

A Review on the Biological Resistance of Terricolous Microorganisms

Mitra Abootorabi*¹

M.A Student of Microbial Biotechnology, Tehran-Shomal Branch,
Islamic Azad University, Tehran, Iran.

<http://dx.doi.org/10.13005/bbra/2648>

(Received: 11 June 2018; accepted: 25 June 2018)

The excessive use of chemical pesticides to confront pests causes environmental pollution. Furthermore, plant pathogens resist chemical pesticides. When such pathogens accumulate in plants or soil, they will cause harmful effects on humans. Biological control is an alternative method that reduces or terminates the use of chemical compounds in agriculture. Biological control is also carried out by microorganisms. Bacteria are the main group of these microorganisms. Due to the extensive presence in the soil, tolerating changes of temperature, pH, and salinity as well as producing endospore resistant species, Bacillus bacteria are used in biological control of soil. Bacillus species are often found in soil and rhizosphere. These bacteria help with the control of plant pathogens by producing siderophore, secretion of enzymes, production of antibiotics and inducing systemic resistance. In this study, various biological control mechanisms which are carried out by microorganisms have been reviewed.

Keyword: metabolite, Bacillus, standard Aspergillus fungi, Fumigatus, Flavus, Niger.

The increasing use of chemicals as pesticides to eliminate plant pathogens has provided effective solutions in agriculture. However, due to the fact that the excessive use of these chemicals such as thiabendazole and o-phenylphenol causes environmental pollution, and as plant pathogenic agents are quickly become resistant to chemical pesticides and considering the high price of pesticides and their accumulation in plants or soil which has harmful effects on humans, extensive researches are being conducted in the world to replace this method with more recent methods to confront fungicidal resistant pathogens. Since the late 1900s, scientists have made great efforts to use natural antagonisms of terricolous organisms

to protect plants. Some bacteria exhibit activities against pathogenic pathogens such as pathogenic fungi due to the ability to produce anti-microbial compounds such as antifungal lipopeptides and some antibiotics. For a long time, aerobic gram-negative bacteria, especially *Pseudomonas* spp, have been widely studied as biological control agents. Despite the desired characteristics of *Pseudomonas* to play a role in biological control, its main weakness as a biocontrol agent is the inability to produce spores, which has recently led to greater attention to bacteria that form Spores of *Bacillus* species (Mavrodi et al., 2017).

Agricultural waste is considered as one of the most important agricultural issues for

*Corresponding author E-mail: mitra.abutorabi54@gmail.com



many reasons, including not observing the correct principles of harvesting, moving, transporting and storing such products. Losses and degradation caused by the action of microorganisms after harvesting result in significant economic losses in agricultural sector. Plant-fungal diseases are one of the most important issues in agriculture and food production in the world. It is estimated that the crop losses due to plant diseases in the Western countries is 25% and in developing countries is about 50%. One hundred and one third of these damages are due to fungal diseases (Gohel et al., 2006). Citrus is one of the most important fruits of the world in terms of economic value, and as before reaching the market and the customer; these fruits are stored, in this time interval, they are more sensitive to post-harvest damages and are exposed to stressed aerobic and anaerobic soil conditions (Usall et al., 2016). Some fungi, especially *Penicillium* species (*p. digitatum*, *p. italicum*), are involved in post-harvest losses (Barkai-Golan 2001; Eckert and Eaks, 1989). Other citrus pathogenic fungi include the *Aspergillus* and *Alternaria*. *Aspergillus* is the most common environmental fungi and can be isolated from citrus fruits, vegetables, tomatoes, corn, pistachios, etc. In citrus, *Aspergillus niger* citrus produces brown rot and *Aspergillus flavus* creates albinism (virescence). *Alternaria* is a species of an incomplete fungus that causes brown to black and fairly soft rot in the lemon. *Alternaria alternata* is one of the most important citrus pathogens in the world (Book 2006). The primary method for controlling the fungal damage to fruits and other agricultural products is the use of chemical fungicides, some of which are not suitable for the treatment of these products, and some have been eliminated due to the possibility of having toxic agents (D'Aquino et al., 2017). Recently, the use of biological control agents, especially bacteria, has attracted a lot of attention due to the ability of some species to suppress different plant diseases and the possibility of combining with other control methods (Arrebola et al., 2010). Therefore, various sources of antibiotic production are screened, among which *Bacillus* especially is an important alternative to extract antibiotics and their industrial production. The soil is considered one of the main sources of microbes and naturally is a habitat for a large group of bacteria that is the source of bioactive products with diverse pharmacological activities.

Soil bacteria, especially the *Bacillus* species, grow rapidly and are characterized by synthesis of secondary metabolites with significant variations in structure and performance and as biocontrol plants (fungicides, bactericides and fertilizers), probiotics and pathogens (Mongkoltharuk 2012; Amin et al., 2012).

Therefore, in the growing trend of the use of secondary bacterial metabolites in medicine and industry, it seems that in the biological control of fungal diseases of the soil, the useful microorganisms of rhizosphere or plant probiotics are appropriate alternatives for the first line of defense against these pathogens. So, the present research studied the effects of various plant pests and diseases and described the biological methods for confronting them using antifungal extracts of bacteria.

Citrus

Citrus is from the family of Rutaceae and the subfamily of Aurantioideae. This subfamily has 33 different species whose three species i.e. *Poncirus*, *Fortunella*, and *Citrus* have a significant economic value in citrus producing countries. The citrus contains salts and is rich in vitamins C, B, and A. It has medicinal and nutritional values, and about 100 industries use citrus to produce their own products. Post-harvest diseases are diseases that occur during harvesting, grading, packaging, storing and transporting the product to the market and ultimately to the consumer. Even at normal room temperature or in the refrigerator, and up to the time of eating the product, pathogens continue to grow (Sivakumar et al., 2007). Post-harvest diseases are mainly caused by fungal and bacterial microorganisms, and fungi are more important pathogens in fruits (Bernat et al., 2017).

Food health is a key component of crop rotation control programs. The failure in controlling some specific storage diseases and the need for more environmentally friendly methods for controlling and confronting plant diseases have led to the emergence of new controlling methods. A society cannot rely on one or two methods of plant disease controlling and it should use all existing methods (Bernat et al., 2017).

Among the available techniques for controlling post-harvest disease, we can point to the biological control and the use of food preservatives (Zhang et al., 2017).

Biological control in plant diseases management

An increase in population and consequently an increase in demand for food as well as the limitation of agricultural land use have led to an increase in crop yields per unit area. In order to achieve sustainability, the need for sustainable agriculture should be felt. Achieving a sustainable lifestyle requires reducing the use of chemical pesticides and applying biological methods against pests and diseases (Stirling, 2017). As the excessive use of chemicals in agriculture causes environmental pollution, throughout the world, comprehensive researches have been conducted to replace this method with newer methods to confront fungal resistant pathogens. An essential solution is the utilization of the activity and function of microorganisms (Nagórska et al., 2007). Biological control reduces the effects of pesticide use in the long term and makes a balance between harmful plant pathogens and their natural enemies. In this regard, antagonistic bacteria and fungi are widely used to control plant diseases (Shahzad et al., 2018).

Biological control mechanisms

Biological control is usually carried out by reducing the concentration of inoculum, replacing pathogens existing in plant residues with saprophytes prior to host culture and preventing proliferation and growth through mechanisms such as competition, antibiosis, predation and parasitism (Stirling, 2017).

Parasitism**Competition**

It is a kind of mutual coexistence between two living organisms, which occurs when different microorganisms within a population attempt to achieve something similar. The target may be a place or food (Stirling, 2017).

Predation

The primarily refers to animals that at the higher stage of nourishment and in the macroscopic world are predations (Stirling, 2017).

Antagonism

It is the negative effect that an organism has on another organism. This is a one-way process and is due to the production of certain compounds such as antibiotic or bacteriocin produced by an organism (Stirling, 2017).

Parasitism

It is a coexisting relation in which two

organisms that are not evolutionally related to each other live together for a long period of time, and as a result of this kind of relation, usually one of these two types of organisms which is physically smaller and is called the parasite, benefits from the other one which is partially damaged and is called the host. The most direct type of competition in a biological control is hyperparasitism in which pathogenic parasites are used to eliminate a pathogenic pathogen. The most direct type of competition in biological control is hyperparasitism, in which obligate parasites are used to eliminate the same plant pathogen (Stirling, 2017). Today, it has been observed that the relation between plants and non-pathogenic microorganisms stimulates the host plant defense systems, which in turn causes biological control of pathogens and significantly reduces the severity of the disease (Stirling, 2017).

Several studies have been done to identify biological control mechanisms in plant diseases, and in most of these studies, there is an antagonistic property that can affect rhizospheric microflora and cause some kind of environmental antagonism and accelerate the host's response to the pathogen (Savini, 2016).

Microorganisms affecting biological control**Fungi**

Several groups of fungi play an important role in the microbial control of insects which are included in Deuteromycete class and Entomophthorales, Saprolegniales and Laeniidiales orders, and the Coelomomycetaceae family.

These fungi are able to attack insect cuticle and can directly penetrate the insect's exoskeleton and make infection, or infect the insects' tracheae. *Trichoderma* and *Gliocladium* are fungi that biologically control fungal pathogens. Through different mechanisms and by producing antimicrobial compounds such as antibiotics with complex structure like gliovirin and gliotoxin, and, most often, through the parasitism relation, they suppress the plant fungal pathogens.

Viruses

Viruses are used for biological control of insect-borne plant pathogens. *Baculoviridae*, *Poxviridae*, *Reoviridae*, *Iridoviridae*, *Parvoviridae*, *Picornaviridae* and *Rhabdoviridae* are used for an effective biological control (Bonning, 2015).

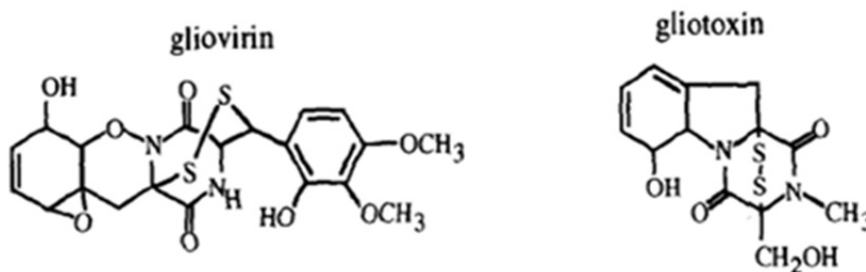


Fig. 1. The structure of two antibiotics produced by fungi which are used for biological control of plant pathogens

Bacteria

Pseudomonas spp

Pseudomonas spp has many characteristics that make them biocontrol, such as colonization and proliferation within the plant, competition with other microorganisms, adaptation to environmental stresses, and the production of a wide range of active biometabolites such as antibiotics, sydrophores, volatile substances, and growth stimulant compounds. Due to this, such bacteria are used to suppress plant pathogens. Among the most common *Pseudomonas* species which have a role in biological control, we can name *P. fluorescens*, *P. chlororaphis*, *P. aureofaciens*, *P. putida* and among non-pathogenic species of this bacteria we can refer to *P. syringae*. These species are used in the suppression of plant diseases such as Take-all (Take-all is a plant disease affecting the roots of grass and cereal plants in temperate climates caused by the fungus *Gaeumannomyces graminis* var. *tritici*. All varieties of wheat and barley are susceptible) and Fire Blight [caused by the bacterium *Erwinia amylovora*, is a common and frequently destructive disease of pome fruit trees and related plants. Pear (*Pyrus* species) and quince (*Cydonia*) are extremely susceptible. Apple, crabapple (*Malus* species), and firethorns (*Pyracantha* species) also are frequently damaged] (Agaras et al., 2015). **Fusarium Head Blight**

Bacillus spp

The *Bacillus* specie was discovered in 1872 by Chon. Gram-positive *Bacillus* spp are rod-shaped, optional aerobic or anaerobic, catalase-positive, and have peripheral cilium. These microorganisms have low chemoorganotrophic metabolism which are dependent to organic

compounds and are used as carbon and energy sources.

The most important characteristic of the members of this specie is the production of endospore, which help with the durability of bacteria in the nature and can last for a very long time, perhaps millions of years (Zimina et al., 2016).

A review on the role of *Bacillus* spp in Biological in biological control of plant diseases

Bacilli associated with the plant are known as plant parasites, saprophytes and biological control agents. Three species of *Bacillus* are considered as plant parasites. These species include *Bacillus megaterium pvcerealis* causing White Blotch Incited in Wheat, *B. circulance* which causes the death of date seedlings and *Bacillus polymyxa* causing blight tomato. Most *Bacillus* species are harmless saprophytes. (Kumar et al., 2015).

Bacillus species are good candidates for biological control due to their specific characteristics. First, they produce anti-fungal and anti-bacterial antibiotics. Their second feature is the ability to produce spores, due to the same characteristic, it is easy to be formulated because comparing with tube cells, it survives longer. Another feature is their permanent presence (because they are part of the general microflora of the soil) in the soil (Balouiri et al., 2015). Among the activities of antibiotics produced by this bacterium, one can name their direct effect on fungi, competition with microorganisms which attack root systems. *Bacillus* bacteria seem to be appropriate solutions to control vascular pathogens due to their ability to colonize the internal organs

of the plant (Pii et al., 2015). The results of the studies conducted by Kim et al. indicate that *Bacillus* spp controls wheat diseases. *B. subtilis* inhibits germination of plant pathogen spores, causes degradation or disruption of their germ tube growth and interferes with the attachment of pathogen to the plant.

Bacillus

Bacillus species include gram-positive bacteria which are rod-shaped, and often move. These bacteria can produce products such as ethanol, H₂, acetone, acetic, formic, lactic, and succinic acids by fermentation of glucose. *Bacillus subtilis* can produce compounds which resist against fungi. Among these compounds one can point to be extracted from the etorin A, which was first extracted from *Bacillus circulans*. This compound is a cyclic lipopeptide that has inhibitory effect on fungal growth while has a little toxic effect on humans. Thus, it is used in the treatment of fungal infections of humans and animals. Other *Bacillus* species that are able to produce Euthorin A is *Bacillus amilolycophasins*. This species of *Bacillus* is used as a biological controller against plant pathogenic fungi (Balouiri et al., 2015). A study on the antifungal metabolites of *Bacillus* species shows that these metabolites are resistant to temperature and pH changes and do not lose their antifungal effect.

Bacillus subtilis is also able to produce a metabolite called surfactin, which is a strong biosurfactant and has an antifungal activity. A compound which is called fusaricidin A also has anti-fungal properties and is obtained from *Bacillus polymyxa*. Fusaricidin A acts against both fungi and gram-positive bacteria.

Bacillus a source of biological active molecules

Most *Bacillus* species are considered as microbial factories which produce a wide range of biologically active molecules that have inhibitory properties towards the growth of pathogens (Passari et al., 2015). One of the most common and well-known microorganisms is *B. subtilis*. An average of 4-5% of its genome is used for antibiotic synthesis and can produce different antimicrobial compounds with different structures (Kumar, 2011). Among the antimicrobial compounds, the potential of cyclic lipopeptides such as Surfactin, etorin and fengycin for biotechnology and pharmacy applications is well-known for their

surfactant properties (Huszcza & Burczyk 2006).

An overview on industrial applications of Bacillus species

Bacillus bacteria are widely used to produce important industrial enzymes, food products, pesticides and insecticides. *Bacillus* secretes extracellular enzymes such as alpha-amylase and protease, which make half of the total commercially produced enzymes (Behera and Ray, 2016).

Certain strains of *Bacillus* are generally safe (GRAS) and are used in industry and agriculture. Bacterium *B. thuringiensis* contains etorins (Hiradate et al., 2002) that is effective in protecting the berry leaves against *Colletotrichum dematium*. Some *Bacillus* species produce very strong natural biosurfactant compounds such as surfactants from *B. subtilis* and lichenysin from *B. licheniformis* which are used to improve the oil refinement. Lantibiotics produce peptide antibiotics containing lanthionine like mersacidin which is produced by HILy85 and 54728 strains of *Bacillus* spp and has meticcillin effect on strains of *Staphylococcus aureus* which resist against antibiotics. Bacteriocin produced by *B. subtilis* ATCC6633 strain inhibits the germination of *Clostridium* sp and *B. cereus* spores (Chatterjee et al., 2005).

Characteristics and biological effects of non-protein toxins from of Bacillus species

Many microbial peptides are synthesized by peptide synthetase which are multienzyme complexes (Heidari, 2016). About 4 to 7 percent of the genomes of *Bacillus subtilis* and *B. amyloliquefaciens* are used to produce biologically active compounds (Stein, 2005). Surfactin, Lichenysin A, fengycin, Tricodine, bacitracin mycosubtilin are produced by non-rhizome peptide synthesis (Koumoutsis et al., 2004). *Bacillus* species produce a wide variety of antibacterial, antiviral and antimicrobial compounds, some of which are toxic for eukaryotic cells. *Bacillus* toxins are associated with various chemical groups whose structure consists of cyclic lipopeptides, cyclic peptides, phospholipid oligopeptides, low molecular weight compounds with NH₂ functional groups as side chains and cationic sugar derivatives of cationic derivatives. The peptides have a molecular weight between 500-4000 daltons and non-peptides have a

molecular weight between 555 and 129 daltons whose average weight is 1000 and 300 daltons, respectively.

Most of the non-protein toxins extracted from *Bacillus* species are listed in the table and their roles as food contaminants are relatively well-known. Most of these materials were discovered before the 1980s, while their toxic properties were identified later.

Bacillus strains produce compounds that in different ways change the function of biological membranes. Some compounds affect the integrity of the plasmid membrane (such as surfactin and lichenysin A) and may cause electrolyte leakage, loss of cell contents, and cell death. The ionophoric materials (such as Gramicidin S, Cruicid, Gramicidin A) form ion channels or act as ion carriers. Such substances change the fluidity of the plasma membrane or the organelles membranes. Protecting transmembrane electrical potential, as well as the proper ionic concentration of cells or organelles, are vital for cellular functions. Many biochemical functions are regulated by the ion flow in the membranes and the change in the structure of the membrane proteins. The change in membrane potential changes the structure of membrane proteins such as Na⁺ / K⁺ channels and may cause cell death (Passari et al., 2015).

CONCLUSION

For many years, agricultural waste has been considered as an important issue due to numerous reasons, including non-compliance with the principles of harvesting, moving, transporting and maintaining such products. Losses and degradation resulted from microorganism activities after harvesting causes significant economic losses to agricultural products. As health is related to the type of diet, the human being who is the main consumer of agricultural products is made to seek foods free from pesticide residues, toxins, and harmful microorganisms. Particular attention to human health and the environment, as well as the resistance of some extracts of pathogens to chemical pesticides and the high price of these materials, motivates human to find alternative methods to fight plant pathogens. Recently, the use of biological control agents, especially bacteria, has attracted a great deal of attention due to the ability

of some species to suppress different diseases of plants through different functional methods and the possibility of combining with other control methods. Biological control reduces the effects of using pesticides in the long term and creates a balance between harmful plant pathogens and their natural enemies.

Terricolous and non-pathogenic bacteria with the antagonistic ability of plant pathogenic fungi and disease prevention are an appropriate alternative to chemical fungicides and are one of the most important factors in establishing and sustaining agricultural systems. Biological control reduces the effects of pesticide in the long run, leads to a balance between harmful plant pathogens and their natural enemies. In this regard, antagonistic bacteria and fungi are widely used to control plant diseases. In comparison with chemical controls, biological control is a healthier and safer control since, unlike some toxic substances, microorganisms are not stored and accumulated in food chains. Biological control is carried out through mechanisms such as competition, antibiosis, predation, and parasitism.

REFERENCES

1. Mavrodi, D. V., Yang, M., Mavrodi, O. V., & Wen, S. 7 Management of Soilborne Plant Pathogens with Beneficial Root-Colonizing *Pseudomonas*. *Advances in PGPR Research*, 2017; **147**.
2. Gohel, Vipul, Anil Singh, Maisuria Vimal, Phadnis Ashwini, and HS Chhatpar. 2006. 'Review-Bioprospecting and antifungal potential of chitinolytic microorganisms'.
3. Usall, J., Ippolito, A., Sisquella, M., & Neri, F. Physical treatments to control postharvest diseases of fresh fruits and vegetables. *Postharvest Biology and Technology*, 2016; **122**: 30-40.
4. Book, Bad Bug. 2006. 'Foodborne pathogenic microorganisms and natural toxins handbook', *Center for Food Safety and Applied Nutrition (CFSAN)*. < <http://vm.cfsan.fda.gov/~mow/intro.htm>.
5. D'Aquino, S., Chessa, I., Inglese, P., Liguori, G., Barbera, G., Ochoa, M. J., ... & Palma, A. Increasing Cold Tolerance of Cactus Pear Fruit by High-Temperature Conditioning and Film Wrapping. *Food and Bioprocess Technology*, 2017; **10**(8): 1466-1478.
6. Arrebola, E, R Jacobs, and L Korsten. 'Iturin A is the principal inhibitor in the biocontrol

- activity of *Bacillus amyloliquefaciens* PPCB004 against postharvest fungal pathogens', *Journal of Applied Microbiology*, 2010; **108**: 386-95.
7. Amin, Adnan, Muhammad Ayaz Khan, Malik Ehsanullah, Uzma Haroon, Sheikh Muhammad Farooq Azam, and Abdul Hameed. 'Production of peptide antibiotics by *Bacillus* sp: GU 057 indigenously isolated from saline soil', *Brazilian Journal of Microbiology*, 2012; **43**: 1340-46.
 8. Amin, Adnan, Muhammad Ayaz Khan, Malik Ehsanullah, Uzma Haroon, Sheikh Muhammad Farooq Azam, and Abdul Hameed. 'Production of peptide antibiotics by *Bacillus* sp: GU 057 indigenously isolated from saline soil', *Brazilian Journal of Microbiology*, 2012; **43**: 1340-46.
 9. Sivakumar, Dharini, Karin Zeeman, and Lise Korsten. 'Effect of a biocontrol agent (*Bacillus subtilis*) and modified atmosphere packaging on postharvest decay control and quality retention of litchi during storage', *Phytoparasitica*, 2007; **35**: 507-18.
 10. Bernat, M., Segarra, J., Casals, C., Teixidó, N., Torres, R., & Usall, J. The relevance of the main postharvest handling operations on the development of brown rot disease on stone fruits. *Journal of the Science of Food and Agriculture* 2017.
 11. Zhang, H., Mahunu, G. K., Castoria, R., Apaliya, M. T., & Yang, Q. Augmentation of biocontrol agents with physical methods against postharvest diseases of fruits and vegetables. *Trends in Food Science & Technology*, 2017; **69**: 36-45.
 12. Stirling, G. R. Biological control of plant-parasitic nematodes. In *Diseases of nematodes* (pp. 103-150). 2017; CRC Press.
 13. Nagórska, Krzysztofa, Mariusz Bikowski, and Michał Obuchowski. 2007. 'Multicellular behavior and production of a wide variety of toxic substances support usage of *Bacillus subtilis* as a powerful biocontrol agent', *ACTA BIOCHIMICA POLONICA-ENGLISH EDITION*-, 54: 495.
 14. Shahzad, S., Rajput, A. Q., & Khanzada, M. A. Effect of Different Organic Substrates and Carbon and Nitrogen Sources on Growth and Shelf Life of *Trichoderma harzianum* 2018.
 15. Stirling, G. R. Biological control of plant-parasitic nematodes. In *Diseases of nematodes* (pp. 103-150). 2017; CRC Press.
 16. Savini, V. *Bacillus cereus* Biocontrol Properties. In *The Diverse Faces of Bacillus cereus*, 2016; (pp. 117-127).
 17. Zimina, M. I., Sukhih, S. A., Babich, O. O., Noskova, S. Y., Abrashina, A. A., & Prosekov, A. Y. Investigating antibiotic activity of the genus *Bacillus* strains and properties of their bacteriocins in order to develop next-generation pharmaceuticals. *Foods and Raw materials*, 2016; **4**(2).
 18. Zakataeva, N. P., Livshits, V. A., Gronsky, S. V., Kutukova, E. A., Novikova, A. E., & Kozlov, Y. I. (2015). *U.S. Patent No. 9,012,182*. Washington, DC: U.S. Patent and Trademark Office.
 19. Kumar, R. M., Kaur, G., Kumar, A., Bala, M., Singh, N. K., Kaur, N., ... & Mayilraj, S. Taxonomic description and genome sequence of *Bacillus campisalis* sp. nov., a member of the genus *Bacillus* isolated from a solar saltern. *International journal of systematic and evolutionary microbiology*, 2015; **65**(10): 3235-3240.
 20. Agaras, B. C., Scandiani, M., Luque, A., Fernández, L., Farina, F., Carmona, M., ... & Valverde, C. Quantification of the potential biocontrol and direct plant growth promotion abilities based on multiple biological traits distinguish different groups of *Pseudomonas* spp. isolates. *Biological Control*, 2015; **90**: 173-186.
 21. Bonning, B. C. Editorial overview: Parasites/Parasitoids/Biological Control: Virus-insect interactions: progress and pitfalls. *Current Opinion in Insect Science*, 2015; **8**, vii-ix.
 22. Balouiri, M., Bouhdid, S., Harki, E. H., Sadiki, M., Ouedrhiri, W., El Abed, S., & Ibsouda, S. K. Study on the Effect of the Antifungal Extract from *Bacillus* sp. on the Physicochemical Properties of *Candida albicans*. *Research Journal of Microbiology*, 2015; **10**(5): 214.
 23. Pii, Y., Mimmo, T., Tomasi, N., Terzano, R., Cesco, S., & Crecchio, C. (2015). Microbial interactions in the rhizosphere: beneficial influences of plant growth-promoting rhizobacteria on nutrient acquisition process. A review. *Biology and Fertility of Soils*, **51**(4): 403-415.
 24. Kumar, K. S., Haritha, R., Mohan, Y. J., & Ramana, T. Screening of marine actinobacteria for antimicrobial compounds. *Research Journal of Microbiology*, 2011; **6**(4): 385.
 25. Huszcza, E., & Bureczyk, B. Surfactin isoforms from *Bacillus coagulans*. *Zeitschrift für Naturforschung C*, 2006; **61**(9-10): 727-733.
 26. Passari, A. K., Mishra, V. K., Saikia, R., Gupta, V. K., & Singh, B. P. Isolation, abundance and phylogenetic affiliation of endophytic actinomycetes associated with medicinal plants and screening for their in vitro antimicrobial biosynthetic potential. *Frontiers in microbiology*, 2015; **6**: 273.
 27. Behera, S. S., & Ray, R. C. Solid state fermentation for production of microbial cellulases: recent advances and improvement strategies. *International journal of biological macromolecules*, 2016; **86**: 656-669.

28. Chatterjee, A., Mayawala, K., Edwards, J. S., & Vlachos, D. G. Time accelerated Monte Carlo simulations of biological networks using the binomial δ -leap method. *Bioinformatics*, 2005; **21**(9): 2136-2137.
29. Heidari, A. Genomics and Proteomics Studies of Zolpidem, Necopidem, Alpidem, Saripidem, Miroprofen, Zolimidine, Olprinone and Abafungin as Anti-Tumor, Peptide Antibiotics, Antiviral and Central Nervous System (CNS) Drugs. *J Data Mining Genomics & Proteomics*, 2016; **7**(3): e125.
30. Stein, T. Bacillus subtilis antibiotics: structures, syntheses and specific functions. *Molecular Microbiology*, 2005; **56**(4): 845-857.
31. Koukoutsis, J. , Smith, J. P., Daifas, D. P., Yayalan, V. , Cayouette, B. , Ngadi, M. And El Khoury, W. *In Vitro* Studies To Control The Growth Of Microorganisms Of Spoilage And Safety Concern In High Moisture, High Ph Bakery Products. *Journal Of Food Safety*, 2004; **24**: 211-230. Doi:[10.1111/J.1745-4565.2004.tb00385.x](https://doi.org/10.1111/J.1745-4565.2004.tb00385.x)