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Research Article

Bacteriocins Prediction and Growth evaluation as a Function of Temperature and pH using Mathematical Modelling Approach

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Abstract

Background: Bacteriocins, peptide-derived molecules created by microorganisms, perform several functions including virulence factors, signaling, and production of antibiotic agents. To date, approximately 500 bacteriocins have been identified which vary among bacterial species. The human skin microbiota contains many microbial cells, which affect many aspects of human physiology. Disturbances in this population can result in various pathological conditions.

Aim: This study aimed to identify novel bacteriocins among bacterial species as antibiotics or probiotics.

Methods: Bioinformatics approaches were used to perform genome mining for retrieval of information related to microbes, bacterial genes, operons, open reading frames, and bacteriocins, and the modelling of bacteriocin production at a particular pH and temperature.

Results: Out of the eight selected species, only six bacterial genomes encode bacteriocins. Each of these six genomes encoded more than one bacteriocin. These results indicate a high degree of bactericidal activity.

Conclusion: These bacteriocins have different modes of action, which might be helpful in developing a mixture of bacteriocins against target living organisms, such as bacteriocins and bacteriocin-producing strains, with probiotic activities as novel medicines in numerous infections, including targeting of recently developing pathobionts associated with several disorders of the skin.

Keywords: Antibiotics, Bacteriocins, Modelling and Simulations, Phylogenetic analysis, Probiotics, Skin microbiome

Introduction

Our skin is home to many microorganisms, including viruses and fungi that make up the skin microbiota. Like those in the gut, skin microorganisms play a fundamental role in protecting against attack pathogens [1]. As the largest organ in the human body and the first line of defense, the skin is colonized by advantageous microorganisms and acts as an effective physical barrier to block pathogen invasion. In a few conditions where the barrier is damaged or when the balance between commensals and pathogens is out, skin ailments or even infections can occur. Human skin may be sebaceous, dry, or oily. However, most of the skin areas are dry, thus developing an unfavorable environment for the growth of mi-

croorganisms, whereas the oily and sebaceous regions favor their growth. Contemplating the structure of the microbiome in various regions of the skin is valuable for explaining the aetiology of common skin ailments such as the high frequency of dermatitis inside the elbow [2] and psoriasis on the outside of the elbow [3]. The human skin microbiome includes Acinetobacter, Corynebacterium, Propionibacterium, Pseudomonas, Staphylococcus, and Streptococcus [4].

Bacteriocins are ribosomal peptides with antimicrobial activity. All types of eubacteria and some archaea produce bacteriocins [5]. Bacteriocins are produced by both Gram-positive and Gram-negative bacteria. Gram-negative microbes produce large bacteriocins ranging from 449 to 629 amino acids [6], whereas gram-positive bacteria produce peptides with less than 70 amino acids [7]. Bacteriocins are characterized based on their peptide structure into three classes: class 1, class 2 (subclasses a, b, c, d), and class 3. They are active against other microbes, either inside similar species or crosswise across genera [8]. With respect to human health, bacteriocins have a limited target range, stability, lower lethality, and strong action, positioning them as feasible options or supplements to existing small antibiotics. The increase in the number of antimicrobial-resistant pathogens and the development of awareness regarding the significance of the microbiome in human health makes the search for bacteriocins more significant [9]. There is an increasing understanding that bacteriocins are key representatives of probiotic strains used to avoid or constrain the growth of diarrheal pathogens. Probiotics are health-enhancing bacteria employed in various industrial settings to improve human health. Probiotic strains are also used to treat a number of diseases, including mucosal surface infections, as alternatives to antibiotics in several ailments, and as antimicrobial agents. Probiotic bacteria such as bifidobacteria, enteric, lactic acid bacteria, Saccharomyces, and streptococci produce bacteriocins as therapeutic agents [10,11]. Some bacteriocins, the most striking Nisin, have a long history of utilization as additives in the food industrial settings, Pyocins (bacteriocin) produced by Pseudomonas aeruginosa, are used to treat several infections, and Streptococcal bacteriocins are used as probiotics and in the resistance [12], these antimicrobials are additionally accepting wider consideration as a potential treatment instead of using antibiotics [13-20]. A few bacteriocins of the skin microbiota and their mechanisms of action are shown in Table 1.

Table 1: Key Bacteriocins reported to be produced in Skin Microbiome.

Skin Microbiota	Bacteriocins	Mechanism	References
Pseudomonas aeruginosa	Pyocins	kill those bacteria which are related to *P. aeruginosa* target cell attachment	14
	S-type bacteriocins	enzymatic activity for lipid cleavage	
	M-type bacteriocins		
	(PseuMs)		
Propionibacterium acnes	Acnecin	Activity is very limited and confined to the inhibition of the growth of *P. acnes* related bacteria	15
Staphylococcus aureus	staphylococcin	Inhibit the growth of several microorganisms.	16
Staphylococcus epidermidis	staphylococcin	Inhibit the growth of several microorganisms.	17
Staphylococcus warneri	Warnerin	Combat bacterial infections against antibiotic-resistant pathogenic bacteria.	18
Streptococcus mitis	Pnc/blp	Active in immunity	19
Streptococcus pyogenes.	Sbp	Active in immunity against other microbes of the nasopharynx	20

As only a limited number of bacteriocins have been identified and reported in the skin microbiota, there is great room for exploration regarding the prediction and characterization of novel bacteriocins from the skin microbiome. Bacteriocins can be identified using various conventional and Insilco methods [21]. To date, in silico bacteriocin screening procedures have prompted the distinguishing proof of numerous novel lantibiotics (class 1 bacteriocins, which act as antibiotics) [22], microcin (very small bacteriocin, removes enteric pathogens from the body) [23], and the sactibiotic (subclass of bacteriocins, plays a role in post-translational modification) [24]. In various examples, standard BLAST-based methodologies have been utilized to recognize bacteriocins, and the BAGEL bacteriocin mining tool has become an especially important asset [25]. BAGEL consolidates the direct mining of structural genes with aberrant mining for genes related to bacteriocin. This is especially helpful for distinguishing peptides that experience critical post-translational alterations, such as those in antibiotics.

Here, we present a new methodology for distinguishing bacteriocins with antimicrobial activity. Our approach is to predict novel bacteriocins and mine microbial genomes to identify genes and ORFs consisting of novel bacteriocins and modelling their production at constant pH and temperature. This modelling will also enable the prediction of the behaviour of microbes at a particular pH and temperature.

Material and Methods

In this section, we propose a novel procedure for bacteriocin prediction. This method is based on the mining of microbial genomes to unravel new insights into the genomes and to predict novel bacteriocins can be used for several purposes. The details of this methodology are presented in Figure 1.

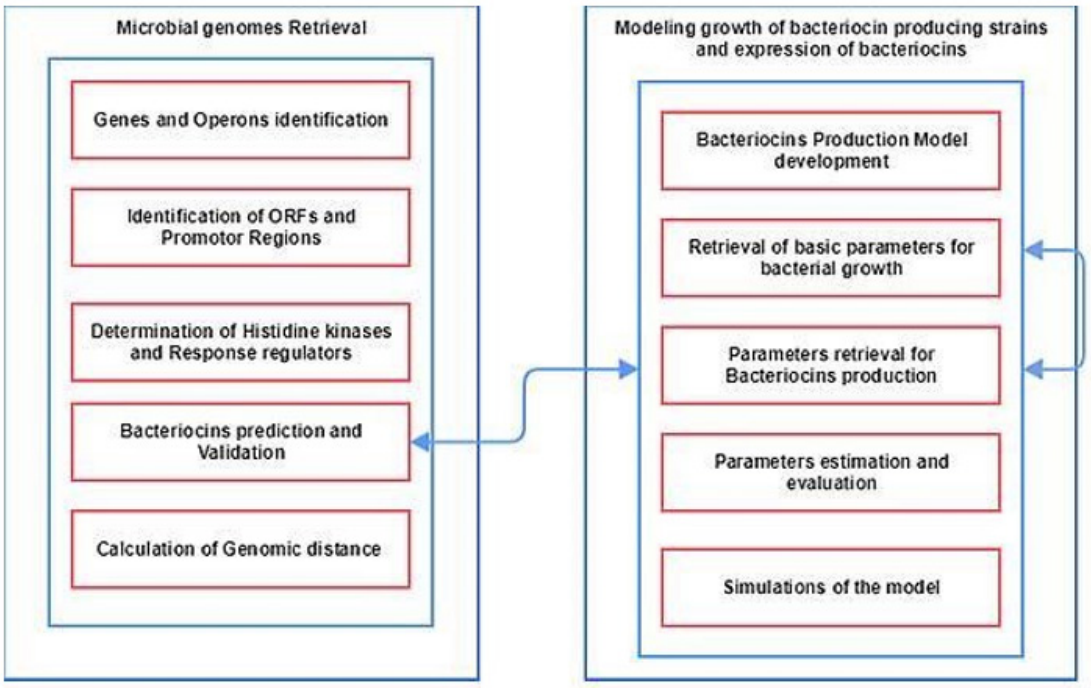

Figure 1: The graphical representation of the methodology used to predict novel bacteriocins and their growth modelling.

Information Retrieval and Screening of Bacterial Genomes

Information about the skin microbes was obtained from the literature [26], and their whole chromosomal and plasmid genomes were retrieved from the NCBI genome browser1 in Fasta format. It contains detailed genomic information, including annotations, assemblies, chromosomes, maps, and sequences.

Identification of Potential Genes and Operons

Potential genes and operons of each microbial strain were identified using the FGenesB tool. This is the most accurate ab initio tool for prokaryotic gene prediction. Its prediction calculation depends on the Markov chain models of coding regions, translation stops, and start sites. The program utilizes specific parameters for the genome learned by the FGENESB-prepare script [27].

Detection of Open reading frames and Promoter Regions

The Open reading frames (ORF) of the microbial species were detected using the ORF Finder tool of NCBI. The minimum ORF length was set to 75 nucleotides as an arbitrary threshold, and the ATG codon was set as the start of each ORF. The promoter regions were identified using the BTSS Finder tool. The promoter is a region of the chromosome that determines where and how transcription of a specific transcript is initiated. Promoter acknowledgment is vital for characterizing the transcription units responsible for gene regulation and particular pathways. The BTSS Finder is a unique tool for the prediction of putative promoter regions in prokaryotes, with an accuracy rate of 86 – 93 % [28].

Identification of Histidine Kinases and Response Regulators

Histidine kinase and response regulator genes in each strain of skin microbes were identified using the P2CS tool [29]. P2CS is a specified database for the two-component systems of prokaryotes, the Two-component system (TCS) is a signal transduction pathway found in each organism, enabling versatile reactions to changes in environmental conditions. However, they are mostly present in microorganisms, where they control various aspects of bacterial digestion, such as cell separation and morphogenesis, digestion, virulence, motility, and biofilm formation. These frameworks are traditionally depicted as the association of two proteins, histidine kinases and response regulators [30].

Identification and validation of Bacteriocins Genes

A typical issue in the annotation of ORFs is the distinguishing proof of genes that are functionally similar to each other but have no sequence homology. This is especially the case for bacteriocins, where ORFs covering bacteriocin genes are regular biosynthetic genes. Using this information, structural bacteriocins could be identified. For this purpose, the BAGEL3 [31] web server was used in this study to distinguish putative bacteriocin ORFs in DNA sequences using novel learning-based bacteriocin databases and motif databases.

Inference of Genome-Genome Distance

Genome sequence data can be utilized to compare similitude among various species, which is also helpful for the assurance of in-

ter-genomic distances between various species. Therefore, keeping this thing in mind, the Genome-Genome distance among all the skin microbial strains was calculated by the GGDC tool [32].

Modelling The Growth of Bacteria and Bacteriocins Expression

The bacteriocin production model for the aforementioned six bacteriocin-producing bacterial strains was developed in the Sim Biology application of MATLAB, and the growing and resting phases of bacteria were also designed to determine bacteriocin production, and the effects of temperature and pH on bacteriocin growth were also generated. It has been revealed that to improve the simulations of the model and to completely understand the expression of each model component, a particular set of parameters is required [33]. For this reason, parameters including half-life, molecular weight, isoelectric point, degradation and elimination rates of bacteria, required temperature, and pH for their growth were obtained from the Bactibase database and literature [34-37], and few parameters were assumed. These parameters are essential for exact simulations of the model.

Parameters Evaluation and Mathematical Formulation

The parameters were evaluated through simulations using the ordinary differential equation (ODE) solver tool of MATLAB. This tool works on the Runge-Kutta estimation strategy in view of unequivocal cycles for the discretization of ODE solutions. After parameter evaluation of the bacteriocin growth mode, differential equations were generated. The model was simulated using the fminsearch algorithm. After parameter evaluation, simulations were performed to determine the rate of expression of bacteriocins and the growth of bacteria in several pH and temperature ranges.

Procedure of Modelling

First, the maximum bacterial growth rate was determined through model simulations at different pH and temperature values. The exponential rate of bacteriocin production and resting phase of the bacteria were also determined. The resting phase was modelled to check for bacterial growth. When the resting phase (in hours) ends, the species starts their growing phase as a function of time, both the resting\ and growing phases are shown by Equations 1 and 2.

$$\frac{d(Resting)}{dt} = \frac{Growing+Resting}{Bmax} * Growing - krs * Resting - kdeath * Resting \quad \text{eq.1}$$

$$\frac{d(Growing)}{dt} = -\frac{Growing + Resting}{Bmax} * Growing - krs * Resting - (kdeath + EFFECT) * Growing + kgrowth * Growing$$

In equations 1 and 2 Bmax shows the maximum production of bacteriocins in both phases under normal pH In the absence of any inhibitory effect, krs shows the response rate of bacteria to a slight change in pH and temperature; kdeath indicates the death of bacteria due to the presence of any inhibitory object, whereas the change in growth rate due to the effect of pH and temperature is shown by EFFECT. The bacteriocin production rate is shown in terms of differential equations 3 and 4 as follows:

$$\frac{d(Central.Bac)}{dt} = \frac{1}{Central} * (-(kdeg * Central.Bac) * Central) \quad \text{eq. 3}$$

$$\frac{d(Biophase.Bac)}{dt} = \frac{1}{Biophase} * ((ke * Central.Bac) * Central - (ke * Biophase.Bac) * Biophase)$$

kdeg shows the degradation rate of bacteriocins after their maximum production, due to changes in temperature and pH, or due to the presence of inhibitory substances.

Results and Discussions

The microbial species that form the skin microbiota, retrieved from the literature, include Acinetobacter Johnsonii, Corynebacterium, Pseudomonas aeruginosa, Propionibacterium acnes, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus warneri, Streptococcus mitis and Streptococcus pyogenes. Acinetobacter johnsonii consists of 1 chromosomal and eight plasmid genomes; Staphylococcus epidermidis has one chromosomal and two plasmid genomes, whereas other microbes have only a single chromosomal genome. The number of potential genes, transcription units, and operons predicted for each microbial genome are presented in Table 2.

Table 2: The number of genes, transcription units, and operons in skin microbial flora predicted through FgenesB server [FgenesB server takes genomic DNA as input and predicts the genes, operons, and their location in the genome.

S.No	Microbe	Genome Type	Number of genes	Number of transcription units	Number of operons
1	*Acinetobacter johnsonii*	Chromosomal genome	3441	2072	681
1	*Acinetobacter johnsonii*	Plasmid genome 1	6	6	0

1	*Acinetobacter johnsonii*	Plasmid genome 2	8	6	2
1	*Acinetobacter johnsonii*	Plasmid genome 3	14	12	2
1	*Acinetobacter johnsonii*	Plasmid genome 4	10	9	1
1	*Acinetobacter johnsonii*	Plasmid genome 5	86	77	8
2	*Propionibacterium acnes*	Chromosomal genome	2602	1428	584
3	*Pseudomonas aeruginosa*	Chromosomal genome	5799	3030	1277
4	*Staphylococcus Aureus*	Chromosomal genome	2753	1503	564
5	*Staphylococcus Warneri*	Chromosomal genome	2463	1392	525
6	*Staphylococcus epidermidis*	Chromosomal genome	2400	1399	477
6	*Staphylococcus epidermidis*	Plasmid genome 1	7	3	1
6	*Staphylococcus epidermidis*	Plasmid genome 2	9	6	2
7	*Streptococcus Mitis*	Chromosomal genome	2119	990	478
8	*Streptococcus pyogenes*	Chromosomal genome	1814	897	405

The genes were predicted because it is the most important step in the understanding of the genome of a species; once the genes are known, the functions of the organisms can be determined, predicting the functions of the genes, and affirming that gene prediction is still challenging and the most demanding task in vivo experimentation [33]. Similarly, the operons were identified, as it is also important to consider operon structures as an essential family among the functional genes. In addition, these units regularly appear in different genomes and perform exceedingly compartmentalized actions in biochemical pathways [34]. Understanding the system that manages gene expression and distinguishing the key administrative components that guide gene expression are noteworthy challenges in molecular biology. Promoters control the expression of each transcriptional unit or gene in the genome [35]. In the present study, the ORFs of each species were also determined. In prokaryotes, genes act as an essential hierarchical unit at the genome level, and compared to eukaryotes, the coding density of bacterial genomes is extremely high [36]. The genome of a regular bacterium is usually 106– 107 base pairs (bp) long, containing approximately 103 to 104 genes. However, the aggregate number of conceivable ORFs is typically in the range 104–105.Although the number and average length of ORFs may differ, microorganisms share normal characteristics due to the distribution of their open reading frame length, which is related to their GC content. Most prokaryotes are considered firmly related based on the same number of ORFs and their lengths [37]. The identified promoter regions and ORFs for each microbial genome are listed in Table 3.

Table 3: The number of promoter regions and ORFs predicted in microbes through BTS finder and ORF finder.

Acinetobacter johnsonii	Chromosomal genome	3509795	6882	295
	Plasmid genome 1	11634	32	29
	Plasmid genome 2	13940	33	61
	Plasmid genome 3	4724	12	87
	Plasmid genome 4	13330	33	66
	Plasmid genome 5	117483	286	262
Propionibacterium acnes	Chromosomal genome	2560265	3945	390
Pseudomonas aeruginosa	Chromosomal genome	6264404	8135	292
Staphylococcus Aureus	Chromosomal genome	2821361	4462	254
Staphylococcus Warneri	Chromosomal genome	2486042	3859	213
Staphylococcus epidermidis	Chromosomal genome	2499279	4822	247
Staphylococcus epidermidis	Plasmid genome 1	4439	12	12
Staphylococcus epidermidis	Plasmid genome 2	6585	17	12
Streptococcus Mitis	Chromosomal genome	2146611	3854	254
Streptococcus pyogenes	Chromosomal genome	1852433	4564	235

Histidine kinases and response regulators were determined for each microbial strain in the skin microbiome. Both histidine kinase and a response regulator form a two-component system (TCS), which is a significant signal transduction system in microor-

ganisms [38]. TCS performs important functions in bacteria, such as bacteriocin production, cell-cell correspondence, adjustment to conditions, and pathogenesis on account of pathogens. Bacterial species usually respond to environmental changes via TCS. Because of their absence in mammals, TCS proteins are viewed as a potential target for developing new antibiotics [39]. Drugs that inhibit TCSs target upstream functions that control these basic proteins. Therefore, anti-TCS drugs work in a different manner than regular medications and are likely to be compelling against drug-resistant bacterial pathogens. Because TCS proteins are missing in humans, drugs that target TCSs may have fewer toxic effects [40]. Therefore, the purpose of identifying TCS was to determine the genes in microbes that produce TCS proteins that may produce bacteriocins. Histidine kinases and response regulators of skin microbial flora retrieved from the P2CS database are displayed in Table 4.

Table 4: The number of Histidine kinases and Response regulators of skin microbial strains retrieved through P2CS database.

S. No	Microbial strains	Histidine Kinases	Response Regulators
1	*Propionibacterium acnes*	125	135
2	*Pseudomonas Aeruginosa*	878	1021
3	*Staphylococcus aureus*	78	78
4	*Staphylococcus Epidermidis*	31	32
5	*Staphylococcus warneri*	12	13
6	*Streptococcus mitis*	16	16
7	*Streptococcus pyogenes*	197	205
8	*Acinetobacter Johnsonii*	NA	NA

From Table 4, it is clear that all six bacteriocin-producing strains produced TCS proteins. Bacteriocins are exceptionally strong bactericidal agents. As mentioned previously, some of them have a restricted range of action, focusing only on firmly related species, especially those produced by lactic acid bacteria, which are active against gram-positive bacteria [34]. Bacteriocins of S. epidermidis are accepted to have advantageous effects on human skin because they may confine the colonization of pathogenic life forms [41-46].

The ability of these S. epidermidis bacteriocins to eliminate human pathogens has sustained therapeutic interest for bacteriocins as a treatment choice [42,44]. Novel bacteriocins of only six bacterial species, Propionibacterium acnes, Pseudomonas auroginosa, Streptococcus pyogenes, Staphylococcus epidermidis, Staphylococcus Warneri, and Staphylococcus aureus are identified in this research study. The predicted bacteriocins are shown in Figure 2. Figure 2 demonstrates novel bacteriocins predicted in skin microbiome along with other genes that play important roles in immunity and regulation through Bagel 3. Only six microbes were found to encode novel bacteriocins (Figure 2). The advantage of Bagel 3 is that it predicts novel bacteriocins by genome mining and aligning [31]. The bacteriocin produced by P. acnes, S. aureus, S, epidermidis, S. pyogens, and P. aeuroginosa shows similarity to Colicin-10 -, which acts as a bacterial killer by forming ion channels. Pyocins-S2 - inhibits lipid synthesis and breaks down chromosomal DNA, S. warneri produces bacteriocins that act as a probiotic against resistant bacterial species. The genome-genome distance and phylogenetic distance among the skin microbial flora were also calculated because the prokaryotic scientific classification has been generally viewed as comprising three interrelated parts: nomenclature, classification, and characterization [43-47]. The organizing rule of microbial scientific categorization is to group related life forms together, which differs from several other groups. The genome-genome distance based on the DNA-DNA hybridization (DDH) method is presented in Table 5. From Table 5, it is clear that all the microbial species are related to each other, with a probable distance ranging from 0.9 – 1.0. Figures 3 shows the high similarity among several species such as Staphylococcus aureus and Staphylococcus warneri, Streptococcus pyogenes and Streptococcus mitis, similarly, Pseudomonas aeruginosa and Acinetobacter johnsonii are highly similar to each other. The remaining Staphylococcus epidermidis and Propionibacterium acnes were closely related up to 99 % to other species. The results of this scientific study have provided a novel dataset of predicted bacteriocins, along with phylogenetic distance and genomic information of the skin microbiome. For the modelling of the bacteriocins, their growth model was developed, as shown in Figure 4.

where some of the parameters were assumed, while others were evaluated by the ODE solver and Fminsearch with the formula used in Equation 5.

Table 5: The genome-genome distance calculation for species based on DDH technique.

Reference genome	DDH	Distance	GC%
Acinetobacter Johnsonii	12.5	1	4.56
Staphylococcus aureus	12.6	0.9912	8.56
Staphylococcus epidermidis	12.5	1	11.38
Propionibacterium acnes	12.5	1	11.38
Staphylococcus warneri	12.7	0.9901	8.7
Pseudomonas aeruginosa	12.7	0.9906	9.34
Streptococcus mitis	12.6	0.9921	1.45
Streptococcus Pyogenes	12.7	0.9902	2.92

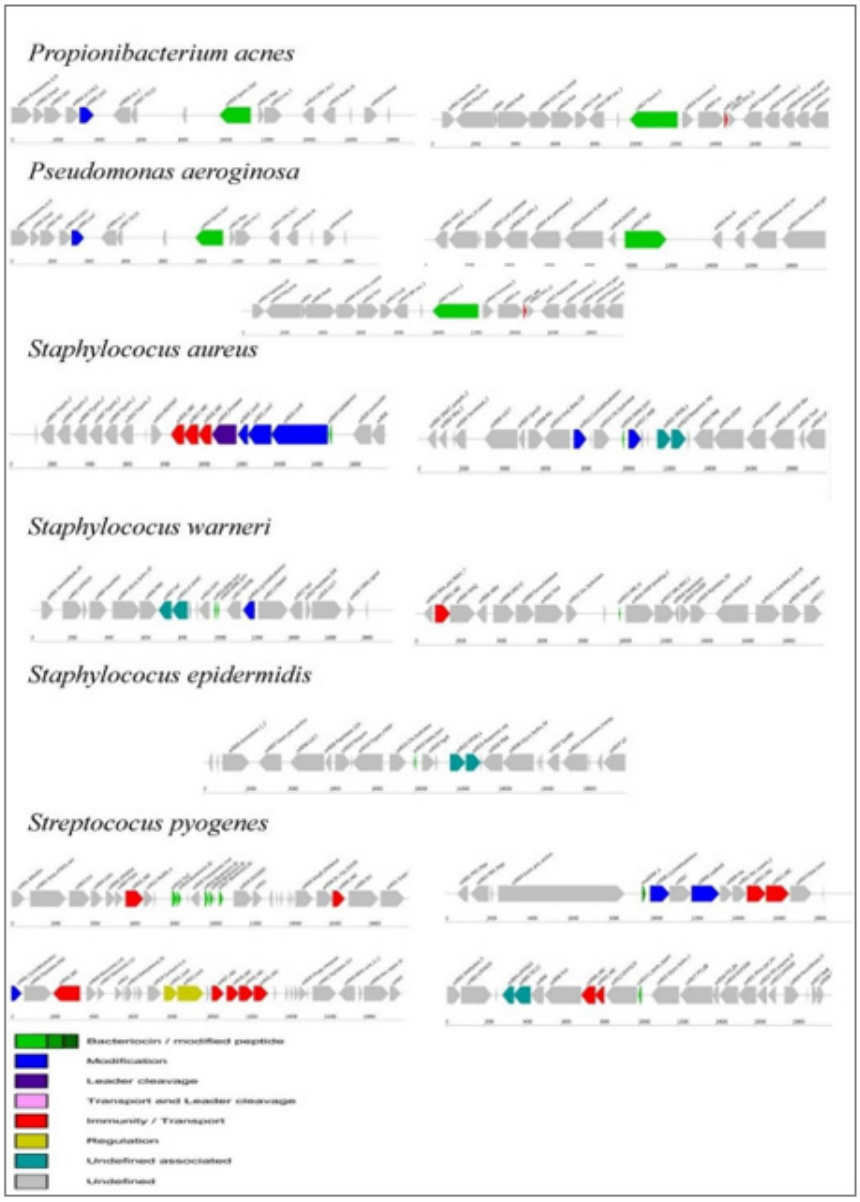

Figure 2: the Bagel 3 analysis for bacteriocins and other important genes in the skin microbiome, out of 8 genomes only 6 encode novel bacteriocin.

$[t, y] = ode45([t, y] = ode45(odefun, tspan, y0, options)$ eq. 5

where @fun is the function vector showing the action of bacterial species, tspan symbolizes the time consumed in the simulation process, and y0 is the state variable for differential equations. The fminsearch function reduces the error functions and assigns the evaluated values to each parameter. In Figure 4, the production of bacteriocin is represented by the growth rate constant kgrowth, where the growing phase represents the time when bacteriocin production acquires its maximum development in a particular medium; the growth reaction is controlled by the kdeath+effect rule, according to which, if any bacterial species do not receive proper pH and temperature or if any substance causes an inhibitory effect on bacterial growth, resulting in the death of a species and the bacteriocins will not be produced; on the other hand, after production of bacteriocins, the bacterial species moves to the resting phase. Some of the parameters used for this model were assumed and the others were evaluated. The assumed parameters and their evaluated values for the modelling of bacteriocins are listed in Table 6.

Table 6: The parameters and their values used for the bacteriocins production model.

Name	Value	Units
K-e (Elimination rate of bacteria)	100	1/hour
K-deg (Degradation rate of bacteria)	0	1/hour
K-death (Death rate of bacteria)	0.179	Milligram/liter
pH (pH value required for bacterial growth)	0 – 8	1/hour
Temp (Temp value required for bacterial growth)	0 – 50	1/hour
B-max (Maximum bacterial growth)	4.15×10^{-8}	Molecule
Krs (Resting rate of bacteria)	0	1/hour
K-growth (Growth rate of bacteria)	1.39	1/hour
pI (Isoelectric point)	0.679	1/hour
B (Production of bacteriocin)	1	Molecule
Effect (Effect of pH and Temp on bacteriocin production)	1	1/hour

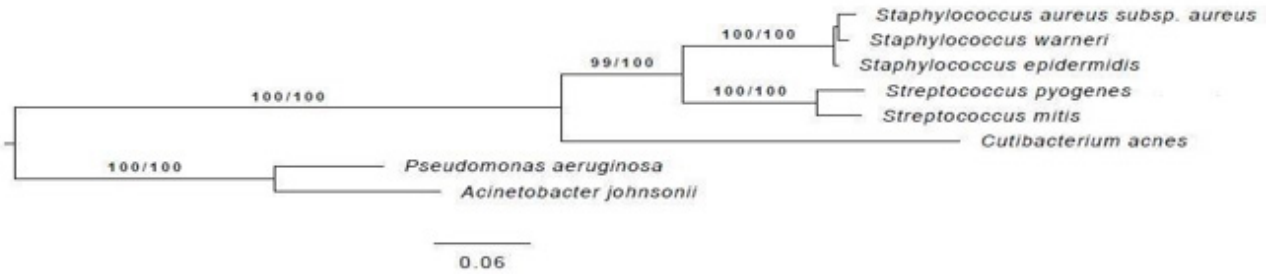

Figure 3: The phylogenetic tree constructed for the skin microbiome developed through Genome-genome distance calculator tool.

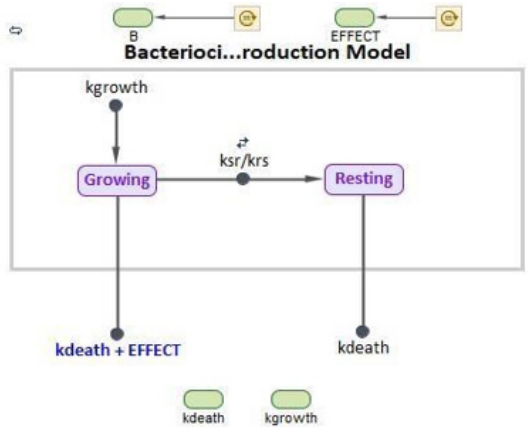

Figure 4: The Bacteriocins production and growth model.

For each bacterial species, several variants were developed with different values of K-deg, K-e, pI, pH, and temperature. However, the other parameters were kept constant. A relationship between pH and temperature was established, and the parameters were fitted to the model for a particular pH and temperature. The production rate of bacteriocin was related to the temperature and pH, and the function f(pH), assessed at different pH values (pH 0–8) and temperature (0-50°C), was modelled for each bacteriocin-producing species. For modelling the growth of bacteriocins of Propionibacterium acnes the pH was set to 6.5, Temp at 400C, for Pseudomonas auroginosa the values are 7.0 pH and temperature 400C, Streptococcus pyogenes requires 370C and 7.6 pH, for Staphylococcus epidermidis the pH was set to 6.8 and temp 300C, 4500C and 6.5 pH for Staphylococcus Warneri, and for Staphylococcus aureus the parameter values were 370C and pH 7.0. The simulation results for bacteriocin growth are shown in Figure 5 and 6.

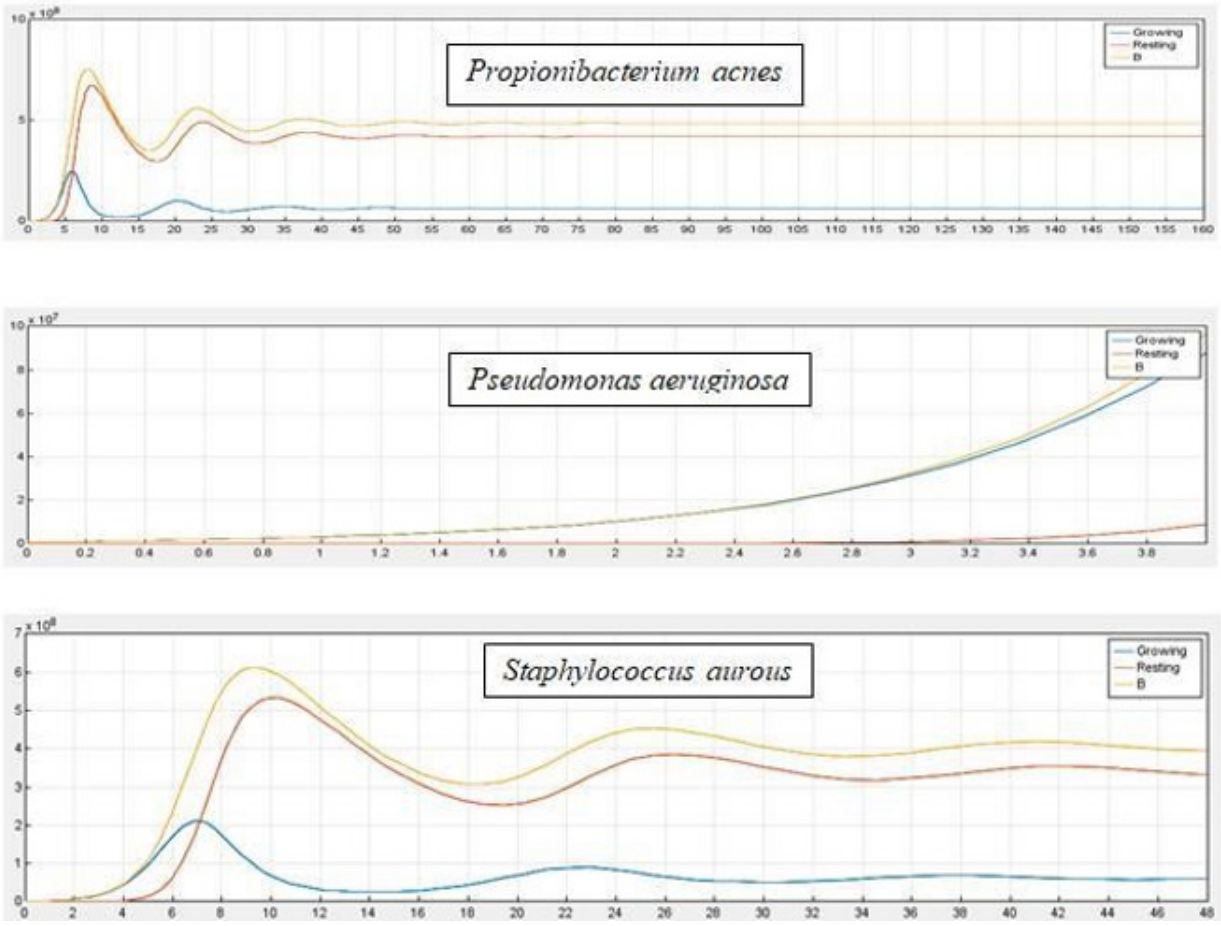

Figure 5: The modelling and simulations analysis of bacteriocins production and growth of bacterial species.

In Figure 5 and Figure 6, the X-axis represents the number of hours required for bacterial species to grow and produce their desired bacteriocins, and the Y-axis shows the rate of bacteriocin production. Yellow lines represent the growth rate of bacteriocins, blue lines show the growth rate of bacteria, and red lines indicate the resting phase of bacteria after the production of bacteriocins. From Figure 5 and Figure 6, it is clear that, at a particular pH and temperature, all the bacteria started to produce bacteriocins after 4 hours and the concentration reached 10 × 107 to 10 × 108. A slight reduction in pH or temperature results in a decrease in the production of bacteriocins. Propionibacterium and Psuodomonas produced small amounts of bacteriocins, whereas the bacteriocin production rates of staphelyococi and Streptococi were observed to be better. Therefore, for the appropriate production of bacteriocins, the aforementioned temperature and pH can be applied to specific bacteria.

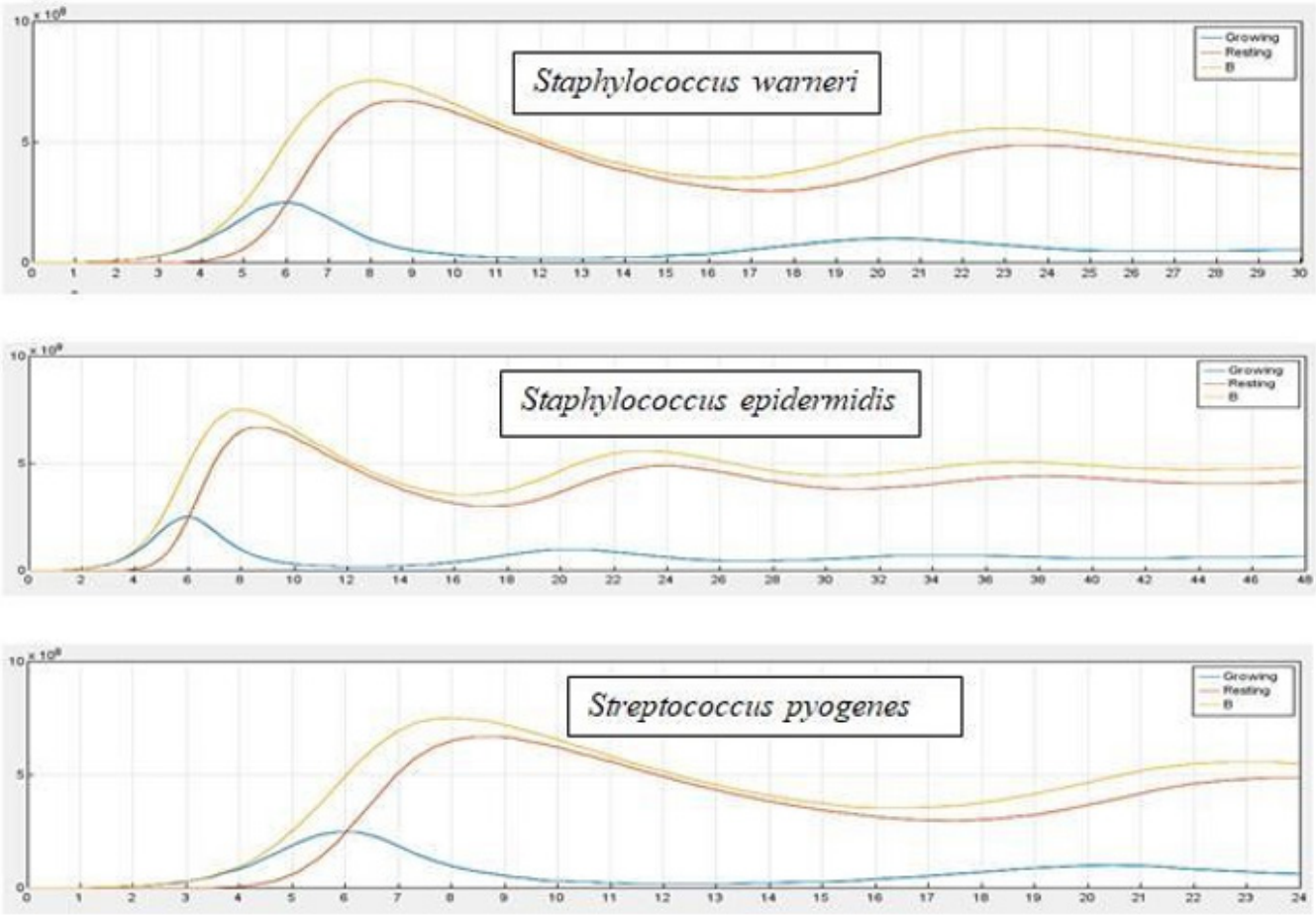

Figure 6: The modelling and simulations analysis of bacteriocins production and growth of bacterial species.

Conclusion

In this study, the genomes of skin microbial flora were gathered and mined to unravel interesting pieces of information and bacteriocins. It has been reported that 30–99 % of microorganisms can produce bacteriocins. This in silico study identified only six microbial strains that produced more than one novel bacteriocin, along with several other genes important for immunity and regulation. Simulation analysis of the bacteriocin growth model provided the specific pH and temperature for the appropriate production of bacteriocins. These bacteriocins have diverse modes of action that may be helpful in developing a mixture of therapeutics with synergistic effects against target living organisms. The evolutionary development of bacteriocins from other microorganisms can also be predicted using the same approach.

Author contributions:

AM: Assisted in the data collection, prepared and drafted the manuscript, contributed to the analysis and interpretation of data for the manuscript and revised the work for critically important intellectual content.

AJ: conceived the study, its design and methodology, contributed to the analysis, data interpretation, manuscript writing and revised the work for critically important intellectual content and acted as the corresponding author.

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