Egypt. J. Chem. **Vol. 67**, No. 11. pp. 449 - 469 (2024)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Valorization of Sugarcane By-Products for Valuable Compounds Production Using Fusarium Solani

Mennatallah Abdou Basuiony,[a] Sherif Helmy Ahmed,[a] Rania Saber Yousef [a*]

[a]*Biochemistry Department, Faculty of Agriculture, Cairo University, Giza, Egypt.*

Abstract

Sugarcane by-products have the efficacy of alternative, low-cost culture media that could be used for the cultivation of a wide range of fungi. Various formulations of culture media are used for the growth of *Fusarium* species, which can provide a variety of famous bioactive compounds. This study investigates the bioactive compounds and biological activities of the fungal strain *Fusarium solani* when cultivated on sugarcane by-products as different carbon sources (bagasse, vinasse, and molasses). The obtained results revealed the highest growth rate of *Fusarium solani* detected in T9 (molasses: vinasse with a ratio of 1:1). The maximum phenols and flavonoids content was recorded by a fungal strain grown on the same treatment (T9) with concentrations of 360.09 and 111.56 mg/mL, respectively. *Fusarium solani* exhibited the highest free radical scavenger in T9 and T11 (molasses: vinasse with a ratio of 1:3). According to the previous *F. solani* cultivated on T9, that produced a high concentration of active metabolites (48.02 mg/L), which was analyzed by HPLC analysis. In addition to that, the fungus showed better antibacterial activity against *Staphylococcus aureus* when grown on T9. This finding suggests that sugarcane industrial wastes can be used as a growth culture economic medium to be substituted by the synthetic medium as potato dextrose liquid for *Fusarium solani,* as this fungus has various useful pharmaceutical and agricultural applications due to its produced secondary metabolites that exhibit potential antioxidant and antibacterial activities.

Keywords: Industrial waste treatment; Secondary metabolites; Antioxidants; Antimicrobial.

1. Introduction

Fungi act as a potential source of natural products that are found in a variety of plant species [1]. The fungal species are essential for new drug creation due to their metabolic diversity and unique genetics, such as the *Fusarium* species, which provide various secondary metabolites with a broad spectrum of biological activities [2]. Secondary metabolites produced by fungal strains were described as low-molecular weight molecules, which cannot be essential for the growth and development of microbial species as primary metabolites, while their synthesis is influenced by various carbon sources [3]. The main four classes of fungal secondary metabolites were indole alkaloids, terpenes, polyketides, and non-ribosomal peptides that are helpful for agricultural, pharmaceutical, and medicinal aspects [3, 4]. Fungal secondary metabolite biosynthesis begins with Acetyl-CoA, which is formed by the breakdown of carbohydrates. Nevertheless, there are various pathways for the production of FSMs, such as volatile terpenes synthesized by the mevalonate pathway, while fumonisins and naphthoquinone pigments are produced through the polyketide pathway [3].

The synthesis of secondary metabolites by a fungal strain depends on physical and chemical culture conditions such as pH, temperature, C/N ratio, and carbon and nitrogen sources [5]. The medium composition influences the production of anhydrofusarubin, polyketides, javanicin, bostrycoidin, and fusarubin that are formed by *Fusarium solani* [6]. In addition to that, valuable

*Corresponding author e-mail: dr.raniasaber@cu.edu.eg
Receive Date: 23 February 2024, Revise Date: 31 March 2024, Accept Date: 09 April 2024
DOI: 10.21608/ejchem.2024.272306.9382

secondary metabolites (monoterpenes, sesquiterpenes, and naphthoquinone pigments) were produced by *Fusarium verticillioides* when cultivated on a medium supplemented by various carbon sources (monosaccharides and disaccharides), as well as the formation of the mycotoxins FB_1 and FB_2 [7]. Plants are rich in bioactive compounds (phytochemicals) with diverse applications, such as sugarcane industrial by-products, which have active ingredients such as phenolics, flavonoids, triterpenoids, lignins, and phytosterols. These bioactive compounds are used for treating cystitis, burning urination caused by high acidity, nephritis, and an enlarged prostate. In addition to that, sugarcane constituents showed potential biological activities, for instance, anti-inflammatory, anti-thrombotic, anti-hyperglycemic, analgesic, diuretic, and anti-hypercholesterolemic [8]. An inexpensive raw material, sugarcane molasses, was used to enhance biofilm production for the biosynthesis of an alkaloid, Fumigaclavine C, from the endophytic filamentous fungus *Aspergillus fumigatus* CY018 that showed vital biological activities such as anti-inflammatory, anti-atherogenic, and antitumor effects [9].

Moreover, biofilms can produce potential bio-products such as red pigment by *Penicillium novae-zelandiae*, kojic acid by *Aspergillus oryzae*, cellulase by *Aspergillus niger*, fructooligosaccharides by *Aspergillus phoenicis,* and gliotoxin by *Aspergillus fumigatus* [10-13]. The synthesis of secondary metabolites (phenolic and flavonoid compounds) was enhanced by *Chlorella sorokiniana* when low-cost sugarcane vinasse was used as a cultivated medium supplemented by nitrogen, phosphorus, and potassium sources. These metabolites revealed antioxidant activity that can be used in various applications, such as pharmaceuticals, the dietary industry, and cosmetics [14]. Sugarcane molasses ethanolic extract showed numerous polyphenols such as orientin, chlorogenic acid, vanillin, diosmetin, sinapic acid, swertisin, apigenin, caffeic acid, diosmin, homoorientin, tricin, syringic acid, and vitexin with their antioxidant activity that could be beneficial to human health [15]. Besides, polyphenols have another role in preventing neurodegenerative and cardiovascular diseases, regulating carbohydrate metabolism, and inhibiting enzymes [16-17]. In addition, fungal flavonoids have the ability to inhibit the aldose reductase enzyme [18]. Natural pigments can be used as an alternative to harmful synthetic dyes, which specialize in the food, textile, and cosmetic industries. They provided various biological activities, such as antioxidant and antimicrobial properties [19].

Antioxidants are molecules that delay cell through electrons donating to neutralize free radicals through their free radical scavenging activities [20]. Also, antimicrobial agents have a vital role in treating infectious diseases caused by pathogenic microorganisms in the presence of different modes of action. *Fusarium* is a potential genus producer of antimicrobial secondary metabolites that participated in new drug development, for instance, bacterial terpenes, antiviral enniatins, antiparasitic integracides, antifungal pyridines, and papulacandin [2]. Nevertheless, *Fusarium* species showed a great influence as antibacterial activity against anthropogenic bacteria such as *Bacillus subtilis*, *Escherichia coli*, *Bacillus megaterium*and, and *Clostridium perfringens* due to the presence of sesquiterpens, cyclonerotriol B, fusaravenin alkaloid, naphthoisoxazole amide, zwitter-ionic alkaloid, 1,4-naphthoquinone, and depsipeptide [21].

This study investigates the effect of the addition of agro-industrial by-products of sugarcane, such as bagasse, molasses, and vinasse, to the growth culture of the endophytic fungus *Fusarium solani;* as an alternative medium; on the growth and secondary metabolites produced, in addition to the biological activities such as antioxidant and antimicrobial activities.

2. Materials and Methods

Chemicals and reagents were purchased from E. Merck Co. (Darmstadt, Germany).

2.1. Cultivation of filamentous fungi

The endophytic fungus *Fusarium solani* was discovered by a microscope by Prof. Dr. Ahmed Farahat Sahab, Plant Pathology department, National Research Center, Egypt. The fungal strain was extracted from the rhizosphere soil of *Lupin termis*, according to Brown [22]. Various culture media were prepared for *Fusarium solani* growth conditions at 30 °C for eleven days with pH 5 in a total volume of 600 mL, as mentioned in Table 1.

Table 1 : The composition of different culture media for cultivation of fungal strain *Fusarium solani*

Chemical composition	Treatments										
	T1 (Control)	T2	T3	T4	T5	T6	T7	T8	T9	T10	T11
Prepared potato dextrose broth	Potato120.0 g Dextrose12.0 g	-	-	-	-	-	-	-	-	-	-
Sugarcane bagasse (g)	-	-	60.0	60.0	60.0	-	-	-	-	-	-
Sugarcane molasses(mL)	-	-	-	-	-	600.0	-	290.0	290.0	145.0	145.0
Sugarcane vinasse (mL)	-	-	-	-	-	-	600.0	290.0	290.0	435.0	435.0
Glycerol (g)	-	18.2	-	18.2	18.0	-	-	18.2	18.2	18.2	18.2
Ammonium sulphate(g)	-	0.44	-	-	0.44	-	-	-	0.44	-	0.44
Ferric chloride (g)	-	0.63	-	-	0.63	-	-	0.63	0.63	0.63	0.63

2.2. Growth rate determined as total carotenoids content

An aliquot of the fungal biomass sample was mixed with the acetone-water mixture (80%). The absorbance of the extract should be recorded at 470 nm for the detection of total carotenoids. The pigment's content was calculated according to Yang [23].

2.3. Total carbohydrate, Total amino acids, and Total protein determination

The total carbohydrate content in the fungal culture was determined according to Dubois [24]. An appearance of yellow-orange should be measured at 490 nm.

Total amino acids**:** The 2, 2-dihydroxyindane-1, 3-dione (Ninhydrin) was prepared in citrate buffer, and the glycine standard was prepared in distilled water (1000 µg/mL). An aliquot of 0.1 mL of standard or *Fusarium* culture was mixed with 1.9 mL of ninhydrin reagent, incubated in a boiling water bath (98^{o}C) for 15 min then cooled the tubes and measured the absorbance at 570 nm, against a blank [25].

Total soluble protein in *F. solani* culture was determined according to the method described by Bradford [26]. After 2 minutes, an absorbance of blue color was measured at 595 nm. The standard protein used is albumin bovine serum. To determine, the protein content of unknown samples, by plotting its absorbance against the standard absorbance.

2.4. Total phenols and total Flavonoids content

Total phenols were determined in the fungal culture using the method described by Halliwel and Guttridge [27]. The absorbance was measured at 765 nm using a spectrophotometer. Phenolic contents were calculated based on the standard curve of gallic acid.

Flavonoids compounds were determined in *Fusarium* culture using the method described by Zhishen [28]. The absorbance was measured spectrophotometrically against a blank at 510 nm. Quercetin served as the standard compound for the preparation of the calibration curve.

2.5. High-Performance Liquid Chromatography (HPLC)

The analyses were carried out on HP Series 1100 system that was set to UV-DAD detection between 210 and 400 nm. The chromatograms were recorded at 280 nm, and peaks were blended using HP

chemstation software. This method was described according to Johnsson [29].

2.6. Antioxidant assays

DPPH radical assay: Fusarium extracts were mixed with a DPPH methanolic solution (1mM, 1mL) and then left for 30 minutes at room temperature. The absorbance of the resulting extracts was measured at 517 nm using a spectrophotometer [30].

ABTS radical assay: A known volume (10 µL) of fungal extracts was homogenized with 1 mL of diluted ABTS radical cation ($ABTS^{\bullet+}$), and then absorbance was measured after 1 minute of initial mixing at 734 nm [31].

2.7. Antimicrobial activity

In vitro antimicrobial studies of various *Fusarium solani* culture extracts were carried out by the agar-disc diffusion method against the following test microorganisms, *Staphylococcus aureus* and *Bacillus cereus* (Gram +ve bacteria), while *Escherichia coli* and *Salmonella typhi* (Gram −ve bacteria) were grown on tryptic soy broth culture medium compared to the most common antibiotic standard, tetracycline. The agar-disc diffusion was prepared as sterilized discs (6 mm) loaded with extracts from Whatman No.1 filter paper and dried completely under sterile conditions. Then the sterilized discs were placed on the seeded plates. The inoculated plates were then incubated at 37°C for 24 hours afterwards. Inhibition zones were measured and expressed at the end of the incubation period as the diameter of clear zone including the diameter of paper disc. This method was demonstrated by Bauer [32].

2.8. Molecular docking

Molecular docking studies of the selected compounds were performed using Molecular Operating Environment (MOE) software [33].

2.9. Statistical analysis

Values (three replicates) are presented as means ± SE or SD. Statistical analysis was done utilizing a "costat" statistical computer program. Statistical analysis was established on one-way analysis of variance ANOVA followed by student-Newman Keuls test, and the least significant difference (LSD) at $P< 0.05$.

3. Results and discussions

3.1. Growth rate determined as total carotenoids content

Carotenoids are naturally produced by many microorganisms, such as bacteria, fungi, and algae, which provide yellow, orange, and red pigmentation for various microbes and plant species. The results in Table 2 revealed that total carotenoids content was synthesized by the fungal strain *Fusarium solani* that was grown under a variety of culture media. The highest content was recorded by T9 with a concentration of 15.20 µg/mL, followed by T10 at 13.60 µg/mL, T11 at 12.70 µg/mL, and T8 at 11.30 µg/mL compared to control (T1) at 0.20 µg/mL. So, concentrations of T9, T10, T11, and T8 were folded to untreated strain T1, respectively. These results may be due to the presence of combined sugarcane molasses and vinasse supplemented with another carbon source, glycerol, and a nitrogen source as ammonium sulphate. These results were in agreement with Nafady [34], who reported that the maximum content of β-carotene produced by *Fusarium camptoceras* ASU5 when cultivated on production medium (GAY) supplemented with sugarcane molasses and ammonium phosphate as carbon and nitrogen sources had a content of 508.3 mg/L.

Nevertheless, neurosporaxanthin (carboxylic carotenoid) was yielded by *Fusarium fujikuroi* with a concentration of 8 mg/g dry mass when grown on a culture medium containing a high concentration of sucrose and a low amount of potassium dihydrogen phosphate as a nitrogen source [35]. Besides, neurosporaxanthin is the major carotenoid pigment produced by *Fusarium* species, with a minor content of β-carotene [36]. Another finding was demonstrated by Wit [37], who mentioned that *Fusarium temperatum* synthesized 35.1 ppm of total carotenoids when fungus cultures were exposed to blue light compared to darkness and other sources of light (white and red) with concentrations of 8.9, 11.8, and 15.1 ppm, respectively. Moreover, *Fusarium oxysporum* 4287 produced carotenoid pigments in the presence of illuminated cultures [38]. In addition to that, the maximum carotenoid content was reached at 2611.0µg/L by *Rhodotorula mucilaginosa* F-1 when sugarcane molasses was used as a potential carbon source compared to the control (YM) medium with a concentration of 2337.5µg/L [39]. According to Szotkowski [40] who demonstrated that *Sporobolomyces pararoseus* formed a high content of carotenoids at 24.8 mg/L due to the usage of animal waste fat as a culture medium compared to single carbon sources such as glucose and glycerol.

Table 2 : Total carotenoids content reflect to growth rate of *Fusarium solani* cultivated under different culture conditions

Treatments	Carotenoid (µg/mL)	Relative to control
T1	0.20 ± 0.010^{gh}	-
T2	0.10 ± 0.005^{h}	0.50
T3	0.30 ± 0.015^{g}	1.50
T4	0.20 ± 0.010^{gh}	1.00
T5	0.10 ± 0.005^{h}	0.50
T6	9.10 ± 0.455^{e}	45.50
T7	3.50 ± 0.175^{f}	17.50
T8	11.30 ± 0.565^{d}	56.50
T9	15.20 ± 0.760^{a}	76.00
T10	13.60 ± 0.680^{b}	68.00
T11	12.70 ± 0.635^{c}	63.50

Data are log means ± standard error (SE), n= 3.

3.2. Effect of media composition on fungal primary metabolites

Effects of different carbon and nitrogen sources on the primary metabolites content (carbohydrates, proteins, and amino acids) of *F. solani* are shown in Table 3. The obtained results illustrated that there is a great variation in the primary metabolites content (mg/mL) of *F. Solani,* as follows:

3.2.1. Total carbohydrates content:

These results showed that the maximum of total carbohydrates secreted by the fungal strain cultivated in T8, T9, T11 and T10 with concentrations of 507.88, 481.79, 297.77, and 287.32 mg/mL, respectively, compared to the untreated strain (T1) at 0.23 mg/mL. According to that, the previous treatments were 2208.17, 2094.74, 1294.65, and 1249.22 fold higher than the control (T1). These results may be due to the culture media compositions, such as carbon sources (sugarcane molasses in T6 and combined molasses with vinasse as in T8 till T11), nitrogen sources (ammonium sulphate) and ferric chloride as a mineral element.

These results were in agreement with the results obtained by Tu [41], who reported that the polysaccharide content produced by microbial cells could be enhanced or reduced according to various forms of mineral elements, carbon, and nitrogen sources when added to culture media. Besides, other findings were demonstrated by Banerjee and Nehad [42-43] who mentioned that the two fungal plant pathogens *Alternaria alternate* and *Stemphylium* species can produce a high content of exopolysaccharides when they are cultivated in medium containing mono- and disaccharides such as glucose and sucrose, respectively. Although glucose is an essential carbon source for enhancing biomass and exopolysaccharide production by microbial cells, other saccharides such as fructose, maltose, and starch can serve as main sources. However, rhamnose, as another monosaccharide, has been used as a source of carbon in the cultivation medium of *Fusarium solani* SD5 for the production of extracellular polysaccharides, according to Mahapatra [44]. Moreover, Zeng [45] mentioned that the isolated fungus *Fusarium solani* DO7 from the orchid *Dendrobium officinale* produced two potential polysaccharides, DGS1, and DGS2 when cultivated under solid-state fermentation. These polysaccharides were dominated by vital immunomodulatory and antioxidant activities. Nevertheless, another study by Obruca [46] reported that white-rot basidiomycetes formed from various enzymes, such as cellulases and xylanases, produced by the filamentous fungal strain *Fusarium solani* F-552, are responsible for lignocellulosic material's saccharification, which enhances polysaccharide content and reduces lignin's yield.

3.2.2. Total amino acids and protein content:

The obtained data in Table 3 revealed that the highest amino acid and protein content were recorded by the *Fusarium* strain when grown on T6 as 80.63 and 25.56 mg/mL, respectively, compared to T1 with the content of 10.55 and 0.03 mg/mL, respectively. Accordingly, T6 was folded to T1 with 7.64 and 852.00, respectively.

These results were in agreement with those by Tang [47], who reported that the deficiency of nitrogen sources in the cultivated medium of *Mucor circinelloides* WJ11 led to inhibition of the biosynthesis of amino acids, which caused a reduction in protein expression. Another study, demonstrated by Ferreira [48], revealed that the amino acid composition of Eucalyptus clones was influenced by nitrogen starvation. In the plant root, the contents of arginine, methionine, and proline were reduced, while threonine, tyrosine, alanine, and methionine were decreased in the leaves of that plant due to the limitation of nitrogen content. Another study [49] revealed that the protein was decomposed due to the absence of the nitrogen source ($NaNO_3$) in the cultivated medium of microbial cells. The crude

protein and real protein of marine microalgae *Tisochrysis lutea* were reduced to nitrogen-free medium compared to other concentrations of nitrogen source ($NaNO_3$) of 0.88, 0.66, 0.44, and 0.22 mM, respectively, while the soluble protein was enhanced when exposed to the same treatments.

Table 3: Primary metabolites content in *Fusarium solani* culture cultivated under different conditions

Treatments	Total carbohydrates (mg/mL)	Relative to control	Total amino acids (mg/mL)	Relative to control	Total proteins (mg/mL)	Relative to control
T1	0.23 ± 0.01^{i}	-	10.55 ± 0.53^{g}	-	0.03 ± 0.002^{h}	-
T2	0.22 ± 0.01^{i}	0.95	2.85 ± 0.14^{k}	0.27	0.04 ± 0.002^{h}	1.33
T3	0.74 ± 0.03^{h}	3.22	4.41 ± 0.22^{j}	0.42	0.04 ± 0.002^{h}	1.33
T4	2.19 ± 0.11^{g}	9.52	6.06 ± 0.30^{i}	0.57	0.18 ± 0.01^{g}	6.00
T5	0.84 ± 0.04^{h}	3.65	7.83 ± 0.39^{h}	0.74	0.01 ± 0.001^{h}	0.33
T6	134.68 ± 6.73^{e}	585.56	80.63 ± 4.03^{a}	7.64	25.56 ± 1.28^{a}	852.00
T7	75.50 ± 3.78^{f}	328.26	26.88 ± 1.34^{f}	2.55	16.11 ± 0.81^{f}	537.00
T8	507.88 ± 25.39^{a}	2208.17	60.63 ± 3.03^{b}	5.75	18.30 ± 0.92^{d}	610.00
T9	481.79 ± 24.09^{b}	2094.74	46.25 ± 2.31^{c}	4.38	16.67 ± 0.83^{e}	555.66
T10	287.32 ± 14.37^{d}	1249.22	36.88 ± 1.84^{e}	3.49	20.00 ± 1.00^{b}	666.66
T11	297.77 ± 14.89^{c}	1294.65	40.63 ± 2.03^{d}	3.85	18.89 ± 0.94^{c}	629.66

Data are log means ± standard error (SE), n= 3.

3.3. Effect of media composition on production of secondary metabolites by Fusarium solani

Fusarium sp. are endophytic fungi that can produce many bioactive compounds such as terpenes, polyketides, nonribosomal peptides, and anthraquinones with antimicrobial, anti-inflammatory, and cytotoxic activities. These secondary metabolites are formed during the late growth phase of the producing microorganisms. The synthesis of these metabolites can be influenced by manipulating the type and concentration of the nutrients in the culture medium. The obtained results in Table 4 revealed that there is a great variation in secondary metabolites content, such as total phenols and total flavonoids of *Fusarium solani* during cultivation under different culture media. The total phenols content produced by the fungus was enhanced in T9 (360.09 mg/mL), followed by T8,

T11, and T10 (346.98, 324.17, and 298.22 mg/mL, respectively) compared to the untreated strain T1 (0.84 mg/mL). According to that, the flavonoids content of these treatments was folded to T1 with 656.24, 632.35, 505.53, and 465.06, respectively. These results were equivalent to the HPLC analysis of the active metabolites produced by *Fusarium solani*.

These results may be due to low nitrogen content and high carbon sources such as mono and polysaccharides in a mixed culture of sugarcane molasses and vinasse 50:50%,v/v, in addition to glycerol and ferric chloride that are present in T9, which interfere with the high accumulation of secondary metabolites, especially phenol and flavonoid compounds. These results were in agreement with Shalapy [18], who reported that *Fusarium oxysporum* synthesized high concentrations of phenols and flavonoids at 2.87 and 2.01 µg/mg dry weights, respectively. *Fusarium solani* produces 1.12 and 0.92 µg/mg dry weight when cultivated on Czapek-Dox broth medium, which is supplemented by glucose as a main carbon source and a variety of nitrogen sources. In addition, the Kroneikiolive cultivar produced a maximum content of total phenols when infected by root rot pathogens *Fusarium solani* and *Fusarium konzum* at 0.781 and 0.339 mg/g fresh weight, respectively, compared to the control (un-inoculated) with a concentration of 0.331 mg/g fresh weight [50].

Another study was demonstrated by Ming [51], who mentioned that total phenols were enhanced in the leaves, pseudostems, and roots of berangan banana plants (274.0, 263.1, and 362.5%, respectively) when infected by the fungal strain *Fusarium oxysporum*. Also, total flavonoids were recorded at the highest percentage (184.9, 222.2, and 206.7%, respectively) compared to healthy plants. Besides, the total phenolic content revealed by the endophytic fungus *Fusarium proliferatum* (ACQR8) was 78.02 µg GAE/mg, while the flavonoids content was 85.53 µg RE/mg when cultivated on potato dextrose broth [52]. Moreover, the highest phenolic content was registered by wheat bran fermented with *Aspergillus niger* at 10,707.5 µg/g, followed by *Aspergillus awamori*, *Aspergillus oryzae* with concentrations of 5362.1 and 7462.65 µg/g, respectively, compared to the unfermented sample (wheat bran) at 1531.5 µg/g [53]. Nevertheless, a finding was done by Gulsunoglu [54], who reported that fermented apple peel with *Aspergillus niger* ZDM2 produced high levels of total phenols and flavonoids of 1440 and 382 mg/g dm, respectively, followed by *Aspergillus tubingensis* ZDM1, which revealed 1202 and 495 mg/g dm, respectively, which may be due to mold fermentation. Total phenolic compounds were extracted from the leaves of cauliflower fermented with *Aspergillus sojae*as at a concentration of 321 mg/100g fresh weight compared to unfermented plant leaves at a concentration of 113 mg/100g fresh weight [55].

Table 4 : Secondary metabolites content of of *Fusarium solani* culture that cultivated under different culture

Treatments	Total phenols (mg/mL)	Relative to control	Total flavonoids (mg/mL)	Relative to control
T1	0.84 ± 0.04^{g}	-	0.17 ± 0.01^{hi}	-
T2	0.13 ± 0.01^{g}	0.15	0.09 ± 0.01^{j}	0.53
T3	1.14 ± 0.06^{g}	1.36	0.59 ± 0.03^{g}	3.47
T4	2.08 ± 0.10^{g}	2.48	0.63 ± 0.03^{g}	3.71
T5	1.76 ± 0.09^{g}	2.09	0.54 ± 0.03^{g}	3.18
T6	147.23 ± 7.36^{f}	175.27	41.41 ± 2.07^{f}	243.59
T7	238.53 ± 11.93^{e}	283.96	80.31 ± 4.02^{e}	472.41
T8	346.98 ± 17.35^{b}	413.07	107.50 ± 5.38^{b}	632.35
T9	360.09 ± 18.00^{a}	428.68	111.56 ± 5.58^{a}	656.24
T10	298.22 ± 14.91^{d}	355.02	79.06 ± 3.95^{e}	465.06
T11	324.17 ± 16.21^{c}	385.92	85.94 ± 4.30^{c}	505.53

Data are log means ± standard error (SE), n= 3.

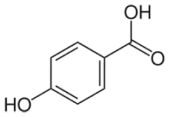
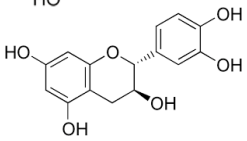
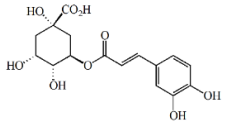
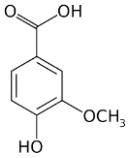
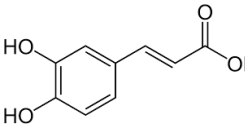
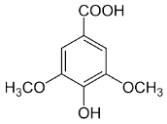
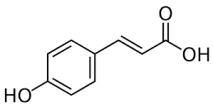
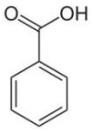
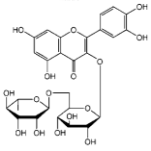
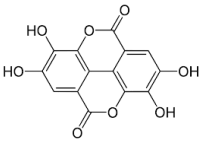
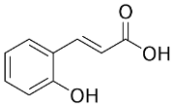
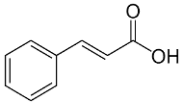
3.4. HPLC analysis

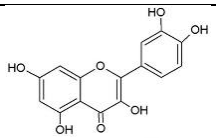
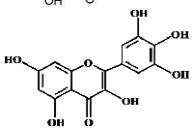
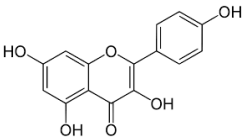
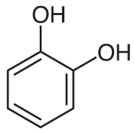
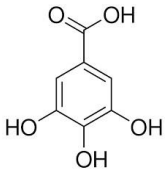
The HPLC analysis of vital secondary metabolites produced by the endophytic fungus *Fusarium solani* cultivated on different treatments (T8, T9, T10, and T11) compared to untreated strain T1 is shown in Table 5. The highest content of secondary metabolites reached 48.02 mg/L in T9, followed by T10, T8, and T11, with concentrations of 19.25, 11.82, and 9.91 mg/L, respectively, compared to control (T1) at 0.11 mg/L. These results may be due to media composition that affected the production of bioactive metabolites such as kampherol synthesized by a fungal strain when cultivated on T9 (combined molasses and vinasse 50:50% v/v, glycerol, $FeCl_3$ and $(NH_4)_2SO_4$) compared to others. Also, quercetin exhibited the maximum concentration in the same treatment (T9) at 18.00 mg/L, followed by T8 at 4.51 due to the absence of a nitrogen source in T8. These results were in agreement with Kristensen [56], who reported that polyketides produced from *Fusarium solani* were affected by different carbon and nitrogen

sources found in a cultivated medium, such as bostrycoidin, which was produced in the presence of maltose and ammonium tartrate, while fusarubin, anhydro fusarubin, and javanicin were formed in media containing sucrose and sodium nitrate with different concentrations. Another finding by Chimón [7] demonstrated that the highest content of useful metabolites such as monoterpenes, sesquiterpenes, and naphthoquinone pigments was produced by *Fusarium verticillioides* when submerged medium contained fructose, followed by lactose, and xylose. Nevertheless, *Fusarium oxysporum* can be used in many pharmaceutical applications due to the biosynthesis of some bioactive metabolites such as vanillin, gallic acid, chlorogenic acid, ferulic acid, gallate, catechin, coumaric acid, naringenin, kaempferol, daidzein, and rutin compared to *Fusarium solani,* which produced the same profile with different concentrations except catechin, coumaric acid, rutin, and kaempferol were absent, while ellagic acid was present [18].

According to Song [57], *Fusarium decemcellulare* F25 is a promising source of bioactive metabolites that synthesize pentaene diacid, isocoumarin, and pyrrolidinone derivatives when grown on a rice-based medium. Moreover, a variety of secondary compounds, such as emodin, fusaisocoumarin A, and sesquiterpenoid phytohormone abscisic acid, were extracted from the endophytic fungus *Fusarium verticillioides* WF18 [58]. Also, the ethyl acetate extract of *Fusarium prolifertatum* ACQR8 revealed active metabolite as 2,4-Di-tert-butylphenol with a concentration of 16.94% [52]. In addition to that, *Fusarium chlamydosporum* exhibited various secondary metabolites, such as four pyrones, three cyclohexadepsi peptides, and three indole derivatives [59]. A study was demonstrated by Khan [60], who revealed that *Fusarium solani* isolated from *Cassia alata* Linn. exhibited a variety of active metabolites, for instance, anhydrofusarubin, 3-deoxyfusarubin, fusarubin, bostrycoidin, ergosterol, 3,5,9-trihydroxyergosta-7,22-diene-6-one, and 4-hydroxybenzaldehyde, when cultivated on potato dextrose agar medium for 28 days. Moreover, inoculated *Triticum aestivum* (winter wheat) with the fungus *Fusarium culmorum* revealed the highest content of various secondary metabolites such as kaempferol, luteolin, naringenin, quercetin, rutin, and vitexin with a concentration of 0.81, 0.44, 0.91, 0.48, 0.65, and 0.80 mg/Kg, respectively, compared to the control (non-inoculated) at 0.70, 0.36, 0.60, 0.31, 0.29, and 0.65 mg/Kg, respectively [61].

Table 5 : HPLC analysis of phenolic compounds extracted from *Fusarium solani* cultivated on different culture media

SN	RT	Chemical compound	Chemical structures	T (mg/L)	T8 (mg/L)	T9 (mg/L)	T10 (mg/L)	T11(mg/L)	Biological activity	Reference
1	6.90	p-Hydroxy benzoic acid		ND	ND	0.91	0.48	0.32	Antioxidant and antibacterial activities	[62]
2	7.49	Catechin		ND	0.06	0.20	0.13	0.07	Antioxidant and antibacterial activities	[63]
3	8.49	Chlorogenic acid		ND	0.24	0.76	0.37	0.28	Antioxidant and antibacterial activities	[64]
4	9.01	Vanillic acid		ND	1.33	5.68	2.75	1.36	Antioxidant and antibacterial activities	[65-66]
5	9.73	Caffeic acid		0.07	0.53	1.31	0.58	0.42	Antioxidant	[67]
6	10.5	Syringic acid		0.004	ND	ND	0.05	ND	Antioxidant and antibacterial activities	[68]
7	12.1	p-Coumaric acid		ND	ND	0.15	0.12	ND	Antioxidant and antibacterial activities	[69]
8	12.8	Benzoic acid		ND	ND	ND	0.23	ND	Antibacterial	[70]
9	14.6	Rutin		ND	1.45	5.62	3.12	1.93	Antioxidant	[71]
10	15.2	Ellagic acid		ND	ND	0.18	0.16	0.11	Antioxidant	[72]
11	15.9	O-Coumaric acid		ND	0.14	0.31	0.11	ND	Antioxidant	[73]
12	19.2	Cinnamic acid		ND	ND	0.09	0.06	ND	Antioxidant and antibacterial	[74]

SN	RT	Chemical compound	Chemical structures	T (mg/L)	T8 (mg/L)	T9 (mg/L)	T10 (mg/L)	T11(mg/L)	Biological activity	Reference
13	19.8	Quercitin		ND	4.51	18.00	ND	ND	Antioxidant and antibacterial	[75]
14	21.6	Myricetin		ND	3.25	11.74	10.59	5.09	Antioxidant and antibacterial	[57]
15	23.1	Kampherol		ND	ND	1.86	ND	ND	Antioxidant and antibacterial	[76]
16	4.75	Catechol		0.04	ND	ND	0.50	ND	Antibacterial	[77]
17	2.75	Quinol		ND	0.12	0.20	ND	0.06	Antioxidant and antibacterial	[78-79]
18	3.09	Gallic acid		ND	0.19	1.01	ND	0.27	Antioxidant and antibacterial	[80]
Total bioactive compounds produced by *Fusarium solani* (mg/L)				0.11	11.82	48.0	19.25	9.91		
Percentage of antioxidant compounds (%)				63.64	100.0	100.0	96.21	100.00		
Percentage of antibacterial compounds (%)				36.36	82.06	84.5	79.38	75.18		

*RT (Retention time)

3.5. Antioxidant activity

The results mentioned in Fig. 1 revealed the antioxidant activity of *Fusarium solani* grown on various culture media using the DPPH assay. The highest scavenger free radical was shown by T11 at 84.90%, followed by T10, T8, and T9 with concentrations of 84.00, 82.90, and 78.20%, respectively, compared to the untreated strain (T1) at 56.80%. While the ABTs assay showed T9 registered the highest antioxidant content with a concentration of 67.30% compared to control T1 with 59.90%, as recorded in Fig. 2. The lowest scavenging free radical was T2 (45.40%) compared to others. These results may be due to the presence of bioactive compounds extracted from *Fusarium solani* grown on T8, T9, T10, and T11 compared to control T1, as mentioned in Table 5, that showed vital antioxidant activity with a percentage of 100.00, 100.00, 96.21, and 100.00 %, for T8, T9, T10, and T11, respectively, compared to control T1 at 63.64%. These results were in agreement with Khan [60], who demonstrated that

fusarubin extracted from *F. solani* showed potential antioxidant activity with IC_{50} values of 34.8 µg/mL, followed by 4-hydroxybenzaldehyde, anhydrofusarubin and bostrycoidin with the content of 28.9, 12.4, and 1.6 µg/mL, respectively, compared to positive control IC_{50} values such as BHA 1.2 µg/mL, trolox 1.3 µg/mL, and ascorbic acid 1.5 µg/mL.

Several studies have discussed a substantial correlation between quinone derivatives and the antioxidant activities of endophytic and related Actinomycetes extracts [81-82]. The DPPH scavenging assay of extracted fractions of *Alternaria alternata* achieved the highest antioxidant activity when compared with α-tocopherol; that activity refers to the presence of the benzoxazole derivatives [83]. Sun [84] described that *Fusarium oxysporum* GU-7 showed potential antioxidant activity because of the presence of the coumarins scopoletin and fraxetin. Nevertheless, *Fusarium* sp. isolate OQ-Fus-2-F, which was isolated from *Euphorbia* sp. Stem, exhibited the maximum IC_{50} values in ABTS with a concentration of 37.5 µg/mL, due to the presence of some potential active compounds as alkaloids, steroids, and terpenoids when cultivated on malt extract glucose medium [85]. According to Shalapy [18], *Fusarium oxysporum* can be used as a potential antioxidant agent because of its abundant content of phenosl and flavonoids. The methanolic extract of *F. lateritium* showed free radical scavenging activity with a concentration of 29.95%, which was significantly lower than that of *Xylaria* sp. at 95.82% because of the appearance of potential phenolic compounds in the *Xylaria*crude extract [86]. Another finding was demonstrated by Elshahawy [87], who revealed that *Fusarium oxysporum* presented antioxidant activity due to the presence of bioactive compounds such as phenolics and flavonoids.

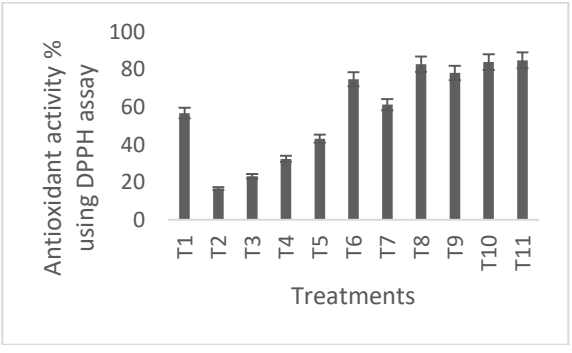


Fig. 1. Antioxidant activity (%) of ethanolic extracts of *Fusarium solani* cultivated under different culture media after 11 days against DPPH.

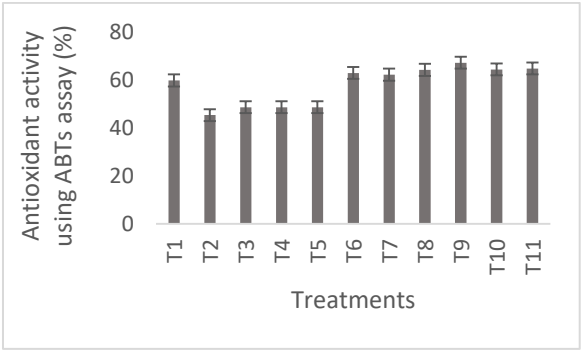


Fig. 2. Antioxidant activity (%) of ethanolic extracts of *Fusarium solani* cultivated under different culture media after 11 days against ABTS.

3.6. Anti-microbial activity

The results in Tables 6 and 7 showed the antimicrobial activity of *Fusarium solani* against various bacterial strains, such as *Staphylococcus aureus, Escherichia coli, Salmonella typhi*and, and *Bacillus cereus*. The highest zone of inhibition was recorded by the *Fusarium* strain when cultivated on T9 against *Staphylococcus aureus* at 16.50 mm, compared to control T1 at 9.50 mm which was 2.10-fold higher than of the untreated strain (T1) and 1.46 times higher than the most common standard tetracycline. These may be due to the presence of eleven bioactive compounds, which exhibited the maximum percentage of antibacterial activity of the fungal strain on T9 at 84.55%, followed by T8, T10 and T11 with the content of 82.06, 79.38, and 75.18%, respectively, compared to T1 at 36.36% as mentioned in Table 5. Also, the natural source of quercetin produced by *Fusarium solani* in T9, as shown in Table 5, acts as a potent inhibitor against penicillin-binding protein-2a (PBP-2a) of *Staphylococcus aureus,* as mentioned in Table 7 and Figure 3, which exhibited the highest antibacterial activity. These results were in agreement with Shi [88], who demonstrated that *Fusarium* sp. TP-G1 had antimicrobial activity against MRSA, *Staphylococcus aureus,* and *Acinetobacter baumannii* due to the presence of some potential secondary metabolites such as trichosetin, beauvericin, enniatin, fusaric acid, and dehydrofusaric acid in crude fermentation extracts of the *Fusarium* strain.

In addition to that, Yuniati [89] revealed that two antibacterial compounds, 1,8-dihydroxy-3-methoxy-6-methylanthracene-9,10-dione, and 1,3,8-trihydroxy-6-methoxyanthracene-9,10-dione were isolated from *Fusarium* sp. and showed necessary antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhi*, *Pseudomonas aeruginosa,* and *Streptococcus mutans*. Nevertheless, Chutulo [90] reported that

Fusarium oxysporum can form therapeutic agents against pathogenic microorganisms due to its antimicrobial activity against gram-positive and gram-negative bacteria. Moreover, bioactive compounds such as isocoumarin derivatives, pentaene diacid, and pyrrolidinones isolated from *Fusarium decemcellulare* F25 showed a potential antifungal activity against *Colletotrichum musae* [91]. A study by Singh [52] revealed that the endophytic fungus *Fusarium proliferatum* ACQR8 exhibited a variety of secondary metabolites such as phenolics, terpenoids, and unsaturated alkenes that showed the most promising antifungal and antibacterial activities against phytopathogenic species. Nevertheless, fusarielins and their derivatives extracted from *Fusarium* species exhibited mild antibacterial effects against *Staphylococcus aureus* [92].

Another finding, altersolanol, fusaraichromenone, 4-hydroxydihydronorjavanicin, and 5-hydroxy-7-methoxy-2-isopropylchromone, as active metabolites produced from *Fusarium* species, showed adverse antimicrobial activity. Besides, tyrosol and beauvericin extracted from the filamentous fungus *Fusarium solani* showed potential antifungal activity against pathogenic *Cladosporium* strains [1]. Also, bikaverin formed from *Fusarium oxysporum* CCT7620 that was cultivated in a rice medium exhibited antimicrobial activity. The crude extract of *F. proliferatum* (ACQR8) exhibited a broad spectrum of antibacterial activity against gram-positive and gram-negative bacteria such as *Staphylococcus aureus*, *Shigella boydii*, *Salmonella typhi*, *Aeromonas hydrophila*, *Escherichia coli*, *Enterococcus faecalis*, and *Klebsiella pneumonia*. The highest zone of inhibition was recorded by *Shigella boydii* with a concentration of 23.0 mm [52]. Also, 3-deoxyfusarubin-isolated endophytic fungus *Fusarium solani*showed significant antibacterial activity against *Bacillus megaterium*, *Staphylococcus aureus*, *Pseudomonas aeruginosa,* and *Escherichia coli* with zones of inhibition of 34, 26, 24, and 25 mm, respectively, compared to other active compounds anhydrofusarubin, 4-hydroxybenzaldehyde, bostrycoidin, and fusarubin [60].

Table 6.
Antibacterial activity as agar disc diffusion assay (mm) of *Fusarium solani* extracts cultivated under different culture conditions against gram-negative bacteria

Treatments	Bacterial species					
	Escherichia coli	Relative to control (T1)	Relative to standard	*Salmonella typhi*	Relative to control (T1)	Relative to standard
T1	11.00 ± 0.55^{d}	-	0.48	10.50 ± 0.53^{b}	-	1.03
T2	12.80 ± 0.64^{b}	1.16	0.56	7.80 ± 0.39^{i}	0.74	0.76
T3	11.00 ± 0.55^{d}	1.00	0.48	9.30 ± 0.47^{f}	0.89	0.91
T4	12.00 ± 0.60^{c}	1.09	0.52	11.00 ± 0.55^{a}	1.05	1.08
T5	8.50 ± 0.43^{i}	0.77	0.37	10.50 ± 0.53^{c}	1.00	1.03
T6	10.30 ± 0.52^{e}	0.94	0.45	8.00 ± 0.40^{h}	0.76	0.78
T7	11.00 ± 0.55^{d}	1.00	0.48	9.00 ± 0.45^{g}	0.86	0.88
T8	8.30 ± 0.42^{j}	0.75	0.36	9.00 ± 0.45^{g}	0.86	0.88
T9	9.00 ± 0.45^{g}	0.82	0.39	9.50 ± 0.48^{e}	0.90	0.93
T10	8.80 ± 0.44^{h}	0.80	0.38	7.50 ± 0.38^{j}	0.71	0.74
T11	9.80 ± 0.49^{f}	0.89	0.43	7.00 ± 0.35^{k}	0.67	0.69
Tetracycline		23.00 ± 1.15^{a}			10.20 ± 0.51^{d}	

Data are log means ± standard error (SE), n= 3.

Table 7
Antibacterial activity as agar disc diffusion assay (mm) of fungal extracts cultivated under different culture conditions against gram-positive bacteria

Treatments	Bacterial species					
	Bacillus cereus	Relative to control (T1)	Relative to standard	*Staphylococcus aureus*	Relative to control (T1)	Relative to standard
T1	7.50 ± 0.38^{h}	-	0.75	8.00 ± 0.40^{i}	-	0.69
T2	10.00 ± 0.50^{d}	1.33	1.00	11.00 ± 0.55^{e}	1.38	0.96
T3	10.50 ± 0.53^{b}	1.40	1.05	11.00 ± 0.55^{e}	1.38	0.96
T4	14.00 ± 0.70^{a}	1.86	1.40	14.00 ± 0.70^{b}	1.75	1.22
T5	8.80 ± 0.44^{e}	1.17	0.88	11.80 ± 0.59^{c}	1.48	1.03
T6	10.00 ± 0.50^{d}	1.33	1.00	10.30 ± 0.52^{f}	1.29	0.89
T7	8.30 ± 0.42^{g}	1.11	0.83	7.50 ± 0.38^{j}	0.94	0.65
T8	8.80 ± 0.44^{e}	1.17	0.88	10.00 ± 0.50^{g}	1.25	0.87
T9	8.50 ± 0.43^{f}	1.13	0.85	16.80 ± 0.84^{a}	2.10	1.46
T10	8.30 ± 0.42^{g}	1.11	0.83	8.80 ± 0.44^{h}	1.10	0.77
T11	10.30 ± 0.52^{c}	1.37	1.03	8.00 ± 0.40^{i}	1.00	0.69
Tetracycline		10.00 ± 0.50^{d}			11.50 ± 0.58^{d}	

Data are log means ± standard error (SE), n= 3.

3.7. Molecular docking

Molecular docking is a type of computational modeling of complexes that depends on the interaction between two or more molecules. The results in Table 8 and Figs. 3a, b, and c revealed that molecular binding between quercetin and the active site (acyl-Penicillin binding protein 2a) from methicillin-resistant *Staphylococcus aureus* showed binding affinity of -16.22 Kcal/mol and tetracycline as - 21.32 Kcal/mol compared to co-crystalized ligand (penicillin G) with an energy score of -18.97 Kcal/mol. These results may be due to the presence of two hydroxyl groups in the *meta* position of the benzene ring (A) and two hydroxyl groups in the *ortho* position of the benzene ring (B) in the quercetin compound, which were significant for the anti-methicillin-resistant *Staphylococcus aureus* activity as shown in Fig. 3c. These results were in agreement with Alves [93], who reported that the presence of two (OH) groups in *ortho* and *para* positions of the benzene ring and OCH_3 groups in the *meta* position and carboxylic acid were vital for anti-MRSA activity.

Another finding was demonstrated [91], who suggested that coumarin derivatives as compound 18 exhibited the greatest binding energy against the penicillin-binding protein of MRSA at − 91322 Kcal/mol compared to quinazolinone−71098 Kcal/mol. Nevertheless, natural bioactive compounds such as luteolin, kaempferol, chlorogenic acid, sinigrin, zingiberene, 1-Methyl-4-(6-methylhepta-1,5-dien-2-yl) cyclohex-1-ene, and curcumin presented significant binding energies against methicillin-resistant *Staphylococcus aureus* (MRSA) infections as −8.6, −8.4, −8.2, −7.5, −7.4, −7.3, and −7.2 Kcal/mol, respectively [94]. In addition, plant-based phenolic compounds act as antibacterial agents

against the MRSA [95]. Moreover, quercetin 3-O-rutinoside displayed a vital PBP2a inhibition of -91.56 Kcal mol^{-1}, followed by quercetin -78.75 Kcal mol^{-1} compared to the standard antibiotic ceftobiprole -73.17 Kcal mol^{-1}. Besides, Verma [96] mentioned that various flavonoids such as naringin, hesperidin, neohesperidin, didymin, and icariin yielded the best docking score with PBP-2a of *S. aureus* with concentrations of -9.6, -9.2, -9.0, -8.8, and -8.6 Kcal/mol, respectively, compared to the most common to standard inhibitor, methicillin, at -7.1 Kcal/mol. According to Masumi [97], natural flavonoids such as kaempferol 3-rutinoside-7-sophoroside presented the highest binding affinity with SauPBP2a at −14.4 Kcal/mol, followed by rutin−9.7 Kcal/mol. Nevertheless, streptomyces is an essential antibiotic-producing bacterium because of the bioactive compound 1-acetyl-β-carboline, which displayed the lowest binding energy with PBP2a such at -7.12 Kcal/mol compared to ceftaroline at -6.32 Kcal/mol [98].

Table 8
Docking results of quercetin compared to tetracycline with the *Staphylococcus aureus* active site PBP2a

Compound name	Binding energy (Kcal/mol)	Amino acid residue
Quercetin	- 16.22	Tyrosine 446
		Serine 598
		Threonine 600
		Asparagine 464
Tetracycline	- 21.32	Threonine 600
		Serine 598

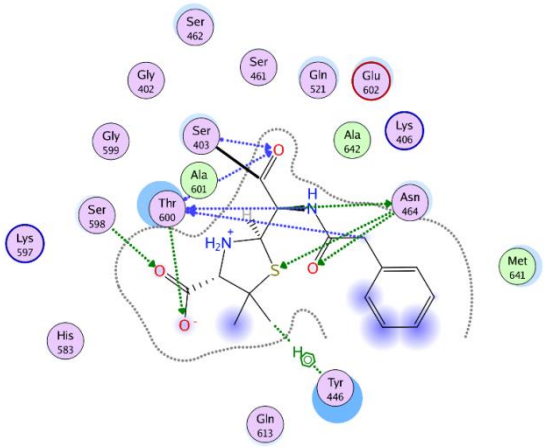


Fig. 3a. 2D structure of penicillin Ginteracted with the *Staphylococcus aureus* active site PBP2a.

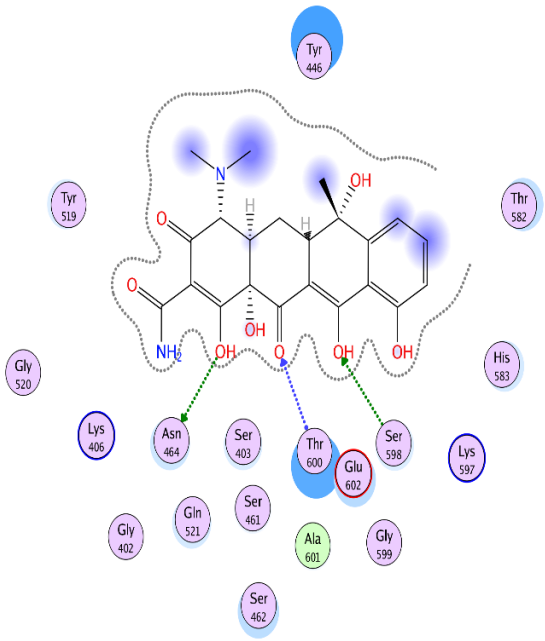


Fig. 3b. 2D structure of tetracyclineinteracted with the *Staphylococcus aureus* active site PBP2a.

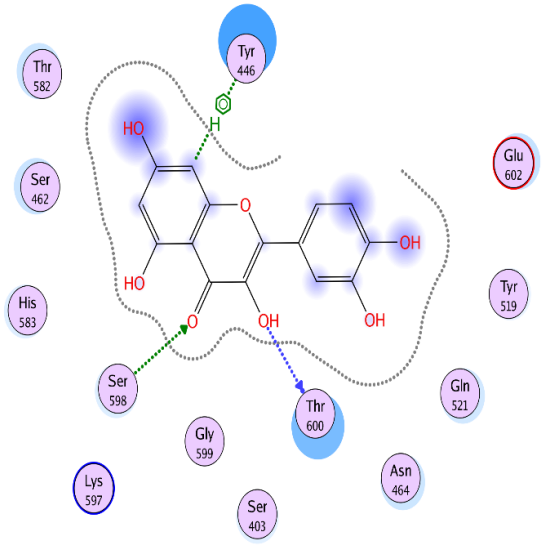


Fig. 3c. 2D structure of quercetin interacted with the *Staphylococcus aureus* active site PBP2a.

Conclusion

Several priorities stand out for ongoing research to use industrial by-products as low-cost cultural media. This study focused on using sugarcane by-products (bagasse, molasses, and vinasse) in the growth culture of *Fusarium solani,* which reflected a significant increase in growth levels, primary metabolites, total phenols, and flavonoids content. According to the antioxidant testing, T9 and T11 exhibited the highest free radical scavenging activity as they have a high concentration of active metabolites when analyzed by HPLC. Also, the fungus *Fusarium* showed an increase in its antibacterial activity against *Staphylococcus aureus*. For future studies, it is necessary to give priority to focus on the various uses of industrial wastes in increasing the production of vital compounds from microorganisms.

4. Conflicts of interest

There are no conflicts to declare.

5. Funding sources

Not Applicable.

6. Acknowledgments

Not Applicable.

7. References

[1] Vieira N, Cortelo P, Castro-Gamboa I (2020) Rapid qualitative profiling of metabolitespresent in *Fusarium solani*, a rhizosphericfungus derived from *Senna spectabilis*, usingGC/MS and UPLC-QTOF/MSE techniquesassisted by UNIFI information system. European journal of mass spectrometry. 281-291. DOI: 10.1177/1469066720922424.

[2] Xu M, Huang Z, Zhu W, Liu Y, Bai X, Zhang H (2023) *Fusarium*-derived secondary metabolites with antimicrobial effects. Molecules. (28): 1-15. https://doi.org/10.3390/molecules28083424.

[3] Keller N (2019) Fungal secondary metabolism:regulation, function and drug discovery. Microbiology. 17: 167-180. https://doi.org/10.1038/s41579-018-0121-1.

[4] Devi R, Kaur T, Guleria G, Rana K, Kour D, Yadav N, Yadav A, Saxena A (2020) Fungal secondary metabolitesand their biotechnologicalapplications for human health. New and future developments in microbial biotechnology and bioengineering. 147-161. https://doi.org/10.1016/B978-0-12-820528-0.00010-7.

[5] Knox B, Keller N (2015) Biosynthesis and molecular genetics offungal secondary metabolites. Biosynthesis and molecular genetics of fungal secondary metabolites. 67–79.

[6] Kristensen S, Pedersen T, Nielsen M, Wimmer R, Muff J, Sørensen J (2021) Production and selectivity of key fusarubins from *Fusarium solani* due to media composition. Toxins. 13:1-12. https://doi.org/10.3390/toxins13060376.

[7] Achimón F, Krapacher C, Jacquat A, Pizzolitto R, Zygadlo J (2021) Carbon sources to enhance the biosynthesis of useful secondarymetabolites in *Fusarium verticillioides* submerged cultures. World journal of microbiology and biotechnology. 37(78): 1-11. https://doi.org/10.1007/s11274-021-03044-z.

[8] Wani A, Rahayu F, Fauziah L, Suhara C (2023) Advances in safe processing of sugarcane and bagasse for the generation ofbiofuels and bioactive compounds. Journal of agriculture and

food research. 1-12. https://doi.org/10.1016/j.jafr.2023.100549.

[9] Tao J, An F, Pan Z, Lu Y (2018) Stimulatory effects of sugarcane molasses on Fumigaclavine C biosynthesis by *Aspergillus fumigatus* CY018 via biofilm enhancement. Journal of microbiolog and biotechnology. 28(5): 748–756. https://doi.org/10.4014/jmb.1801.01073.

[10] Ogawa A, Wakisaka Y, Tanaka T, Sakiyama T, Nakanishi K (1995) Production of kojic acid by membrane-surface liquid cultureof *Aspergillus oryzae* NRRL484. Journal of fermentation and bioengineering. 80(1): 41-45.

[11] Aziani G, Terenzi H, Jorge J, Guimarães L (2012) Production of Ffructooligosaccharides by *Aspergillus phoenicis* biofilm on polyethylene as inert support. Food technology and biotechnology. 50 (1): 40–45.

[12] Hailei W, Ping L, Yufeng L, Zhifang R, Gang W (2012) Overproduction of a potential red pigment by a specificself-immobilization biomembrane-surface liquid cultureof *Penicillium novae-zeelandiae*. Bioprocess and biosystems engineering. 35: 1407–1416. DOI 10.1007/s00449-012-0729-x.

[13] Gamarra N, Villena G, Gutiérrez-Correa M (2010) Cellulase production by *Aspergillus niger* in biofilm,solid-state, and submerged fermentations. Applied microbiology and biotechnology. 87: 545–551. DOI 10.1007/s00253-010-2540-4.

[14] Ansilago M, Ramos M, Mussury R, de Carvalho E (2021) Enhancing secondary metabolite production by *Chlorella sorokiniana* using analternative medium with vinasse. Research, society and development journal. 10(5): 1-11. DOI: http://dx.doi.org/10.33448/rsd-v10i5.15237.

[15] Deseo M, Elkins A, Rochfort S, Kitchen B (2020) Antioxidant activity and polyphenol composition of sugarcane molasses extract. Food chemistry. 1-39. doi: https://doi.org/10.1016/j.foodchem.2020.126180.

[16] Ji J, Yang X, Flavel M, Shields Z, Kitchen B (2019) Antioxidant and Anti-Diabetic Functions of aPolyphenol-Rich Sugarcane Extract. Journal of the American College of Nutrition. 1-11. https://doi.org/10.1080/07315724.2019.1587323.

[17] Scalbert A, Manach C, Morand C, Remesy C, Jimenez L (2005) Dietary polyphenols and the prevention of diseases. Critical reviews in food science and nutrition. 45: 287–306. DOI: 10.1080/1040869059096.

[18] Shalapy N, Kang W (2022) *Fusarium oxysporum&Fusarium solani*: Identification, characterization, and differentiation the fungal phenolic profiles by HPLC and the fungal lipid profiles by GC-MS. Journal of food quality. 1-12. https://doi.org/10.1155/2022/4141480.

[19] Menezes B, Solidade L, Conceição A, Junior M, Leal P, de Brito E, Canuto K, Mendonça S, de Siqueira F, Marques L (2020) Pigment production by *Fusarium solani*BRM054066 and determination of antioxidantand anti-inflammatory properties. AMB Express. https://doi.org/10.1186/s13568-020-01054-y.

[20] Lobo V, Patil A, Phatak A, Chandra N (2010) Free radicals, antioxidants and functional foods: Impacton human health. Pharmacognosy reviews. 4: 118-126. DOI: 10.4103/0973-7847.70902.

[21] Jiang C, Li J, Zhang J, Jin X, Yu B, Fang J, Wu Q (2019) Isolation, identification, and activity evaluation of chemical constituents from the soil fungus *Fusarium avenaceum* SF-1502 and endophytic fungus *Fusarium proliferatum* AF-04. Journal of agricultural and food chemistry. 1-36. DOI: 10.1021/acs.jafc.8b05576.

[22] Brown W (1924) Two mycological methods: II- A method of isolating single strains of fungi by cutting out a hyphal tip. Oxford journal (38): 402-404.

[23] Yang C, Chang K, Yin M, Huang H,(1998) Methods forthe determination of the chlorophylls and their derivatives. Taiwania. 43(2): 116-122.

[24] Dubois M, Gilles K, Hamilton J, Rebers P, Smith F (1956) Colorimetric method for determination of sugars and related

substances.

[25] Lee Y, Takahashi T (1966) An Improved Calorimetric Determination of amino acids with the use of ninhydrin. Analytical biochemistry (14): 71-77.

[26] Bradford M (1976) Rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Analytical biochemistry (72): 248-254.

[27] Halliwel B, Guttridge J (1989) Free radicals in biology and medicion. 2nd ed. London: Clarendon Press.

[28] Zhishen J, MengCheng T, Jianming W(1999) The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chemistry (64): 555-559.

[29] Johnsson P, Kamal-Eldin A, Lundgren L, Aman P (2000) HPLC method for analysis of secoisolariciresinol diglucoside in flaxseeds. Journal of agricultural and food chemistry. 48 (11): 5216-5219.

[30] Yen G, Chen H (1995) Antioxidant activity of various tea extracts in relation to their antimut agenicity. Journal of agricultural and food chemistry. 43: 27-32.

[31] Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-evans C (1999) Antioxidant activity applyingan improved ABTS radical cation decolorization assay. Free radical biology and medicine. 26: 1231–1237.

[32] Bauer A, Kirby W, Sherris j, Turck M (1966) Antibiotic susceptibility testing by a standardized single disk method. American journal of clinical pathology. 45 (4): 493–496.

[33] Kant K, Lal U R, Kumar A, Ghosh M (2019) A merged molecular docking, ADME-T and dynamics approaches towards the genus of Arisaema as herpes simplex virus type 1 and type 2 inhibitors. Comput. Biol. Chem. 78: 217–226.

[34] Nafady N, Bagy M, Abd-Alla M, Morsy F, Mahmoud G (2016) Bio-enrichment of β-carotene production by *Fusarium camptoceras* grown on sugarcane molasses using statistical approach. International journal of advanced biotechnology and research. 7(3): 1186-1203.

[35] Parra-Rivero O, de Barros M, Prado M, Gil J, Hornero-Méndez D, Zacarías L, Rodrigo M, Limón M, Avalos J (2020) Neurospora xanthin overproduction by *Fusarium fujikuroi* and evaluation of its antioxidant properties. Antioxidants. 9: 1-17: doi:10.3390/antiox9060528.

[36] Avalos J, Pardo-Medina J, Parra-Rivero O, Ruger-Herreros M, Rodríguez-Ortiz R, Hornero-Méndez D, Limón M (2017) Carotenoid Biosynthesis in *Fusarium*. Journal of fungi. 1-16: 3(39). doi:10.3390/jof3030039.

[37] Wit M, Jabłońska E, Mirzwa-Mróz E, Ochodzki P, Warzecha R, Lewandowska A, Wakuliński W (2020). Variability of carotenoid biosynthesis in meiotic offspring of *Fusarium Temperatum* strains. International journal of sciences: Basic and applied Research. 50(1): 156-166.

[38] Rodríguez-Ortiz R, Michielse C, Rep M, Limón M, Avalos J (2012) Genetic basis of carotenoid overproduction in *Fusarium oxysporum*. Fungal genetics and biology. 49: 684–696. http://dx.doi.org/10.1016/j.fgb.2012.06.007.

[39] Cheng Y, Yang C (2016) Usingstrain*Rhodotorula mucilaginosa*toproducecarotenoidsusing foodwastes. Journal of the taiwan instituteof chemical engineers. 1–6. http://dx.doi.org/10.1016/j.jtice.2015.12.027.

[40] Szotkowski M, Byrtusova D, Haronikova A, Vysoka M, Rapta M, Shapaval V, Marova I (2019) Study of metabolic adaptation of red yeasts to waste animal fat substrate. Microogranisms. 7: 1-28. doi:10.3390/microorganisms7110578.

[41] Tu Z, Liu L, Lin W, Xie Z, Luo J (2018) Potential of using sodium bicarbonate as external carbon source to cultivate microalga in non-sterile condition. Bioresource technology journal. 109-115.

[42] Banerjee D, Jana M, Mahapatra S (2009) Production of exopolysaccharide by endophytic Stemphylium sp. Micologia aplicada international journal. 57-62.

[43] Nehad E, El-Shamy A (2010) Physiological studies on the production of exopolysaccharide by Fungi. Agriculture and biology journal. 1303-1308.

[44] Mahapatra S, Banerjee D (2013) Optimization of a bioactive exopolysaccharide production from endophytic *Fusarium solani* SD5. Carbohydrate Polymers journal. 627–634.

[45] Zeng Y, Yang H, Wu X, Peng F, Huang Z, Pu L, Zong M, Yang J, Lou W (2019) Structure and immunomodulatory activity of polysaccharides from Fusarium solani DO7 by solid-state fermentation. International journal of biological macromolecules. 568-575.

[46] Obruca S, Marova I, Matouskova P, Haronikova A, Lichnova A (2012) Production of lignocellulose-degrading enzymes employing Fusarium solani F-552. Folia Microbiologica journal. (57): 221–227.

[47] Tang X, Zan X, Zhao L, Chen H, Chen Y, Chen W, Song Y, Ratledge C (2016) Proteomics analysis of high lipid-producing strain *Mucor circinelloides* WJ11: an explanation for the mechanism of lipid accumulation at the proteomic level. Microbial cell factories journal. 35:15.

[48] Ferreira E, Novais R, Dubay G (2016) Nitrogen supply affects root and shoot amino acid composition in Eucalyptus clones. Austr. J. Crop Sci. 10:3.

[49] Almutairi A (2020) Improvement of chemical composition of *Tisochrysis Lutea* grown mixotrophically under nitrogen depletion towards biodiesel production. Molecules journal. 25: 1-14. doi:10.3390/molecules25204609.

[50] Sabet K, Ghanem G, Radwan F, Allam L (2016) Olive cultivar reaction and biochemical changes due to infection by root rot pathogens. The egyptian journal of phytopathology. 44(2): 261-282.

[51] Ming F, Razali Z, Somasundram C (2021) Involvement of phenolic compounds and their composition in the defense response of *Fusarium oxysporum* infected berangan banana plants. Sains Malaysiana. 50(1):23-33. http://dx.doi.org/10.17576/jsm-2021-5001-03.

[52] Singh A, Kumar J, Sharma V, Singh D, Kumari P, Nishad J, Gautam V, Kharwar R (2021) Phytochemical analysis and antimicrobial activity of an endophytic*Fusarium proliferatum* (ACQR8), isolated from a folk medicinal plant *Cissus quadrangularis* L. South african journal of botany. 87-94. https://doi.org/10.1016/j.sajb.2021.03.004.

[53] Yin Z, Wu W, Sun C, Lei Z, Chen H, Liu H, Chen W, Ma J, Min T, Zhang M, Wu H (2018) Comparison of releasing bound phenolic acids from wheat bran byfermentation of three *Aspergillus* species. International journal of food science and technology. 53: 1120–1130. doi:10.1111/ijfs.13675.

[54] Gulsunoglu Z, Purves R, Karbancioglu-Guler F, Kilic-Akyilmaz M (2020) Enhancement of phenolic antioxidants in industrial apple waste by fermentation with*Aspergillus* spp. Biocatalysis and agricultural biotechnology. https://doi.org/10.1016/j.bcab.2020.101562.

[55] Huynh Th, Smagghe G, Gonzales G, Camp J, Raes K (2016) Extraction and bioconversion of kaempferol metabolites fromcauliflower outer leaves through fungal fermentation. Biochemical engineering journal. 1-7. http://dx.doi.org/10.1016/j.bej.2015.12.005.

[56] Kristensen S, Pedersen T, Nielsen M, Wimmer R, Muff J, Sørensen J (2021) Production and selectivity of key fusarubins from*Fusarium solani* due to media composition. Toxins. (13):1-12. https://doi.org/10.3390/toxins13060376.

[57] Song X, Tan L, Wang M, Ren C, Guo C, Yang B, Ren Y, Cao Z, Li Y, Pei J (2020) Myricetin: A review of the most recent research. Biomedicine and pharmacotherapy. 134:1-13. https://doi.org/10.1016/j.biopha.2020.111017.

[58] Ebrahim W, Ozkaya F, Ebada Sh (2020) Antifungal metabolites from endophytic fungus *Fusarium verticillioides*strain WF18. South african journal of botany. 133:40-44. https://doi.org/10.1016/j.sajb.2020.06.029.

[59] Wang Z, Zhang W, Xiao L, Zhou Y, Du F (2018) Characterization and bioactive potentials of secondary metabolites from *Fusarium chlamydosporum*. Natural product research. https://doi.org/10.1080/14786419.2018.1508142.

[60] Khan N, Afroz F, Begum N, Rony S, Sharmin S, Moni F, Hasan C, Shaha K, Sohrab H (2018) Endophytic *Fusarium solani*: A rich source of cytotoxic and antimicrobialnapthaquinone and aza-anthraquinone derivatives. Toxicology reports. 970–976. https://doi.org/10.1016/j.toxrep.2018.08.016.

[61] Buśko M, Góral T, Ostrowska A, Matysiak A, Walentyn-Góral D, Perkowski J (2014) The effect of *Fusarium* inoculation and fungicide application on concentrations of flavonoids (apigenin, kaempferol, luteolin, naringenin, quercetin, rutin, vitexin) in winter wheat cultivars. American journal of plant sciences. 5: 3727-3736. http://dx.doi.org/10.4236/ajps.2014.525389.

[62] Wang J, Jiang Z (2022) Synthesis, characterisation, antioxidant and antibacterial properties of p-hydroxybenzoic acid-grafted chitosan conjugates. International journal of food science and technology. 57:1283–1290.

[63] Alavi M, Hamblin M, Aghaie E, Mousavi S, Hajimolaali M (2023) Antibacterial and antioxidant activity of catechin, gallic acid, and epigallocatechin-3-gallate: focus on nanoformulations. Cellular, molecular, and biomedical reports. 3(2): 62-72.

[64] Wang L, Pan X, Jiang L, Chu Y, Gao S, Jiang X, Zhang Y, Chen Y, Luo Sh, Peng C (2022) The biological activity mechanism of chlorogenic acid and its applications in food industry: A review. Frontiers in nutrition. 9:1-22. doi: 10.3389/fnut.2022.943911.

[65] Ingole A, Kadam M, Dalu A, Kute Sh, Mange P, Theng V, Lahane O, Nikas A, Kawal Y, Nagrik Sh, Patil P (2021) A review of the pharmacological characteristics of vanillic acid. Journal of drug delivery and therapeutics. 11:200-204.

[66] Adekola H, Adeleye A, Adesetan T, Folorunso J, Odeyemi F (2022) Antibacterial activity of vanillic acid against *Staphylococcus aureus*, *Salmonella typhi*, and *Proteus mirabilis*. Microbes, infection and chemotherapy. 2: 1-6.

[67] Cizmarova B, Hubkova B, Bolerazska B, Marekova M, Birkova A (2020) Caffeic acid: a brief overview of its presence, metabolism, andbioactivity. Bioactive compounds in health and disease. 3(4): 74-81.

[68] Zochedh A, PriyaM, Chakaravarthy C, Sultan A, Kathiresana T (2022) Experimental and computational evaluation of syringic acid – structural, spectroscopic, biological activity and docking simulation. Polycyclic aromatic compounds. 43: 6516-6548.

[69] Ferreira P, Victorelli F, Fonseca-Santos B, Chorilli M (2018) A review of analytical methods for p-coumaric acid in plant-based products, beverages, and biological matrices. Critical reviews in analytical chemistry. 1-11. https://doi.org/10.1080/10408347.2018.1459173.

[70] Synowiec A, Żyła K, Gniewosz M, Kieliszek M (2021) An effect of positional isomerism of benzoicacid derivatives on antibacterial activity against *Escherichia coli*. Open life sciences. 16: 594–601. https://doi.org/10.1515/biol-2021-0060.

[71] Enogieru A, Haylett W, Hiss D, Bardien S, Ekpo O (2018) Rutin as a potent antioxidant: Implications for neurodegenerative disorders. Oxidative medicine and cellular longevity. 1-17. https://doi.org/10.1155/2018/6241017.

[72] Sharifi-Rad J, Quispe C, Castillo C, Caroca R, Lazo-Vélez M, Antonyak H, Polishchuk A, Lysiuk R, Oliinyk P, De Masi L, Bontempo P, Martorell M, Daştan S, Rigano D, Wink M, Cho W (2022) Ellagic acid: A review on its natural sources, chemical stability, and therapeutic potential. Oxidative medicine and cellular longevity. 1-24. https://doi.org/10.1155/2022/3848084.

[73] Khan R, Naseem I (2023) Antiglycation and antioxidant potential of coumaric acid isomers: a comparative in-vitro study. Journal of biomolecular structure and dynamics. https://doi.org/10.1080/07391102.2023.2267699.

[74] Deng H, Xu Q, Guo H, Huang X, Chen F, Jin L, Quan Z, Shen Q (2022) Application of cinnamic acid in the structural modification of natural products: A review. Phytochemistry. 206. https://doi.org/10.1016/j.phytochem.2022.113532.

[75] Mohammed F, Sevindik M, Uysal I, Şabik A (2023) Quercetin: Derivatives,

biosynthesis, biological activity, pharmacological and therapeutic effects. Prospects in pharmaceutical sciences. 21(3): 49-56. https://doi.org/10.56782/pps.147.

[76] Jan R, Khan M, Asaf S, Asif L, Kim K (2022) Bioactivity and therapeutic potential of kaempferol and quercetin: new insights for plant and human health. Plants journal. 11:1-18. https://doi.org/10.3390/plants11192623.

[77] Ibrahim H, Soliman H, Hamed F, Marrez D, Othman S (2020) Antibacterial activity of vanillic acid and catechol producedby microbial biotransformation of caffiec acid. Journal of pharmaceutical sciences and research. 12(6): 740-743.

[78] Jeyanthi V, Velusamy P, Kumar G, Kiruba K (2021) Effect of naturally isolated hydroquinone in disturbing the cell membraneintegrity of *Pseudomonas aeruginosa* MTCC 741 and *Staphylococcus aureus*MTCC 740. Heliyon. 1-7. https://doi.org/10.1016/j.heliyon.2021.e07021.

[79] Giner R, Ríos J, Máñez S (2022) Antioxidant activity of natural hydroquinones. Antioxidants journal. 11:1-21. https://doi.org/10.3390/antiox11020343.

[80] Kahkeshani N, Farzaei F, Fotouhi M, Alavi S, Bahramsoltani R, Naseri R, Momtaz S, Abbasabadi Z, Rahimi R, Farzaei M, Bishayee A (2018) Pharmacological effects of gallic acid in health and diseases: Amechanistic review. Iranian journal of basic medical sciences. 22(3): 225-237.

[81] Singh R, Dubey A K (2023) Diversity and Applications of Endophytic Actinobacteria of Plants in Special and Other Ecological Niches. Frontiers in Microbiology, vol. 9. https://www.frontiersin.org/articles/10.3389/fmicb.20 18.01767

[82] Hamed A A, El awady M E, Abdel-Razik G, Gomaa M, Hassan M G (2024) Bioactive metabolites from Streptomyces sp. RSE with potential anticancer and antioxidant activity. Egypt. J. Chem. 67(4).

[83] Khalil N M, Yousef R S (2020) Efficacy of *Alternaria alternata* NMK1 Secondary Metabolites against Some Seed-Borne Fungi. Egypt. J. Bot. 60 (2): 537-548. DOI: 10.21608/ejbo.2020.21766.1425

[84] Sun Y, Ren G, Shi Q, Zhu H, Zhou N, Kong X, Jiang D, Liu C (2023) Identification of a novel coumarins biosynthetic pathway in the endophytic fungus *Fusarium oxysporum* GU-7 with antioxidant activity. Applied and environmental microbiology. 89(1): 1-14. DOI: 10.1128/aem.01601-22.

[85] Al-Qaralleh O, Al-Zereini W, Al-Mustafa A (2021) Antibacterial, antioxidant and neuroprotective activities of crudeextract from the endophytic fungus *Fusarium* sp. isolate OQ-Fus-2-Ffrom *Euphorbia* sp. plant. Journal of pharmacy and pharmacognosy research. 9(6):755-765.

[86] Hamzah T, Lee Sh, Hidayat A, Terhem R, Faridah-Hanum I, Mohamed R (2018) Diversity and characterization of endophytic fungi isolated from the tropical mangrove species,*Rhizophora mucronata*, and identification of potential antagonists against the soil-borne fungus, *Fusarium solani*. Frontiers in Microbiology. 9:1-17. doi: 10.3389/fmicb.2018.01707.

[87] Elshahawy O A M, Zeawail M E F, Hamza M A, Elateeq A A, Omar M A (2022) Improving the Production of Total Phenolics and Flavonoids and the Antioxidant Capacity of Echinacea purpurea Callus through Biotic Elicitation. Egypt. J. Chem. 65(12): 137–149. doi:10.21608/EJCHEM.2022.145210.6328

[88] Shi S, Li Y, Ming Y, Li C, Li Z, Chen J, Luo M (2018) Biological activity and chemical composition of the endophytic fungus *Fusarium* sp. TP-G1 obtained from the root of *Dendrobium officinale* Kimura et Migo. Records of natural products. 12(6): 549-556.

[89] Yuniati Y, Rollando R (2018) Isolation of antibacterial compounds from endophyte fungal of *Fusarium* sp. in *phyllanthus niruri* linn. leaves. Journal of pharmaceutical sciences and research. 260-264.

[90] Chutulo E, Chalannavar R (2020) Antimicrobial activity of Fusarium oxysporum, endophytic fungus, isolated from *Psidium guajava*L. (white fruit). International journal of pharmaceutical

sciences and research. 11(11):.5844-5855.

[91] Song Z, Sun Y, Xu Sh, Li G, Yuan C, Zhou K (2023) Secondary metabolites from the endophytic fungi *Fusarium decemcellulare* F25 and theirantifungal activities. Frontiers in microbiology. 1-10. DOI 10.3389/fmicb.2023.1127971

[92] Tchoukoua A, Hasegawa R, Hendracipta K, Sato S, Koseki T, Shiono Y (2017) Structure elucidation of new fusarielins from *Fusarium* sp.and their antimicrobial activity. Magnetic resonance in chemistry. 56:32–36.

[93] Alves M, Ferreira I, Froufe H, Abreu R, Martins A, Pintado M (2013) Antimicrobial activity of phenolic compounds identified in wildmushrooms, SAR analysis and docking studies. Journal of applied microbiology.

[94] Nandhini P, Gupta P, Mahapatra A, Das A, Agarwal S, Mickymaray S, Alothaim A, Rajan M (2023) In-Silico molecular screening of natural compounds as a potential therapeutic inhibitor for Methicillin-resistant *Staphylococcus aureus* inhibition. Chemico-Biological Interactions. 374.

[95] Alhadrami H, Hamed A, Hassan H, Belbahri L, Rateb M, Sayed A (2020) Flavonoids as potential anti-MRSA agents through modulation of PBP2a: A computational and experimental study. Antibiotics. 1-16:9. doi:10.3390/antibiotics9090562

[96] Verma A, Ahmed F, Hossain Sh, Bhojiya A, Mathur A, Upadhyay S, Srivastava A, Vishvakarma N, Barik M, Rahaman M, Bahadur N (2021) Molecular docking and simulation studiesof flavonoid compounds against PBP-2a ofmethicillin-resistant *Staphylococcus aureus*. Journal of biomolecular structure and dynamics. 1-17. https://doi.org/10.1080/07391102.2021.1944911

[97] Masumi M, Noormohammadi F, Kianisaba F, Nouri F, Taheri M, Taherkhani A (2022) Methicillin-Resistant *Staphylococcus aureus*: Docking-based virtual screeningand molecular dynamics simulations to identify potential Penicillin-Binding Protein 2a inhibitors from natural flavonoids. International journal of microbiology. 1-14. https://doi.org/10.1155/2022/9130700.

[98] Laksono A, Asnani A, Iswanto P (2020) Interaction of mutant PBP2a and bioactive compounds fromStreptomyces with anti-MRSA activities. Materials science and engineering. 1-7. doi:10.1088/1757-899X/959/1/012031.