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The Activity of Antimicrobials-Producing Extremophile Bacteria from Lake Magadi, Kenya

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Abstract

Background: Drug resistance poses a challenge in managing microbial infections, highlighting the urgency to develop novel, effective antimicrobials. The natural environment is a proven source of novel antimicrobial agents. This study explored unique and exploitable antimicrobial-producing bacteria from the extreme habitat of Lake Magadi.

Methodology: Soil samples were purposively collected from five sites representing the different physiochemical conditions around Lake Magadi. A total of 163 bacterial types were recovered and screened for antimicrobial activity using the agar well diffusion. Selected isolates underwent biochemical, physiological, and molecular characterization.

Results: Ten isolates demonstrated good antimicrobial activity against *Bacillus subtilis* (ATCC 6633), *Shigella dysenteriae* (ATCC 13313), *Salmonella typhimurium* (ATCC 19028), *Staphylococcus aureus* (ATCC 23922), *Candida albicans* (ATCC 90028), *Escherichia coli* (ATCC 25922), *and Pseudomonas aeruginosa* (ATCC 29212). The 16S rRNA sequence gene analysis identified the best antimicrobial-producing bacteria as *Brevibacillus laterosporus*. The ethyl acetate extract from *Brevibacillus laterosporus* showed an MIC of 6.25 µg ml^{-1} against *Escherichia coli* and *Bacillus subtilis*. The isolate also showed positivity for cellulase, amylase, and xanthanase enzymes.

Conclusion: Lake Magadi harbors bacteria that produce bioactive compounds that can be explored to develop novel antibiotics. These compounds offer promising potential for pharmaceutical and enzymatic applications.

Significance and impact of the study: Drug resistance is a public health threat; therefore, it is necessary to develop novel drugs. Our findings highlight the potential of antimicrobial compounds from *Brevibacillus laterosporus* for pharmaceutical use.

Keywords: Extremophiles, secondary metabolites, antimicrobial activity, antimicrobial resistance

Introduction

Antimicrobial agents are important in managing infectious diseases. Microbes' wide range of defense mechanisms includes broad-spectrum antibiotics, by-products of metabolism such as organic acids, and lytic agents. Some bioactive peptides with a bactericidal effect, such as protein exotoxins and bacteriocins, have been described. This biological repository has a remarkable diversity and abundance, as some substances are produced only by certain bacteria and others by a wide range of species [1]. Actinomycetes have produced approximately two-thirds of the naturally occurring antibiotics [2], where 75% are used in medicine and 6]% in agriculture [3]. Most of the microbes are from the *Streptom*yces and *Micromonospora* genera. *Actinomycetes* have been isolated from various environments such as soil, mountains, swamps, and marine settings. Globally, multi-drug-resistant microbes, the constant rise in resistance to existing antibiotics, and the rapid development of cross-resistance to new antibiotics are pressing public health issues. Multi-drug-resistant organisms (MDRO) include Vancomycin-resistant *Enterococci* (VRE), Methicillin-resistant *Staphylococcus aureus* (MRSA), and Extended Spectrum β-Lactamase (ESBL) producing strains like *Klebsiella pneumoniae* and *Escherichia coli.* As resistant pathogens evolve, treatment options are reduced, with certain organisms demonstrating total resistance to all available antibiotics [4]. Natural products are a reliable source of novel bioactive secondary metabolites. Studies indicate that microbes have produced many bioactive antimicrobials. There is a need to explore potential habitats for novel antibiotic-producing *Actinomycetes*. *Brevibacillus laterosporus* habituates various environments and is rarely pathogenic to humans[5]. The microbe has been used as a biocontrol against mosquitos [6], a pesticide against lepidoptera, diptera, nematodes, mollusks [7] and *Tenebrio molitor* L. [Coleoptera] larvae[8]. Extracts from *B. laterosporus* have anticancer activity[9]. Bacteria habiting adverse environments display survival strategies such as producing antagonistic secretions against competitive microorganisms. Extremophiles could have unique physiological adaptations, including producing complex biomolecules that can survive in harsh environments [10]. Previous studies have covered the microbial diversity of Lake Magadi, however our study searched for bioactive actinomycetes. The extreme physical-chemical properties of Lake Magadi could have led to the emergence of actinobacteria with unique adaptations that may produce novel bioactive compounds [11]. This study explored the bioactive secondary metabolites produced by halophilic bacteria at Lake Magadi and particularly reports the activity of *Brevibacillus laterosporus*.

Materials and Methods

Sampling Technique

Samples were collected purposively at five sites, representing different physicochemical conditions, at the margins of the hypersaline Lake Magadi (1.88° S and 36.28° E). The Lake covers approximately 100 km^2 and is situated in the southern region of the Gregory Rift, a branch within the Kenyan Rift Valley and North of Tanzania's Lake Natron. The major water sources are saline hot springs (up to 86° C) that feed alkaline lagoons at the lake margins. Large salt beds are left due to evaporation during dry seasons, frequently above 40°C. The pH ranges between 9-12.5. Eighty soil samples (50g each) were collected at each site ranging from the hot springs to more cool lake areas, in triplicate, placed in 50 ml sterile falcon tubes, transported in a cool box, and stored at 4° C. The physicochemical parameters for the sample collection sites were determined.

Isolation and Cultivation of Actinomycetes

The soil sample (0.1 g) was inoculated in 1 ml sterile tryptone soy broth medium prepared with lake water and then incubated at 37 ° C for 24h. A 10-fold dilution was done to the enriched cells then 100 µl of 10^{-8}, 10^{-9}, and 10^{-10} dilutions spread plated on *Actinomycetes* selective media; Yunnan Institute of Microbiology (YIM) culture 14 i.e., YIM14, YIM17, YIM21, YIM 47, YIM 171, and YIM 711, actinomycetes agar, Horikoshi, and sodium propionate. The media were supplemented with cycloheximide, nalidixic acid, and nystatin to inhibit fungal growth and a 50 µl vitamin mixture to enhance proliferation. Plates were incubated

at 30 °C until colonies appeared (7-21 days). Pure colonies were cultured on tryptone soy agar at 30° C for 7 days.

Screening the isolates for the secretion of bioactive compounds

The bacteria were cultured in antibiotic production broth media (PM3) containing Glucose (5.0 g), glycerol (2.5g), oatmeal (5.0g), soya bean flour (5.0 g), dry yeast (0.5 g), casamino acid (2.0 g), agar (15 g) and distilled water (1 L). Sporulation salts ($MnCL_2$ (12.58 mg/ml), $CaCl_2$ (156mg/10ml) and $MgCl_2$ (190mg/10ml)) were added. The cultures were incubated while shaking at 30°C and 100 rpm for one week. Screening the production of bioactive compounds activity was done on Mueller Hinton agar (MHA) (pH 8 and 5% NaCl), using the agar well diffusion technique, against *Bacillus subtilis* (ATCC 6633), *Shigella dysenteriae* (ATCC 13313), *Salmonella typhimurium* (ATCC 19028), *Staphylococcus aureus* (ATCC 23922), *Candida albicans* (ATCC 90028), *Escherichia coli* (ATCC 25922), *and Pseudomonas aeruginosa* (ATCC 29212). The pathogenic bacteria (100 µl) were spread plated on MHA, 10 µl broth containing the test isolate introduced in agar wells, and the plates incubated at 30°C for 24 h. Positive and negative controls were kanamycin ((1 mg/ml) CAS 25389-94-0, sigma Aldrich) and blank plates, respectively. Zones of inhibition were scored as a measure of inhibitory activity.

The minimum inhibitory concentration (MIC) was determined using a standard macro-dilution test against seven test organisms. A stock of *Brevibacillus laterosporus* extract 2,000 µg/ml was prepared and diluted with 1 % DSMO (in sterile distilled water) to 1000 µg/mL, then inoculated into the test pathogenic bacterial broth. The cultures were incubated at 35° C for 24h, and growth was observed. The minimum bactericidal concentration (MBC) was determined against seven test organisms [12]. Approximately 100 µl broth from the tubes not visibly showing growth was plated on nutrient agar and grown in triplicate for 24 h at 35 °C. The lowest concentration at which bacteria did not grow was the MBC.

Morphological and Physiological Characterization

The morphological traits of bacterial colonies were determined using standard microbiological techniques. Growth of the isolates at 0%, 5%, 10%, 15%, and 20% NaCl levels, 25–40°C temperature ranges, and 6.0-10.0 pH was determined. The optical absorbance at 600nm was recorded after 24 hours as a determinant for growth. The results were recorded and presented in graphs.

Screening for Enzymatic Activity of the Bacterial Isolates

Screening for enzymatic activity was evaluated by spot-inoculating the isolates on a basal media enriched with starch substrates, xanthan, cellulose, skim milk, tween 20, and tween 80. The isolates were grown at 30°C for 48h and then assayed to produce the respective enzyme. The formation of clear zones indicated enzymatic activity.

Molecular Characterization of the Bacterial Isolates

Genomic DNA was extracted and used as a template for a polymerase chain reaction (13). The 16S ribosomal RNA (rRNA) gene was amplified using a universal bacterial primer pair of 8 F forward 5′-AG(A/G) GTTTGATCCTGGCT-3′ and 1492 R reverse, 5′-CGGCTACCTTGTTACGACTT-3′. Amplicons were generated on a SureCycler 8800 (Agilent Technologies) in a total reaction volume of 50 µl (30.0 µl PCR [polymerase chain reaction] water, 10.0 µl polymerase buffer, 2.5 µl of each primer, 1.0 µl of dNTPs, 1.0 µl of MgCl2, 1.5 µl of dimethyl sulfoxide (DMSO), 0.3 µl Taq polymerase, and 1.0 µl of genomic DNA). The PCR reaction conditions were as follows: 5 min at 95°C followed by 35 cycles (1 minute of denaturing at 94°C, 1 minute of annealing at 53°C, 1 minute of extension at 72°C) followed by a final extension step of 5 min at 72°C. Amplified products were separated on 1% agarose gel in Tris base, acetic acid, and EDTA (TAE) buffer and visualized under UV light after staining with a fluorescent dye. The amplified fragments were cleaned by mixing 12.5 µl of PCR product with 2.5 µl of ExoSAP-IT™ (Thermo Fisher Scientific) and incubated at 37°C for 30 min followed by heating the mixtures at 95°C for 5 min to stop the reaction. The PCR

products were sequenced using the same universal primers 8 F and 1492 R at Inqaba Biotech, South Africa. The gene sequences from the isolates were edited using Chromas Lite (https://technelysium.com.au/wp/chromas) and compared to the sequences in the public databases using the basic local alignment search tool (BLAST) on the National Centre for Biotechnology Information (NCBI) website (www.ncbi.nih.gov).

Results and Discussion

Isolation of Actinomycetes

Sampling was done at different sites with unique physicochemical characteristics to maximize bacterial diversity, as shown in Table 1.

Table 1: Physicochemical properties of different sites at Lake Magadi

Properties/ element	Site 2 Sed	Site 3 Sed	Site 4 Sed	Site 5 Sed	Site 6 Sed
Ph	10.18	10.12	10.11	10.37	10.07
*EC Salts (uS/cm)	86800	171000	114000	11700	38200
Phosphorus (ppm)	2.91	18.6	17.3	27.6	26.0
Potassium (ppm)	2440	3780	4580	1700	2100
Calcium (ppm)	5450	914	2400	3520	1830
Magnesium (ppm)	16.0	24.6	39.5	103	64.7
Manganese (ppm)	35.9	112	118	173	99.8
Sulfur (ppm)	71.2	262	478	135	258
Copper (ppm)	0.35	< 0.20	1.43	1.86	0.48
Boron (ppm)	55.6	82.0	57.1	20.7	35.0
Zinc (ppm)	1.93	5.33	7.58	3.01	1.83
*Sodium (ppm)	52300	80900	64000	11200	24200
Iron (ppm)	24.6	228	417	482	504
*Nitrates (ppm)	1.92	0.74	0.76	1.23	1.84
*Ammonium (ppm)	2.92	4.96	11.4	10.9	9.44
*Organic carbon (%)	0.24	0.30	0.31	0.57	0.38
Calcium (%)	10.3	1.23	3.92	24.4	7.51
Magnesium (%)	0.05	0.055	0.11	1.19	0.44
Potassium (%)	2.37	2.61	3.84	6.03	4.42
Sodium % (ESP)	86.0	94.8	90.8	67.4	86.3
Other Bases (%)	1.22	1.28	1.29	1.03	1.33
Hydrogen (%)	0.00	0.00	0.00	0.00	0.00
Ca: Mg Ratio (%)	204	22.3	36.5	20.5	17.0
*C.E.C meq/100g	264	371	306	72.3	122

Key: S - Site, Sed – Sediment

A total of 163 isolates were recovered. Sites 5, 3, and 4 had the most diversity of isolates at 48, 46, and 39, respectively. Sites 6 and 2 had 16 and 14 isolates, respectively. The slight differences in the sampling sites' conditions showed minimal influence on the bacterial diversities. However, bacterial type abundance differed among sites 3,4, and 5, having a higher variety at 45, 36, and 45, respectively. Sites 3 and 4 had high Na^+ levels at 80900 and 64000 ppm, respectively. Site 5, despite the relatively high bacterial abundance, had a Na^+ level of 11200 ppm. Sites 2 and 6 had 14 and 11 unique isolates recovered, respectively. Site 2 and 6 had Na^+ at 52,300 and 24,200ppm, respectively. Halophiles grow in highly saline conditions and were likely found at sites 2,3 and 4.

Antimicrobial screening of the Bacterial Isolates

Ten of the 163 isolates recovered showed good antimicrobial activity against seven common bacterial laboratory reference strains (Table 2).

Figure 1: Graphs showing the activity of selected isolates against common human pathogens

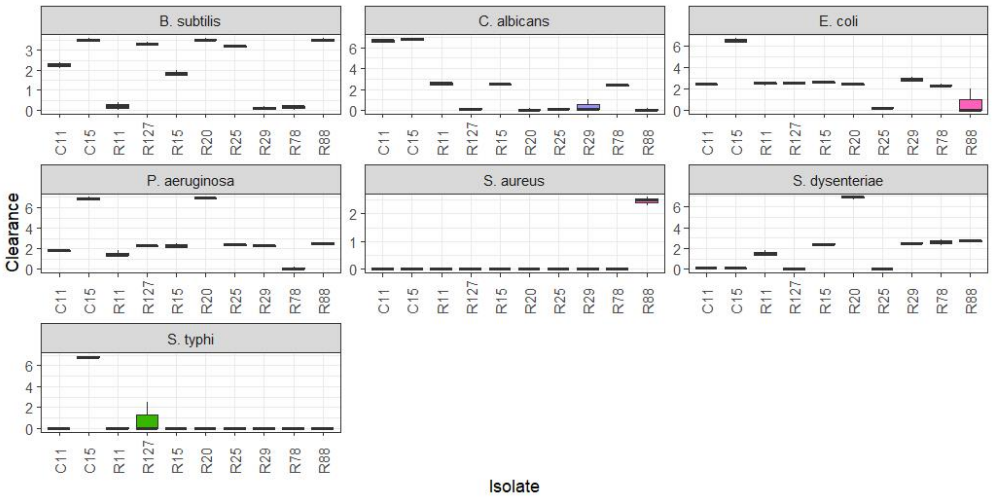

Figure 2: R plots showing the activity of selected isolates against common human pathogens

Isolate C15 metabolites showed activity against a wide spectrum of the test organisms with MIC values at: *E. coli* (6.25µg/ml), *B. subtilis* (6.25 µg/ml), *C. albicans* (12.5 µg/ml), *S. dysenteriae* (25 µg/ml), *P. aeruginosa* (12.5 µg/ml), *S. typhimurium* (25 µg/m-

l), and *S. aureus* (50 µg/ml) (Table 3). This shows that the isolate secretes bioactive antimicrobial compounds that can be potentially developed.

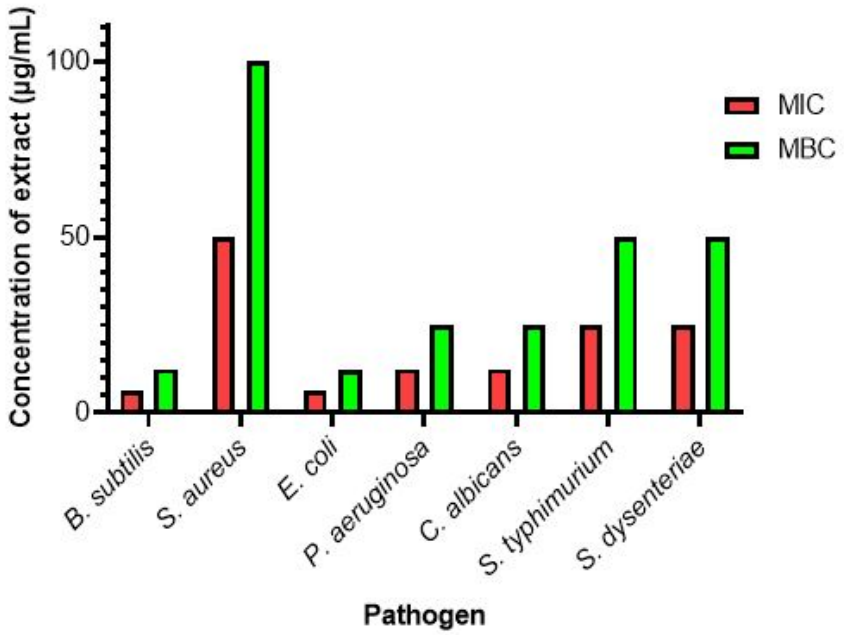

Figure 3: MIC and MBC (µg/ml) of isolate C15 extract against test organisms

Studies show that extreme environments may harbor novel bacterial strains capable of producing new antimicrobial drugs. A novel species closely related to *Nocardiopsis* species was isolated from a Salt Lake in Algeria; it had activity against Gram-positive bacteria and antifungal properties [14]. This study selected 10 bacterial isolates from the hypersaline Lake Magadi. The varying activity patterns against the targeted microorganisms suggest a diversity of produced active biomolecules. A notable isolate, C15, which produces antifungal and antibacterial active biomolecules, was found to be phylogenetically related to *Brevibacillus laterosporus*. Studies show that *Brevibacillus laterosporus* produces antimicrobial compounds such as bacteriocin, possibly contributing to its antibacterial and antifungal effects. Bacteriocin was found to be stable under varying pH and temperature conditions [15]. *Brevibacillus laterosporus* also produces the antibiotic peptides gramicidin and tyrocidine, which can disrupt the lipid membranes of microorganisms [16]. Yang et al. [17] reported similar results on the antimicrobial potential of metabolite extracted from *Brevibacillus* species against antibiotic-resistant Gram-positive bacteria. A novel antibacterial peptide, Tostadin, was obtained from *Brevibacillus laterosporus* and strongly inhibited *Staphylococcus aureus* and *Escherichia coli* [18]. Isolates C11 and C15 showed high activity against *Candida albicans*, which corroborates findings where *Brevibacillus* species exhibited activity against *Candida* strains [19]

Morphological and Biochemical Characterization of The Bacterial Isolates

The bacteria showed diverse macroscopic and microscopic characteristics under the microscope, as shown in Table 4.

Table 2: Morphological characterization

Isolate	Media	Site	Shape	Size	Margin	Chromogenesis	Opacity	Surface	Consistency	
R11	Y601	S2	Round	small	Entire	light yellow	translucent	flat	smooth	mucoid
C11	SP	S4	Irregular	small	Entire	White	translucent	flat	smooth	friable
R15	SP	S4	Round	small	Entire	light brown	translucent	flat	smooth	mucoid
C15	SP	S4	Round	small	Entire	Yellow	opaque	convex	smooth	viscid

R20	Y711	S3	filamentous	large	Filamentous	Cream	opaque	flat	rough	mucoid
R29	HM	S2	Round	medium	Undulate	Cream	opaque	flat	rough	butyrous
R75	AA	S3	Round	small	Entire	Orange	opaque	convex	smooth	mucoid
R78	Y711	S5	Irregular	medium	filamentous	Cream	opaque	raised	rough	viscid
R88	SP	S3	Round	small	Cream	Translucent	cream	flat	rough	friable
R127	Y21	S4	Round	medium	Entire	Cream	opaque	undulate	smooth	friable

Key: SP – Sodium propionate, HM – Horikoshi, AA – Actinomycetes agar, Y - Yunnan Institute of Microbiology culture

The isolates showed high activity (> 6mm inhibition zones) for cellulase, amylase, and xanthanase production. Isolates R29 and R78 showed high lipase activity (> 6mm) by utilizing tween 20 efficiently, followed by R127(3.8 mm), whereas the other bacteria showed slight lipase-secreting ability. Isolates R11 and R29 efficiently utilized tween 80, followed by C15, R20, R78, and R88 (Table 4).

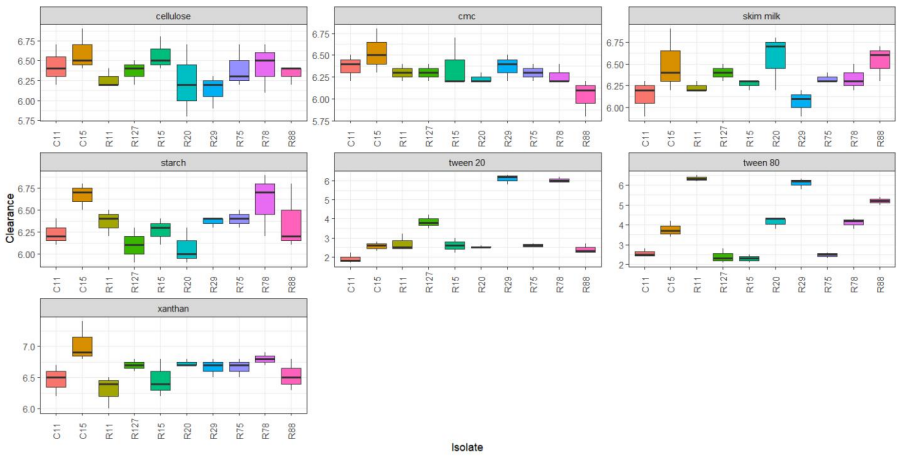

Figure 4: Utilization of various substrates by the bacterial isolates

Figure 5: Cellulose hydrolysis

Figure 6: Carboxymethyl cellulose

Figure 7: Skim milk

Figure 9: Tween 20

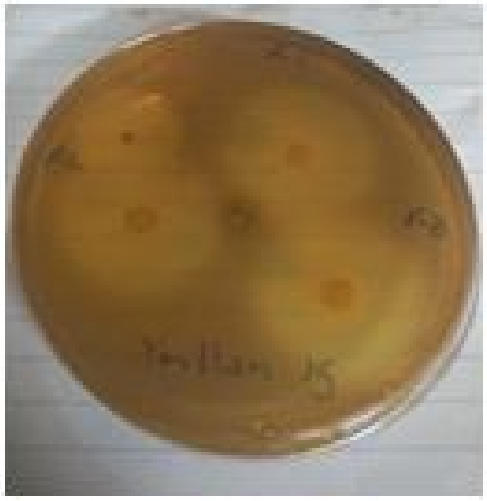

Figure 10: Xanthan

The secretion of extracellular hydrolytic enzymes by halophiles and haloalkaliphiles has been reported. The secretion of various extracellular enzymes by the bacterial isolates in this study corroborates previous findings [20] which reported that haloalkaliphilic bacteria from Lake Magadi could produce protease, amylase, lipase, cellulase, and pectinase enzymes. The bacterial isolates exhibited combined hydrolytic activities. Similarly, halophilic bacteria have been isolated from a hypersaline lake that produces hydrolytic enzymes such as protease, amylase, lipase, pectinase, cellulase, and xylanase [21]. The disparity in lipase production by the isolates might be due to genetic variations. The variability in lipase production by the isolates has been attributed to their capacity to regulate their growth and metabolic processes [22]. The ability of the isolates to secrete extracellular enzymes at high salinity, temperatures, and alkalinity shows the potential of the enzymes for industrial application.

Physiological characterization of the bacterial isolates

Most of the organisms grew optimally at pH 7.0-9.0; pH 7 (R78), pH 8 (R11, C11, R15, R29, R78, and R127), and pH 9 (C15, R20, and R75) (Figure 11). This supported the alkaliphilic observation for the isolates. However, R127 grew optimally at pH 6, showing alkali tolerance.

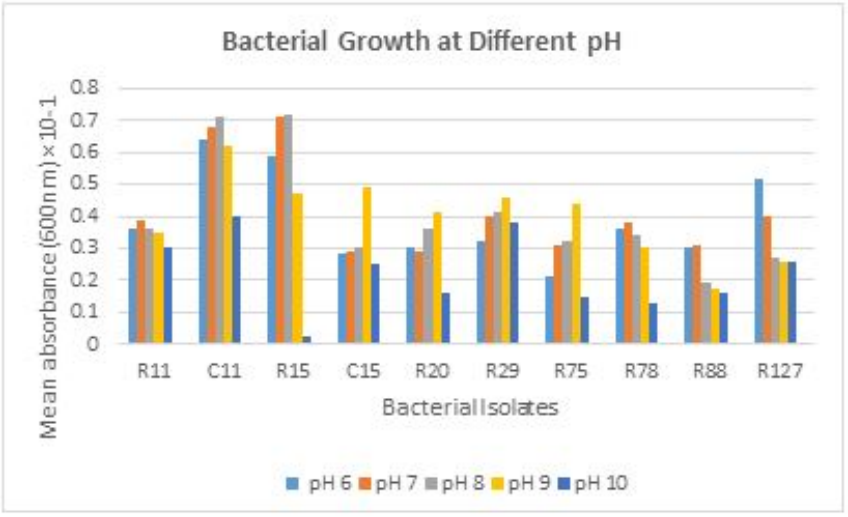

Figure 11: Growth pH of bacteria isolates at different pH levels

These findings correspond with the documented pH ranges commonly observed among alkaliphilic bacteria isolated from East African soda lakes with growth pH ranges between 7.0 and 11.0 [23–25]. The isolates demonstrated the capacity to thrive in mild acidity, indicating their ability to withstand a broad pH range.

The ideal growth temperature for the bacterial isolate R88 was 25°C, with 40°C being optimal for the other isolates [Figure 12]. This indicates that isolates are thermophiles, whereas R88 is thermotolerant.

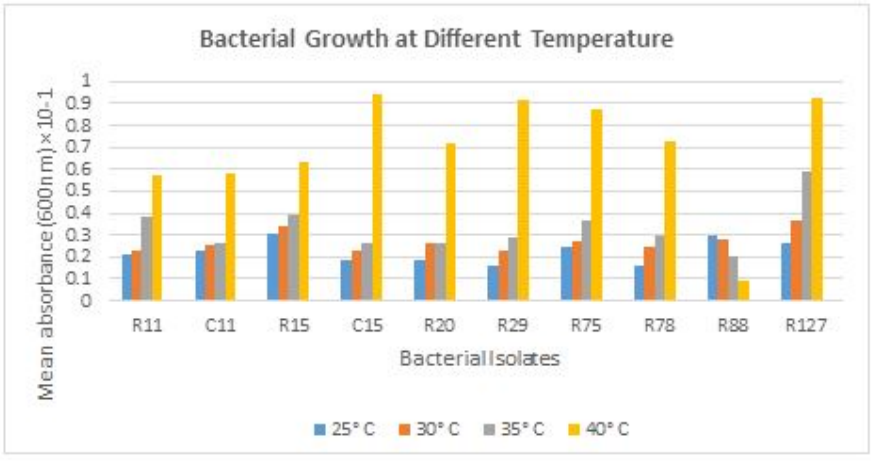

Figure 12: Growth of bacterial isolates from Lake Magadi at different temperatures

Our results agree with data isolated from hypersaline lakes [26], which isolated protease-producing bacteria from soil samples of Lake Wadi El-Natrun that thrived at a temperature range of 25-55°C.

The optimal growth salinity was 5% for most of the isolates (moderate halophiles) except N75 and N88 (0% salinity (halotolerant)). Isolate C11 showed optimal growth at 20% salinity (extreme halophile) (Figure 13).

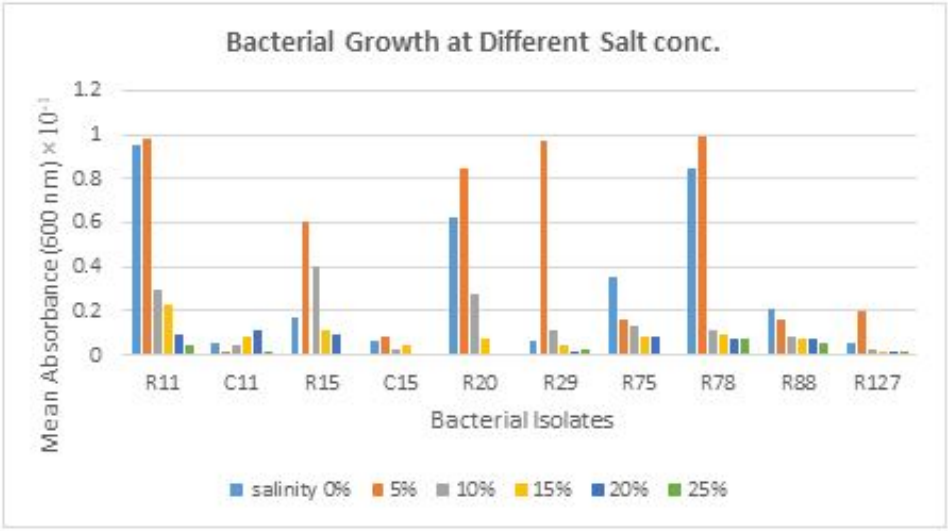

Figure 13: Growth of bacteria from Lake Magadi at different salt levels

Halophiles are categorized as slight (1.7-4.8% (seawater is 3.5%)), moderate (4.7-20%), and extreme halophiles (20-30%) based on the environmental salinity. Halophiles need NaCl to grow, whereas halotolerant microbes can grow under salty conditions, which is not mandatory. We observed slow bacterial growth in the presence of 20% NaCl. Elevated salt concentrations have been linked to cellular dehydration, enzyme inhibition, and reduced oxygen availability in the environment.

Molecular characterization of the bacterial isolates

The phylogenetic affiliation of the 10 selected bioactive isolates was evaluated using BLAST analysis to the nearest neighbors following a partial sequence of the 16S rRNA (Figure 14). The result was expressed as percentage similarity (Table 3). Sequence analysis revealed that seven isolates were affiliated with the *Bacillus* genus, exhibiting 91-96% similarity. Isolate C11 was affiliated with *micrococcus*, R7 *Streptococcus* (94.74%), and R123 *Polynucleobacter* (100%).

Table 3: BLAST analysis of bacterial isolates from Lake Magadi

Isolate code	Description	Per. Identity	Accession
R11	*Salipaludibacillus agaradhaerens*	*91.55%*	*NR_026142.1*
C11	*Micrococcus aloeverae*		
R15	*Bacillus bataviensis strain*	96.35%	NR_041571.1
C15	*Brevibacillus laterosporus*		
R20	*Salipaludibacillus agaradhaerens*	93.35%	NR_026142.1
R29	*Bacillus urumqiensis*	93.10%	NR_149288.1
R75	*Streptococcus hongkongensis*	94.74%	NR_117974.1
R88	*Salipaludibacillus agaradhaerens*	95.49%	NR_026142.1
R78	*Polynucleobacter aenigmaticus*	100.00%	NR_159080.1
R127	*Salipaludibacillus agaradhaerens*	94.77%	NR_026142.1

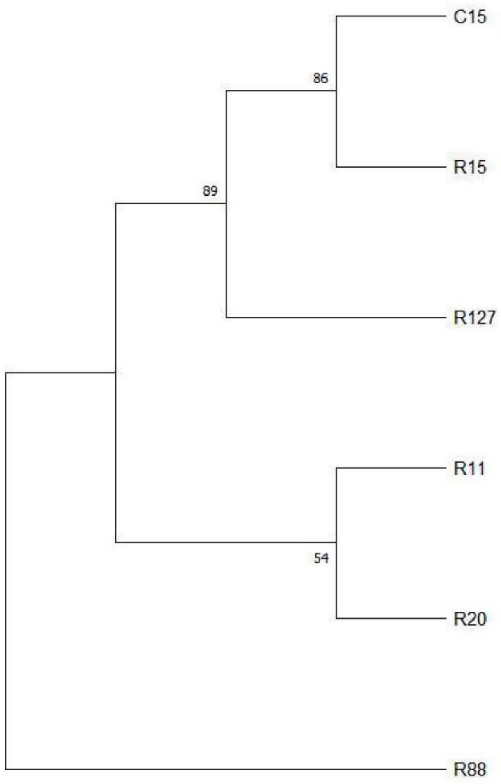

Figure 14: A phylogenetic tree showing the recovered isolates

Genera *Bacillus* and *Micrococcus* have been recovered from hypersaline and alkaline habitats. *Bacillus* is the most dominant group from a highly alkaline condition of saline soda lime in Poland [27]. Additionally, 90% of the isolates from deep sea sediments were affiliated with the genus *Bacillus* [28]. The high prevalence of the genus *Bacillus* within these ecosystems indicates high adaptation to endure salt and alkaline habitats, which is linked to their endospore dormant stages. Species of *Bacillus* and *Micrococcus* were isolated from Lake Magadi [29]. M*icrococcus* were also isolated from sediments and water samples of the alkaline Lonar Lake in India[30]. To our knowledge, *Polynucleobacter aenigmaticus* has not previously been reported from Lake Magadi. Isolates R11, R20, R29, R75, and R127 exhibited 91-94% sequence similarity, suggesting they could represent new genera. Isolates R15 and R88 showed sequence similarity at 96% and 95%, respectively, indicating a probability of representing new species.

In conclusion, our study showed that Lake Magadi contains antimicrobial-producing bacteria, especially Brevibacillus laterosporus, which can be explored for novel antibiotics and enzymes. The extracellular hydrolytic enzymes produced at high temperatures, salinity, and pH may have potential biotechnological applications.

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Data and Material Availability

All the data used in the current study can be made available upon request.

Competing Interest

The authors declare no conflict of interest.

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