 2018) and the identification and removal of residues of this toxin in aqueous samples is essential. MOS-5 strain Bacillus thuringiensis isolated from organophosphate-contaminated agricultural wastewater uses malathion as a source of carbon and energy and completely degrades it (Zeinat kamal et al, 2008).

Crude oil is an important source of pollution in the environment and its events today have become an environmental and social disaster, which affects the biodiversity and distribution of microorganisms in an environment (Das and Mukherjee, 2007). Strains of Bt have been isolated from oil stains that use petroleum compounds as a carbon source and decompose them in vitro for 27 days (Thamer et al, 2013). These reports indicate the high potential of Bt strains for environmental cleanup and bioremediation and highlight the importance of further research in this area.

Production of microbial biopolymers (intracellular inclusions):

Microbial biopolymers are a good alternative to petroleum-derived plastics. These biopolymers have many advantages over conventional hard biodegradable plastics (due to their high molecular weight), including biodegradability, environmental friendliness, and renewable resources.

PHA (Polyhydroxy Alkanoate), Polyhydroxy Alkanoate is a polyester of four hydroxy acids that are naturally synthesized using bacteria to store carbon. PHAs have the properties of thermoplastics and biodegradable elastomers and their synthesis system for the production of large quantities of polymers at the lowest cost, and on cost-effective substrates (Ojumu et al, 2004). In Brazil, agricultural waste (Rice husk, mango peel (the most successful source of carbon), potato peel, bagasse, etc.) as a cheap source of carbon for IAM 12077 strain by acid hydrolysis pretreatment or the use of bacterial enzyme, polymer production (Gowda and shivakumar, 2014).

PHB (polyhydroxybutyrate) is the best known PHA, which has polypropylene-like properties and can be easily decomposed in air. Some strains of Bacillus thuringiensis are considered good candidates for large-scale production of PHB, which uses sugarcane extract as a source for economic production (Thammasittirong et al, 2017). The NG strain is a new strain of Bacillus thuringiensis that It is isolated from the effluent outlet of the beverage production plant, which is capable of simultaneously producing polyhydroxybutyrate and 4 other types of polyhydroxy alkanoate (Gholamveisi et al, 2017).

Bacillus thuringiensis in nanobiotechnology:

Silver nanoparticles have been considered due to their wide applications in life sciences and other sciences. Initially, bulk materials were broken down to nanoscale using physical and chemical approaches to form nanoparticles. The biggest problem with the physical approach is the roughness created at the surface of the nanoparticle structure, which has major effects on the physical and chemical properties of the nanoparticle surface, while at the same time a lot of energy was required to maintain pressure and temperature. In the chemical approach, the molecular structure is preserved with high accuracy (Kowshik et al, 2003), but the regenerating and stabilizing chemicals used in this method are often toxic and flammable and cannot be removed due to environmental problems. Are easily disposed of (Jain et al, 2010), so nanoparticle fabrication is a non-green method in this way, and due to these disadvantages, a clean, environmentally friendly and informal method is required to produce nanoparticles. Biological methods are safe, cost-effective and environmentally friendly green methods (Narayanan and sakthivel, 2010). In the production of nanoparticles using microorganisms, bacteria and fungi due to more advanced technology has received more attention than actinomycetes and yeast (Zhang et al, 2011). In the meantime, bacteria have been given a lot of attention for making metal nanoparticles, and the reason is the relative ease of working with them. In addition, there is the possibility of genetic manipulation and increased production and control of particle shape and size (Parikh et al, 2008). By reducing and precipitating, Bacillus thuringiensis converts toxic mineral ions dissolved in silver nitrate into non-toxic and insoluble ions of silver nanoparticles. Silver resistance genes, type C cytochromes, peptides, cellular enzymes and reducing cofactors play an important role in the synthesis of silver nanoparticles (Singh et al, 2015). In addition to known applications of nanoparticles, including: molecular residue detection, diagnostic applications, antibacterial, catalytic, microelectronic, photonic, optical, DNA sequencing, high-level Raman spectroscopy and pharmaceuticals, in recent years silver nanoparticles synthesized by Korstaki strain (Btk-AgNPs) have been considered as nanoparticle-based insecticides (Atef et al, 2017).

Application of Bacillus thuringiensis in industry:

Bacillus thuringiensis produces a variety of extracellular enzymes, each of which has a wide range of applications in different industries. Amylase is a large group of enzymes that break down starch and other oligosaccharides and polysaccharides, which has many applications in industry due to its high thermal resistance of the bacterial type. It is widely used in textile, distillation, pharmaceutical and bread baking industries.

Cellulose is known to be the most abundant plant biomass on Earth and its purpose is to decompose it as a renewable energy alternative to fossil fuels. Although many microbes were known for their decomposition of cellulose, their applications were not very satisfactory because they did not meet the specific requirements such as high catalytic performance on insoluble cellulose substrates, stability at high temperatures and pH, tolerance to the final product (Percival et al, 2006). Bacillus thuringiensis strains produce new cellulases that have the ability to release glucose from cellulose, carboxymethylcellulose (CMC) and insoluble cellulose crystals. Extracted cellulose can be used to convert lignocellulosic biomass to fermentable sugars (Lin et al, 2012). Chitin, a linear N-acetyl glucosamine polymer that is the most abundant biomass on earth after cellulose (Lee et al, 2000). Production of cheap chitinolytic enzymes is an important element in the use of oyster waste and shrimp farms, etc., which not only solves environmental problems, but also strengthens the economic value of seafood (Kuzu et al, 2012). Found in a wide range of organisms such as bacteria, plants, fungi, insects and hardwoods. And since chitin is not found in vertebrates, the use of chitinase is recommended for the treatment of fungal and parasitic infections (Reyes-remirez et al, 2006). Creatine is an insoluble protein found in the structure of feathers, hair, wool, and horns, and is a large amount of slaughterhouse waste that is resistant to many proteolytic enzymes such as trypsin and pepsin, resulting in the accumulation of large amounts of creatine waste in nature. High cysteine content is a property that distinguishes creatine from other proteins such as collagen and elastin. Bacillus strains produce and secrete large amounts of extracellular enzymes that are able to break down these proteins (Badrud Duza and Mastan, 2014). In the leather industry, a suitable proteolytic enzyme should be used that does not degrade collagen and creatine, as their degradation reduces the quality of leather. Findings on keratinase isolated from TS2 strain Bacillus thuringiensis indicate that this enzyme may have such an industrial application (Sivakumar et al, 2012). Lipases are the most important hydrolytic enzymes produced by various microorganisms, including bacteria. And are used in food and pharmaceutical industries. Research results indicate the high potential of Bacillus thuringiensis lipase enzyme for use in industry (Badrud Duza and mastan, 2014).

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