Biotechnological
Communication

BBRC
Bioscience Biotechnology
Research Communications

Biosc.Biotech.Res.Comm. Vol 13 (2) April-May-June 2020 Pp-410-423

Biological Production of Antimicrobial Peptides Against Plants as Well as Human Pathogens

Farwa Basit[1], Sana Asghar[2] and Taswar Ahsan[3*]

1Institute of Crop Sciences, College of Agriculture and Biotechnology, Zhejiang University, P.R, China,

[2]Department of Molecular Biology and Biochemistry, Institute of life Sciences, Zhejiang University, P.R, China

[3]Faculty of Sciences, University of Central Punjab, Lahore, Pakistan

ABSTRACT

Antimicrobial peptides (AMPs) are one of the natural defense compounds grounded on drugs because of its vast potential as a novel biopharmaceutical product for both humans and plants. Antimicrobial Peptides (AMP) have gathered attention as a feasible clarification to this serious matter and are existence discovered for their prospective antimicrobial applications. These are small, cationic and characteristically have hydrophobic residues and play an important role in biological activities by creating interaction with the cell membranes. These compounds are extracted and purified by natural hosts like bacteria as well as fungi etc trough ribosomal or non-ribosomal synthesis .Plants and agricultural production are affected by various diseases that are caused by bacteria, fungi and viruses. Anti-microbial peptide are used as bio-pesticides which are concealed from many microorganisms alongside it about transgenic plants too rapid it to control the plant infections and plant pathogens but there are some social concerns and limitations because of less toxicity and less stability of these compounds that's why transgenic plants are not commercially marketed.Now a day, instead of using chemical peptides researchers are paying attention on numerous antimicrobial peptides which based on structural analog design and can overcome plant disease as commercial bio pesticides. This valuation will assess the work of bacterial cloning and its mechanism to supply the recombinant proteins in against of plant pathogens for instance bacteria, fungi, nematodes, and viruses that reason of plant disorder. It can help to exploit the recognition of peptide–antibiotic amalgamations that will meritoriously eradicate resistant bacteria.Various techniques such as gene editing, protein engineering or computational tools can provide help to face the industrial requirements which could stimulate development to squeeze proteins or peptides as well as can be used to screen latent peptide sequences with antimicrobial properties, and for computer-aided discovery of AMPs as well.

KEY WORDS: ANTIMICROBIAL PEPTIDES, BIOPHARMACEUTICAL, RIBOSOMAL SYNTHESIS, NON RIBOSOMAL SYNTHESIS.

Article Information:*Corresponding Author:*taswar.micro@gmail.com*
Received 17/03/2020 Accepted after revision 10/06/2020
Published: 30th June 2020 Pp-410-423

Published by Society for Science & Nature, Bhopal India.
Available at: https://bbrc.in/
Article DOI: http://dx.doi.org/10.21786/bbrc/13.2/08

INTRODUCTION

Natural products are selected according to subordinate metabolites from an innumerous list of sources, just as creatures, oceanic living beings, organisms, earthly plants, and spineless creatures (Chin, et al., 2006). These synthetically and fundamentally various molecules act as an uncommon class of therapeutics to recuperate various maladies. The preliminary documentation of the use of normal items to recoup human constitution goes back to the ancient Mesopotamia's advanced restorative framework from 2900 - 2600 BCE, (Reisel et al., 2002, Rahman, et al., 2014). The natural product portion can't just zone that has encountered extensive development or utilizations useful items created in/from living creatures. Prokaryotic and eukaryotic bacterial cells, in blend with the advancement of recombinant DNA strategies, have been liable for a blast of biologics. Biologics are a lot of atoms whose active therapeutic materials are resulting from living beings, for example, creatures, microorganisms, plants, human blood items, and tissue transplants that are too multi-layered to even think about being delivered through organic synthesis (Revers, et al., 2010 Park et al., 2019).

Biologics can be separated into five superior classes: First one is monoclonal antibodies, as trastuzumab (HerceptinR) and rituximab (RituxanR); Second one is blood factor subsidiaries, similar to coagulation factor VIIa (NovoSeven RTR) and epoiten alfa (EpogenR); Third one is Immunization; Fourth one is Enzymes; and Fifth one is recombinant proteins, for instance immunomodulatory cytokines, and thrombolytic mediators (Lacana, et al., 2007).Bacteriocins are a protein delivered by microorganisms of one strain and dynamic against those of a firmly related these are specific peptides known as antimicrobial peptides which are formed by Gram-negative bacteria. These molecules have included generous concern; particularly those made by GRAS (Commonly Renowned as Nontoxic)) microbes, by way of normal nourishment preservers inside nutrient production fields. These peptides likewise indicate likely replacements to obsolete antibiotics which is utilized for cure of poisonousness within persons and food assembly creatures.(Cotter, et al., 2005; Desriac et al., 2010; Svetoch et al.,2010) besides, supplementary investigations, reveal probable such as medicines designed for tumor cure (Ravikant, et al., 2015).

The further most dynarnic requisite for this inspection is production of wide phases of energetic bacteriocin by using biological ways. Though specific peptides could be sterilized after their local making bacterial strains, these techniques required some additional time period, work besides bacteriocin productions are frequently decrease (Fernández, et al.,2003). Artificial manufacture is an important opportunity in few research works, nonetheless hassle of a number for the bacteriocins as well as cost for various manner restriction used for high amount production. (Dong, Chen et al. 2012, Park, Yoon et al. 2019,Dong et al., 2012; S. R. Park et al., 2019).

These straining, which might be food-grade creatures, provide an inoffensive preference for commercial foodstuffs, in addition to offer inherited as well as secretory apparatus for dynamic LAB bacteriocin assembly. Though, countenance bacterial strains accessibility are enormously certain and its effect in production are quiet unsatisfactory at manufacturing level, limiting variability and production of bacteriocin amount. Expected of these boundaries, *Escherichia coli*, has been the furthest generally utilized creature for heterologous protein manufacturing, it is a generous choice for representing the expression of heterologous bacteriocin owing to the situation, it shows quick development on low-price media, studying on its widespread inherited classification along with accessibility of multipurpose cloning techniques, structural expressions as well as various bacterial strains, (Fernández et al., 2003; Mergulhao, et al., 2004; Rosano et al., 2014 Li et al., 2016, Mesa-Pereira, et al.,2018).

This may cause an ease for efficient description besides establishing a beneficial formation method for production of different kinds of bacteriocins which are considered as tricky for their development, By adding toward the ones bacteriocins found out for elimination of its information through microbial genomes which arrange in particle order (Kuo & Huang, et al., 2013), Growing their capability for production and profit-oriented by using meals and therapeutic productions (Ongey & Neubauer, 2016). However, this technique isn't underprivileged of difficulties which may upward thrust throughout the expression, production or processing of these particle containing of two or further amino acids it's peptide in *E. coli* (J. Choi & Lee, et al., 2004).Advanced the powerful manufacturing of the recombinant human being insulin HumulinR , *E.coli* quickly developed the highest expression platform with in the 1980s when the bio-pharmaceutical area appeared and become monitored by means of yeast *Saccharomyces cerevisiae*, (Romero-Garcia, et al., 2016). Bacterial cells create the mainstream of hosts working in the production of currently allowable recombinant medicines for human being treatment, mostly due to their absence of uncommon post-translational modifications, terrible solubility and origination of cell stress responses, proteolytic ambiguity (Graumann et al., 2006; Mesa-Pereira et al., 2018).

This verifies that microbial hosts signify convenient and full of life systems for the well-prepared manufacturing of recombinant proteins despite a few blocks and complications. This assessment will evaluate the tasks of bacterial cloning and its mechanism to supply the recombinant proteins in contradiction of plant pathogens alike bacteria, fungi, nematodes, and viruses that reason of plant infections.

Mechanism designed for anti-microbial peptide protein production through microbial cloning: The host cell's exquisite qualities which prove as protein production device will yield treasured protein that will provoke define its entire procedure which designates understanding desirable for this approach; it's a

multiplicity of molecular apparatuses, methods, and substances. Amongst microbes, host schemes which are obtainable encompass microbes, algae, fungi, and yeast. All have strengths and weaknesses and their preference possibly concern to protein of interest (Adrio & Demain, 2010) Like, A prokaryotic expression scheme won't be suitable, uncertainty eukaryotic post-translational amendments are desirable. (Sahdev, et al., 2008). The benefits of use of the *Escherichia coli* for the reason that host entity are familiar. (i) lt contains unequaled reckless rate of growth.

In glucose and salts medium as well as assumed an optimum ecological circumstances, its repetition period is around 20min (Rosano, et al., 2014). So, its means that's culture injected through a 1/100 diluted of sterilized appetizer culture might also immobile stage inside rare times. Although, it need to remain as well-known which show expression of include are combinant protein might inform a metabolic load at mobe, producing a considerable reduction in gene proportion time (Pinfold, et al.,1996) (ii) Cell cultures with greater width are smoothly attained.Speculative thickness limit liquid culture of an *Escherichia coli* that is assessed around two hundered gram dry cellular weightiness /lorroughly1× 1013 possible microorganisms/ml.(Restaino et al., 2013). It is investigated that their physicochemical capabilities as well as, secondary structures, and appliances of action, and associated them with the peptides inside AMP database(Lei et al., 2019). Gram-positive bacteria that have habitat inside soil and 98% of identified AMPs likewise originated from natural bases such as skin excretions of frogs besides toxins from diverse species (Lei et al., 2019)

Existence a work horse creature, these plans ascended appreciations to the prosperity of understanding around its physiology like composition, functions and structures study. (iii) Opulent multifarious media may be crafted from keenly obtainable as well as reasonable mechanisms (Bakare, Fadaka, Klein, & Pretorius, 2020). (iv) Conversion through exogenic DNA remains reckless and calm as well. Plasmid conversion of Escherichia coli could implement tiny such as for five min, (Aranishi, Okimoto, & Izumi, 2005). Its structural physiognomies subsidize to their amphipathicity which permits for segregating obsessed by the membrane lipid bilayer (Bechinger & Gorr, 2017), in that way ornament their antimicrobial accomplishments, consequently impacting actual membrane absorbency on a assortment of cytoplasmic objectives, (Bakare et al., 2020).

Genetic factors that understanding repetition as free units, for instance plasmids, comprise are plicon. It consist of one supply of replication collectively with its associated cis-acting manipulate components A huge drawback is to having lack of awareness during selection of a suitable vector in duplicate amount. Duplication Controller amount be located in the replicon, (Turgeon, et al., 2008). Generally used vectors, like the pET collection, have the pMB1 foundation, 15 to 60 duplicates; (Bolivar et al., 1977) although a modified form of pMB1 starting place is existing within pUC sequences 500 to 700 duplicates for each cell; (Minton 1984). Alternative kind wild form ColE1 basis 15 to 20 duplicates to each cell; (Minton, et al., 1984). Alternative kind wild-kind ColE1 basis (15–20 duplicates (Lazzaro, et al., 2020) to each cell (Lin-Chao, et al., 1986; Lee et al., 2006). AMPs are ubiquitous among multicellular eukaryotes , with most plant and animal species expressing dozens of distinct AMP genes in epithelial tissues and in response to infection (Chen, et al., 2020; Waghu, et al., 2020). The diversity and potency of AMPs make them attractive candidates for translational application, and several are already in clinical trials (Lazzaro et al., 2020).

So it could inside the pQE vectors (Qiagen). These are totally suitable with identical mismatch institution which means that they can't be extent composed in the alike cell by way of their challenge with separately towards replication technology (Del Solar, et al., 1998; Joseph et al., 2010) . On behalf of twofold expression of specific recombinant proteins the usasge of double plasmids, schemes with pISA are reachable (pBAD and pACYC plasmids collection, ten to twelve duplicates per cell (Guzman, et al.,1995).

The foremost in research of prokaryotic promoter is irrefutably *luc promoter*, and rnost vital essential of loc operon (Müller, et al.,1996). Accrued material inside working of an organization is permissible because of its extensive usage for expression of vectors. For initiation of the system is Lactose sources and this sugar can be usage for production of protein. Though, overview remains challenging for existence of willingly resources of metabolized carbon for example glucose. If the both lactose or glucose are prevailing, lac promoter's expression is not entirely influenced till entirely the glucose has been used .At this estimation (small amount of glucose),cyclic adenosine monophosphate is designed (Bakare et al., 2020), that is vital intended for entire beginning of lac operon (Skrzypczak, et al., 1994; Wöhrl, et al., 1990).Many AMPs have the potential to fold into amphipathic a-helices with hydrophilic (Lei et al., 2019) and hydrophobic sides (top, left). This conformation is schematically represented as an amphiphilic cylinder (Lazzaro et al., 2020; Waghu et al., 2020), with hydrophobic (red) and hydrophilic (blue) halves. AMPs bind to the membrane surface with the hydrophobic side groups anchored in the hydrophobic lipidic core of the bilayer, leading to different outcomes (center) (Bakare et al., 2020).

This optimistic mechanism of expression is called catabolite repression .In agreement, cyclic adenosine monophosphate (cAMP) elevations are small in cells rising luc operon suppressing sucrose, as well as acquaintances by lesser charges of lac operon's expression. (Hsiao, et al.,1977). To sign the development of plasmid permitted cells, are confrontation indicator is added to support of plasmid. Inside system of *Escherichia coli*, resistance of antimicobial genome is naturally utilized for its resolution (Bhopale, et al., 2020). Ampicillin's confrontation is deliberated through bla gene which

causes enzyme (Nesa et al., 2020; Tincho, et al., 2020) Nevertheless, in place of b-lactamase is unremittingly covered, deprivation of antibiotic shadows as well a pair of times, ampicillin is closely fatigued (Rosano, et al., 2014). physicochemical properties and mechanism of action which governs their penetration into microbial cell (Boparai et al.,, 2020).

The budget of antibiotics and the distribution of antibiotic opposition are foremost uncertainties in plans deals with important values. Plentiful struggle has been pre in the progress about free of antibiotics plasmid schemes. These organizations are originated upon an idea of plasmid obsession, process which happens when plasmid cells are not accomplished for development or else alive (Peubez et al., 2010; Zielenkiewicz et al., 2001). In few cases, significant gene can detach from genome of microbe and positioned on a plasmid. Therefore, when division of cells is happened then, a microbe which is free from plasmid is died Various sub categories of plasmid-obsession schemes occur conferring to their purpose: (i) toxins or anti-toxin built schemes, (ii) metabolic rate- built systematic organization (iii) System of (ORT) operator repressor titration (Kroll et al., 2010).

However this favorable skill has been confirmed positive in extensive fermenters (Peubez et al., 2010; Pohlmann et al., 2006) Systems of expressions created on plasmid fascination are still not broadly disseminated. If physical, biological or chemical learning based on recombinant protein are essential, At the same time, synthesis companion necessity can eradicate from recombinant proteins. Identifiers of Peptide should must separate since it can impede structure as well as action of protein (Rosano, et al., 2014), then it can left inside residence level for learning of crystallography, (Falquet et al., 2002; Schmid et al., 2009). Identifiers might be abolished moreover enzymatic cleavage or chemical discontinuity occurs. A quick exploration in research paper or an appropriate *E. coli* straining for usage of it as host will produce for many potential contestants. Altogether it has many benefits as well as flaws. Aimed at an initially expression shade, solitary few of *E.coli* strains are vital: 21 (DE3) and approximately byproducts of K- 12 descent. At this detail, it would be richer in quantity of choices which scheming is knowingly up to an expression system.

Selecting the faultless mixture is not thinkable; consequently numerous circumstances must confirm the required protein achievement. lf there two protein are introduced to express duplication inside six unlike vectors of expressions, each partial in three unlike expressions sequences, then there would be 36 tribunals of expression. This quantity might be uniformly enhanced while additional variables are occupied inside version. This kinds of trials might be contains end errors as well as its time wasting more, experimental learning can be complete earlier. If micro expressional tests are attained at earlier level, then limited screens can accomplish within 96 fine plates and 2-m1 tubes (Li, et al., 2002). Extraordinary, through place procedures familiarizing involuntary fluid handling robots have been designated, creating it thinkable for a solitary individual to examine further than 1000 culture circumstances within a week.

Antimicrobial peptides produced by Bacteria against plant pathogens: Bacteriocins, a various collection of anti-bacterial ribosomaly formed peptides, contains probable such as biopreservers inside wide spreading diversity of diets besides forthcoming therapeutics for obstruction of antimicrobial confrontation microbes. However, numerous bacteriocins have been categorized, Many aspects border manufacture intimate enormous amounts, prerequisite to create their commercialized feasible for diet and uses of pharmacy as well. New bacteriocins are classified by databank removal has been bright; nonetheless their consideration remains stimulating toward assess inside non-appearance of appropriate manifestation organizations. *E. coli* has utilized as non-homologous toward construction of recombinant proteins for ages as well as devours a general set of manifestation vectors and bacterial strains reachable as well (Mesa-Pereira et al., 2018).

Peptaibols are linear peptides, collection of both C-terminal amino alcohol and an acyl N-terminus, that are preposterous in dialkylated amino acids for example a-diaminobutyric acid (Degenkolb, et al., 2003). The lipopeptaibols is the small peptide with anti-microbial action ensure an acylated N-terminus tranquil of a minor fatty acid chain (Toniolo, et al., 2001). Their production is attained by vast multi-purpose non-ribosomal peptide synthetase is an enzyme that has been duplicated (Jarvis, et al., 2002). Peptaibols is well-defined in numerous fungi. Their anti-microbial actions effects characteristically fungi as well as also plant infective agent Gram positive bacteria (pathogenic bacteria) through process of membrane interference. The explanations might either be the antibiotic resistance to the obtainable therapeutic particles or the sluggish rate of creating satisfactory therapeutic routines to challenge the fast development of novel infective syndromes, as well as the poisonousness of present behavior routines. (Lazzaro et al., 2020; Tincho et al., 2020).

Trichokonins be located dynamic in contradiction of plant infective bacterium is *Clavibacter michiganensis* (Bhopale, et al., 2020; Lazzaro et al., 2020) besides the fungi infective bacterium such as there are five kinds Bipolaris sorokiniana (Zhong et al., 2020), *Fusarium oxysporum, Rhizoctonia solani, Botrytis cinerea* in addition *Colletotrichum ssp*. (Zhuang, et al., 2006), antifungal association in contradiction of *Sclerotium cepivorum* by Trichorzins and harzianins (Rebuffat, et al., 1995). Recently, deeper evaluation of the molecular evolution and population genetics of AMP genes reveals more evidence for adaptive maintenance of polymorphism in AMP genes than has previously been appreciated, as well as adaptive loss of AMP activity (Lazzaro et al., 2020).

Table 1. Various antimicrobial peptides with specific characteristics obtained from different origins

Name	Specificity	Origin	References
Endolysins	Antimicrobial Compound	*Various bacteriophage*	(Challinor, et al.,2015; Mamo, et al.,2016)
Andropin	Antibiotic	*Drosophila melanogaster*	(Mookherjee, et al.,2020; Zhang et al., 2020)
Liamocin	-	*Aureobasidium pullulans*	(Price, et al., 2017)
Laparaxin	-	*Lactobacillus paracasei*	(S. Liu et al., 2012)
Harzianins	Compound	*Trichoderma harzianum*	(Phazang, et al.,2020)
Unknown	-	*Bacillus sp*	(Seal et al., 2018)
Erythromycin A	Antibiotics	*Saccharopolyspora erythraea*	(Alt, et al., 2013; McGuire et al., 1952)
Antifungal heliomicin	Compound	*Heliothis virescens*	(Lei et al., 2019)
NaD1	Antibiotics	*Pathogenic fungi*	(Breen, et al.,2015)
Tetracycline	-	*Streptomyces rimosus*	(Chopra, et al.,2001; Demain, et al., 2009)
Vancomycin	-	*Amycolatopsis orientalis*	(Marsboom et al., 2012; Schatz, et al., 1944)
Nisin	-	*Lactococcus lactis*	(Gyawali, et al., 2014; J. W.-H. Li et al., 2009)
Amphotericin B	Antifungal agents	*Streptomyces nodosu*	(Abu-Salah, et al., 1996; Tevyashova et al., 2013)
Lipopeptin A	Antibiotics	*Pyricularia oryzae*	(Tsuda et al., 1980; Zhang et al., 2020)
Coronamycins	Antibiotics	*Pythium ultimum*	(Zhang et al., 2020)
Ieodoglucomide C	-	*Bacillus licheniformi*	(Dahrouj, et al., 2015)
Inceptins	-	*Vigna Unguiculata*	(Wagh et al., 2020)
Bleomycin		*Anticancer, Antitumor Streptoalloteichus hindustanus, Streptomyces verticillus*	(Beck et al., 2002; Demain, et al.,2011)
Cahuitamycins(	Biofilm inhibitory agents	*Streptomyces gandocaensis*	(Park et al., 2016)
Plantaricin Pln1 (Class II)	Bacteriocin	*Lb. plantarum* 163	(Huang, et al.,2016)
Aurein	Antibiotic	*Litoria aurea*	(Bakare et al., 2020; Zhong et al., 2020)
Subtilosin A (Sactipeptide)	-	*B. subtilis* 168	(Himes, et al.,2016)
Plantaricin E (Class IIb, two-peptide bacteriocin)	-	*Lb. plantarum* 163	(M. Li et al.,2017)
Plantaricin EF (Class IIb, two-peptide bacteriocin)	-	*Lb. plantarum*	(Galluzzi et al., 2018)
Plantaricin K	-	*Soil metagenome*	(Arora, et al., 2014)
Abaecin	Antibiotic	*Apis mellifera L.*	(Bakare et al., 2020)

Almost reports have revealed that pathogen against tomato like *Clavibacter michiganensis* subsp. michiganensis conceals protein which is 14-kDa, *C. michiganensis* subsp. *michiganensis* AMP-I, which ends development of *Clavibacter michiganensis* sub *Sp sepedonicus*, significant intermediate of microbial sphere potato's deterioration. Through tryptic fragments achieved sequences, we have gene coding *CmmAMP*-I is acquainted then we necessity recombinant deliberate protein via an N-terminal intein (section of protein) tag. Sequence of gene is accessible to *CmmAMP*-I which includes distinctive N-terminal signal peptide on behalf of Sec-dependent excretion. The recombinant protein was enormously vigorous, per 50 percent progression reticence (IC50) around

10 pmol; on the other hand, it was not poisonous for potato shrubberies or else stems. CmmAMP-I does not appearance like slightly recognized protein and hence indicates a completely fresh thoughtful of bacteriocin. Owed to its rich in antimicrobial movement and its very tinny inhibitory spectrum, battling potato ring rot disease might be attention of CmmAMP-1 (Liu et al., 2013).

Considering to (Fouhy et al., 2012), laboratory bacteriocins are categorized in which they are changed post-transnationally (class I) and unaffected considerably changed peptides (class II). Class I could be distributed in many parts such as lantibiotics it's contain features of lethionine (with lanthionine channels), linaridins, proteusins, lined azoleor azoline-containing peptides (Az peptide) cyanobactins, thiopeptides its don't have action in contradiction of Gram negative bacteria, lasso peptides, sactibiotics (comprise sulfur a carbon associations), bottromycins, glycocins (anti-microbial peptide) , as well as more different microcins which won't fit more sub catogeries. Class II is additional detached inside class IIa is first sub class its pediocin alike the bacteriocins, Class IIb is second sub class in this dual peptide alike bacteriocins, ClassIIc is third sub-class it's like round bacteriocins, ClassIId is forth class unaffected, undeviating, non-pediocin alike, sole peptide bacteriocins which won't suitable to further sub category), and ClassIIe is the fourth sub class in this microcin E492- alike bacteriocins).

Herein taxonomy, enormous (more than 10 kDa), warmth labile anti-microbial peptides bacteria lysine and its class III bacteriocins remained disconnected through cluster of bacteriocin. Correspondingly, bacteriocins which is related to Gram-negative bacteria could alienate inside petty peptides, for instance microcins including [class I (alterations occurrence) and classII (unchanged)], besides huge peptides for instance colicins (Boparai, et al., 2011). In multipurpose (Chen et al., 2020), the manufacture of bacteriocins inside ordinary congregation wants many genes counting physical gene which codes pre-peptide (Waghu et al., 2020). Additional genes encrypt a protein which have resistance, specific excretion apparatus and in several investigations proteins expert implementation, alterations and monitoring systems (Nes et al.,1999; Tincho et al., 2020).Furthermore, the novel peptides also used high constancy to trypsin, serum, salts and diverse pH atmospheres. Furthermost particularly, the novel peptides presented a little propensity to grow bacterial resistance and they showed ideal antimicrobial activity in contradiction of the attained resistant strains (Zhong et al., 2020).

In furthest case, the appearance of physical gene and developed classification be located abundant to create vigorous bacteriocin. About instances comprise carnobacteriocin B2 (Jasniewski, Cailliez-Grimal, Gelhaye, & Revol-Junelles, 2008), divercin both AS7 as well as V41 (Bowman, et al.,2004; Drozdzynska et al., 2014; Ingham et al.,2005; Kendir, et al., 2007), epidermicin NI01also include (Sandiford & Upton, 2012), gassericin A isd another type (Choi et al., 2003), or sakacin P is the last one (Dong et al., 2012) Physical gene expressed together by genes intricate inside post-translational alterations on alike and also unlike plasmids exist obligatory for heterologous appearance of lantibiotics for instance lichenicidin (Al Toma et al., 2015; Lee et al., 2011), another example is nukacin ISK-1 (Hosomi et al., 2005), these are some more examples included like prochlorosin, haloduracin, nisin(Dabashi, et al., 2011), suicin(Jiang, et al., 2014).

Antimicrobial peptides produced by Fungi against plant pathogens: AMPs have been the entity of consideration in prior ages as candidates for defense products of plant. So they are minor peptides sequence, through regularly less than fifty amino acid remains designated in the living organizations, which are primaril defense line in animals or plant life. Valuations of Anti-microbial peptide have been approved out in the microbes (Jack et al., 2000; Montesinos, et al., 2007; Raaijmakers, et al., 2006; Thresh, et al., 2005), pests (Montesinos, 2007), aquatic invertebrates (Zhao et al., 2010), amphibians and mammals animals (Perron, Zasloff, & Bell, 2006; Toke, 2005), and plants. (Feng, et al., 2017; Lay, et al., 2005). Many filar fungi conceal AMPs of 51 to 58 amount of amino acid leftovers alike to protect from plants or animals, with a solid arrangement of anti-equivalent strands alleviated through disulphide networks. The peptides of AFP is belong to *Aspergillus giganteus* have anti-fungal activity (Montesinos, et al., 2007; Vila, Lacadena, et al., 2001),

PAF is belongs to *Penicillium chrysogenum* and another *Penicillium nalgiovense* both have anti-fungal activity (Carlsson et al., 2003; Lazzaro et al., 2020; Ramamourthy, Park, et al., 2020) and Anafp belongs to *Aspergillus niger* also have anti-fungal activity, (Lee et al., 1999; Waghu et al., 2020).AFP is energetic in illogicality of Botrytis cinerea, Pyricularia oryzae and *Fusarium spp.* (Mookherjee et al., 2020) and, but is sluggish in contradiction of microbes (Aniya et al., 2007; Meli, et al., 2001; Ramamourthy et al., 2020).. Antifungal peptides (AFPs) can be established as antibiotic to controller fungal toxicities in agriculture owing to their dissimilar antifungal appliances (Zhang et al., 2020).

There are various anti-microbial peptides which are secondary metabolites designated from fungi, bacteria as well as cyanobacteria which have remains of amino acids such as D or L-forms also allo- and di-amino byproducts. These are organized in the form of cyclical rings and frequently deprived of Disulphide association. Frequent plant-associated as well as soil-inhabiting bacteria which consists of antifunal, antibacterial, cytotoxic and surfactant characteristics plays an important role in formation of specific peptides known as Lipidic cyclopeptides (LCPs). Type of LCPs which are belonged with Pseudomonas ssp. which are generally of the depsipeptide sort as well as are confidential into seven foremost assemblages such as first amphisins, second is corpeptins novel bioactive lipodepsi peptides , third one is putisolvins biofilm development of dissimilar Pseudomonas, forth one is syringomycins, fifth one is

syringopeptins its new photo toxic lipodepsi peptides , six is tolaasins and last is viscosins), and they are beached on the structure of fatty acid and length of fatty acid, and the peptide ring also (Nesa et al., 2020; Raaijmakers et al., 2006).

Syringomicins and another one is syringopeptins both verify itself as virulence issues which are formed in the *Pseudomonas syringae*, nevertheless consistently press the type of bacteria its Gram positive bacteria (Grgurina et al., 2005) as well Botrytis cinerea (Lavermicocc, et al.,1997). The straining which create syringopeptin is the *Pseudomonas syringae* 508 was aggressive to Venturia insufficiencies, the important illustrative of apple coating (Burr, et al., 1996). Tolaasins origin inhibit of the Rhizoctonia solani also another bacteria like Gram-positive bacteria similar the other one is *Rhodococcus fascians*, on the other pointer not to Gram-negative bacteria equivalent to the Erwinia carotovora (Burr et al., 1996; Mookherjee et al., 2020). *Pseudophomins* are attained through the *Pseudomonas fluorescens* BRG100 it comprises anti-fungal ability in battle of *Leptosphaeria maculans* and another *Sclerotinia sclerotiorum* (Burr et al., 1996). Cormycin -A also corpeptins advanced active lipodepsipeptides from the cultures of *Pseudomonas corrugate*-syringomycins and another is syringopeptins which are robust poisonous compounds in illogicality of plants, microbes and animals (Scaloni et al., 2004).

Pseudo-peptides which is performed as plant disorder regulator and contains of intermittent bonds of peptide and multi-layered of amino acid alterations (like nucleosides) are molded by microbes (Mookherjee et al., 2020; Zhang et al., 2020). Pantocines are consequences from the alanine which frustrate transaminase its an enzyme which is catalyzed transamination reaction and its catalyzed amino acid bio development within the bacterium for example Erwinia amylovora, and the vital representative of potency syndrome of rosaceous plants, and they are created through strains of Pantoea agglomerans (Chahardoli, et al., 2018; Kwak et al., 2003; Montesinos, et al., 2007; Phazang et al., 2020). The nucleo-peptide revenues alike polyoxins its anti-fungal antibiotics formed through streptomycetes, nikkomycins it's also related to anti-fungal antibiotics formed through streptomycetes, blasticidin also mildiomycin are similarly pseudo-peptides through antifungal achievement (Copping, et al.,2000).

Polyoxins are oppressed for the mycological plant contamination regulator and are pyrimidine dipeptides that avoid chitin manufacture in fungi equivalent to *Alternaria spp*., another *Botrytis cinerea*, and last *Rhizoctonia solani*. The Nikkomycins are pyridine consequences like to the polyoxins. Blasticidin prevents protein bio-production in the prokaryotes and also signifies its ability in contradiction of *Pyricularia oryzae*. Mildiomycin is a serine derivative energetic in contradiction of powdery fungi like *Podosphera*, another *Sphaerotheca, Erysiphe* and last one Uncinula necator (Lazzaro et al., 2020; Mookherjee et al., 2020). The anti-fungal amide bond surrogates bacilysin,and an alanine-epoxycyclohexane reassured 2 peptides, also *rhizocticin*, a phosphonodipeptide, are formed after crabwise *Bacillus* subtilis straining (Stein, et al., 2005).

Antimicrobial peptides production through transgenic plants: Production of gene that contains of coding of sequence for Anti-microbial peptide which have been expressed on harvest plants provide numerous degrees of defense in inconsistency pathogens of plants and Antimicrobial medications resistant microorganisms have been detected wide-reaching and so alternative growth of antimicrobial peptides has increased attention in human and plants healthcare, (Bhopale, et al., 2020).

Numerous expressive genes of animals have been described as defensive genes exclusive plants. Cecropins A and Cecropins B expressed in the rice which measured resistance in contradiction of *Magneporthe grisea* (Campo et al., 2004) and *Xanthomonas oryzae* (Sharma, et al., 2000), magainin, it's a class of anti-microbial peptides uttered on tobacco deliberates conflict in contradiction of numerous fungi and also bacteria (Gray, et al., 2001), and tachyplesin peptide from crab quantified as protection in potato which was further functioning in contradiction of contagions initiated through *E. carotovora*, (Allefs et al.,1996; Lazzaro et al., 2020).

Plant defensing has been articulated in plants. The Rs-AFP2 radish protecting was conveyed in tobacco as well tomato and dissertations protection in contradiction of *Alternaria longipes* (Broekaert, et al., 1995), Alf-AFP alfalfa protecting uttered in potato defends in contradiction of V. dahlia (Zhou et al., 2000), SPI1 spruce articulates in the tobacco which is offer defense in contradiction of *Heterobasidium annosum* (Elfstrand, et al., 2001), DRR206 pea protecting articulated in canola and also tobacco protects in contradiction of *Leptosphaeria maculans* (Ma, Caldwell et al., 1999), Dm-AMP1 dahlia protecting articulated (Boparai et al., 2020; Tincho et al., 2020) in the eggplant which defend (Su, Wang, & Zhang, 2020) in contradiction of *Botrytis cinerea* and another *Verticillium alboatrum* (Ayi, Turrini, Piga, & Arese, 2004), and last one Mj-AMP1 jalapa protecting articulated in tomato acquires in contradiction of *Alternaria solani* (Piraino et al., 2005). The one another hevein Pn-AMP specified as protector in tobacco in contradiction of *Phytophthora parasitica* (Koo, Kim, & Jeon, 2002) and barley hordothionin expression confidential tobacco intricate it-self as the protector in contradiction of C. michiganensis and another *Pseudomonas syringae pv. Tabaci* (Carmona, et al., 1993). MSI-99 is uttered in the vine of grape protects in contradiction of *Agrobacterium tumefaciens* (Boyer et al., 2006; Chahardoli et al., 2018).

Simulated cecropin correspondents signify protection security to numerous pathogenic bacteria in plants (Zhong et al., 2020). SB-37 defends in difference to *E. carotovora* ssp. *Carotovora* on the potato (Arce, et al.,1999) also MB39 was functioning in contradiction of the plan pathogen bacterium *E. amylovora* on the Royal Gala apple (Liu, et al., 2001). Artificial *cecropin-melittin*

amalgams for instance MsrA2 have been expressed in the tobacco or potato and discuss resistance in contradiction of recurrent phyto-pathogens (Petrenko & Yevtushenko, 2005). The totally artificial peptide which is antimicrobial D4E1 has been articulated in tobacco or potato and poplar also, defensive in contradiction of numerous pathogens (Mentag, et al., 2003; Phazang et al., 2020).

The communicator of indolicidin Rev4 has been articulated in the tobacco and another *Arabidopsis* and was vigorous in contradiction of *Peronospora tabacina*, another one is *Pseudomonas syringae* pv. tabaci and last one is *E. carotovora* contagions (Xu et al., 2006). Artworks of antimicrobial peptides from bacterial basis uttered in the plants are irregular (Phazang et al., 2020; Su et al., 2020). The AFP fungiform protecting from the *Aspergillus* giganteus was uttered in the rice and intricate itself as the shell in contradiction of *M. grisea* (Coca, et al., 2006; Phazang et al., 2020).

It can help to exploit the recognition of peptide–antibiotic amalgamations that will meritoriously eradicate resistant bacteria and by understandings for its natural biology in respect to lesser possibility of security damage as well as circumvent the disaster of resistance. Various techniques such as gene editing, protein engineering or computational tools can provide help to face the industrial requirements which could stimulate development to squeeze proteins or peptides as well as can be used to screen latent peptide sequences with antimicrobial properties, and for computer-aided discovery of AMPs as well.

Future Perspectives: Antimicrobial peptides (AMPs) have a crucial role in natural defense compounds grounded on drugs because of its vast potential as a novel biopharmaceutical product for both humans and plants (Lehel, et al. 2020). There are many investigations which played an important role to provide fundamental resources for the expansion of newly discovered AMP-dependent therapeutics fewer prone to confrontation, a feature essential to circumvent any potential interference with our distinctive immune system (Spohn et al., 2019, Phazang et al., 2020).

Antibiotic-resistant bacteria recurrently demonstrate indemnity sensation to antimicrobial peptides, it will be further helped out to exploit the recognition of peptide–antibiotic amalgamations that will meritoriously eradicate resistant bacteria besides will slow down the novel evolution of resistance towards antibiotics (Lázár et al., 2018; Lei et al., 2019). Scientific based progress, predominantly in mass spectrometry (MS) as well as nuclear magnetic resonance (NMR), have been contributed inside recognizing and illuminating the assembly of innovative AMPs, particularly non ribosomal peptides that cannot be recognized by genomics tactics. Many non-plant AMPs are representing the prospective for plant disease immunity which are frequently verified by in vitro assays analysis. Categorization of AFPs with bio based activities has inordinate connotation for the improvement of novel antifungal therapeutic drugs in contradiction of antibiotic-resistant (Zhang et al., 2020).

Now, the utmost task is remained for the functional authentication of contender AMPs inside plants via transgenic experiments, mainly familiarizing non-ribosomal AMPs into crop yields (Breen et al., 2015; Zhang et al., 2020). Furthermore, these peptides highlighted the effective results towards its efficiency, wide specificity, low toxicity, fewer drug interfaces, biologically multiplicity as well as various characteristics for direct targeting. Pharmaceutical industries should demeanor specific clinical trials for better peptide drugs developments. There is a need to perform various de novo preclinical as well as clinical trials for effective peptides drug development so that modification of pre-treated peptides can be done at including its chemicals as well as physical characteristics (Boparai, et al. 2020).

It is essential to produce Imitation and enduring AMP analogs so that the drawbacks of their natural peptides should be overwhelmed besides the latent complications for the drug applicants can also be solved (Lei et al., 2019). The inclusive continuum of actions for these peptides will permit the chance to reconnoiter their paybacks as alimentary supplements as well as , (Bakare et al., 2020, Lazzaro et al., 2020). Peptides which have proved themselves as bacterial and fungal resistants by membranolytic as well as non-membranolytic mechanisms such as KW4 peptides, provide specific template progress of novel classes of antifungal or antibacterial drugs by showing themselves no cytotoxic activity to cultured humanoid keratinocyte cells. Nonlytic mechanism of action makes further open the doors toward the future anti-candidal agents, (Ramamourthy et al., 2020).

Natural AMPs of various bacteria are beneficial can demonstrate the strategy of AMP variants for undertaking the intensifying numeral of multi-drug-resistant contagions, as an appropriate supernumerary for conformist antibiotics (Nesa et al., 2020). It can also provide basic understandings for its natural biology in respect to lesser possibility of security damage as well as circumvent the disaster of resistance which is presently encrustation orthodox antibiotics. Various techniques such as gene editing, protein engineering or computational tools can provide help to face the industrial requirements which could stimulate development to squeeze proteins or peptides. These techniques and tools can e utilized screen latent peptide sequences with antimicrobial properties, as well as for computer-aided discovery of AMPs

CONCLUSION

Antimicrobial peptides can play their crucial role in field of agriculture to enhance the food production and crop development by overcoming the plant pathogens as well as controlling various diseases of plants. AMPs are environment friendly, less cost and can be utilized instead of chemical pesticides. AMPs are used as bio-pesticides

which are secreted from numerous microorganisms beside it some transgenic plants also express it to control the plant diseases and plant pathogens but there are some social concerns and limitations because of less toxicity and less stability of these compounds that's why transgenic plants are not commercially marketed. There is need to utilize various latent techniques of biotechnology so that toxicity of these compounds can be reduced as well as stability of it can be enhanced. Though, it can prove as a novel compound in the drug discovery.

REFERENCES

Abu-Salah, K. (1996). Amphotericin B: an update. British journal of biomedical science, 53(2), 122-133.

Adrio, J.-L., & Demain, A. L. (2010). Recombinant organisms for production of industrial products. Bioengineered bugs, 1(2), 116-131.

Al Toma, R. S., Kuthning, A., Exner, M. P., Denisiuk, A., Ziegler, J., Budisa, N., & Süssmuth, R. D. (2015). Site-Directed and Global Incorporation of Orthogonal and Isostructural Noncanonical Amino Acids into the Ribosomal Lasso Peptide Capistruin. ChemBioChem, 16(3), 503-509.

Allefs, S. J., De Jong, E. R., Florack, D. E., Hoogendoorn, C., & Stiekema, W. J. (1996). Erwinia soft rot resistance of potato cultivars expressing antimicrobial peptide tachyplesin I. Molecular Breeding, 2(2), 97-105.

Alt, F. W., Zhang, Y., Meng, F.-L., Guo, C., & Schwer, B. (2013). Mechanisms of programmed DNA lesions and genomic instability in the immune system. Cell, 152(3), 417-429.

Aniya, M., Enomoto, H., AOKI, T., Matsumoto, T., Skvarca, P., Barcaza, G., Isenko, E. (2007). Glaciological and geomorphological studies at Glaciar Exploradores, Hielo Patagonico Norte, and Glaciar Perito Moreno, Hielo Patagonico Sur, South America, during, 2003-2005 (GRPP03-05).

Aranishi, F., Okimoto, T., & Izumi, S. (2005). Identification of gadoid species (Pisces, Gadidae) by PCR-RFLP analysis. Journal of Applied Genetics, 46(1), 69-73.

Arce, H. E. (1999). Report. Accreditation: the Argentine experience in the Latin American region. International Journal for Quality in Health Care, 11(5), 425-428.

Arora, P. K., Srivastava, A., & Singh, V. P. (2014). Bacterial degradation of nitrophenols and their derivatives. Journal of Hazardous Materials, 266, 42-59.

Ayi, K., Turrini, F., Piga, A., & Arese, P. (2004). Enhanced phagocytosis of ring-parasitized mutant erythrocytes: a common mechanism that may explain protection against falciparum malaria in sickle trait and beta-thalassemia trait. Blood, 104(10), 3364-3371.

Bakare, O. O., Fadaka, A. O., Klein, A., & Pretorius, A. (2020). Dietary effects of antimicrobial peptides in therapeutics. All Life, 13(1), 78-91.

Bechinger, B., & Gorr, S.-U. (2017). Antimicrobial peptides: mechanisms of action and resistance. Journal of dental research, 96(3), 254-260.

Beck, S. D., Foster, R. S., Bihrle, R., Ulbright, T., Koch, M. O., Wahle, G. R., . . . Donohue, J. P. (2002). Teratoma in the orchiectomy specimen and volume of metastasis are predictors of retroperitoneal teratoma in post-chemotherapy nonseminomatous testis cancer. The Journal of urology, 168(4), 1402-1404.

Bhopale, G. M. (2020). Antimicrobial peptides: A promising avenue for human healthcare. Current Pharmaceutical Biotechnology, 21(2), 90-96.

Boparai, J. K., & Sharma, P. K. (2020). Mini Review on Antimicrobial Peptides, Sources, Mechanism and Recent Applications. Protein and peptide letters, 27(1), 4-16.

Bowman, S. M., Wenstrom Jr, R. F., Steckel, M., & Craig, E. V. (2004). Suture buttress: Google Patents.

Boyer, L. A., Plath, K., Zeitlinger, J., Brambrink, T., Medeiros, L. A., Lee, T. I., Ray, M. K. (2006). Polycomb complexes repress developmental regulators in murine embryonic stem cells. Nature, 441(7091), 349-353.

Breen, S., Solomon, P. S., Bedon, F., & Vincent, D. (2015). Surveying the potential of secreted antimicrobial peptides to enhance plant disease resistance. Frontiers in plant science, 6, 900.

Broekaert, W. F., Terras, F., Cammue, B., & Osborn, R. W. (1995). Plant defensins: novel antimicrobial peptides as components of the host defense system. Plant physiology, 108(4), 1353.

Burr, G. W., Mok, F. H., & Psaltis, D. (1996). Holographic memory with angle, spatial and out-of-plane multiplexing: Google Patents.

Campo, S., Carrascal, M., Coca, M., Abián, J., & San Segundo, B. (2004). The defense response of germinating maize embryos against fungal infection: a proteomics approach. Proteomics, 4(2), 383-396.

Carlsson, G. E., Möller, A., Blomstrand, C., Ueda, T., Mizushige, K., Yukiiri, K., Chern, C.-M. (2003). European stroke initiative recommendations for stroke management–update 2003. Cerebrovascular Diseases, 16(4), 311-337.

Carmona, C. A. (1993). A arbitragem no processo civil brasileiro: Malheiros Editores.

Chahardoli, M., Fazeli, A., Niazi, A., & Ghabooli, M. (2018). Recombinant expression of LFchimera antimicrobial peptide in a plant-based expression system and its antimicrobial activity against clinical and phytopathogenic bacteria. Biotechnology & Biotechnological Equipment, 32(3), 714-723.

Challinor, V. L., & Bode, H. B. (2015). Bioactive natural products from novel microbial sources. Annals of the

New York Academy of Sciences, 1354(1), 82-97.
Chen, C. H., & Lu, T. K. (2020). Development and Challenges of Antimicrobial Peptides for Therapeutic Applications. Antibiotics, 9(1), 24.
Chin, Y.-C. (2006). Solid-state semiconductor light emitting device: Google Patents.
Choi, J., & Lee, S. (2004). Secretory and extracellular production of recombinant proteins using *Escherichia coli*. Applied microbiology and biotechnology, 64(5), 625-635.
Choi, S.-K., Olsen, S., Abe, K., Abe, T., Adachi, I., Ahn, B. S., . . . Akemoto, M. (2003). Observation of a narrow charmoniumlike state in exclusive B± →K±π+ π− J/→ decays. Physical review letters, 91(26), 262001.
Chopra, I., & Roberts, M. (2001). Tetracycline antibiotics: mode of action, applications, molecular biology, and epidemiology of bacterial resistance. Microbiol. Mol. Biol. Rev., 65(2), 232-260.
Coca, S. G., Krumholz, H. M., Garg, A. X., & Parikh, C. R. (2006). Underrepresentation of renal disease in randomized controlled trials of cardiovascular disease. Jama, 296(11), 1377-1384.
Copping, L. G., & Menn, J. J. (2000). Biopesticides: a review of their action, applications and efficacy. Pest Management Science: Formerly Pesticide Science, 56(8), 651-676.
Cotter, P. D., Hill, C., & Ross, R. P. (2005). Bacteriocins: developing innate immunity for food. Nature Reviews Microbiology, 3(10), 777-788.
Dabashi, H. (2011). Shi'ism: Harvard University Press.
Dahrouj, H., Douik, A., Rayal, F., Al-Naffouri, T. Y., & Alouini, M.-S. (2015). Cost-effective hybrid RF/FSO backhaul solution for next generation wireless systems. IEEE Wireless Communications, 22(5), 98-104.
Degenkolb, T., Berg, A., Gams, W., Schlegel, B., & Gräfe, U. (2003). The occurrence of peptaibols and structurally related peptaibiotics in fungi and their mass spectrometric identification via diagnostic fragment ions. Journal of peptide science: an official publication of the European Peptide Society, 9(11-12), 666-678.
Del Solar, G., Giraldo, R., Ruiz-Echevarría, M. J., Espinosa, M., & Díaz-Orejas, R. (1998). Replication and control of circular bacterial plasmids. Microbiol. Mol. Biol. Rev., 62(2), 434-464.
Demain, A. L., & Sanchez, S. (2009). Microbial drug discovery: 80 years of progress. The Journal of antibiotics, 62(1), 5-16.
Demain, A. L., & Vaishnav, P. (2011). Natural products for cancer chemotherapy. Microbial biotechnology, 4(6), 687-699.
Desriac, F., Defer, D., Bourgougnon, N., Brillet, B., Le Chevalier, P., & Fleury, Y. (2010). Bacteriocin as weapons in the marine animal-associated bacteria warfare: inventory and potential applications as an aquaculture probiotic. Marine drugs, 8(4), 1153-1177.
Dong, X., Chen, J., Ma, Y., Wang, J., Chan-Park, M. B., Liu, X., . . . Chen, P. (2012). Superhydrophobic and superoleophilic hybrid foam of graphene and carbon nanotube for selective removal of oils or organic solvents from the surface of water. Chemical communications, 48(86), 10660-10662.
Drider, D., & Rebuffat, S. (2011). Prokaryotic antimicrobial peptides: from genes to applications: Springer Science & Business Media.
Drozdzynska, A., Pawlicka, J., Kubiak, P., Kosmider, A., Pranke, D., Olejnik-Schmidt, A., & Czaczyk, K. (2014). Conversion of glycerol to 1, 3-propanediol by Citrobacter freundii and Hafnia alvei–newly isolated strains from the Enterobacteriaceae. New biotechnology, 31(5), 402-410.
Elfstrand, M., Fossdal, C. G., Swedjemark, G., Clapham, D., & Olsson, O. (2001). Identification of candidate genes for use in molecular breeding-A case study with the Norway spruce defensin-like gene, Spi 1. Silvae Genetica, 50(2), 75-81.
Falquet, L., Pagni, M., Bucher, P., Hulo, N., Sigrist, C. J., Hofmann, K., & Bairoch, A. (2002). The PROSITE database, its status in 2002. Nucleic acids research, 30(1), 235-238.
Feng, P., Wang, Z., & Yu, X. (2017). Predicting antimicrobial peptides by using increment of diversity with quadratic discriminant analysis method. IEEE/ACM transactions on computational biology and bioinformatics.
Fernández, M. L., & Castro, Y. R. (2003). Evaluación Del Sexismo Ambivalente En Estudiantes Gallegos/As/Assessment Of Ambivalent Sexism In Galician Students. Acción psicológica, 2(2), 131.
Fouhy, F., Guinane, C. M., Hussey, S., Wall, R., Ryan, C. A., Dempsey, E. M., Stanton, C. (2012). High-throughput sequencing reveals the incomplete, short-term recovery of infant gut microbiota following parenteral antibiotic treatment with ampicillin and gentamicin. Antimicrobial agents and chemotherapy, 56(11), 5811-5820.
Galluzzi, L., Vitale, I., Aaronson, S. A., Abrams, J. M., Adam, D., Agostinis, P., Andrews, D. W. (2018). Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. Cell Death & Differentiation, 25(3), 486-541.
Graumann, K., & Premstaller, A. (2006). Manufacturing of recombinant therapeutic proteins in microbial systems. Biotechnology Journal: Healthcare Nutrition Technology, 1(2), 164-186.
Gray, D. E. (2001). Accommodation, resistance and transcendence: Three narratives of autism. Social Science & Medicine, 53(9), 1247-1257.

Grgurina, I., Bensaci, M., Pocsfalvi, G., Mannina, L., Cruciani, O., Fiore, A., Takemoto, J. Y. (2005). Novel cyclic lipodepsipeptide from *Pseudomonas syringae* pv. lachrymans strain 508 and syringopeptin antimicrobial activities. Antimicrobial agents and chemotherapy, 49(12), 5037-5045.

Guzman, L.-M., Belin, D., Carson, M. J., & Beckwith, J. (1995). Tight regulation, modulation, and high-level expression by vectors containing the arabinose PBAD promoter. Journal of bacteriology, 177(14), 4121-4130.

Gyawali, R., & Ibrahim, S. A. (2014). Natural products as antimicrobial agents. Food control, 46, 412-429.

Himes, B. E., & Weitzman, E. R. (2016). Innovations in health information technologies for chronic pulmonary diseases. Respiratory research, 17(1), 38.

Hosomi, M., Yamagishi, H., Yamamoto, T., Bessho, K., Higo, Y., Yamane, K., Fukumoto, C. (2005). A novel nonvolatile memory with spin torque transfer magnetization switching: Spin-RAM. Paper presented at the IEEE InternationalElectron Devices Meeting, 2005. IEDM Technical Digest.

Hsiao, S., Epstein, A. N., & Camardo, J. S. (1977). The dipsogenic potency of peripheral angiotensin II. Hormones and behavior, 8(2), 129-140.

Huang, L.-C., Ahlstrom, D., Lee, A. Y.-P., Chen, S.-Y., & Hsieh, M.-J. (2016). High performance work systems, employee well-being, and job involvement: An empirical study. Personnel Review.

Ingham, E., & Fisher, J. (2005). The role of macrophages in osteolysis of total joint replacement. Biomaterials, 26(11), 1271-1286.

Jack, R. W., & Jung, G. (2000). Lantibiotics and microcins: polypeptides with unusual chemical diversity. Current opinion in chemical biology, 4(3), 310-317.

Jarvis, J., Beach, D., & Wiest, S. (2002). The jazz educator's handbook: Kendor Music.

Jasniewski, J., Cailliez-Grimal, C., Gelhaye, E., & Revol-Junelles, A.-M. (2008). Optimization of the production and purification processes of carnobacteriocins Cbn BM1 and Cbn B2 from Carnobacterium maltaromaticum CP5 by heterologous expression in *Escherichia coli*. Journal of microbiological methods, 73(1), 41-48.

Jiang, X., Jiang, H., Shen, Z., & Wang, X. (2014). Activation of mitochondrial protease OMA1 by Bax and Bak promotes cytochrome c release during apoptosis. Proceedings of the National Academy of Sciences, 111(41), 14782-14787.

Joseph, S., Camps-Arbestain, M., Lin, Y., Munroe, P., Chia, C., Hook, J., Singh, B. (2010). An investigation into the reactions of biochar in soil. Soil Research, 48(7), 501-515.

Kendir, O., & Yildirim, R. (2007). Sensing device for firearm laser training system and method of simulating firearm operation with various training scenarios: Google Patents.

Koo, J., Kim, Y., & Jeon, H. (2002). ZrO2 gate dielectric deposited by plasma-enhanced atomic layer deposition method. Japanese journal of applied physics, 41(5R), 3043.

Kroll, J., Ng, N., Canagaratna, M., Zhang, Q., Jimenez, J., Tian, J., Murphy, S. (2010). Organic aerosol components observed in Northern Hemispheric datasets from Aerosol Mass Spectrometry.

Kuo, C.-K., & Huang, C.-H. (2013). Paper molded box: Google Patents.

Kwak, Y. T., Guo, J., Prajapati, S., Park, K.-J., Surabhi, R. M., Miller, B., Gaynor, R. B. (2003). Methylation of SPT5 regulates its interaction with RNA polymerase II and transcriptional elongation properties. Molecular cell, 11(4), 1055-1066.

Lacana, E., Amur, S., Mummanneni, P., Zhao, H., & Frueh, F. (2007). The emerging role of pharmacogenomics in biologics. Clinical Pharmacology & Therapeutics, 82(4), 466-471.

Lavermicocca, P., Iacobellis, N. S., Simmaco, M., & Graniti, A. (1997). Biological properties and spectrum of activity of *Pseudomonas syringaepv*. syringaetoxins. Physiological and molecular plant pathology, 50(2), 129-140.

Lay, F., & Anderson, M. (2005). Defensins-components of the innate immune system in plants. Current Protein and Peptide Science, 6(1), 85-101.

Lazzaro, B. P., Zasloff, M., & Rolff, J. (2020). Antimicrobial peptides: Application informed by evolution. Science, 368(6490).

Lee, C. S., López, S. R., Hernández, L., Colby, S. M., Caetano, R., Borrelli, B., & Rohsenow, D. (2011). A cultural adaptation of motivational interviewing to address heavy drinking among Hispanics. Cultural diversity and ethnic minority psychology, 17(3), 317.

Lee, S., Choi, H., Suh, S., Doo, I.-S., Oh, K.-Y., Choi, E. J., Lee, Y. (1999). Oligogalacturonic acid and chitosan reduce stomatal aperture by inducing the evolution of reactive oxygen species from guard cells of tomato and Commelina communis. Plant physiology, 121(1), 147-152.

Lei, J., Sun, L., Huang, S., Zhu, C., Li, P., He, J., He, Q. (2019). The antimicrobial peptides and their potential clinical applications. American journal of translational research, 11(7), 3919.

Li, G. J., Hyde, K. D., Zhao, R. L., Hongsanan, S., Abdel-Aziz, F. A., Abdel-Wahab, M. A., Ariyawansa, H. A. (2016). Fungal diversity notes 253–366: taxonomic and phylogenetic contributions to fungal taxa. Fungal diversity, 78(1), 1-237.

Li, J. W.-H., & Vederas, J. C. (2009). Drug discovery and natural products: end of an era or an endless frontier? Science, 325(5937), 161-165.

Li, M., & Wan, Y. (2017). Terminal device: Google Patents.

Li, S.-L. (2002). Tape measure: Google Patents.

Liu, S., Wilkinson, B. J., Bischoff, K. M., Hughes, S. R., Rich, J. O., & Cotta, M. A. (2012). Novel antibacterial polypeptide laparaxin produced by Lactobacillus paracasei strain NRRL B-50314 via fermentation.

Liu, Y.-J. (2001). Dendritic cell subsets and lineages, and their functions in innate and adaptive immunity. Cell, 106(3), 259-262.

Liu, Z., Ma, P., Holtsmark, I., Skaugen, M., Eijsink, V. G., & Brurberg, M. B. (2013). New type of antimicrobial protein produced by the plant pathogen Clavibacter michiganensis subsp. michiganensis. Appl. Environ. Microbiol., 79(18), 5721-5727.

Ma, C.-P., Caldwell, R., Bode, P., & Wang, L. (1999). The mass power spectrum in quintessence cosmological models. The Astrophysical Journal Letters, 521(1), L1.

Mamo, G. (2016). Anaerobes as sources of bioactive compounds and health promoting tools Anaerobes in Biotechnology (pp. 433-464): Springer.

Marsboom, G., Toth, P. T., Ryan, J. J., Hong, Z., Wu, X., Fang, Y.-H., Pogoriler, J. (2012). Dynamin-related protein 1–mediated mitochondrial mitotic fission permits hyperproliferation of vascular smooth muscle cells and offers a novel therapeutic target in pulmonary hypertension. Circulation research, 110(11), 1484-1497.

McGuire, J., Bunch, R., Anderson, R., Boaz, H., Flynn, E., Powell, H., & Smith, J. (1952). Ilotycin, a new antibiotic. Antibiotics & chemotherapy (Northfield, Ill.), 2(6), 281-283.

Melis, J., & Vila-Masot, O. (2001). Frequency controlled half-bridge inverter for variable loads: Google Patents.

Mentag, R., Luckevich, M., Morency, M.-J., & Seguin, A. (2003). Bacterial disease resistance of transgenic hybrid poplar expressing the synthetic antimicrobial peptide D4E1. Tree Physiology, 23(6), 405-411.

Mergulhao, F. J., Monteiro, G. A., Cabral, J. M., & Taipa, M. A. (2004). Design of bacterial vector systems for the production of recombinant proteins in *Escherichia coli*. Journal of microbiology and biotechnology, 14(1), 1-14.

Mesa-Pereira, B., Rea, M. C., Cotter, P. D., Hill, C., & Ross, R. P. (2018). Heterologous expression of biopreservative bacteriocins with a view to low cost production. Frontiers in microbiology, 9, 1654.

Minton, N. P. (1984). Improved plasmid vectors for the isolation of translational lac gene fusions. Gene, 31(1-3), 269-273.

Montesinos, E. (2007). Antimicrobial peptides and plant disease control. FEMS microbiology letters, 270(1), 1-11.

Mookherjee, N., Anderson, M. A., Haagsman, H. P., & Davidson, D. J. (2020). Antimicrobial host defence peptides: Functions and clinical potential. Nature Reviews Drug Discovery, 1-22.

Müller, J., Oehler, S., & Müller-Hill, B. (1996). Repression oflacPromoter as a Function of Distance, Phase and Quality of an AuxiliarylacOperator. Journal of molecular biology, 257(1), 21-29.

Nes, I. F., & Eijsink, V. (1999). Regulation of group II peptide bacteriocin synthesis by quorum-sensing mechanisms. Cell-cell signaling in bacteria. ASM Press, Washington, DC, 175.

Nesa, J., Sadat, A., Buccini, D. F., Kati, A., Mandal, A. K., & Franco, O. L. (2020). Antimicrobial peptides from Bombyx mori: a splendid immune defense response in silkworms. RSC Advances, 10(1), 512-523.

Ongey, E. L., & Neubauer, P. (2016). Lanthipeptides: chemical synthesis versus in vivo biosynthesis as tools for pharmaceutical production. Microbial cell factories, 15(1), 97.

Park, S. R., Yoon, Y. J., Pham, J. V., Yilma, M. A., Feliz, A., Majid, M. T., Reynolds, J. M. (2019). A review of the microbial production of bioactive natural products and biologics. Frontiers in microbiology, 10, 1404.

Park, W., Yoo, D. H., Jaworski, J., Brzezicki, J., Gnylorybov, A., Kadinov, V., Kang, S. W. (2016). Comparable long-term efficacy, as assessed by patient-reported outcomes, safety and pharmacokinetics, of CT-P13 and reference infliximab in patients with ankylosing spondylitis: 54-week results from the randomized, parallel-group PLANETAS study. Arthritis research & therapy, 18(1), 25.

Perron, G. G., Zasloff, M., & Bell, G. (2006). Experimental evolution of resistance to an antimicrobial peptide. Proceedings of the Royal Society B: Biological Sciences, 273(1583), 251-256.

Petrenko, A., & Yevtushenko, N. (2005). Testing from partial deterministic FSM specifications. IEEE Transactions on Computers, 54(9), 1154-1165.

Peubez, I., Chaudet, N., Mignon, C., Hild, G., Husson, S., Courtois, V., Sodoyer, R. (2010). Antibiotic-free selection in *E. coli*: new considerations for optimal design and improved production. Microbial cell factories, 9(1), 65.

Phazang, P., Negi, N. P., Raina, M., & Kumar, D. (2020). Plant Antimicrobial Peptides: Next-Generation Bioactive Molecules for Plant Protection Phyto-Microbiome in Stress Regulation (pp. 281-293): Springer.

Pinfold, J. V., & Horan, N. J. (1996). Measuring the effect

of a hygiene behaviour intervention by indicators of behaviour and diarrhoeal disease. Transactions of the royal society of tropical medicine and hygiene, 90(4), 366-371.

Piraino, B., Bailie, G. R., Bernardini, J., Boeschoten, E., Gupta, A., Holmes, C., Mujais, S. (2005). Peritoneal dialysis-related infections recommendations: 2005 update. Peritoneal Dialysis International, 25(2), 107-131.

Pohlmann, A., Fricke, W. F., Reinecke, F., Kusian, B., Liesegang, H., Cramm, R., Schwartz, E. (2006). Genome sequence of the bioplastic-producing "Knallgas" bacterium Ralstonia eutropha H16. Nature biotechnology, 24(10), 1257-1262.

Price, N. P., Bischoff, K. M., Leathers, T. D., Cossé, A. A., & Manitchotpisit, P. (2017). Polyols, not sugars, determine the structural diversity of anti-streptococcal liamocins produced by Aureobasidium pullulans strain NRRL 50380. The Journal of antibiotics, 70(2), 136-141.

Raaijmakers, J. M., De Bruijn, I., & de Kock, M. J. (2006). Cyclic lipopeptide production by plant-associated Pseudomonas spp.: diversity, activity, biosynthesis, and regulation. Molecular Plant-Microbe Interactions, 19(7), 699-710.

Rahman, Z., Siddiqui, A., Bykadi, S., & Khan, M. A. (2014). Determination of tacrolimus crystalline fraction in the commercial immediate release amorphous solid dispersion products by a standardized X-ray powder diffraction method with chemometrics. International journal of pharmaceutics, 475(1-2), 462-470.

Ramamourthy, G., Park, J., Seo, C., J Vogel, H., & Park, Y. (2020). Antifungal and Antibiofilm Activities and the Mechanism of Action of Repeating Lysine-Tryptophan Peptides against Candida albicans. Microorganisms, 8(5), 758.

Ravikant, K. T., Gupte, S., & Kaur, M. (2015). A review on emerging fungal infections and their significance. J Bacteriol Mycol, 1, 00009.

Rebuffat, S., Goulard, C., & Bodo, B. (1995). Antibiotic peptides from Trichoderma harzianum: harzianins HC, proline-rich 14-residue peptaibols. Journal of the Chemical Society, Perkin Transactions 1(14), 1849-1855.

Reisel, D., Bannerman, D. M., Schmitt, W. B., Deacon, R. M., Flint, J., Borchardt, T., Rawlins, J. N. P. (2002). Spatial memory dissociations in mice lacking GluR1. Nature neuroscience, 5(9), 868-873.

Revers, L., & Furczon, E. (2010). An introduction to biologics and biosimilars. Part II: Subsequent entry biologics: Biosame or biodifferent? Canadian Pharmacists Journal/Revue des Pharmaciens du Canada, 143(4), 184-191.

Romero-Garcia, S., Moreno-Altamirano, M. M. B., Prado-Garcia, H., & Sánchez-García, F. J. (2016). Lactate contribution to the tumor microenvironment: mechanisms, effects on immune cells and therapeutic relevance. Frontiers in immunology, 7, 52.

Rosano, G. L., & Ceccarelli, E. A. (2014). Recombinant protein expression in *Escherichia coli*: advances and challenges. Frontiers in microbiology, 5, 172.

Sahdev, S., Khattar, S. K., & Saini, K. S. (2008). Production of active eukaryotic proteins through bacterial expression systems: a review of the existing biotechnology strategies. Molecular and cellular biochemistry, 307(1-2), 249-264.

Sandiford, S., & Upton, M. (2012). Identification, characterization, and recombinant expression of epidermicin NI01, a novel unmodified bacteriocin produced by Staphylococcus epidermidis that displays potent activity against *Staphylococci*. Antimicrobial agents and chemotherapy, 56(3), 1539-1547.

Schatz, A., Bugle, E., & Waksman, S. A. (1944). Streptomycin, a Substance Exhibiting Antibiotic Activity Against Gram-Positive and Gram-Negative Bacteria Proceedings of the Society for Experimental Biology and Medicine, 55(1), 66-69.

Schmid, C. D., Melchior, B., Masek, K., Puntambekar, S. S., Danielson, P. E., Lo, D. D., Carson, M. J. (2009). Differential gene expression in LPS/IFNγ activated microglia and macrophages: in vitro versus in vivo. Journal of neurochemistry, 109, 117-125.

Seal, B. S., Drider, D., Oakley, B. B., Brüssow, H., Bikard, D., Rich, J. O., Bertin, G. (2018). Microbial-derived products as potential new antimicrobials. Veterinary research, 49(1), 66.

Sharma, A. (2000). Seasonal to interannual rainfall probabilistic forecasts for improved water supply management: Part 3—A nonparametric probabilistic forecast model. Journal of Hydrology, 239(1-4), 249-258.

Skrzypczak, W., Janus, K., Muszczynski, Z., & Jankowiak, D. (1994). The effect of spironolactone (aldactone) on electrolyte balance and renal functions of calves. Acta Veterinaria Brno, 63(1), 19-23.

Stein, T. (2005). *Bacillus subtilis* antibiotics: structures, syntheses and specific functions. Molecular microbiology, 56(4), 845-857.

Su, Q., Wang, K., & Zhang, Z. (2020). Ecotopic Expression of the Antimicrobial Peptide DmAMP1W Improves Resistance of Transgenic Wheat to Two Diseases: Sharp Eyespot and Common Root Rot. International journal of molecular sciences, 21(2), 647.

Svetoch, E., & Stern, N. (2010). Bacteriocins to control Campylobacter spp. in poultry—a review. Poultry science, 89(8), 1763-1768.

Tevyashova, A. N., Olsufyeva, E. N., Solovieva, S. E., Printsevskaya, S. S., Reznikova, M. I., Trenin, A. S., Mirchink, E. P. (2013). Structure-antifungal activity relationships of polyene antibiotics of the amphotericin B group. Antimicrobial agents and chemotherapy, 57(8), 3815-3822.

Thresh, J., & Cooter, R. (2005). Strategies for controlling cassava mosaic virus disease in Africa. Plant pathology, 54(5), 587-614.

Tincho, M. B., Morris, T., Meyer, M., & Pretorius, A. (2020). Antibacterial Activity of Rationally Designed Antimicrobial Peptides. International Journal of Microbiology, 2020.

Toke, O. (2005). Antimicrobial peptides: new candidates in the fight against bacterial infections. Peptide Science: Original Research on Biomolecules, 80(6), 717-735.

Toniolo, C., Crisma, M., Formaggio, F., & Peggion, C. (2001). Control of peptide conformation by the Thorpe-Ingold effect (Cα-tetrasubstitution). Peptide Science: Original Research on Biomolecules, 60(6), 396-419.

Tsuda, K., Nihara, T., Nishii, M., Nakamura, G., Isono, K., & Suzuki, S. (1980). A new antibiotic, lipopeptin A. The Journal of Antibiotics, 33(2), 247-248.

Turgeon, N., Laflamme, C., Ho, J., & Duchaine, C. (2008). Evaluation of the plasmid copy number in B. cereus spores, during germination, bacterial growth and sporulation using real-time PCR. Plasmid, 60(2), 118-124.

Vila, L., Lacadena, V., Fontanet, P., del Pozo, A. M., & Segundo, B. S. (2001). A protein from the mold *Aspergillus giganteus* is a potent inhibitor of fungal plant pathogens. Molecular Plant-Microbe Interactions, 14(11), 1327-1331.

Waghu, F. H., & Idicula-Thomas, S. (2020). Collection of antimicrobial peptides database and its derivatives: Applications and beyond. Protein Science, 29(1), 36-42.

Venerupis philippinarum

Wöhrl, B. M., Sprenger, G. A., & Lengeler, J. W. (1990). Construction of a new catabolic pathway for D-fructose in *Escherichia coli* K12 using an L-sorbose-specific enzyme from Klebsiella pneumoniae. Archives of microbiology, 154(2), 162-167.

Xu, Y., Xing, Y., Chen, Y., Chao, Y., Lin, Z., Fan, E., Shi, Y. (2006). Structure of the protein phosphatase 2A holoenzyme. Cell, 127(6), 1239-1251.

Zhang, D., Lu, Y., Chen, H., Wu, C., Zhang, H., Chen, L., & Chen, X. (2020). Antifungal peptides produced by actinomycetes and their biological activities against plant diseases. The Journal of Antibiotics, 1-18.

Zhao, J., Qiu, L., Ning, X., Chen, A., Wu, H., & Li, C. (2010). Cloning and characterization of an invertebrate type lysozyme from *Venerupis philippinarum*. Comparative biochemistry and physiology Part B: Biochemistry and molecular biology, 156(1), 56-60.

Zhong, C., Zhu, N., Zhu, Y., Liu, T., Gou, S., Xie, J., . . . Ni, J. (2020). Antimicrobial peptides conjugated with fatty acids on the side chain of D-amino acid promises antimicrobial potency against multidrug-resistant bacteria. European Journal of Pharmaceutical Sciences, 141, 105123.

Zhou, Q., & Gao, T. (2000). Microbiology of environmental engineering. HEP, Beijing.

Zhuang, L., Jing, F., & Zhu, X.-Y. (2006). Movie review mining and summarization. Paper presented at the Proceedings of the 15th ACM international conference on Information and knowledge management.

Zielenkiewicz, U., & Cegłowski, P. (2001). Mechanisms of plasmid stable maintenance with special focus on plasmid addiction systems. Acta Biochimica Polonica, 48(4), 1003-1023.