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Original article

Antioxidant and antibacterial activity of soil *Streptomyces* isolates against beta-lactamase-resistant bacteria

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ABSTRACT

Background: Antimicrobial drug resistance has become a global health problem. There is a need for a newer, more efficient, and potent source of antibiotics against these drug-resistant pathogens, especially the Beta-lactamase drug-resistant organisms. This study examines the antibacterial activity of *Streptomyces* isolates on Beta-lactamase bacteria. **Method:** Soil Samples were collected from various sites within Mogadishu and screened for the isolation of *Streptomyces* following the conventional microbiological method. The soil samples were analyzed for their proximate content and were pretreated and inoculated onto a Czepadox agar modified with 50mg/mL cycloheximide and incubated for 5 – 7 days at 37ºc. Streptomyces-like isolates were purified and tested for various biochemical and sugar fermentation tests. The Antimicrobial activity of the *Streptomyces* isolates against Beta-lactamase organisms (Penicillin +Oxacillin resistant *Staphylococcus aureus*, Streptomycin resistant *Shigella dysenterae*, Oxacillin-resistant *Pseudomonas aeruginosa*, Carbapenem-resistant *Salmonella typhi*, Penicillin resistant *Escherichia coli)* was examined. The radical scavenging activity of *Streptomyces* isolates was examined. **Results:** Seventy-two **(**72) *Streptomyces* isolates were recovered, but only 10 isolates expressed high antibacterial activity against beta-lactamase-resistant bacteria. *Streptomyces* isolate GS 4 demonstrated the highest activity among the examined isolates. All the isolates had considerably high antioxidant activity. **Conclusion:** There was a high antibacterial activity of *Streptomyces* isolates recovered from the soil of Mogadishu against beta-lactamase-resistant bacteria. This study offers essential knowledge on soil properties and the potential of *Streptomyces* isolates for use in biotechnology and pharmaceutical industries and provides source material for bioactive antibiotics.
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Introduction

The challenge of antimicrobial resistance (AMR) has become increasingly significant in worldwide public health, posing a substantial obstacle to the effectiveness of conventional antibiotics [1]. The core of this problem is the rapid increase in bacteria that possess β-lactamase enzymes, which provide them with resistance against a broad range of β-lactam antibiotics, including well-established ones like penicillins, cephalosporins, and carbapenems [2]. The continuous development and spread of these bacteria that produce β-lactamase highlight the urgent requirement for creative approaches to address the threat posed by infections resistant to several drugs [3]. Researchers have responded

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promptly to this urgent demand by directing their attention towards the natural world, aiming to discover innovative antibacterial medicines [2,3].

The soil is a valuable source of microbial variety, including a wide range of living forms waiting to be discovered [4]. Amidst the diverse collection of microorganisms, *Streptomyces* species stand out for their remarkable capacity to produce a wide range of secondary metabolites, which have the potential to yield remarkable therapeutic benefits [5]. *Streptomyces*, commonly found in soil environments, have fascinated researchers with their ability to produce various structurally complex chemicals. *Streptomyces* have a wide range of capabilities, from medicines that have significantly impacted medicine to substances that may combat fungal infections, viral attacks, and even malignant growths [6]. Nevertheless, the less familiar aspects of their secondary metabolites - their significant antioxidants and antibacterial properties - provide great potential for therapeutic exploration and advancement [7].

The bioactive compounds from *Streptomyces* possess significant antioxidant properties, which have important therapeutic implications [8]. These compounds have the potential to protect against diseases caused by oxidative stress [8]. By scavenging detrimental reactive oxygen species (ROS) in living organisms, they provide hope in reducing cellular injury and preventing the development and advancement of many diseases [9]. In addition, their ability to fight against β-lactamase resistance makes them a promising solution in the ongoing fight against antibiotic-resistant microorganisms [8].

To fully harness the therapeutic capabilities of soil *Streptomyces*, it is crucial to understand the complex interaction between these highly skilled microorganisms and their resilient opponents, the β-lactamase resistant bacteria. Researchers can only utilize the bioactive arsenal for developing new therapeutic approaches by gaining a deeper grasp of the underlying mechanisms that control their interplay. Equipped with this information, they set out on a mission to discover new potential drugs that are more effective and resistant to developing resistance mechanisms [4,10]. This will bring about a new era in the battle against antibiotic resistance. The menace of antimicrobial resistance has stirred the need for an effective, safe alternative to antimicrobial resistance. The latter necessitates this study.

Methods

Collection and pre-treatment of soil sample

Soil samples were collected from various ecological habitats, such as grassland, cultivated fields and refuse dump sites. Using a shovel, soil samples were dug from 5 to 10 cm depths, carefully placed in sterile polythene bags and labeled accordingly [4]. The soil samples were subjected to an initial air-drying phase, carefully carried out for 3 to 4 hours at a controlled temperature of 45°C [4]. Afterward, the desiccated samples were carefully ground into a fine powder and sifted to guarantee consistency before being considered appropriate for isolating *Streptomyces* species. A rigorous pre-treatment procedure was carried out [5]. This involved subjecting the samples to a hot water bath set at a specific temperature of 56°C, which was maintained for 30 minutes. The samples were diluted using sterilized water to reach a dilution factor of 10^{-5}. Afterward, an exact volume of around 100 microliters from each diluted sample was carefully distributed evenly across the isolation media surface, guaranteeing consistent coverage [11]. The inoculated medium was carefully incubated for 2 to 4 weeks in a controlled environment with a constant temperature of 28 ± 2°C and high humidity [12]. After the incubation period, a thorough examination of the cultured media was conducted, and putative colonies of *Streptomycetes* were carefully recognized based on their specific morphological traits. The suspected colonies were carefully separated and purified using a modified Czepadox agar medium to maintain the integrity and purity of the resulting culture. A series of biochemical and sugar fermentation tests were carried out following standard protocols [13].

Antimicrobial activity of *Streptomyces* on the Beta-lactamase resistant test organisms and *candida*

The isolates were subjected to preliminary screening for antibiotic activity on a Muller Hinton agar medium using the streak-plating technique. The plates were prepared and inoculated with a *Streptomyces* isolate using a single streak of inoculum applied to the top end of the Petri dish. Following a 5-day incubation period at 28ºC, the plates were inoculated with test organisms using a single streak perpendicular to the *Streptomyces* strains [4]. The microbial interactions were seen and

analyzed using the zone of inhibition method. The measurements were taken to the closest millimeter after 24 hours of incubation at 37 degrees Celsius. Test organisms bacteria (Penicillin +Oxacillin resistant *Staphylococcus aureus*, Streptomycin resistant *Shigella dysenterae*, Oxacillin resistant *Pseudomonas aeruginosa*, Carbapenem-resistant *Salmonella typhi* and Penicillin resistant *Escherichia coli*) were used to determine the antimicrobial activity of the isolated *Streptomyces* strains. As mentioned earlier, the bacteria were cultivated in Nutrient Agar (NA) (Difco) at a temperature of 37±0.1°C for 24 hours. Subsequently, they were preserved in a Nutrient Agar slant at a temperature of 4°C [14].

Antioxidant properties

The DPPH radical scavenging assay was utilized to assess the quenching ability of the isolates, following the method described by Espindola et al. [9]. A solution of DPPH in methanol (0.15%) was combined with serial dilutions (200–1,000 μg/ml) of the isolates. The mixture was left undisturbed for ten minutes, and then the absorbance was measured at a wavelength of 513 nm. The radical scavenging activity was quantified using the IC50 value (μg/ml), which is the dose necessary to achieve a 50% inhibition. Vitamin C served as the reference standard [8].

Statistical analysis

The diameter zones of inhibition of extracts are presented as the average value plus or minus the standard deviation. The study's statistical analysis was conducted using the student's t-test. The data about biochemical and physiological parameters were analyzed and presented as the mean value ± standard error of the mean (SEM).

Results

Table 1 thoroughly examines soil samples obtained from four separate locations, each distinguished by specific physicochemical characteristics. The parameters encompassed are texture, pH levels, and the concentration of essential elements such as potassium (K), phosphorus (P), calcium (Ca), zinc (Zn), magnesium (Mg), copper (Cu), aluminum (Al), iron (Fe), manganese (Mn), electrical conductivity (EC), organic matter (OM), and total nitrogen (TN). The soil texture of Site 1 is mainly categorized as Sandy-Silt, with significant amounts of clay, sand, and silt. The pH level is slightly acidic, measuring 7.42, and the concentrations of essential elements exhibit variation, with notable levels of potassium (K) and organic matter (OM), as presented in Table 1. Site 2 displays a sandy soil texture characterized by significantly elevated sand content and relatively low amounts of clay and silt. The pH level of the soil is 8.60, indicating an alkaline nature.

Additionally, the soil exhibits high levels of calcium (Ca) and organic matter (OM). Site 3, on the other hand, exhibits a loamy silt texture, which encompasses features of both sandy and silty soils, as presented in Table 1. The pH level of the soil is somewhat acidic, measuring at 7.29. Additionally, the soil is abundant in phosphorus (P) and magnesium (Mg). Site 4 exhibits a sandy silt texture characterized by moderate amounts of clay, sand, and silt. The pH level is somewhat alkaline at 8.16, and the soil exhibits diverse amounts of vital components, notably high levels of aluminum (Al) and iron (Fe).

The provided outcome in Table 2 highlights the identification of *Actinomycetes* strains from numerous sample locations, emphasizing the enumeration of colony-forming units (CFUs) detected on different growth conditions. Site 1 displayed the total colony-forming units, with particularly remarkable numbers on Czepadox agar and Sabouraud dextrose agar. Site 2 similarly showed a notable number of CFUs, although the CFUs' distribution over the media differed from that of Site 1. Meanwhile, Sites 3 and 4 had somewhat lower CFU totals, indicating possible variations in the number or variety of *Actinomycetes* among the examined locales.

The *Streptomyces* isolates display various colors ranging from cream, white, and gray to yellowish-green and brown. Similarly, the substrate's visual characteristics range from white and grey to cream and yellow, and specific isolates exhibit pigments that can diffuse, such as brown, yellow, and ox-blood, as represented in Table 3. All the *Streptomyces* isolates consistently exhibit good results for catalase and Gram stain. However, there is variation among the strains in terms of coagulase, citrate utilization, and indole synthesis. The isolates exhibit distinct fermentation patterns for sorbitol, arabinose, xylose, sucrose, and maltose, as represented in Table 3.

Table 4 presents the outcomes of the secondary screening of *Streptomyces* isolates for their antibacterial activities using the disc diffusion method. The isolates were subjected to testing against a range of antibiotic-resistant bacterial

strains, such as *Staphylococcus aureus*, resistant to Penicillin and Oxacillin, *Shigella dysenteriae*, resistant to Streptomycin, *Pseudomonas aeruginosa* resistant to Oxacillin, Salmonella typhi resistant to Carbapenem, and *Escherichia coli* resistant to Penicillin as represented in Table 4. Various levels of inhibitory zones were identified against the investigated bacterial strains in the isolates labeled GS 2, GS 4, DM 6, DM 8, CP 9, CP 4, DM 5, GS 3, and DM 2, as represented in Table 4. Significantly, several isolates demonstrated varying degrees of efficacy against bacterial strains. Isolate GS 4 exhibited significant inhibition against Streptomycin-resistant *Shigella dysenteriae* and Carbapenem-resistant *Salmonella typhi*, with 28 mm and 24 mm inhibition zone sizes, respectively. In contrast, GS 3 exhibited comparatively reduced activity against all examined bacterial strains compared to the other isolates, as represented in Table 4.

The study evaluated the antioxidant activity of different isolates, and the findings are displayed in Figure 1. Out of the isolates, GS 4 showed the highest level of radical scavenging activity, measuring 33.34%. It was closely followed by CP 4, which had a scavenging activity of 31.03%. By comparison, isolates such as CP 9 and GS 5 exhibited comparatively lower levels of radical scavenging activity, with 19.34% and 19.29%, respectively. In addition, the control sample, ascorbic acid, exhibited a markedly greater level of radical scavenging activity at 73.45%, acting as a standard for comparison.

Table 1. Physicochemical analysis of soil samples

Texture	Sandy-Silt	Sandy	Loamy Silt	Sandy Silt
Clay	19.37	4.93	8.66	10.02
Sandy	48.98	90.29	82.74	53.48
Silt	26.37	5.64	8.60	36.05
pH	7.42	8.60	7.29	8.16
K	1.62	2.51	2.05	1.39
P	0.41	0.01	1.84	0.35
Ca	2.85	21.25	6.03	1.04
Zn	0.02	0.04	0.24	0.03
Mg	2.01	0.42	3.28	2.11
Cu	0.03	----	---	0.02
Al	4.87	1.82	3.94	7.62
Fe	13.74	2.02	5.22	13.05
Mn	0,21	0.07	0.02	0.24
EC	0.22	0.29	0.26	0.31
OM	3.52	5.34	5.68	7.85
TN	0.21	0.29	0.30	0.25

Table 2. Isolation of *Actinomycetes* strains

Sampling sites	Colony forming unit				
	Czepadox agar	Yeast extract	Potato Dextrose	Saboaurad dextrox agar	
Site 1	70	12	18	16	116
Site 2	48	26	22	5	101
Site 3	52	7	7	6	72
Site 4	35	9	4	5	53
Total	205	54	51	32	342

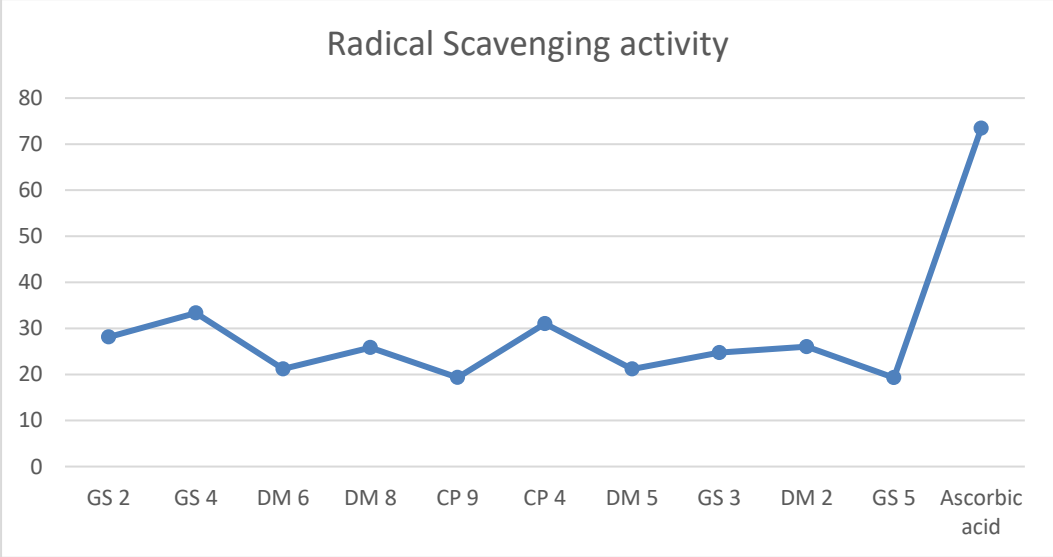
Table 3. Morphological characteristics of *Streptomyces* species

	Streptomyces isolates									
Characteristics	**GS 2**	**GS 4**	**DM 6**	**DM 8**	**CP 9**	**CP 4**	**DM 5**	**GS 3**	**DM 2**	**GS 5**
Morphological features										
Aerial appearance	Cream	White	Cream	Grey	White	Grey	White	Yellowish green	Yellow	Brown
Substrate appearance	white	Grey	Cream	Yellow	Yellow	Grey	Grey	cream	cream	Cream
Diffusible pigment	-	Brown	-	-	Brown	-	-	-	Yellow	Ox-blood
Biochemical test										
Catalase	+	+	+	+	+	+	+	+	+	+
Gram Stain	+	+	+	+	+	+	+	+	+	+
Coagulase	-	+	+	+	+	+	-	+	+	+
Citrate	+	-	+	+	+	-	+	+	+	+
Indole	+	-	-	+	-	-	+	-	-	-
Sugar fermentation										
Sorbitol	+	+	-	+	-	+	+	+	+	+
Arabinose	+	+	+	+	+	+	+	+	+	+
Xylose	+	+	+	+	+	-	+	+	-	+
Sucrose	+	-	+	+	+	+	+	+	+	+
Maltose	+	+	+	+	-	+	+	+	+	-

Table 4. Secondary screening of *Actinomycetes* isolates for antimicrobial properties using disc diffusion method.

Isolates	Penicillin +Oxacillin resistant *Staphylococcus aureus* (mm)	Streptomycin resistant *Shigella dysenterae* (mm)	Oxacillin resistant *P. aeruginosa* (mm)	Carbapenem resistant *Salmonella typhi* (mm)	Penicillin resistant *E. coli* (mm)
GS 2	18	22	18	23	13
GS 4	22	28	20	24	16
DM 6	19	27	17	21	20
DM 8	19	24	19	20	19
CP 9	20	27	18	16	15
CP 4	19	24	19	17	19
DM 5	19	23	22	21	20
GS 3	17	20	17	19	19
DM 2	19	22	21	19	20
GS 5	20	19	19	22	23

Figure 1. Antioxidant activity of Streptomyces isolates collected from soil of Mogadishu.



Discussion

The problem of antimicrobial resistance has changed the narrative of therapeutic medicine, as previously efficacious drugs are now almost useless in the battle against pathogenic bacteria [1,15,16]. The latter has necessitated the need to source newer, productive means of curbing the antimicrobial menace [17]. This study thoroughly examines Streptomyces isolated from soil samples from different sites, their antibacterial activity against some beta-lactamase bacteria, and their radical scavenging activity.

There were myriad chemical compositions from the various sites where the soil was collected, and the nutritional composition of the soil enhanced the proliferation of Streptomyces in the soil. The latter are in alliance with the reports of others [11,12,18,19]. The differences in soil features can impact microbial populations, such as Actinomycetes, which are recognized for their abundant synthesis of bioactive chemicals that may possess antibacterial capabilities. The growth of Streptomyces on different cultural media indicates a diverse microbial population with possible antibacterial properties, the latter following the findings of Abdirasak et al. [5].

Various morphological traits and biochemical tests in Streptomyces populations indicate their variability, which may lead to differences in antibacterial capabilities across different isolates [4]. The evaluation of the antimicrobial properties of Streptomyces isolates against antibiotic-resistant bacterial strains demonstrated significant inhibitory effects, suggesting their potential as a valuable source of innovative antimicrobial drugs. Notably, some strains demonstrated substantial inhibition against antibiotic-resistant bacteria that are clinically relevant, indicating their effectiveness in fighting antimicrobial resistance [20]. The high antibacterial activity of the Streptomyces isolates against beta-lactamase test organisms in this study is unclear. Still, it could be attributed to active secondary metabolites with high antimicrobial properties. The latter are in alliance with the findings of others [21,22]

Furthermore, the assessment of antioxidant activity among the isolates revealed different levels of ability to remove radicals, with specific isolates displaying significant antioxidant capacity. Although not directly linked to antimicrobial resistance, the found antioxidant activity highlights the various roles of Streptomyces in ecosystem functioning and their potential as sources of bioactive chemicals with a wide range of biological activities [23–25]. The findings of this study contribute to our understanding of natural sources of antimicrobial substances and provide valuable information for developing new approaches to combat antimicrobial resistance by identifying unique bioactive compounds.

Conclusion

The Streptomyces isolates exhibited significant antibacterial activity against beta-lactamase organisms, providing a viable alternative for exploring potent novel antibiotic sources.

Streptomyces microbes can synthesize various bioactive compounds, such as antibiotics, pigments, and enzymes. These chemicals have diverse applications in medicine, food, biotechnology, and laboratory environments. The ability of Streptomyces to create enzyme inhibitors reveals a new aspect of microbial antagonism called anmesalism.

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Conflicts of interest

The authors declare that they do not have any conflict of interest.

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