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REVIEW ARTICLE

Potential applications of *Bacillus thuringiensis* Berliner in agriculture, medicine and environment

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Abstract

Bacillus thuringiensis (*Bt*) is renowned for its insecticidal activity against a wide range of target pests. *Bt* formulations offer safe alternatives to chemical insecticides, effectively eliminating insects using toxins and enzymes such as chitinases and metalloproteases. This bacterium has transformed pest management through the development of genetically modified insect-resistant crops, providing targeted protection. Beyond pest control, *Bt* serves as an alternative to antibiotics, fertilizers, bioremediation agents and for nanomaterial synthesis. While its effectiveness in insect control contributes to sustainable farming practices, *Bt* further promotes plant growth as a biofertilizer and growth enhancer. Additionally, it plays various roles in medicine and environmental applications. Bacteriocins, proteins produced by *Bt*, exhibit high efficacy against pathogenic bacteria and demonstrate some fungicidal activity, offering potential applications in medicine and food preservation. *Bt*'s influence extends to environmental bioremediation, where it targets heavy metals and dyes. It is also involved in the synthesis of metal nanoparticles and exhibits anti-cancer activity by targeting various cancerous cells. Overall, *Bt* showcases a broad spectrum of activity across agriculture, medicine and environmental sectors, highlighting its potential to enhance crop productivity, improve human health and reduce environmental pollution.

Keywords

antimicrobial; *Bacillus thuringiensis*; bacteriocins; biopesticides; parasporins; PGPB

Introduction

Since the 1960s, industrialized nations have extensively relied on synthetic chemical pesticides to manage pests and increase crop yields (1). However, the widespread use of artificial pesticides has sparked discussions regarding their environmental impact, effects on non-target organisms and the development of resistance among major insect pests (2). Therefore, it is essential to adopt alternative methods for managing insect pests.

Currently, the use of microorganisms has emerged as an alternative for pest management, offering increased specificity and toxicity against target insect pests (3). Recently, there has been a notable increase in the use of biopesticides, which play a vital role in Integrated Pest Management.

Biopesticides can be classified as microbial, plant or animal-based biopesticides (4). One of the beneficial microorganisms employed as a biocontrol agent is the entomopathogenic bacterium, *Bacillus thuringiensis* (*Bt*) (Bacilliales : Bacillaceae). *Bt* is a common Gram-positive bacterium present in various environments, including soil, water, grain storage and decomposing insects (5, 6).

During the sporulation phase of its life cycle, *Bt* produces crystal proteins. As the bacterium prepares to form a spore, it also synthesizes these crystal proteins, which aggregate to form crystals or paracrystalline inclusions. These crystals are composed of Crystal (Cry) or Cytolytic (Cyt) proteins that are deposited alongside the bacterial spores. In addition to Cry proteins, *Bt* also produces Vegetative Insecticidal Proteins (VIP), which have different mechanisms of action and are secreted during the vegetative phase of the bacterium.

Bt-producing spores contain insecticidal protein crystals known as δ-endotoxins or Cry proteins (7). These crystals exhibit different shapes, like bipyramidal, spherical and cuboidal (8). When consumed by susceptible insects, these proteins are activated in the alkaline environment of the insect midgut, binding to specific receptors on the insect cell membrane. This interaction disrupts epithelial cells in the insect gut, primarily by creating pores in the cell membrane, ultimately leading to insect death (9). Although *Bt* contributes to insect mortality, high concentration of the endotoxins is necessary for effective pest control (10).

Bt-based bioinsecticides are recognized for their selectivity and species-specific targeting of various insect species, providing a safe and environmentally friendly pest management option. The preferred term for these insecticidal proteins has shifted to "pesticidal proteins" rather than Cry toxins or *Bt* toxins (11). *Bt* comprises a diverse family of subspecies classified as entomopathogens, found in various habitats and characterized by 72 antigenic groups (12). Based on amino acid sequence similarities, 74 *cry* gene families (*cry1–cry74*) with a total of 770 different *cry* genes have been identified, along with 3 *cyt* families (*cyt1–cyt3*) which consist of 38 *cyt* genes.

Additionally, vegetative insecticidal proteins (Vips), produced during the vegetative phase of growth, include approximately 138 *vip* genes categorized into 4 groups (*vip1–vip4*). The specific activity of these proteins toward various pests, such as lepidopterans, dipterans, coleopterans, hymenopterans and even other invertebrates like mites and nematodes, is determined by the contents of Cry, Cyt, Sip (secreted insecticidal proteins) and Vip proteins (13-15).

Recent research has revealed additional capabilities of *Bt* strains, including the promotion of plant growth, remediation of heavy metals, anti-cancer properties and antagonistic effects against plant and animal pathogenic microorganisms (Fig. 1). Efforts are ongoing to enhance these byproducts by developing new production techniques and incorporating more potent *Bt* strains. This review compiles the various roles exhibited by *Bt* and its potential applications.

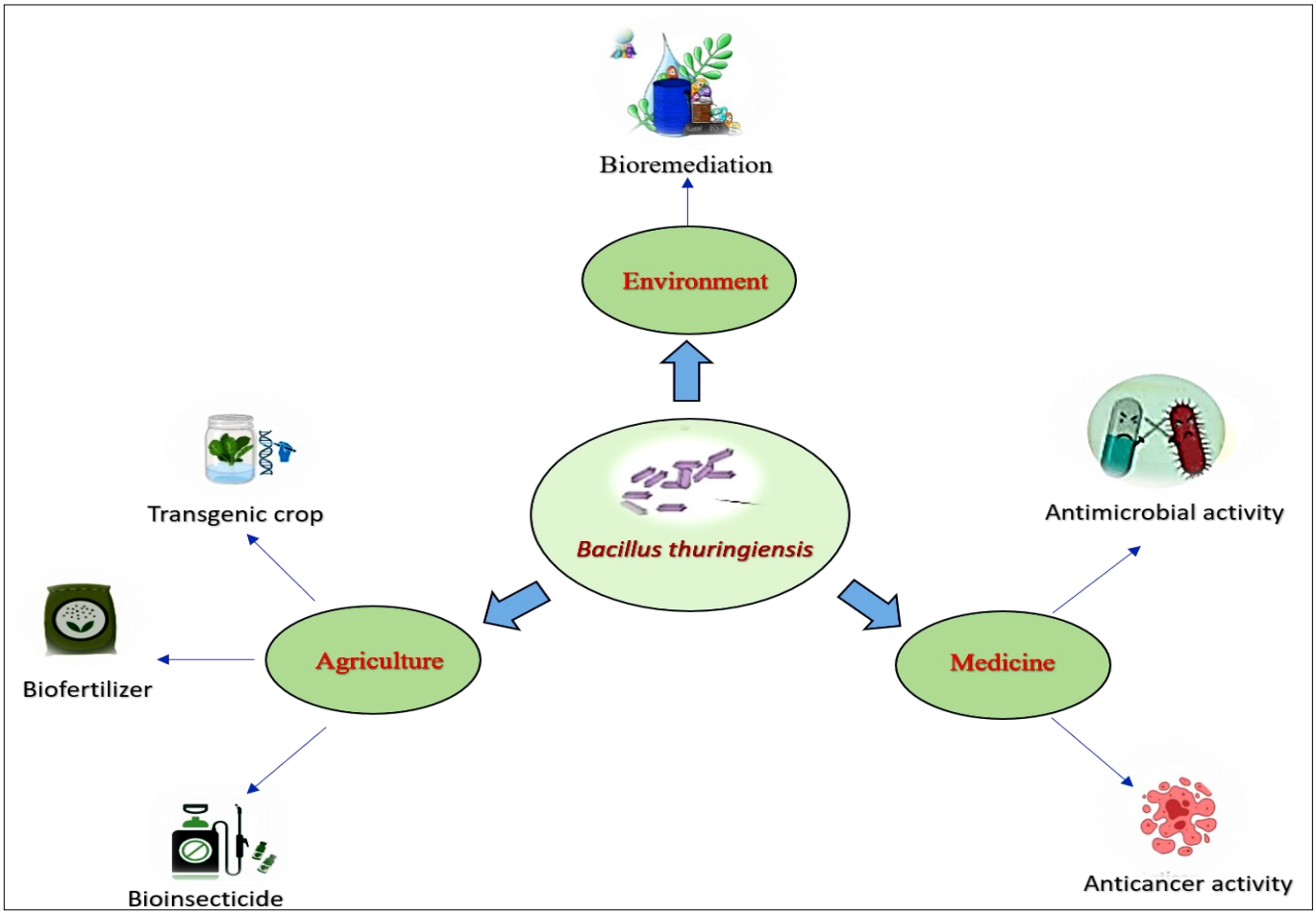

Fig. 1. Overall function of *Bacillus thuringiensis*.

Role of Bt as Bioinsecticide

With the rising costs and risks associated with synthetic insecticides, advances in biotechnology have enabled the efficient development of microbial insecticides. Microbial pesticides, especially those developed using *Bt*, holds great promise for pest management. *Bt*-based products are the most widely as commercial biopesticides in the biocontrol industry, accounting for nearly 97 % of the global biopesticide market (16). Early *Bt* formulations, such as Sporeine and Thuricide, faced challenges in competing with synthetic chemical insecticides due to their lower efficacy (17).

Bt-based biopesticides are available in different formulations *viz.,* powder formulation, liquid formulation, nanoencapsulation, etc. Liquid formulations are cost-effective and user-friendly but face stability issues. In contrast, powder formulations are more stable, although their production involves a complex and costly drying process. However, the addition of specific additives in powder formulations improves stability while maintaining cost-effectiveness (18).

Advanced *Bt* products with higher efficacy have been developed for pest control, targeting insect pests from orders such as Lepidoptera, Diptera and Coleoptera. The use of advanced methods facilitated the selection of strains with highly effective or novel toxin combinations, improving the specificity and efficacy of *Bt*-based bioinsecticides (19). One of the key advantages of *Bt* as a bioinsecticide is its environmental safety. Its low residual action prevents contamination of water and soil, unlike chemical pesticides. Additionally, it is highly selective, making it safe for non-target organisms such as fish, birds and mammals (20).

Wettable powder formulations were developed *viz*., Belthirul and Biolep using *Bt* isolate KD2 combined with different compounds (21). Belthirul was found to cause 78 % mortality in *Helicoverpa armigera*, while Biolep resulted in 53 % mortality. It was prepared a freely-flowing WDG formulation using *Bt* strain DOR *Bt*-127, which was tested against *Spodoptera litura* (22). Furthermore, a new aqueous formulation developed from an indigenous strain of *Bt. israelensis* VCRC B646 proved effective in controlling mosquito vectors (23).

In addition to Cry and Cyt toxins, *Bacillus thuringiensis* (*Bt*) produces proteinaceous toxins, like Vip and Sip families, which also exhibits insecticidal activity targeting specific insect orders. *Bt* synthesizes various enzymes and compounds, including chitinases, metalloproteases, cytolysins, antibiotics and β-exotoxins, all of which contribute to its virulence and host specificity.

Bt chitinases, members of the glycoside hydrolase 18 (GH18) family, plays a critical role in degradation of chitin, a major component of insect exoskeletons and peritrophic membranes. These enzymes are essential in chitin assimilation as a carbon source, contributing to *Bt's* pathogenicity and potentially influencing host specificity by targeting diverse insect peritrophic structures (24, 25).

Metalloproteases aid in toxin penetration through barriers like chitin-rich peritrophic membranes and mucin layers during infection. These enzymes, belonging to the M60, M6, M9 and M73 families, enhance *Bt*'s adaptability and pathogenicity across various stages of infection. For example, Enhancin-like Metalloproteases (M60 family) degrade intestinal mucin, increasing the effectiveness of the Cry1Ac toxin (26). InhA Metalloproteases (M6 family) neutralize insect immune peptides, help *Bt* escape phagocytosis by cleaving membrane proteins and collaborate with Cry toxins to enhance cytotoxicity, contributing to the overall complexity of *Bt*'s virulence. (27). ColB Metalloprotease (M9 family) facilitates *Bt*'s penetration into the haemocoel by breaking down the basal lamina (28). Additionally, metalloproteases like CalY (M73 family) support biofilm formation, further aiding in the pathogen's adaptability (29).

Cytolysins such as sphaericolysin produced by *Lysinibacillus sphaericus*, create pores in cellular membranes, causing cellular lysis. These proteins act as virulence factors, affecting a wide range of species and contributing to host-pathogen interactions (30). Similarly, Zwittermycin A (ZwA), a unique antibiotic produced by some *Bt* strains, exhibits broad-spectrum activity and works synergistically with other *Bt* toxins, further impacting a wide range of species (31).

Bt also produces β-exotoxins, such as thuringiensin (Thu), which are low-molecular-weight toxins with a broad insecticidal spectrum. These toxins are also effective against mites and nematodes (32, 33). However, they have been reported to cause harmful effects in mammals, including inflammatory responses and lung tissue damage (34). This diversity of virulence factors reveals their complex infection strategies, from ingestion to invasion of host body cavities, offering valuable insights into developing novel pest control methods (35).

Bt gene-based transgenic crops

While *Bt* formulations are considered environmentally safer pesticides, they face several limitations, e.g., repetitive application, short efficacy durations and difficulty in targeting specific insect species. Recent advancements in plant transformation technology have addressed some of these issues by incorporating foreign genes into crops, resulting in insect-resistant plants. *Bt* transgenic crops are genetically modified to express proteins derived from *Bacillus thuringiensis* (*Bt*), which provide resistance to insect pests. This innovation has significantly advanced agricultural pest management, reducing the need for biopesticide sprays. The first transgenic crop that reaches the United States commercial markets was *Bt* potato in 1995. Following that, *Bt* corn and cotton were introduced in 1996, offering resistance to pests like the European corn borer, southwestern corn borer, tobacco budworm, cotton bollworm, pink bollworm and Colorado potato beetle. The lepidopteran-specific *vip* and *cry* genes, including *cry1Ac*, *cry1Ab*, *cry2Ab*, *cry1Fa* and *vip3Aa*, confer resistance to various lepidopteran pests. Additionally, the *cry34Ab1–cry35Ab1* and *cry3A* genes have been used to develop approximately

34 and 60 genetically modified (GM) crops respectively, providing resistance to coleopteran pests (36). *Bt* toxins from the Cry1A class exhibit dual specificity, targeting both Coleoptera and Lepidoptera (37). To further enhance resistance and delay the development of insect resistance, techniques like gene pyramiding and fusion technologies have been employed. These methods, which involve the expression of multiple genes in a single crop, have been successfully demonstrated in a variety of crops (38). Moreover, *Bt* Cry proteins have shown promise in inhibiting the growth of larvae from various insect species, highlighting the potential for developing even more resistant crops (39).

Farmers benefit significantly from *Bt* crops, experiencing reduced pest damage, improved crop quality and fewer losses during storage and transportation. Additionally, *Bt* crops contribute positively to sustainable agriculture by promoting healthier soils and reducing pest risks through enhanced pest management. Numerous studies have demonstrated that the adoption of *Bt* crops boosts agricultural productivity and economic gains in various regions of the world (40). Globally, the cultivation of biotech crops, also known as genetically modified organisms (GMOs), has reached an average of 191.7 million ha. over the past 22 years. These crops are now grown in approximately 70 countries since their commercialization (41). To date, 577 transgenic events have been developed across 32 different crops worldwide, with cotton, corn and potato having the highest number of approved GM events—51, 230 and 30 events respectively. Currently, 10 insect-resistant transgenic crops, representing 354 events, have been approved for cultivation. These include cotton, cowpea, eggplant, maize, poplar, potato, rice, soybean, sugarcane and tomato, with most incorporating insecticidal genes derived from *Bt* (42). In India, *Bt* cotton has been commercially cultivated since 2002. However, due to legal challenges and public opposition, other GM crops like *Bt* brinjal and GM mustard, though approved for commercial release by the Genetic Engineering Appraisal Committee (GEAC), have not been widely adopted.

Continuous cultivation of transgenic crops can lead to the development of resistance in insects against the *Bt* crops over time. For example, certain pests may evolve to resist *Bt* toxins, as observed with the cotton pink bollworm developing resistance to *Bt* cotton, reducing the crop's long-term efficacy. Despite these challenges, the use of *Bt* crops remains controversial regarding their impact on the environment and mammals. Some scientists, based on laboratory and field studies, support *Bt* crop cultivation, asserting that these crops are safe. However, others argue that *Bt* crops may pose risks to human health (43).

Studies have shown that *Bt* corn or cotton do not have significant adverse effects on beneficial insects or non-targeted organisms. In addition, the remains or pollen of *Bt* crops have not been found to harm non-target plants in *Bt* crops fields (44). However, challenges have arisen, such as severe infestations of sucking mirid insects in *Bt* cotton fields in China, which have become major pests (45). Similarly in India, *Bt* cotton has faced problems with aphids and mealybugs (46). However, it was reported that feeding larvae of *Chrysoperla carnea* on aphids reared on *Bt* corn did not affect the predator's pupation or adult emergence (47). Furthermore, studies on honey bee survival indicated that Cry proteins do not negatively impact honey bee populations (48).

Role of Bt against pathogenic bacteria

Bt strains demonstrate antimicrobial activity against plant and human pathogenic bacteria as well as bacteria involved in food degradation. This antimicrobial effects results from the production of antimicrobial small peptides known as bacteriocins and the disruption of bacterial communication signals through enzyme activity (49, 50).

Bacteriocins are thermotolerant antimicrobial peptides produced by *Bt* during specific growth stages, playing a vital role in defending against other microorganisms. *Bt* strains, produce these bacteriocins during critical phases, such as sporulation and protein synthesis (49). Previous research has identified and characterized 18 distinct types of bacteriocins from various *Bt* subspecies, including *morrisoni, kurstaki, kenyae, entomocidus, tolworthi, tochigiensis* and *thuringiensis*. These bacteriocins act similarly to antibiotics, being effective against antibiotic-resistant strains. Their protein-based composition, coupled with low oral toxicity, allow for degradation after consumption, with effects ranging from inhibiting bacterial growth to causing death (51).

The disruption of bacterial communication is facilitated by enzymes that degrade N-acyl-homoserine lactone (AHL), thereby interfering with bacterial signaling and potentially affecting their coordinated behaviors (50). The diverse bacteriocins produced by *Bt* strains have promising applications in combating various pathogenic bacteria, making them valuable in agriculture, medicine and food safety. In agriculture, combining *Bt* with other bacterial and fungal antagonists enhances its effectiveness in controlling plant diseases, such as *Ralstonia solanacearum* in Naga chili (52), tomato (53) and eucalyptus (54).

Certain *Bt* bacteriocins also show potential for controlling human and animal pathogens, offering alternatives to traditional antibiotics. These bacteriocins can be used as safe food preservatives, helping to prevent the growth of enterotoxigenic bacteria and extending the shelf life of food products. For instance, *Bt* fengycin-like lipopeptides and other bacteriocins have demonstrated antibacterial properties against pathogens like *Escherichia coli*, *Staphylococcus epidermidis*, *Bacillus cereus* and *Vibrio cholerae* (55). Thuricin S is another example of a *Bt* bacteriocin with antibacterial effects against a wide range of bacteria, including *Listeria monocytogenes*, *Bacillus cereus* and *Pseudomonas aeruginosa*, showing promise as a natural food preservative. Other compounds, such as Morricin 269, Kurstacin 287, Kenyacin 404, Entomocin 420 and Tolworthcin 524, exhibit broad-spectrum activity against foodborne pathogens and human pathogens, demonstrating their potential in food safety and health applications (56, 57).

Entomocin 110, another *Bt* bacteriocin, has proven

effective against *Paenibacillus* larvae, the causative agent of foulbrood disease in honeybee larvae, offering a natural and environmentally friendly alternative for antibiotics (57). The versatility of *Bt* strains as antagonists against plant, human and animal pathogens highlighting their potential for biocontrol and food preservation. Supplementary Table S1 presents a list of *Bt* strains and their antagonistic effects on various bacteria, emphasizing *Bt's* role in biocontrol through natural bactericidal or bacteriostatic compounds.

Bt against fungi

The antagonistic activity of *Bt* against plant pathogenic and human pathogenic fungi is well-documented through several mechanisms, including the production of antibiotics, lipopeptides, siderophores, volatile organic compounds, secondary metabolites and cell wall-degrading enzymes. While Cry proteins synthesized by *Bt* do not exhibit antifungal activity, certain specific *Bt* strains have demonstrated effectiveness against various plant pathogenic fungi, including *Fusarium* (58), *Sclerotium* (59), *Colletotrichum* (58), *Rhizoctonia* (60) and *Botrytis* (61).

Chitinase production in *Bt* strains has shown high efficacy against fungi that cause diseases in animals and humans such as *Aspergillus niger*, *Candida albicans* and *P. chrysogenum* (62). Additionally, *Bt* induces systemic resistance in plants against fungal pathogens by promoting the production of defense-related enzymes and metabolites. The lipopeptide fengycin and volatile compounds produced by *Bt* also inhibit the growth of phytopathogenic fungi, with fengycin displaying notable toxicity (63). Various *Bt* strains targeting different fungal pathogens and their activities are listed in Supplementary Table S2. Recent studies have provided evidence of *Bt*'s effectiveness in controlling various phytopathogenic fungi and promoting plant growth through direct or indirect mechanisms (64, 65).

The indirect mechanisms though which *Bt* may suppress plant pathogens and enhance the plant growth include the synthesis of bacteriocins, autolysins, lactonases, siderophores, β-1,3- glucanase, chitinases, antibiotics and hydrogen cyanide and the degradation of indole-3-acetic acid (IAA) (66). In contrast, direct mechanisms may involve stimulating plant growth by supplying nitrogen and soluble nutrients as well as through the activity of 1-aminocyclopropane-1-carboxylic acid (ACC) deaminase and the synthesis of plant hormone such as IAA, gibberellic acid and cytokinins (65).

The antifungal activity of *Bt* varies among different strains, with distinct morphological effects observed on fungal cell walls. These effects include inhibition of mycelial growth and spore germination, spore lysis, disruption of hyphal tips and reduced germ tube elongation (67). Notably, *Bt* has been demonstrated to suppress phytopathogenic fungi through the application of bacterial suspensions, supernatants, crude extracts containing chitinases and purified chitinase enzymes. However, information on *Bt*'s antagonistic effects against human and animal pathogenic fungi is limited, indicating a need for further research to explore potential applications in plant protection, medicine and the food industry.

Overall, the multifaceted antifungal properties of *Bt* position it as a promising biocontrol agent with broader applications. The activity of *Bt* against fungal plant pathogens has been demonstrated in earlier studies (68, 69). For example, the active ingredient of the commercial bioinsecticide, XenTari® (*Bt* Serovar *aizawai* strain ABTS-1857) can potentially suppress *Botrytis cinerea* in tomato (70). It was reported that both the spores and proteins of *Bt* directly act against the fungus *B. cinerea*, helping to improve yields in tomatoes (71). In addition, they also demonstrated *Bt* induced plant resistance in tomato against powdery mildew fungus, *Oidium neolycopersici* and *Leveillula taurica.*

Role of Bt as Plant growth-promoting Bacteria

In general, Plant Growth-Promoting Rhizobacteria (PGPR) positively impacts plant growth and development. Bacterial strains that enhance promote plant growth are referred to as Plant Growth-Promoting Bacteria (PGPB). The application of PGPB has been demonstrated to enhance seedling emergence and overall plant growth (72). Growth-promoting mechanisms include improving nutrient mobilization, siderophore production for increased iron availability in the rhizosphere, synthesizing plant growth regulators, boosting photosynthetic rates and exhibiting antimicrobial activity against plant pathogens (Fig. 2) (73).

Despite the perception that *Bacillus* has lower rhizocompetence, recent genetic studies show that specific strains of *Bt* exhibit a notable ability to compete in the rhizosphere. *Bt* is notable for its capacity to reduce plant diseases through systemic resistance while indirectly promoting plant growth. The inherent variability in *Bt*'s interactions with plants, influenced by differences in soil composition and bacterial colonies associated with plants, is significant for promoting plant growth (74).

Bt is recognized as a plant growth promoter and its ability to establish itself as an endophyte in various crops, such as cabbage, cotton, soybean and rice emphasizes its potential as an effective plant growth-promoting agent. As an endophyte, *Bt* has the potential to enhance nutrient uptake, bolster disease resistance and contribute to overall plant health, thereby facilitating robust growth across diverse agricultural environments (75). Phytohormones, essential compounds produced by bacteria that colonize plant roots, play a crucial role in regulating plant growth, pathology and interactions with microorganisms. *Bt* is explored for its role in promoting plant growth through the production of indole-3-acetic acid (IAA), ACC deaminase and siderophores as well as organophosphorus phosphatases (OPPs) that solubilize organic phosphate (76). The positive impact of IAA-producing *Bt* strains on various crops, including cabbage, lettuce, pea, lentil and soybean, along with their ability to enhance nodulation, growth and yield, emphasizes their potential as growth promoters (70).

Bt strains such as C25 (77) and KR1 (78) have been shown to enhance growth in *Lactuca sativa* and soybean. The production of ACC-deaminase by *Bt* strains stimulates

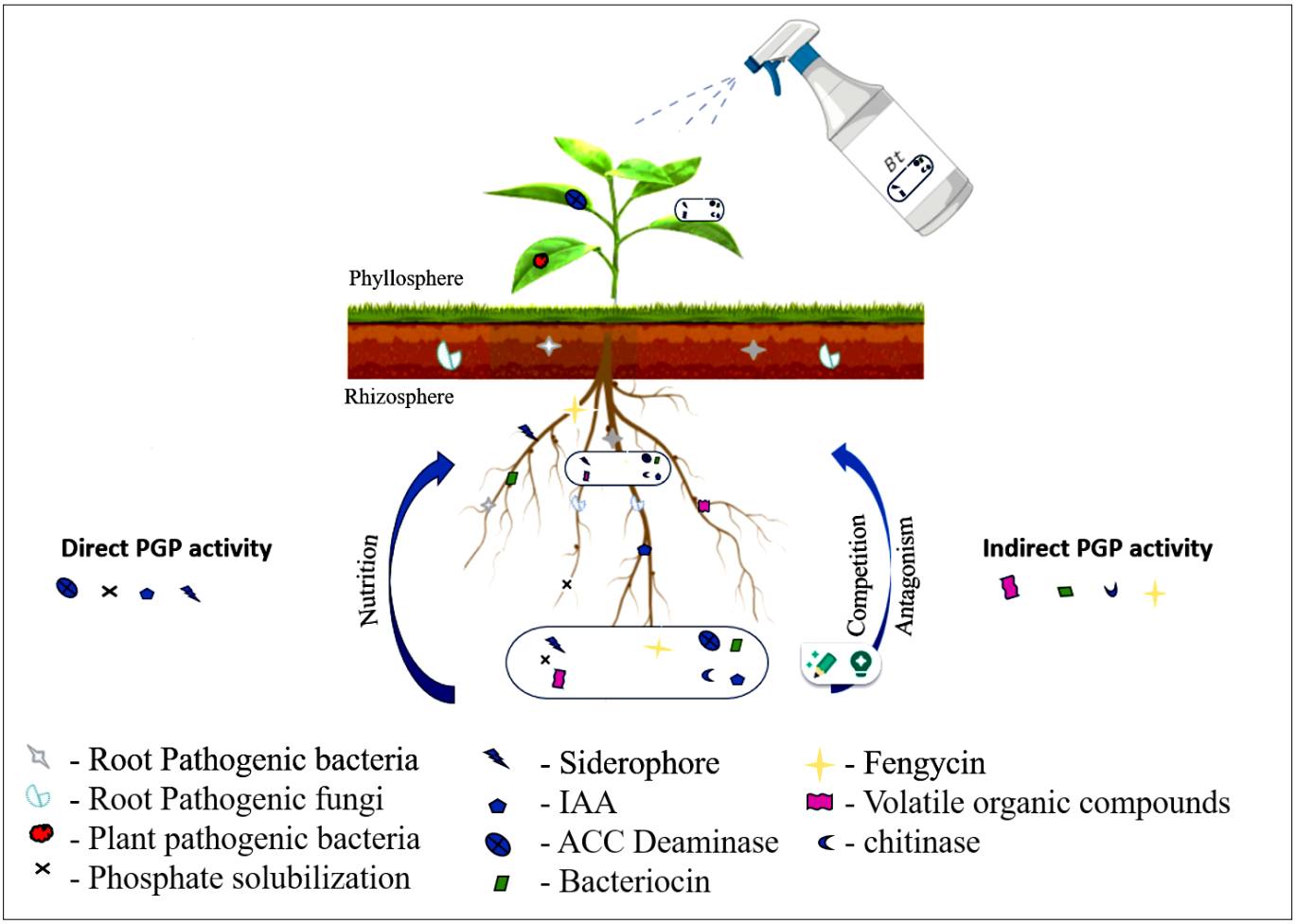

Fig. 2. Role of *Bacillus thuringiensis* in plant growth regulation.

root elongation, supporting overall plant development. Additionally, *Bt* strains like SNKr10 and native strains with ACC-deaminase activity contribute to root growth by reducing stress hormone levels in *Vigna radiata* (79). The colonization of seedling roots and the positive effects on host plant physiology make *Bt* a promising growth promoter, especially under challenging conditions like drought. *Bt* holds significant promise for promoting plant growth, further research is essential to optimize its application and understand its interactions with diverse plants and environments.

Biofertilizers consist of living microorganisms that play a vital role in enhancing a plant's intake and transport of mineral nutrients. PGPR in biofertilizers employs various mechanisms to promote growth and stress tolerance in plants. They achieve this by accumulating osmolytes (OS), phosphate and potassium solubilization, boosting nutrient uptake, nitrogen fixation, increasing water absorption capacity, siderophore sequestration and enhancing antioxidant enzymes (AEs) activity (80, 81).

Bt is recognized as significant phosphate-solubilizing bacteria, transforming non-soluble organic phosphate into a soluble form through enzymatic activity using organophosphorus phosphatases (82). Plant growth often encounters challenges due to iron deficiency, especially in calcareous soils where iron dissolution is problematic. Iron is an essential cofactor for enzymes in plants, prompting the release of soluble organic compounds like siderophore, which facilitates the crucial dissolution of Fe^{3+} for effective iron uptake (83). Siderophores produced by *Bt* play a vital role in enhancing plant growth by sequestering iron from pathogens. The *Bt* ATCC 33679 strain, produces bacillibactin, a siderophore with a high affinity for iron, which potentially aid in plant development and controls phytopathogenic fungi through iron competition (84).

The incorporation of *Bacillus* spp. in commercial biofertilizers, renowned for promoting plant growth, underscores the importance of iron in ensuring optimal plant nutrition. Despite the availability of various commercial PGPR products, there is a notable absence of commercial plant growth-promoting products based on *Bt*. The use of *Bt* and methods of application as a biofertilizer and growth promoter in various crops are listed in Supplementary Table S3.

Role of Bt in metal nanoparticle synthesis

Metal nanoparticles (NPs) are valued for their advanced characteristics and wide-ranging applications across various industries. Traditional chemical methods for nanomaterial synthesis often involve used are toxic, flammable chemicals, which pose challenges for environmentally safe disposal. In addition, these chemical synthesis processes can introduce toxic substances onto the nanoparticle surface, potentially leading to adverse effects in medical applications.

In contrast, biological approaches for green synthesis utilizes bacteria, fungi and plant extracts, offering advantages like cleanliness, non-toxicity and eco-

friendliness under ambient conditions (85, 86). Bacterial strains, including *Bt*, have been harnessed to generate metal NPs (87, 88). Recent studies have demonstrated the ability of *Bt* to synthesize silver and cobalt nanoparticles, with silver NPs exhibiting significant toxicity against drug-resistant human pathogenic bacteria, including *E. coli, P. aeroginosa* and *S. aureus*. Specific *Bt* strains possess reducing enzymes that facilitates the reduction of metal ions for NP biosynthesis. Moreover, *Bt*-synthesized cobalt NPs exhibit noteworthy larvicidal effects against malaria and dengue vectors (87).

These nanoparticles show promise for various applications, such as biopesticides, antifungal agents and protective coatings. Current research efforts aim to develop cost-effective processes for NP biosynthesis, leveraging *Bt*'s potential for eco-friendly nanoparticle synthesis and its applications in various fields. It was reported that compounds like proteins, reducing sugars, phenolic compounds and aromatic compounds in *Bt* may be involved in the synthesis process of *Bt*-Ag_2O (89). A study reported that *Bt*-Ag_2O NPs synthesized using *Bt* could function as pesticides and anti-fungal agents for stored products (90). Ag NPs demonstrated high insecticidal activity by generating reactive oxygen types, inducing oxidative stress, causing protein unfolding, disrupting cell membrane and leading to inflammation and insect mortality (91). These nanoparticles can also serve as carriers for *Bt* crystal proteins, with higher toxicity while minimizing environmental pollution and safety risks (92). It was reported that the encapsulation of *Bt* protein (Cry1Ab) could enhance its effectiveness against *Ostrinia nubilalis* under environmental conditions (93). Table 1 describes the synthesis of metal nanoparticles by various *Bt* strains, their applications, methods of confirmation and their activity against multi-drug-resistant bacteria or larvae.

Bt as an agent in Bioremediation

Heavy metals, pesticides, herbicides and petroleum derivatives pose significant threats to higher trophic levels by entering the food chain, raising concerns about their impact on ecosystems and human health. Heavy metal contamination has become a severe environmental challenge in wastewater, where conventional physical separation methods are ineffective at lower concentrations and traditional physicochemical methods may further harm the environment (94, 95).

Biological approaches offer hope, utilizing microorganisms to eliminate pollutants in a cost-effective and widely accepted manner. Eco-friendly technologies such as bio-stimulation, bioaugmentation, bioaccumulation, biosorption, phytoremediation and rhizoremediation harness the metabolic capabilities of microorganisms for the extraction and removal of heavy metals in both aquatic and terrestrial ecosystems. These methods promote detoxification, biotransformation and the effective degradation of various toxic pollutants, highlighting microorganisms' ability to accumulate, degrade or mineralize harmful heavy metals (96).

Microorganisms can thrive even in low concentrations of heavy metals, influencing the composition and function of microbial communities. Understanding these

Table 1. List of *Bt* strains involved in synthesis of metal nanoparticles.

Sl. No.	Strain	Application	Confirmation of nano materials	Activity	References
1	*Bt* strain IS1 (Soils of Bikaner (Rajasthan))	Silver NPs (AgNPs)	UV-Vis, X-ray diffraction (XRD), Transmission electron microscopy	High toxicity against multi-drug-resistant bacteria (*Escherichia coli, Staphylococcus aureus* and *Pseudomonas aeruginosa*)	(115)
2	*Bt* (MTCC-6941)	Cobalt NPs (Co NPs)	X-ray diffraction (XRD), Fourier transform infrared (FTIR), Field-emission scanning electron microscopy (FESEM) with energy dispersive X-ray spectroscopy and Transmission electron microscopy (TEM)	Larvicidal activity against *Aedes aegypti*	(88)
3	*Bt* rhizosphere soil (black soil) of cotton Kalloorani, Aruppukottai, Virudhunagar district) Tamil Nadu	Silver NPs (AgNPs)	UV-Vis	High mortality rates against *Aedes aegypti* larvae	(116)
4	*Bt*	Silver NPs (AgNPs)	UV-Vis absorbance spectra, attenuated total reflection Fourier transform infrared spectra, zeta analysis and field emission scanning electron micrographs	Antibacterial Activity - Stronger against *E. coli* than commercial AgNPs	(87)
5	*Bt* MRS2 from Farmland, cattle rangeland and metal recycling dumpsite	AgNP Synthesis	Anistropic, irregular shape; Plasmon resonance peak at 440 nm; FT-IR peaks at 3379 and 1643 cm	*E. coli* (strain 2), *S. aureus, K. pneumoniae*	(117)
6	*Bt* CR2 from Farmland, cattle rangeland and metal recycling dumpsite	AgNP Synthesis	Anistropic, irregular shape; Plasmon resonance peak at 434.5 nm; FT-IR peaks at 3379 and 1643 cm	*E. coli* (strain 2), *S. aureus, K. pneumoniae*	(117)
7	*Bt* (ACCC 03343)	*Bt*-Ag_2O	UV-vis spectroscopy, FTIR, XRD, SEM, EDS, HR -TEM, zeta potential analysis	Synthesis of Ag_2O nanoparticles (*Bt*-Ag_2O NPs), antifungal activity against *Aspergillus flavus* and *Penicillium chrysogenum*, with *Aspergillus flavus* being more sensitive.	(90)

complex interactions; shaped by factors such as metal type and availability is crucial for the success of bioremediation strategies (97). *Bt* strains demonstrate significant flexibility in degrading persistent pollutants, including pesticides, herbicides and petroleum derivatives. However, there are currently no commercially available *Bt*-based products on the market for bioremediation, underscoring the need for further research and development projects to facilitate their future commercialization. The use of *Bt* strains in bioremediation for cleaning contaminated sites and managing waste is listed in Table 2.

Role of Bt as an Anti-cancerous agents

Cancer is the leading cause of human mortality worldwide, with new types of the disease continuously emerging. However, the development of new treatments has been slow, often ineffective and significantly expensive. Parasporins (PS) are specific proteins found exclusively in *Bacillus thuringiensis* (*Bt*), known for their selective cytotoxicity against cancer cell types while causing minimal or no harm to healthy human cells, making them promising candidates for cancer treatment (98). For decades, *Bt* has been recognized for its crystal-shaped toxins that effectively control insect pests and disease vectors. However, some *Bt* proteins, which lack insecticidal activity, have demonstrated significant cytotoxicity against various cancer cells, thereby expanding the potential of *Bt* beyond pest management.

Table 2. List of *Bt* strains in bioremediation and environmental applications.

Sl. No.	Strain	Extracted from	Specific activity	Compounds	References
1	*Bt* var. *thuringiensis*, serotype 1	Polluted environments	Biosorption of heavy metals	Mercury, Copper	(118)
2	*Bt* MTCC 4714	Distillery sludge	Phytoremediation	Distillery effluent	(119)
3	*Bt* MTCC 4714	Distillery sludge	Bioaugmentation, Synthetic melanoidin (GGA, GAA, SGA, SAA) decolorization	GGA, GAA, SGA, SAA	(120)
4	*Bt* strain 4G1	Collected from *Bacillus* genetic stock center Ohio State University	Bio decolourisation	Methylene blue	(121)
5	*Bt* MOS-5	Agricultural wastewater near Berket El-Sabaa Egypt	Cometabolic degradation	Malathion	(122)
6	*Bt serovar israelensis*	Bacteries Entomopathogens, Institute Pasteur, Paris, France	Chicken feather degradation, mosquitocidal toxin production	Bacterial toxins (not specified)	(123)
7	*Bt* var. *kurstaki* HD-1	Collected from the Laurentian Forestry Centre, Canada	Bioaugmentation, combined biocontrol/bioremediation strategies	Dimethyl phthalate (DMP)	(124)
8	*Bt* SRDD	Dye-contaminated soil and water	Biodecolourisation, Acid azo dye decolorization (including AR-119)	Acid red-119 (up to 5000 ppm), Acid brown 14, Acid black 210, Acid violet 90, Acid yellow 42	(125)
9	*Bacillus* sp. L14	Cadmium hyperaccumulator *Solanum nigrum* L.	Bioaccumulation of heavy metals	Cd (II), Pb (II), Cu (II)	(126)
10	*Bt* NA2	Petroleum oil contaminated site	Bioaugmentation	Fluoranthene, Pyrene	(127)
11	*Bt*	Sugarcane field soil with fipronil history	Biostimulation and bioaugmentation	Fipronil	(128)
12	*Bt*		Bioaugmentation	Light crude oil	(129)
13	*Bt* RUN1	Soil samples obtained from a garbage disposal site around Redemption City, Nigeria	Bioaugmentation, Enzymatic Degradation Laccases, Malachite green (triphenylmethane dye) decolorization and degradation	Malachite green	(130)
14	*Bt* strain PSU9	Songkhla Province, Thailand	Exact mechanism that bacteria used to degrade EtBr was not unraveled	Ethidium bromide	(131)
15	*Bt* OSM29	The rhizosphere of cauliflower grown in soil with industrial effluents	Heavy metal biosorption (Cd, Cr, Cu, Pb, Ni)	Cd, Cr, Cu, Pb, Ni	(132)
16	*Bt* GDB-1	Roots of *Pinus sylvestris*	Phytoremediation	Arsenic, copper, lead, nickel and zinc	(133)
17	*Bt*	Cotton field soil	Bioaugmentation, microbial consortia development	Dimethyl phthalate (DMP)	(134)
18	*Bacillus thuringiensis* PW-05	Odisha coast	Mercury volatilization, biofilm formation, exopolysaccharide production	$HgCl_2$, $CdCl_2$, $ZnSO_4$, $PbNO_3$, Na_2HAsO_4, amoxycillin, ampicillin, methicillin, azithromycin, cephradine	(135)

19	*Bt* strain KUNi1	Industrial waste-contaminated soil	Bioaccumulation	Ni, Zn, Cu, Co, Cd (Ni resistance highest)	(136)
20	*Bt* BRC-ZYR2	Uranium deposit	Bioaugmentation	- Cr (VI) reduction - Insecticidal crystal proteins (ICPs: cry1Ba, cry1Bb, cry1Be/cry1Bf, cry9Ca, cry9Da)	(137)
21	*Bt* strain BRC-ZYR3	Uranium mine	Uranium bioaccumulation and transformation	Uranium (VI)	(138)
22	*Bt* strain 016	Collected from Northeast Agricultural University, China	Biosorption	Lead	(139)
23	*Bt* var *kurstaki* strain 4D4	Donated by Dr. Daniel R. Zeigler (BGSC Director, Ohio, USA	Biostimulation	Chlorpyrifos	(140)
24	*Bt* ZS-19	pyrethroid-contaminated	Pyrethroid (particularly cyhalothrin) degradation	Cyhalothrin, 3-phenoxybenzoic acid (intermediate), 3-phenoxyphenyl acetonitrile (intermediate), N-(2-isopro-xy-phenyl)-4-phenoxy-benzamide (intermediate), other pyrethroids (fenpropathrinn, deltamethrin, beta-cypermethrin, cyfluthrin, bifenthrin)	(141)
25	*Bt* strain BRC-HZM2	Chlorpyrifos-contaminated samples	Bioaugmentation, soil amendment	Chlorpyrifos	(142)
26	IS1 (*Bt* strain "Simi")		Bioaccumulation of heavy metals	Zinc, Lead	(143)
27	*Bt* strain	*Bt* from marine sediment	Bioaugmentation	Phenanthrene (PAH) - Imidacloprid (pesticide) (Degradation pathways for both established)	(144)
28	*Bt* strain Cr-S1	samples of wastewater	Bioaccumulation	Chromium	(145)
29	*Bt* B1(2015b)	the soil of the chemical factory "Organika-Azot" in Jaworzno, Poland	Cometabolic degradation	Naproxen and Ibuprofen	(146)
30	*Bt*	Agricultural soil	Assimilation	Phthalic acid esters (dimethyl, diethyl, dipropyl and dibutyl phthalate)	(147)
31	*Bt* J20	Olive waste in Palestine	Immobilize J20 cells using sodium alginate	phenol	(148)
32	*Bt* strain SG4	Cypermethrin-contaminated agricultural soil samples from Pantnagar, Uttarakhand	Immobilized the culture with sodium alginate/agar discs	Cypermethrin	(149)
33	*Bt* strain H2	hypersaline Lake Tuz in Turkey	Degradation of halogens	halogen-polluted marine/hypersaline environments	(150)
34	*Bt* with engineered atzA enzyme	Collected from *Bacillus* Genetic Stock Center (Columbus, Ohio)	Atrazine (ATR) detoxification through chlorohydrolase activity	Atrazine	(151)
35	*Bt*		Bisorption and bioaugmentation;inoculated into the aquaculture water to directly remove contaminants	Ammonia-nitrogen (NH_3-N) removal, nitrite-nitrogen (NO_2-N) removal, nitrate-nitrogen (NO_3-N) removal, metal removal (Ni, Cr, Se, Al, Cd, Mn, Fe, B)	(152)
36	*Bt*	Oil-contaminated places	Biosurfactant production Decanoic acid, oleamide	Effective bioremediation of petroleum oil residues in contaminated sites	(153)
37	*Bt* (V45)	Tannery industry sediment	Chromium (VI) bioreduction	Chromium (VI)	(154)
38	*Bt* subsp. *israelensis*	*Bacillus* Genetic Stock Center 4Q2-81	Atrazine (ATR) detoxification to hydroxyatrazine (HA)	Atrazine	(155)
39	*Bt* JNU01	Landfill site	Biodegradation of polyethylene (PE)	Polyethylene (PE)	(156)
40	*Bt* SE1C2	Tissue interior of *Catharanthus roseus* grown in magnesite mining area, Salem, India	Phytoremediation	Cd and Zn	(157)
41	*Bt* (Acc MW979616)	*Salix alba* roots	Phytoremediation	Cd Reduction 80 %; Treatment: *Bt* seeds + $CdSO_4$ 400 mg + 0.5 g root powder	(158)
42	*Bt* x-27	Uranium-contaminated soil	Uranium (VI) bioreduction	Uranium (VI) bioreduction, Anaerobic culture with electron donor, Sodium lactate, intracellular NADH dehydrogenase-ubiquinone system	(159)

It was first to identify a specific group of proteins

known as parasporins, which exhibit a remarkable ability to kill human cancer cells (99). They later isolated and sequenced an 81 kDa protein from the A1190 strain of *Bt* and named it parasporin (100). Sequence analysis revealed 5 conserved regions similar to Cry proteins, although there was less than 25 % overall identity to known Cry and Cyt proteins. Initially, defined as non-insecticidal proteins that exclusively target cancer cells, the definition of parasporins has since been broadened to include *Bt* and related bacterial proteins that are non-hemolytic but specifically cytotoxic to cancer cells (101). Similar to insecticidal Cry protein, parasporins are produced as inactive precursors during *Bt* sporulation. Proteolytic cleavage, facilitated by alkaline conditions at the N- or C-terminus, activates these precursors into their cytotoxic form (102). Interestingly, the functional boundaries between Cry proteins and parasporins are not entirely distinct, as certain parasporins exhibit dual activity, demonstrating effectiveness against both insects and cancer cells (103).

The presence of non-insecticidal *Bt* strains contributes to more than 90 % of species diversity in the natural environment, indicating the vast and largely unexplored biodiversity hotspots with potential applications that extend well beyond classical agriculture and pest control. A study was conducted using indigenous *Bt* isolates from the rich biodiversity of the Western Ghats in India to explore the parasporin diversity. This paradigm of *Bt* strains producing parasporins extends to these environments as ecosystem and bioprospecting platforms for novel compound design, facilitating advancements in human health (104).

Parasporins are categorized into 2 classes: pore-forming toxins and 3-domain structures, based on a 4-stage nomenclature system. They are classified into 6 different families: PS1, PS2, PS3, PS4, PS5 and PS6. Among these, PS1, PS3 and PS6 are larger parasporins that exhibit a 3-domain structure. Initially inactive at around 80 kDa, they become active after proteolytic processing, resulting in smaller forms ranging from 60 to 70 kDa (105). In contrast, PS2, PS4 and PS5 are smaller parasporins associated with MTX-like Cry toxins, with lower molecular weights. These are initially inactive, ranging from 31 to 27 kDa and their active forms range from 27 to 30 kDa (106). The committee defines parasporins as non-hemolytic proteins derived from *Bt* and related bacteria, characterized by cytotoxicity towards cancer cells. Recent investigation of parasporins reveals their promising potential for applications in cancer therapy (107). Phylogenetic relationships among these anticancer proteins were analysed using *Bt* strains with diversified parasporins genes. Protein sequences were retrieved from the NCBI database and a phylogenetic tree was constructed using MEGA software 11 (Fig. 3).

Parasporin 1

PS1, found in the *Bt* strain A1190, is a protein that exhibits limited sequence similarity with Cry and Cyt toxins (102). Its activation involves proteolytic cleavage, converting it into an active form that induce apoptosis in cancer cells, mainly in the HL60 line and HeLa cell line (101). PS1 operates via increasing intracellular calcium concentration and has been shown to interact with the tumor suppressor protein beclin-1, indicating its role in regulation of autophagy and apoptosis (108).

Parasporin 2

PS2, derived from *Bt serovar dakota* strain A1547, lacks the structural complexity of PS1 and is activated through Protease K processing. It exhibits potent toxicity against HepG2 and CACO-2 cells through a mechanism that involves cell membrane permeabilization and pore formation (103). It interacts with GPI-anchored proteins and cholesterol in the cancer cell membrane, causing cell lysis (109). Researchers have also discovered that PS2 is 10 times more effective against these cancer cells than previously reported, suggesting that its mechanism of action may vary depending on the cell type (110).

Parasporin 3

PS3 possesses a 3-domain structure feature and its activation require proteolytic cleavage, which contributes to its specific toxicity against cancer cells such as HL-60 and HepG2. It triggers cell death via pore formation and necrosis, possibly in a ROS-independent mechanism (102). Additionally, PS3 contains a unique richin domain that is absent in other Cry proteins, enhancing its specificity for cancer cells through sugar binding that interacts with carbohydrates (111).

Parasporin 4

PS4 isolated from the *Bt* strain A1470, differs markedly from other parasporins and Cry proteins, having no conserved regions and structural similarity (104). It functions as a cholesterol-independent pore-forming toxin, exhibiting high cytotoxicity against several cancer cell lines, including Sawano, TCS, MOLT-4, HL60, HepG2, Caco-2 cells. This cytotoxicity is associated with nuclear shrinkage and cell bursting, causing release of lactate dehydrogenase and the uptake of FITC-dextran by affected cells (112). Notably, the action of this toxin does not involve the activation of caspase-3 and 7, suggesting a unique mechanism of action that distinguishes it from other parasporins (113).

Parasporin 5

PS-5 derived from *Bt tohokuensis* A1100, demonstrates cytotoxic effects against leukemic T cells (MOLT-4) and a wide range of mammalian cell lines through C-terminal cleavage with proteinase K (106). Unlike other parasporins, it shows low sequence similarity to Cry toxins, although it does exhibit some resemblance to Cry toxins and aerolysin -type pore-forming toxins. However, it lacks a clear mechanism of action, emphasizing a need to bridge gap in the area (102).

Parasporin 6

PS6 isolated from *Bt* M109 exhibits partial similarity to Cry2 toxins but is distinguished by unique structural features and cytotoxic effects against HepG2 and HeLa cells (105, 112). It is activated by N-terminal protease treatment under alkaline conditions, which leads to membrane damage and various pore-forming effects, suggesting its poten-

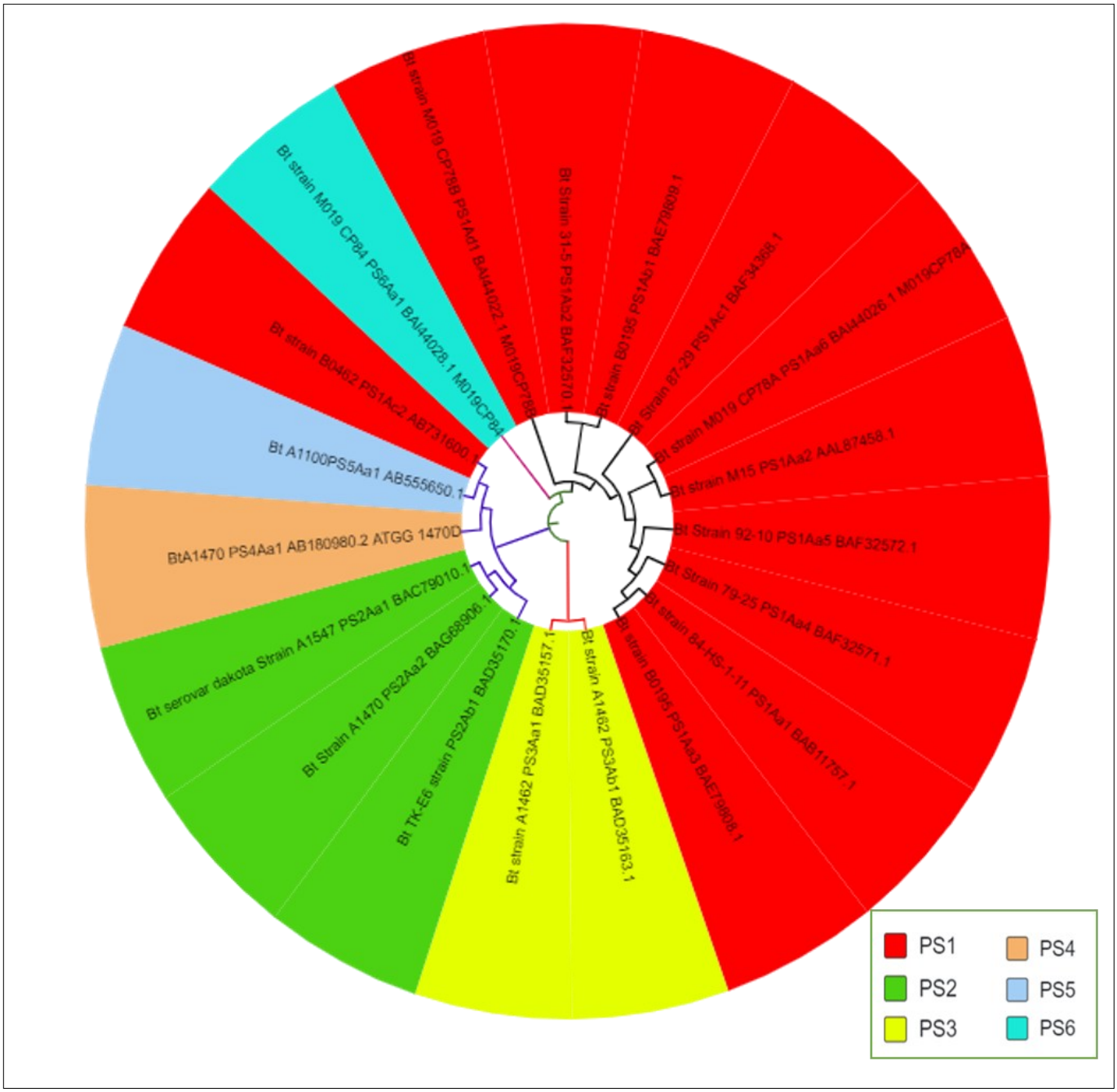

Fig. 3. Phylogenetic relationships among the anticancer proteins. Protein sequences were retrieved from the NCBI database and a phylogenetic tree was constructed with the help of MEGA software 11.

tial for cancer therapy (105).

Among PS proteins, PS1 and PS2 show promise for cancer treatment. PS1 triggers apoptotic signalling and selectively impacts various cell lines. PS2 is identified as a selective pore-forming toxin that induces morphological changes and activates apoptosis in cancer cells. Although PS3, PS4, PS5 and PS6 exhibit cytotoxicity, their mechanisms remain largely unknown, with fewer studies conducted compared to PS1 and PS2 (114). Current investigation includes identifying and evaluating novel native strains of *Bt* that demonstrate increased cytotoxic activity against cancer cells. Selected strains will undergo genetic enhancement to boost toxin activity. PS proteins are emerging as a promising alternative for cancer treatment, potentially offering advantages over current methods by reducing side effects. This advancement seeks to improve treatment outcomes and enhance the overall quality of life for individuals undergoing cancer therapy.

Currently, pharmaceuticals derived from *Bt* with anticancer properties are not commercially available. However, exploring the mechanisms by which *Bt*-parasporins act against various cancer types indicates the possibility for these proteins to be developed as anticancer pharmaceuticals in the future. Transitioning from lab-based research to real-world medical treatments is a complex process fraught with challenges. Extensive research is required to validate treatments efficacy, determine optimal delivery method and ensure safety of patients. The potential of specific *Bt* strains to produce toxins with anticancer activity against a range of human cancer cell lines, including leukemia, cervical, hepatocellular and colon cancer cells are listed in Table 3.

Conclusion

Beyond its traditional role as a biopesticide, *Bt* (*Bacillus*

Table 3. *Bt* strains producing toxins with anticancer activity against human cancer cell lines.

Sl. No.	Current Name	Old name	Isolated from	Cells	Protoxin (kDa)	Active Toxin (kDa)	*Bt* Strain	References
1	PS1Aa1	Cry31Aa1	Soil Isolate from Hiroshima Prefecture, Japan	MOLT-4, HeLa cells	81	15 and 56	*Bt* strain 84-HS-1-11	(100)
2	PS1Aa2	Cry31Aa2	Dead two-spotted spider mites (*Tetranychus urticae*)	HeLa, TCS, HL-60, Jurkat, HepG2 cells	83	55 and 70	*Bt* strain M15	(160)
3	PS1Aa3	Cry31Aa3	Soil sample in Japan	HeLa cells	81	56	*Bt* strain B0195	(161)
4	PS1Aa4	Cry31Aa4	Urban soil, Hanoi, Vietnam		81	NP	*Bt* strain 79-25	(162)
5	PS1Aa5	Cry31Aa5	Urban soil, Hanoi, Vietnam		81	NP	*Bt* strain 92-10	(162)
6	PS1Aa6	Cry31Aa6	Japan, Caribbean, Canada	HepG2 cells and HeLa cells	70	15 and 55	*Bt* strain M019, CP78A	(105)
7	PS1Ab1	Cry31Ab1	Soil sample in Japan	HeLa Cells	82	56	*Bt* strain B0195	(161)
8	PS1Ab2	Cry31Ab2	Urban soil, Hanoi, Vietnam		82	NP	*Bt* strain 31-5	(162)
9	PS1Ac1	Cry31Ac1	Urban soil, Hanoi, Vietnam	HeLa and HepG2 cells	87	NP	*Bt* strain 87-29	(162)
10	PS1Ac2	Cry31Ac2	Pond water in Seigenji, Kurumeshi, Fukuoka, Japan	HeLa Cells	81	15 and 60	*Bt* strain B0462	(163)
11	PS1Ad1	Cry31Ad1	Japan, Caribbean, Canada	HepG2 and HeLa cells	73	14 and 59	*Bt* strain M019, CP78B	(105)
12	PS2Aa1	Cry46Aa1	Soil sample collected in the city of Hino, Tokyo, Japan	MOLT-4, Jurkat, Sawano and HepG2 cells	37	30	*Bt* serovar dakota strain A1547	(164)
13	PS2Aa2	Cry46Aa2	Soil sample collected in the city of Hino, Tokyo, Japan	MOLT-4, Jurkat, Sawano and HepG2 cells	30	28	*Bt* strain A1470	(165)
14	PS2Ab1	Cry46Ab1	Soil in Ehime Prefecture, JapanJurkat	Jurkat, HEK293, HeLa and MOLT-4 cells	33	29	*Bt* TK-E6 strain	(166)
15	PS3Aa1	Cry41Aa1	Japan	HL60 and HepG2 cells	88	64	*Bt* strain A1462	(167)
16	PS3Ab1	Cry41Ab1	Japan	HL60 and HepG2 cells	88	64	*Bt* strain A1462	(167)
17	PS4Aa1	Cry45Aa1	Soil sample collected in the city of Hino, Tokyo, Japan	CACO-2 cells	31	28	*Bt* A1470	(112)
			Soil sample collected in the city of Hino, Tokyo, Japan	MOLT-4 cells	31	28	*Bt* A1470	(168)
18	PS5Aa1	Cry64Aa1	Japan	MOLT-4, HepG2, TCS, HeLa, COS7, Vero and Sawano cell	33	30	*Bt* A1100	(106)
19	PS6Aa1	Cry63Aa1	Japan, Caribbean, Canada	HepG2, HeLa, CaCo-2	85	14 and 59	*Bt* strain M019, CP84	(105)

thuringiensis) also highlights its multifunctionality across various sectors, including agriculture, medicine and environmental science. The use of recombinant toxin genes has significantly enhanced crop protection, while transgenic crops contribute substantially to sustainable agricultural practices. Pyramiding, which involves integrating toxin genes into wild-type or genetically modified plants, improves pest control and delays the development of resistance. Extensive research has revealed that *Bt* plays numerous roles, ranging from the genetic improvement of crops and disease resistance to the development of new cancer therapies. Additionally, *Bt* regulates and enhances plant growth, fixes nitrogen and produces phytohormones, all of which are essential for increasing crop yields. In the medical field, *Bt*'s anticancer properties, particularly through parasporins, open up new therapeutic avenues, potentially leading to more effective and targeted cancer treatments. Furthermore, *Bt* has shown promise in bioremediation, aiding in the removal of pollutants and heavy metals as well as the synthesis of nanoparticles. This exploration in material science emphasizes environmental concerns and may have significant implications for both medical and industrial applications.

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Authors' contributions

All authors contributed to the study conception, design and manuscript preparation. Data collection was done by VS. The first draft of the manuscript was written by VS, RG and MS. Figures were prepared by RR. BN and JM critically reviewed and edited the manuscript. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

Ethical issues: None.

Supplementary data

Table S1. List of *Bt* strains and their contribution to their antagonistic effects on different pathogenic bacteria.

Table S2. List of *Bt* strains and their contribution to plant health and protection through biological control of fungal diseases.

Table S3. List of *Bt* strains and their effectiveness in plant growth.

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