In silico molecular modeling of cold pressed garden cress (Lepidium sativum L.) seed oil toward the binding pocket of antimicrobial resistance Staphylococcus aureus DNA-gyrase complexes

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Abstract. – OBJECTIVE: The seeds of garden cress, Lepidium sativum L., are a fantastic source of phytochemicals and proteins. The purpose of the current study was to use solvent extraction techniques to examine the physicochemical characteristics and biological activities of garden cress (L. sativum) seed oil extracts and compounds against Staphylococcus aureus, in vitro, molecular docking and pharmacokinetics.

MATERIALS AND METHODS: Cress seed oil were collected from Sakaka, Saudi Arabia’s Al-Jouf market. Seeds were crushed in 80% ethanol for several extraction. The oil extraction was forced through a perforated tube, and the meal was expelled via a calibrated aperture. After that, a centrifuge was used to separate the oil from the plant debris (15 min). Study the anti-Staphylococcus aureus of cress seed oil by Well-Diffusion Assay, while cress oil molecules docked against Staphylococcus aureus target (pdb-id: 2XCS) by MOE 19.0901 Software. The pharmacokinetics (ADMET) and Lipinski’s rules were predicted by pKCSM online server (available at: https://biosig.lab.uq.edu.au/pkcsm/prediction).

RESULTS: The outcome showed that the oil yield for seed oil extract, the specific gravity (0.93) and concentration (33%) was substantially greater. Our findings included a maximal zone of inhibition (23 mm), a minimum inhibitory concentration (MIC) of 80 µg/mL, and a minimum bactericidal concentration (MBC) of 170 µg/mL of cress oil against Staphylococcus aureus. The docking results indicated that the affinity score of Quercetin-3-O-glucosylgalactoside docked against pdb-id: 2XCS was 9.48, while RMSD 1.59 Å compared with the co-crystallized ligand showed an affinity score of -7.58 kcal/mol and RMSD 1.32 Å.

CONCLUSIONS: Our findings suggest that Cress seed oil might be utilised to protect food from S. aureus infection that is resistant to antibiotics.

Key Words: In silico, Cress seed oil, Bacterial infections, Antimicrobial, Cytotoxic, Staphylococcus aureus, Docking, DNA-gyrase, Antibiotic resistance.

Introduction

According to the WHO, general, unchecked use of anti-bacterial drugs is to blame for the
rise in death and morbidity from antimicrobial resistance in low-income and middle-income countries. The WHO report of 2020 “Prioritization of Pathogens to Guide Research and Development of New Antibiotics” discusses several infections as being of utmost importance, including the carbapenem-resistant *Pseudomonas aeruginosa*. The high priority pathogens list includes methicillin-resistant Gram-negative bacterium as well as *Staphylococcus aureus* as a vancomycin.

One of the biggest plant families is *Brassicaceae*, which has 1,500 species of food, medicinal, and vegetable crop plants spread across 300 genera. *Brassicaceae* family contains 103 species and 53 genera; the most prevalent of them are *Anstatica*, *Arabis*, *Diplotaxis*, *Zilla*, and *Lepidium*. A variety of species of the genus *Lepidium* thrive in warm climates. This family’s species are widespread around the globe, with the Mediterranean, West and Central Asia, and some regions of North America having the most diversity. In *Brassicaceae* family members such as, *Lepidium sativum* L. are annual plants. *L. sativum* is also referred to as garden pepper cress, pepper grass, pepperwort, garden cress, poor man’s pepper, and pepper grass in various regions.

Phenolic acids, polyphenols, flavonoids, terpenoids, and other phytochemicals are found in medicinal and herbal plants. Biofilm production may be decreased, quorum sensing can be inhibited, bacterial adhesion to mucosal surfaces can be prevented, cell surface hydrophobicity can be influenced, and glycolytic enzymes can be decreased by phytochemicals. The shape and structure of the target pathogen govern the antibacterial action of plant components. This result is consistent with our earlier research on complexes of “smart” triiodides that were created by adding molecular iodine. In several formulations containing AgNP and/or iodine, we used plant extracts of *Zingiber officinale* (ginger), *Aloe vera barbadensis* M. (AV), *Cinnamomum zeylanicum* (Cinn), *Salvia officinalis* L. (sage), and *Capsicum frutescens* (paprika).

*L. sativum*, popularly known as curly garden cress, is a plant that contains several compounds. Saudi Arabia and other Arab nations frequently employ the *Lepidium sativum* plant, a member of the *Brassicaceae* family, for both nutritional and therapeutic purposes. In the past, people in ancient Saudi Arabia and India used *L. sativum* to cure a wide range of ailments, including arthritis, inflammation, and the mending of bone fractures. The seed extracts have been used to treat dysentery, stomachaches, gastrointestinal ailments, indigestion, febrile diseases, and skin issues in local traditional medicine. Also, the anti-microbial efficiency of *L. sativa* seed extracts against several microbial pathogens has been recorded.

Based on these facts, the objective of this investigation is to inspect the possible link between antibiotic resistance in the bacterial isolates studied and the antimicrobial activities of the oil of Cress obtained from Saudi Arabia, and study the effect of it on the multi-drug resistance *S. aureus* strains. Next, we have performed detailed *in silico* molecular modeling study and pharmacokinetics to investigate the binding affinity of the bioactive compounds of Cress seed oil toward the binding pocket of *S. aureus* Gyrase complex.

### Materials and Methods

#### Extraction and Plant Material

Cress seed oil were collected from Sakaka, Saudi Arabia’s Al-Jouf market. Seeds were crushed up and combined with standard pellets. Cress seed oil (2 kilograms) were subjected to several extractions in 80% methanol at room temperature. To get 100 g of concentrated extract, the extract was filtered and concentrated under decreased pressure.

#### Oil Extraction

*L. sativum* seeds were cold-pressed. The following step involved grinding and compressing the seeds (2 kg) using a conical screw rotation. The extracted oil was forced through a perforated tube, and the meal was expelled via a calibrated aperture. After that, a centrifuge was used to separate the oil from the plant debris (15 min). It was then filtered and stored at a temperature of 4°C.

#### Well-Diffusion Assay

The original stock cultures of antimicrobial resistance *S. aureus* were used in all tests to avoid the loss of antibiotic resistance that might occur when frequently subculturing. From the pure and fresh *S. aureus* growth, 0.5 McFarland suspensions were prepared using sterile normal saline. We used a sterile cotton swab to inoculate all of the *S. aureus* isolates onto Müller-Hinton agar and then added the oil extraction to *S. aureus* cultures (petri dish). For 24 hours, the plates were
incubated at 37°C. The next step was to check for and measure millimeter-sized inhibitory zones (mm). Zones of inhibition suggest antibacterial action when they are present.\textsuperscript{13}

**Molecular Docking Study**

**Preparation of targeted proteins**

Using MOE 19.0901 Software\textsuperscript{16} (available at: https://www.chemcomp.com/Products.htm), the binding site for the \textit{S. aureus} Gyrase complex with DNA was created from the co-crystallized ligand inside the crystal protein [PDB codes: 2XCS (available at: https://www.rcsb.org)]. We prepared target protein by utilizing protein report and utility and clean protein choices, crystallographic disorders and unfilled valence atoms were fixed. Applying MMFF94 force fields helped to reduce the amount of protein energy. By using fixed atom constraint, it was possible to create the stiff structure of the binding site. The necessary amino acids for proteins have been identified and prepped for docking.

**Preparation of tested ligands**

Using MOE 19.0901 Software\textsuperscript{16}, the saved file was opened, 3D structures were protonated, partial charges were corrected, and energy was reduced by applying 0.1 RMSD kcal/mol. MMFF94 force field. 2D structures of tested ligands were created using Chem-Bio Draw Ultra 17.0 and saved in MDL-SD file format. The reduced structures were then ready for docking using a procedure called ligand preparation.

**Molecular docking**

The receptor was prepared, and the prepared ligands were selected for molecular docking. The placement was scored by binding affinity and the refinement was scored by Generalized Born/Volume Integral (GB/VI)/WSA $\Delta$G. The ligands were permitted to be flexible during the refining while the receptor was kept stiff. Each molecule was given the opportunity to interact with the protein in ten distinct ways. Then, using the docking scores (interaction energy) of the best-fit postures with the active site at the \textit{S. aureus} Gyrase complex with DNA, a 3D image was produced by the Discovery Studio 2019 Client program. The projected binding mechanism, and preferred orientation and affinity of each docking posture and binding are all predicted using these techniques.\textsuperscript{16}

**Validation of molecular docking**

The suggested docking algorithm’s reliability and repeatability were first tested by redocking the co-crystallized ligand into the appropriate receptor’s active site while calculating the root mean square deviation (RMSD). The \textit{S. aureus} Gyrase complex with DNA(2XCS) was docked with a co-crystallized ligand, and the RMSD 1.32 exceeded 2.00 as showing a validated algorithm in comparison to the crystallographic structure.

**Toxicity Properties and Pharmacokinetic**

The kinetic study of ADMET is the study of how drugs are absorbed, distributed, metabolized, and eliminated. [A] Absorption: it is the process through which a medication enters the bloodstream from the place of administration. [D] Distribution: the transport of blood into and out of tissues is referred to as distribution. [M] Metabolism: enzymes are often engaged in drug metabolism, which is the chemical alteration of the drug with the aim of eliminating it. [E] Elimination: it is the complete and permanent expulsion of the parent medication from the body. Enzymes are often engaged in drug metabolism, which is the chemical alteration of the drug with the aim of eliminating it. [T] Toxicity: this filter is used to evaluate the worth of a substance and its metabolites, as its name implies.\textsuperscript{17-19} Lipinski’s rules are a set of recommendations made by Pfizer’s Chris Lipinski to assist in designing compounds with excellent convenience. The 4 recommendations are: (1) The compound must be 500 g/mol or less in molecular weight. (2) There should not be more than five hydrogen bond donors (HBDs) in the molecule. These OH and NH groupings predominate. (3) There should not be more than 10 hydrogen bond acceptors per molecule. In essence, there are the atoms of oxygen and nitrogen in the molecule. (4) The molecule’s logP-assessed lipophilicity cannot be higher than 5. These are known as “Lipinski’s Rules” or “Rule of 5”.\textsuperscript{20,21} Lipinski\textsuperscript{20,21} said that in order to have a decent probability of having advantageous oral bioavailability, the molecules should follow at least three of the four recommendations. Therefore, Lipinski’s principles refer to absorption, having greater effectiveness, or lesser toxicity when we consider ADMET. To enhance oral absorption, these guidelines thus exclusively concentrate on enhancing solubility and membrane permeability.
In silico molecular modeling of cold pressed garden cress toward S. aureus DNA-gyrase complexes

Statistical Analysis

All the data were entered and evaluated by exhausting Statistical Package for Social Science version 24 (IBM Corp., Armonk, NY, USA). Our results are significant when p-value < 0.05.

Results

Assessment of Antimicrobial Activity of Cress Seed Oil

The results revealed a considerable inhibitory capacity of Cress seed oil toward S. aureus activity with inhibition zone diameter of 23 ± 1.01 mm at a concentration of 50 µg/mL and highly significant when compared to negative control and p-value < 0.05. The oil was prepared in dimethyl sulfoxide (DMSO) as a control, sensitive inhibition zone diameter ≥ 11 mm according to Humphries et al. Recorded values of minimal inhibitory concentrations (MIC) were found to be 80 µg/mL, while MIC at 50% was found to be 120 µg/mL and MIC at 90% inhibition was 170 µg/mL. These results showed that Cress seed oil possesses a considerable activity toward S. aureus infection (Table I).

In Silico Molecular Modeling Study

The finding of the molecular docking binding affinity score of Cress (Lepidium sativum L.) seed oil compounds against S. aureus target ranged from -7.53 to -9.38 kcal/mol while RMSD ranged from 1.58 to 1.73 Å, when compared to co-cry stallized ligand with affinity score -7.58 kcal/mol and RMSD 1.32 Å, (Table II).

Our results demonstrated that the binding mode of the co-crystallized ligand exhibited an energy binding of -7.58 kcal/mol toward S. aureus Gyrase complex with DNA. The co-cry stallized ligand formed fourteen Pi-Pi, Pi-sulfur, and Pi-Alkyl interactions with DGF10, DGF11, DCE11, DGE10, MetB1121, AlaB1068, AlaD1068 and Val D1071 amino acid residues. Additionally, the ligand formed two interactions with AspD1083 and AspB1083 amino acid residues (Figure 1a).

Also, the binding mode of Quercetin 3-O-glucoside exhibited an energy binding of -7.53 kcal/mol against S. aureus Gyrase complex with DNA. Quercetin 3-O-glucoside showed four Pi-Alkyl, Pi-Pi and Pi-anion interactions with DGF10, DGF11, DCE11, DGE10 and AlaD1170. Further, Quercetin 3-O-gluc oside engaged in two hydrogen bonds with AspD1083 and AspB1083, at a distance of 2.81 and 1.98. (Figure 1b).

While the binding mode of Quercetin 3-O-rutinoside exhibited an energy binding of -8.45 kcal/mol against S. aureus Gyrase complex with

Table I. Inhibition Zone Diameter and MIC of Cress seed oil against Staphylococcus aureus using agar well diffusion assay.

<table>
<thead>
<tr>
<th>Staphylococcus aureus</th>
<th>Inhibition Zone Diameter</th>
<th>MIC (µg/mL)</th>
<th>MIC</th>
<th>MIC50</th>
<th>MIC90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cress (Lepidium sativum L.) seed oil</td>
<td>23 ± 1.01**</td>
<td>80</td>
<td>120</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>DMSO (Negative control)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

**Highly significant with p-value < 0.05.

Table II. Docking affinity (kcal/mol) of Cress seed oil bioactive compounds against S. aureus Gyrase complex (PDB: 2XCS).

<table>
<thead>
<tr>
<th>Ligand</th>
<th>RMSD value (Å)</th>
<th>Affinity score (kcal/mol)</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-crystallized ligand</td>
<td>1.32</td>
<td>-7.58</td>
<td>Hydrophilic interactions: 3, Pi-interactions: 11</td>
</tr>
<tr>
<td>Quercetin 3-O-glucoside</td>
<td>1.73</td>
<td>-7.53</td>
<td>Hydrophilic interactions: 2, Pi-interactions: 13</td>
</tr>
<tr>
<td>Quercetin 3-O-rutinoside</td>
<td>1.42</td>
<td>-8.45</td>
<td>Hydrophilic interactions: 2, Pi-interactions: 8</td>
</tr>
<tr>
<td>Quercetin 3-O-galactoside</td>
<td>1.80</td>
<td>-7.48</td>
<td>Hydrophilic interactions: 2, Pi-interactions: 15</td>
</tr>
<tr>
<td>Quercetin-3-O-glucosylgalactoside</td>
<td>1.58</td>
<td>-9.38</td>
<td>Hydrophilic interactions: 4, Pi-interactions: 14</td>
</tr>
</tbody>
</table>
DNA. Quercetin 3-O-rutinoside demonstrated thirteen Pi-alkyl and Pi-Pi interactions with DGF10, DGF11, DCE11, DGE10, MetB1121, MetB1075, AlaD1068 and ArgD1122. Additionally, Quercetin 3-O-rutinoside interacted with DGF10, DCE11, and AspD1083 by four hydrogen bonds with distance of 2.35, 2.57, 2.47 and 2.85 Å. Interestingly, Quercetin 3-O-rutinoside interacted with ArgD1122 by ionic interaction (Figure 1c).

On the other hand, the binding mode of Quercetin 3-O-galactoside exhibited an energy binding of -7.48 kcal/mol-1 against *S. aureus* Gyrase complex with DNA. Quercetin 3-O-galactoside formed

![Figure 1](image_url)

**Figure 1.** The ligand docked in *S. aureus* Gyrase complex with DNA. **a,** The Crystal ligand re-docked. **b,** Quercetin 3-O-glucoside. **c,** Quercetin 3-O-rutinoside.
In silico molecular modeling of cold pressed garden cress toward S. aureus DNA-gyrase complexes

In silico molecular modeling of cold pressed garden cress toward S. aureus DNA-gyrase complexes

Quercetin 3-O-galactoside engaged in two hydrogen bonds with AspD1083 and AspB1083, at distances of 1.96 and 2.87 Å, respectively. (Figure 1d). And the binding mode of Quercetin 3-O-glucosylgalactoside exhibited an energy binding of -9.38 kcal/mol against S. aureus Gyrase complex with DNA. Quercetin 3-O-glucosylgalactoside showed eight Pi-Pi and Pi-anion interactions with DGF10, DGF11, DCE11, DGE10 and AlaB1120 amino acid residues. Furthermore, Quercetin 3-O-galactoside engaged in two hydrogen bonds with AspD1083 and AspB1083, at distance of 1.96 and 2.87 Å, respectively. (Figure 1d).

ADMET and Lipinski’s RULES

It is necessary to look at the pharmacokinetic characteristics of novel molecules before they may be identified as prospective drugs. As a result, utilizing online services provided by Pkcsm, the evaluation of ADMET attributes is thought to be the ideal technique to verify and choose the target molecules.

Absorption

According to a study of the literature, substances that produce outcomes (>30 percent abs) are more potent in penetrating the intestinal barrier. According to the findings, absorption ranged between 5-58%, whereas co-crystallized ligand absorption was 91.83%.
Distribution
According to distribution values, *Staphylococcus aureus* DNA-Gyrase compounds have a low value ranging from -1.69 to -2.59 in the permeability of blood-brain barrier, which indicates that they do not penetrate the brain. As a result, adverse effects will be diminished, demonstrating their effectiveness and drug-like behavior.

Metabolism
The chemical biotransformation of a medicine in the body is indicated by computational metabolic behavior; CYP (Cytochrome P450 inhibitors) is important in converting drug molecules. Table III shows that Quercetin 3-O-galactoside are inhibitors and substrates of the 2 major subtypes of CYP, 3A4 and 2D6, suggests that they could be able to be metabolized in the liver.

Excretion and Toxicity
It is assessed for the Ames’ toxicity test (a widely employed method to assess compounds to mutagenic potential using bacteria). The excretion results for all substances indicate an acceptable negative value.

Lipinski’s Rule
The ADMET test has shown that the molecule of cress garden oil that interests us, quercetin 3-O-galactoside, is the least poisonous and safest one that is conceivable. Furthermore, Table IV shows that these Quercetin 3-O-galactoside meet the requirements of Lipinski’s rule: they produced less than 5 H-bond donors and less than 10 H-bond acceptors, had a MW of less than 500 Daltons, and had less than 5 octanol/water partition coefficient. According to Lipinski’s guidelines and the ADMET analysis, the developed Quercetin 3-O-galactoside was in silico confirmed to be a secure pharmaceutical molecule.

The Quercetin 3-O-galactoside showed drug-like characteristics based on the rules of Lipinski. (Table III-IV), This indicated that they had a better chance of being well absorbed after oral administration. Lipinski’s rule said that these compounds had drug-like characteristics.

Discussion
In the current study, we further investigated the antimicrobial activity of Cress seed oil. We have verified the inhibitory action against *Staphylococcus aureus*. The results of the inhibition zone are 23 ± 1.01 and MIC 50 compared to negative control.

The reported inhibition zone diameter of 50 mg/mL of the extract and oil in this study sug-

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**Table III.** The results of the ADMET test with pKCSM of cress garden oil compounds and co-crystallize of docked against *Staphylococcus aureus* DNA-gyrase complexes.

<table>
<thead>
<tr>
<th>Absorption</th>
<th>Distribution</th>
<th>Metabolism CYP</th>
<th>Excretion</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal absorption (human)</td>
<td>Blood-Brain barrier permeability</td>
<td>CYP (Blood-brain permeability)</td>
<td>2D6 Substrate</td>
<td>3A4 Substrate</td>
</tr>
<tr>
<td>Numeric (l % Absorbed)</td>
<td>Numeric (log BB)</td>
<td>Numeric (log PS)</td>
<td>Categorical (Yes/No)</td>
<td>Categorical (Yes/No)</td>
</tr>
<tr>
<td>91.83</td>
<td>-0.981</td>
<td>-2.528</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>35</td>
<td>-2.15</td>
<td>-5.20</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>5</td>
<td>-2.59</td>
<td>-6.25</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>58</td>
<td>-1.69</td>
<td>-4.99</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>10</td>
<td>-2.27</td>
<td>-5.09</td>
<td>NO</td>
<td>NO</td>
</tr>
</tbody>
</table>
In silico molecular modeling of cold pressed garden cress toward S. aureus DNA-gyrase complexes

Table IV. Lipinski’s parameters of all three top compounds and reference in the dataset.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Lipinski’s rule</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HBD</td>
</tr>
<tr>
<td>Co-crystallized ligand</td>
<td>1</td>
</tr>
<tr>
<td>Quercetin 3-O-glucoside</td>
<td>10</td>
</tr>
<tr>
<td>Quercetin 3-O-rutinoside</td>
<td>13</td>
</tr>
<tr>
<td>Quercetin 3-O-galactoside</td>
<td>4</td>
</tr>
<tr>
<td>Quercetin-3-O glucosylgalactoside</td>
<td>11</td>
</tr>
</tbody>
</table>

HBD: number of Hydrogen Bond Donors; HBA: Hydrogen Bond acceptors; RB: number of Rotatable Bonds; t-PS: Total Polar Surface Area, MW: molecular weight; logP: the log of octanol-water partition coefficient.

suggests that oil can be a source for the development of an antimicrobial substance for the control of S. aureus infection, such behavior of the antimicrobial action was also verified by Alqahtani et al.24.

A previous research paper performed by Adam et al.25 demonstrated that L. sativum seed extracts in petroleum ether, aqueous, and methanolic form had antibacterial efficacy against six opportunistic microorganisms: P. aeruginosa, E. coli, K. pneumoniae, S. aureus, Proteus vulgaris, and the fungus C. albicans. In prior research25, it was discovered that petroleum ether, when used at different concentrations (2.5%, 5%, and 10%), performed better than methanol and water in extracting antimicrobial compounds from L. sativum seeds. According to recent studies26,27 conducted in Egypt, L. sativum extract exhibits antimicrobial activity against various gram-positive and gram-negative bacteria. However, in line with our study, there were no appreciable differences between the tested extracts’ susceptibility to the two types of bacteria. In a separate investigation28, the crude extract from Ethiopian L. sativum seeds had antibacterial activity against tested bacteria (S. typhi, E. coli, B. subtilis, and S. aureus) and fungus (F. oxysporum, F. solani, and A. niger)25,26,28,29.

The efficacy of cress oil compounds against S. aureus was also studied using computational approaches since, despite genomics’ success in uncovering new crucial bacterial genes, there are not enough long-term leads in the development of antibacterial drugs to combat the rise in multidrug resistance.

Our results in molecular docking as well as pharmacokinetics and Lipinski’s rules indicated that the best compound against S. aureus DNA gyrase (Pdb id: 2XCS) is Quercetin 3-O-galactoside with affinity score -7.48 kcal/mol and HBD<5; HBA: < 10, MW<500.

Quercetin has been proven in studies30-32 to have broad-spectrum antibacterial activities; not only it effectively inhibits bacteria but also significantly inhibits fungus. The growth of harmful bacteria like Salmonella enteritidis, S. aureus, Proteus sp., Pseudomonas aeruginosa, Escherichia coli, and Aspergillus flavus is effectively inhibited by quercetin, according to several studies30-32. Okayama and Hossion33 discovered that brand-new quercetin acyl glucosides that were artificially created and produced successfully slowed the development of S. aureus, E. coli, and P. aeruginosa. Additionally, MIC values for bayberry extract range from 2.07 to 8.28 mg/mL against Shigella, Listeria, and Salmonella34.

Conclusions

In order to avoid difficulties and the development of antibiotic-resistant strains, it is becoming more important to evaluate the microbiological pattern and the antibiotic sensitivity pattern of the microorganisms to provide empirical antibiotics. In order to prevent the emergence of antibiotic-resistant bacteria and their accompanying consequences, we impulse antimicrobial monitoring and rigorous adherence to antibiotic usage guidelines. Further studies are required to find strains that are resistant to antibiotics utilizing molecular approaches. Our results suggest that the anti-staphylococci of Cress seed oil, gathered in the Al-Jouf area of Saudi Arabia, may be useful in the development of antibacterial drugs against S. aureus, which is resistant to several conventional antibiotics. The active compounds in Cress seed oil that have anti-staphylococcal effect still require more study.
Conflict of Interest
The Authors declare that they have no conflict of interests.

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Authors’ Contribution
Mohammed S. Almuhayawi, Mohammed H. Alruhaili, Hattan S. Gattan, Mohammed Talal Alharbi, Mohanned Talal Alharbi, Mohammed K. Nagshabandi, Samy Selim, Mohammed E. Elnosary: contributed to study conception, design, data analysis, data interpretation, preparing the draft manuscript, and final approval of the version to be published.

Availability of Data and Materials
Data are available upon request to the corresponding author.

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Ethics Approval and Informed Consent
Not applicable.

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In silico molecular modeling of cold pressed garden cress toward S. aureus DNA-gyrase complexes


