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First report on the antibacterial and anti-*Fusarium* activity of methanolic extract of the red alga *Asparagopsis armata*

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This research records the antibacterial and anti-*Fusarium* activity of the methanolic extract (MeOH) from the marine alga, *Asparagopsis armata*, collected in Algeria. The antibacterial activity was screened using the well diffusion method against five pathogenic bacteria strains: *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus cereus*, *Klebsiella pneumoniae* and *Staphylococcus aureus*. The anti-*Fusarium* activity was evaluated using the direct contact method against four *Fusarium* species (*F. culmorum*, *F. graminearum*, *F. poae* and *F. avenaceum*). The results revealed that the methanolic extract of *A. armata* demonstrated notable antibacterial activity against the tested strains with an inhibition zone ranging between 10.2 and 40.6 mm. The crude methanolic extract of *A. armata* exhibited significant antibacterial activity against *S. aureus*, *K. pneumoniae* and *B. cereus* with minimal inhibitory concentration ≤ 2 mg/mL, *P. aeruginosa* appears to be the most resistant strain to the methanolic extract, the MIC > 4.0 mg/mL. Concentration of 80 mg/mL exhibited a total inhibition for all fungal strains except for *Fusarium poae*. The important activity of the extract was attributed to the volatile compounds such as phenol derivatives, halogenated and terpenoid compounds. The red marine alga *Asparagopsis armata* represents an important source of new antibacterial and antifungal agents that can replace the chemical agents used for treatment of human infections and plant diseases.

Keywords: *Asparagopsis armata*; methanol extract; antibacterial activity; anti-*Fusarium* activity.

Introduction

The marine environment is among the most important factors on earth for preserving life, including human life, it is an infinite source of active molecules with an original chemical structure (Carroll et al., 2024). The biodiversity of macroalgae, red (Rhodophyceae), brown (Phaeophyceae) and green (Chlorophyceae) offers the possibility of finding various varieties of natural compounds with interesting biological properties (Bharathi & Lee, 2024). The utmost variety of species exists in the marine environment. Nonetheless, of approximately 220,000 natural substances listed, hardly 10% are derived from marine sources. This means that there is a lot of ignorance and little research on marine organisms, and the main reason for this is because it is hard to get samples. Marine algae are a pertinent source of constituents because of their enormous diversity, occurrence, nutritional and chemical composition.

They have high levels of different types of primary metabolite such as proteins, vitamins and carbohydrates, also secondary metabolites such as phenolic compounds, pigments or terpenoids, which qualifies them for major industrial use (Lourenço-Lopes et al., 2020). Seaweed is rich in bioactive substances and is considered a potential source of new marine therapy. Extracts from a range of macroalgae from around the world have been demonstrated to exhibit several biological activities (Cadar et al., 2025).

There are many studies of algae derived bioactive compounds that have a variety of biological activities, such as antibiotic (Etahiri et al., 2007; Zuorro et al., 2024), antiviral (Hassen et al., 2023), anticandidal (Messahli et al., 2021), anti-inflammatory, antimitotic, antimalarial (Wright et al., 1997), cytotoxic (Ktari & Guyot., 1999), antioxidant (Zubia et al., 2007).

Members of the Rhodomelaceae family are largest biomass producers rich in bioactive metabolites and a great food source (Carpena et al., 2024). The red algae, *Asparagopsis* species such as *Aspargopsis armata* and *Asparagopsis taxiformis*, demonstrated potent antioxidant, antifungal, and antibacterial properties (Devi et al., 2011; Lee et al., 2020). Also, studies have been published showing that red algae *Asparagopsis armata* produce chemical compounds with potential antimicrobial and antitumor activities (Genovese et al., 2009; Alves et al., 2016).

Asparagopsis (Bonnemaisoniaceae, Rhodophyta) species (*A. taxiformis* and *A. armata*) are considered as iconic invaders because they have become distributed in the major tropical and temperate waters of the world (Genovese et al., 2009; Zanolla et al., 2022). *A. armata* was first reported on the Algerian coast in 1923, but since 2003, this species has appeared in several new areas along the Algerian coast (Grimes et al., 2018). This algal species is multiplying and invading Algerian marine ecosystems causing an ecological imbalance threatening the life of aquatic species. Given its richness in active secondary metabolites, it is necessary to valorize this algal biomass.

Antifungal and antibacterial activities of seaweed extracts have been reported from many parts of the world. In Algeria, only anticandida activity has been evaluated (Messahli et al., 2021). But, moreover, to our knowledge this is the first study demonstrating the anti-*Fusarium* and antibacterial activities of *Asparagopsis armata* methanolic extract in Algeria. While many studies have proven the antimicrobial activity of different extracts of red algae, no research has explored the anti-*Fusarium* activity of the methanol extract of *Asparagopsis armata*.

Materials and methods

Asparagopsis armata (red algae) was collected from the intertidal zone (approximately 0.5 m depth) at Salamandre Beach on the western Mediterranean coast of Algeria (35°55'04.49" N 0°34'46.80" E). The algae were gently rinsed with sterile seawater, cleaned of debris and epiphytes, and left to dry at room temperature in the shade. A voucher specimen was confirmed for its botanical identity and deposited in the department of Biology, University of Laghouat (Algeria). The dried algal material was ground into a fine powder using a laboratory blender and preserved away from light at room temperature until extraction. 10 g of red algae powder was extracted with 100 mL of methanol (99.99% purity), under stirring at ambient temperature

for 24 h. After filtration, sterile Whatman No. 1 paper was employed for filtration, the solvent was evaporated using a rotary evaporator at 40 °C. The dried extract was dissolved in dimethyl sulfoxide (DMSO, 10%) at final concentration of 200 mg/mL and stored at +4 °C.

Antibacterial activity was tested on a range of microorganisms:

– Gram-positive bacteria: *Staphylococcus aureus* (ATCC 6538), *Bacillus cereus* (ATCC 25921);

– Gram-negative bacteria: *Klebsiella pneumoniae* IBMC Strasbourg, *Escherichia coli* (ATCC 8739) and *Pseudomonas aeruginosa* (ATCC 27853).

The antibacterial activity of methanolic extract was determined by the well method using the Mueller Hinton agar. Bacterial suspension prepared in physiological water and adjusted to 10^6–10^8 cells/mL. The surface of the agar plate was inoculated by evenly spreading a measured volume of the bacterial inoculum, Then, a 6 mm diameter hole was then punched deeply with a sterile Pasteur pipette. Various volumes ranging from 25 to 50 µL of the MeOH extract were inserted into each well. The petri dishes were incubated at 37 °C for 24 h.

Gentamycin (10 µg), ampicillin (10 µg), amoxicillin (30 µg), and cefotaxim (30 µg) were used as standard reference antibiotics. One of the wells with DMSO only acted as a negative control. The diameter of the inhibition zone environment in the well was measured in millimeters to ascertain the antibacterial activity (Balouiri et al., 2016).

Minimal inhibitory concentration (MIC) according the procedure followed by Wiegand et al. (2008), the broth dilution method, was evaluated for the strains sensitive during the tests of sensitivity in solid medium, this choice is arbitrary (diameter of the inhibition zone ≥15 mm).

We used Brain Heart Infusion Broth (10 mL) containing geometrically increasing concentrations 0.5 to 4 mg/mL of the extract. Then into each tube, 100 µL of inoculum strains previously prepared were poured. Two other series of tubes were prepared, one of which without extract served as a growth indicator and the other without germs served as sterility control. After incubation of petri dishes at 37 °C for 24 h, the growth of bacteria was compared to control. MIC was defined as the minimum concentration of product for which no turbidity was visible compared to control without seaweed extract.

Antifungal activity was tested against four *Fusarium* spp.: *F. poae*, *F. graminearum*, *F. culmorum*, *F. avenaceum*) obtained from the Laboratory of Biological and Agricultural Sciences (University of Laghouat, Algeria) according to the method reported by Kotan et al. (2008).

Discs measuring 6.0 mm in diameter from a fungal preculture on potato dextrose agar (PDA) containing *Fusarium* mycelium were positioned at the center of the PDA plate previously spread with 200 µL of different dilutions of MeOH extract for final concentrations between 2.5 and 80 mg/mL. The petri dishes were incubated at 25 °C for six days.

The diameter of mycelium growth (mm) was measured with a Vernier caliper. All experiments were performed twice, and their data used to calculate the mean and the standard deviation. The effect on fungi was assessed by calculating the inhibition according to the following equation used by Cheng et al. (2008):

$$I = ((D_a - D_b) \times 100) / D_a,$$

where: I – growth inhibition rate (%); D_a – diameter (mm) of the control; D_b – diameter of mycelium colonies in the presence of the extract.

A PDA plate without extract, containing only methanol, was used as negative control and PDA plates handled with nystatin (2.5 to 10.0 mg/mL) were used as positive control.

The antifungal activity was determined based on the percentage rate of inhibition of thallus growth (%) according (Abdellative et al., 2011): low activity – 30% to 40%; moderate activity – 50% to 60%; good activity – 60% to 70%; excellent activity >70%.

To determine the MIC of the *A. armata* methanolic extract, a 200 µL volume of the following dilutions (1–4 mg/mL) of the algal extract were applied with a swab. Then we deposited a disc of mycelium in the centre of the PDA plate of each species of *Fusarium* with diameter 6 mm of a culture, and DMSO was used as a negative control. All petri dishes were incubated at 25 °C, the final cultures were observed on the 6th day, the MIC was visually verified for each petri dish by assessing *Fusarium* growth against positive control.

All procedures, including extractions and measurements, were conducted in triplicate. Results are expressed as mean ± standard deviation (SD).

Results

Results of antibacterial activity of *A. armata* extracts obtained by the well method against bacterial pathogens along with control antibiotics are summarized in Table 1. The methanolic extract of *A. armata* showed broad antibacterial activity against all five tested bacterial strains, with the effects generally increasing in magnitude at higher extract doses. The diameter of zone of inhibition varied according to the concentration and from one microorganism to the other. This antibacterial effect is more or less similar to that obtained with reference antibiotics. DMSO, used as a solvent to dissolve the dry red algal residues, had no antibacterial effect on the studied bacterial strains.

The methanolic extract obtained of *A. armata* revealed appreciable antibacterial activity against all tested bacterial strains. At the highest dose (10 mg), the extract produced large clear zones with *S. aureus* (30.69 ± 0.27 mm), *B. cereus* (23.13 ± 1.19 mm) and *K. pneumoniae* (40.59 ± 0.26 mm, Fig. 1). Moderate inhibition was observed for *E. coli*. Among the tested strains, *P. aeruginosa* exhibited the lowest sensitivity with an inhibition zone of 13.27 ± 0.25 mm observed only at the highest concentration tested. As anticipated, the antimicrobial activity of the extract increased in a dose dependent manner and varied according to the microorganism.

The lowest MIC value of 1.5 mg/mL was recorded in the case of *K. pneumoniae*, which exhibited the highest sensitivity to the methanolic algal extract. The second most inactivated bacteria were *B. cereus* and *S. aureus*, with MIC value of 2 mg/mL.

The antifungal activity of the extract was obtained using the direct contact method. the results presented in Table 2. Inhibition rate of methanol extract against mycelial growth of the fungal strains is shown in Figure 2 and the effect of methanol extract at different concentrations on *Fusarium* is shown in Figure 3.

Methanol extract of *Asparagopsis armata* showed considerable antifungal activity against all fungal strains tested, the percentage inhibition varied from 43.0% for *F. graminerum* and 60.0% on *F. avenaceum* at the concentration of 20 mg/mL, with a high inhibition of 90% at the concentration 80 and 40 mg/mL.

Table 1

Inhibition zones (mm) presented by *Asparagopsis armata* extract against bacterial strains (mean ± SD, n = 3 replicates each containing 5 strains)

Asparagopsis armata extract		Diameter of inhibition zone, mm				
		E. coli	*K. pneumoniae*	*P. aeruginosa*	*B. cereus*	*S. aureus*
Methanol extract, mg/well	5	10.23 ± 0.04	30.46 ± 1.73	8.94 ± 0.06	14.88 ± 1.25	24.05 ± 0.09
	7	12.73 ± 0.25	32.00 ± 1.41	13.99 ± 0.62	18.93 ± 1.32	29.36 ± 0.50
	10	13.93 ± 1.00	40.59 ± 0.26	13.27 ± 0.25	23.13 ± 1.19	30.69 ± 0.27
Control antibiotics	AMP: 10 µg	10.35	6.00	6.00	6.00	41.00
	GEN: 10µg	21.08	20.50	19.65	20.00	27.00
	CTX: 30 µg	28.05	29.75	14.30	6.00	25.20
	AML: 30 µg	10.50	6.00	6.00	6.00	44.55

Notes: AMP – ampicillin, GEN – gentamycin, CTX – cefotaxim, AML – amoxicillin.

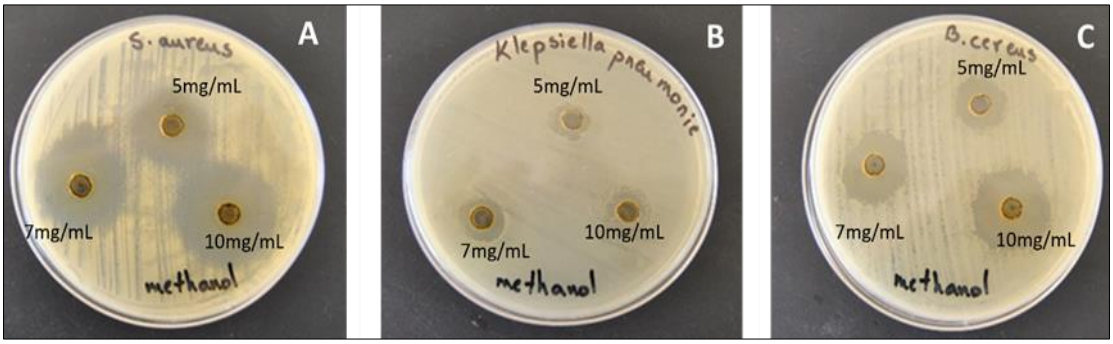

Fig. 1. Results of antibacterial activity of MeOH extract of *A. armata* on *Staphylococcus aureus* (*A*), *Klebseilla pneumoniae* (*B*), *Bacillus cereus* (*C*) obtained by well diffusion method

Table 2
The impact of methanol extract on the diameters of fungal growth (mean ± SD, n = 3 replicates each containing 4 *Fusarium* species)

Extract		Growth diameters, mm			
		F. avenaceum	*F. culmorum*	*F. graminearum*	*F. poae*
Methanolic algal extract, mg/L	0.0	60.43 ± 0.10	64.85 ± 0.92	71.98 ± 1.84	70.81 ± 0.35
	2.5	57.65 ± 1.16	63.12 ± 0.24	61.64 ± 0.13	68.50 ± 0.84
	5.0	54.50 ± 2.57	55.22 ± 1.07	58.83 ± 0.14	62.29 ± 0.30
	10.0	41.80 ± 0.42	51.90 ± 0.85	41.89 ± 1.37	57.10 ± 0.88
	20.0	24.44 ± 0.23	44.92 ± 0.31	41.01 ± 0.03	53.21 ± 0.38
	40.0	6.00 ± 0.00	51.38 ± 1.29	38.01 ± 0.34	40.09 ± 0.29
	80.0	6.00 ± 0.00	6.00 ± 0.00	6.00 ± 0.00	15.01 ± 2.51
Nystatin, mg/L	1.25	37.71 ± 0.44	49.81 ± 1.64	46.36 ± 1.40	55.36 ± 0.14
	2.50	31.70 ± 0.80	44.60 ± 0.88	25.36 ± 0.80	39.14 ± 1.05
	10.00	7.71 ± 2.24	20.03 ± 0.40	19.47 ± 0.87	25.51 ± 0.16

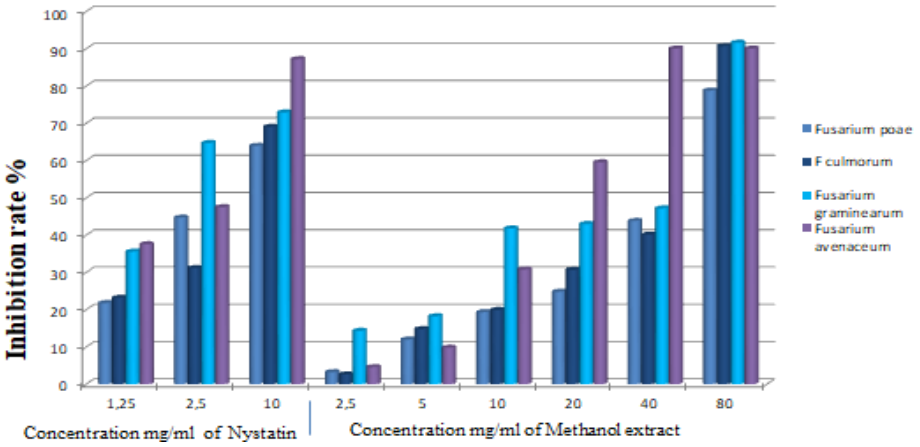

Fig. 2. The inhibition rate of fungal strains by different concentrations of methanol extract and nystatin

Excellent activitiy was observed with the concentration of 80 mg/mL with an almost total inhibition on mycelial growth for all strains except *F. poae*; while the concentrations 10 and 20 mg/mL caused a moderate inhibition of about 40% up to 60% on mycelial growth.

Discussion

The methanolic extract obtained of *A. armata* revealed appreciable antibacterial activity toward all tested strains, these results being consistent with those reported by Lee et al. (2020) who revealed that *A. armata* from Korea has a power source of antibacterial compounds against Gram negative and Gram-positive bacteria. Our result demonstrated that the extract of *A. armata* has a remarkable inhibitory effect against *S. aureus*, using an extract containing a mixture of dichloromethane and methanol (V/V) It was found that this algae is more inhibitory for *S. aureus* compared to other species of red algae, while researchers have also shown that red algae including *A. armata* have strong antibacterial activity compared to brown and green algae.

Also, Bansemir et al. (2006) reported on the antibacterial activities of DMC extracts prepared from 26 seaweed species towards fish-pathogenic bacteria. *A. armata* is most active against all tested bacteria. Paul et al. (2006) showed that the DMC extract of *A. armata* collected from Australia had antibacterial activity against *Vibrio* spp and pathogenic strains. On the contrary, Hmani et al. (2021) reported that the bacterial pathogenic strains (*Pseudomonas cepacia*, *Streptococcus agalactiae*, *Streptococcus aureus*, *Pseudomonas fluorescens*, *Enterococcus faecalis*, and *Aeromonas hydrophila*) were all resistant to methanolic extract of *A. armata* collected from the coast of Tunisia. In addition, the study of Bouhlal et al. (2010) indicated that the MeOH extract of *A. armata* did not cause any inhibition of the strains *E. faecalis* and *E. coli*, but had a positive effect for *S. aureus*. Etahiri et al. (2007) advised that the methanolic extract of *A. armata* from the Atlantic coast of Morocco was found to be inactive against *S. aureus*. Moreover, Pinteus et al. (2020) indicated that the high inhibitory activity of *A. armata* extract toward *S. aureus* and *P. aeruginosa* growth was caused by cytoplasmatic membrane disruption and DNA damage. The majority of active fractions were mainly composed of fatty acids and bromoditerpenes. The chemical compounds present at the level of the algae *A. armata* having antibacterial activity can therefore be more or less hydrophobic, such as terpenic compounds and lipids (Paul et al., 2006).

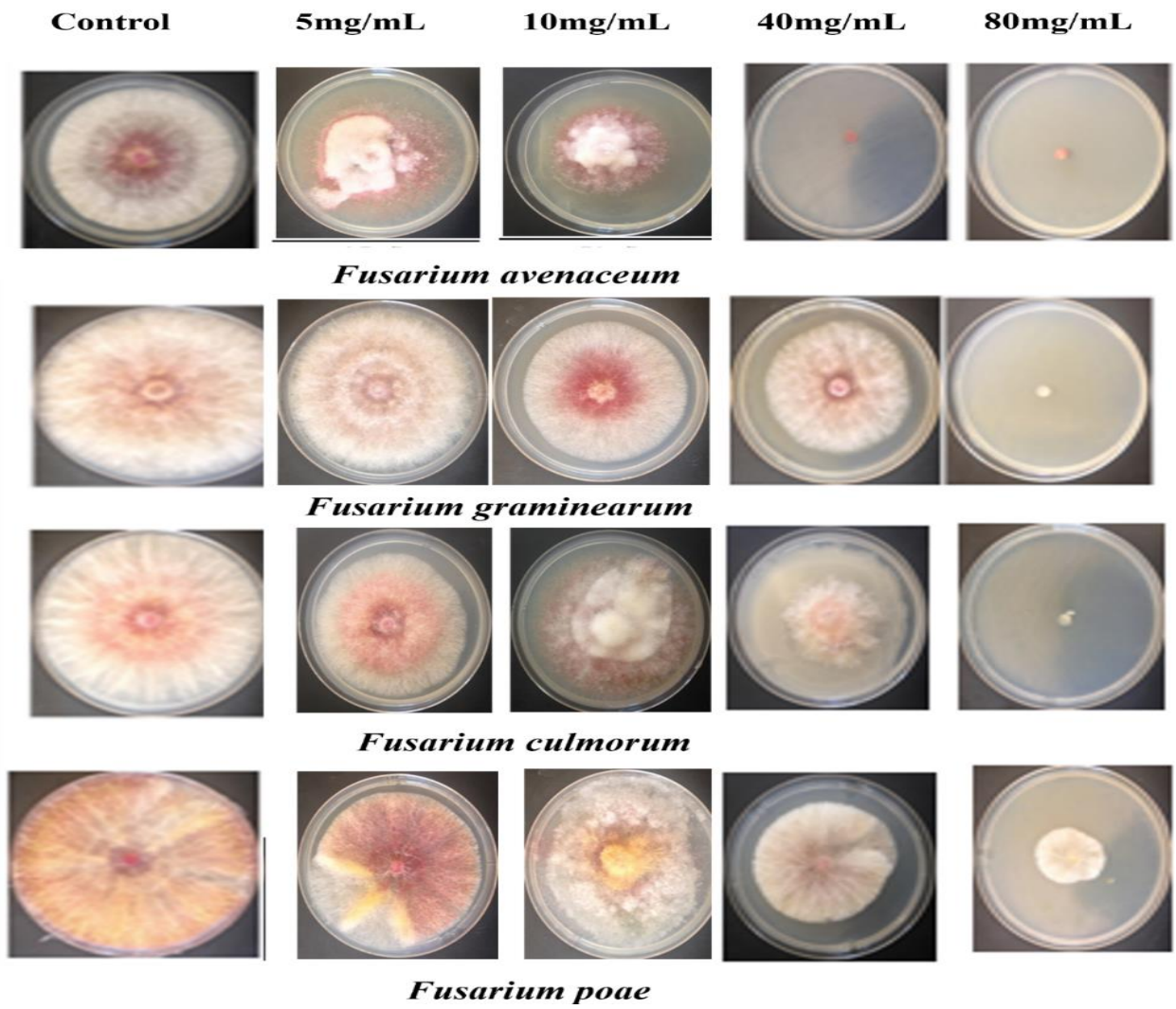

Fig. 3. The effect of methanol extract at different concentrations on four *Fusarium* species

Furthermore, the differences of the minimal inhibitory concentration value could be due to the morphological structure of the bacterial cells and their composition in the cells. The weak activity of the extract against the Gram-negative microorganisms can be associated with the presence of defensive enzymes and an outer membrane and a periplasmic space in $Gram^-$ bacteria, which are absent in $Gram^+$ bacteria (Horta et al., 2019). The results also showed that the effect of the inhibition of bacterial growth increased with increasing extract concentrations. Moreover, the solvent's extraction systems were crucial in obtaining notable antibacterial activity from plants including algae. *P. areuginosa* was the most resistant strain against the methanolic algal extract, which presents a CMI value higher than 4 mg/mL.

The antifungal activity results obtained in this study show that the methanolic extract effectively inhibits the mycelial growth of *Fusarium*. The extract obtained from *A. armata* using DMC/methanol mixture as extraction solvent has no activity toward the growth of *Cryptococcus neoformans*. Hmani et al. (2020) also reported that the methanol extract of *A. armata* species collected from the Tunisian coast presented no activity against *Candida albicans*. Also it found that the methanolic extract of *Asparagopsis taxiformis* elicited modest activity towards *Candida albicans* and *Penicillium* sp. furthermore, the results recorded show that the methanolic extract of *Hyneamus ciformis* (red algae) present a puissant activity against *C. albicans*, *Penicellium* sp. and *Aspergillus* sp. (Saim et al., 2021). In addition, Pinteus (2015) indicate that the dichloromethane extracts (1 mg/mL) of three red algae, among them *A. armata*, induced an inhibitory activity of 86% against *Saccharomyces cerevisiae*.

The results obtained from the minimum inhibitory concentration analysis showed that the methanol extract produced a MIC of 0.4 mg/mL against *Fusarium avenaceum* and showed a higher MIC of 0.8 mg/mL against *F. graminearum* and *F. culmorum*, therefore *F. avenaceum* is more sensitive to the methanolic extract of *A. armata* than other species.

Several studies have shown that seaweed is endowed with antifungal and anti-bacterial activity (Zinedine et al., 2004; Eouatassi & Louastel, 2012). The antifungal effect of the extracts of red algae comes following the interaction of the active principles with the lipids at the level of the mycelial wall, leading after their peroxidation to morphological alterations of the thalli of the fungi. A few red seaweeds have been reported to produce chemicals with potent biological activity (Küpper et al., 1998; Harper et al., 2001).

Yin & Tsao (1999) reported the inhibitory action on fungi strains It is possible that this is because of the formation of a hydrogen liaison between the active sites of the target enzymes and the hydroxyl group of phenolic compounds.

The antimicrobial effects of phenolic compounds may be influenced by several mechanisms, such as inhibition of microbial enzymes by oxide compounds, or by their non-specific actions on microbial protein, also the mechanism of phenol toxicity to fungi is based on the inactivation of fungal enzymes that contain the HS group in their active site (Cowan et al., 1999).

Most compounds with antimicrobial activity are terpenic derivatives (Etahiri et al., 2001; Wang et al., 2009; Chakraborty et al., 2010; Mahizan et al., 2019), phenolic (Etahiri et al., 2007; Choi et al., 2012; Daglia, 2012; Manso et al., 2022) and lipid (Paul et al., 2006). Red algae are able to produce bioactive molecules that can be used in the pharmaceutical industry.

Studies have shown that the genus *Asparagopsis* synthesizes various natural products such as halogen compounds, methane, ketones, acetates and acrylates (Genovese et al., 2009). Some parameters have

an effect on antimicrobial activity, such as harvest season and certain physicochemical parameters such as light, temperature, mineral salts and water movement (Amimi et al., 2007; El Omari et al., 2013) – they constitute the essential ecological parameters in the determination of the fertility of algae and therefore significantly affect the presence of bioactive molecules responsible for the biological activity.

Mc Connell & Fenical (1977), reported that the halogenated organic compounds of algae, which are thought to be at the origin of their antibacterial and antifungal activity, have 1 to 4 carbon atoms and are highly volatile. In addition, the red algae produce terpenes and acetogenins, substances from the polymerisation of acetates. Kladi et al. (2004) and Dembitsky & Srebnik (2002) have shown also that extracts of red seaweed inhibit the development of several fungal strains. These same authors also suggest that volatile compounds of red algae such as phenol derivatives and halogenated fatty acids, terpenoids and halogenated secondary metabolites are responsible for this antifungal activity. Among all marine algae, the Rhodophyta class has the greatest richness, offering a unique biosynthetic pathway for the synthesis of organohalogens. Algae produce halogenated organic compounds as a protective system against microorganism infections (Goodwin et al., 1997).

Furthermore, according to Jacinto et al. (2013), the powerful antimicrobial properties of *A. armata* is explained by the synthesis of halogenated compounds, derived from bromine.

Based on these results, the red alga *A. armata* is found to be rich in antimicrobial inhibitors. The extraction method used in our work has probably made it possible to obtain extracts that contain several active ingredients responsible for the inhibition of bacterial strains. We can deduce that the difference or concordance of our results with those of other works on the same species can be explained by: biosynthesis of secondary metabolites associated with seasonal variations or sexual phase of the algae, solvent type, nature and or concentration of bioactive molecules present in the species and their solubility in the chosen solvent and methods used to assess antimicrobial activity and choice of microorganisms to test and the differences in the extraction protocols to retrieve the active metabolites (Pinteus et al., 2015).

Conclusion

This study detected significant antimicrobial activities of the red alga *A. armata* extracts *in vitro* assays. Methanol was confirmed to be the most effective extraction solvent. The results showed that *A. armata* evidenced high antibacterial activity, as it inhibited the growth of Gram-negative and Gram-positive bacteria. Our finding shows that the antimicrobial activities obtained are related to the tested strain, the concentration of the active ingredient and the nature of the solvent of extraction.

The methanol extract was revealed to be an active antifungal agent, and seems to be the best extraction solvent given its high antifungal activity, so it can therefore be valued as a natural source of antifungal agents that can be used in the fight against mycotoxinogenic fungi. This study confirmed the considerable capacity of this alga for the production of bioactive molecules, which can be proposed as a natural source of antimicrobial agents that can be used to fight diseases and used in the pharmaceutical industry. In order to complete this study, it would be possible to determine the bioactive compounds responsible for these properties.

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