Marine-Derived Bioactive Substances' Microbicidal Mechanisms

Subjects: Others

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Marine natural compounds suppress or kill plant pathogenic pathogens through different mechanisms, including affecting microbial cell wall synthesis, cell membrane permeability, fatty acid metabolism, respiratory system, cytoskeleton, bacterial quorum sensing (QS), as well as inducing plant immune system for inhibition.

marine natural products | plant pathogens | bioactive substances | chemical control | antimicrobial mechanism

1. Affect Cell Wall Structures

Cell wall is the outermost structure of the plant pathogenic fungi and bacteria, which plays important role in maintaining cell shape and integrity. It also maintains normal metabolism, ion exchange, and osmotic pressure in cells [1]. Some marine compounds can inhibit the formation of microbial cell walls, thus suppress the growth or kill the pathogens. For instance, Chakraborty et al. isolated compounds **13**–**17** from a marine bacterium *B. subtilis* 109GGC020. Compounds **13**–**17** inhibit cell wall synthesis of *M. oryzae* to inhibit its growth [2]. Marine natural products can destroy structure of the fungal cell wall component glucosamine to inhibit the cell wall synthesis and growth. For example, microalgal phenolic extracts (MPE) were isolated from marine microalgae *Nannochloropsis* sp. and *Spirulina* sp., which can destroy the glucosamine structure of *F. graminearum* CQ244 and reduce glucosamine production by 15% [3]. Chitin is another fungal cell wall key component, which can be degraded by chitinase [4]. A chitinase was identified from the marine bacterium *B. pumilus* JUBCH08, which was proved to degrade the cell wall of *F. oxysporum* and inhibit its growth [5].

2. Affect Cell Membrane Permeability

The cell membrane is a lipid bilayer semi-permeable membrane, which controls the two-way flow of substances inside and outside the cell of the plant pathogens. The microbial cell membrane is another most common target of marine natural compounds. For example, antifungal ethyl acetate extract from marine-derived *Streptomyces* sp. AMA49 can destroy the cell membrane of *M. oryzae* to suppress fungal growth [6]. A series of other marine-derived natural compounds can also achieve their antibacterial effects by destroying the cell membrane of different plant pathogens [7][8][9][10][11][12]. Compound **9** isolated from *B. velezensis* 11-5 can selectively bind with phospholipids in the cell membrane of *M. oryzae*, thus affecting the membrane structure [13]. The microalgal phenolic extracts, which are isolated from *Nanochoropsis* and *Spirulina*, can combine with ergosterol on the membrane (MPE) of *F.*

graminearum cells to elevate plasma membrane permeability and lead to the leakage of proteins, nucleotides, amino acids, sugars, and salts, therefore leading to the death of fungi [14].

3. Affect Fatty Acid Metabolism

Fatty acid metabolism is very important for the functional appressorium formation in some plant pathogenic fungi. When the fatty acid metabolism of fungi is blocked, the fungi cannot penetrate plant cells [15][16][17]. Interestingly, it is reported that halisulfate 1 and bromophenols, the marine-derived metabolites, could inhibit the activity of *M. oryzae* isocitrate lyase, thus inhibiting the fatty acid metabolism, which will affect mature appressorium formation and penetration of *M. oryzae* [18][19].

4. Affect Respiratory System

Marine natural compounds can also target the respiratory electron transport system of plant pathogens to inhibit their respiration, through which they can inhibit the growth of pathogens. For example, compound **26** (Figure 1) isolated from marine *Myxobacterium* can breaking the electron flow by targeting the cytochrome b-c1 segment [20], and therefore inhibits the growth of plant pathogens.

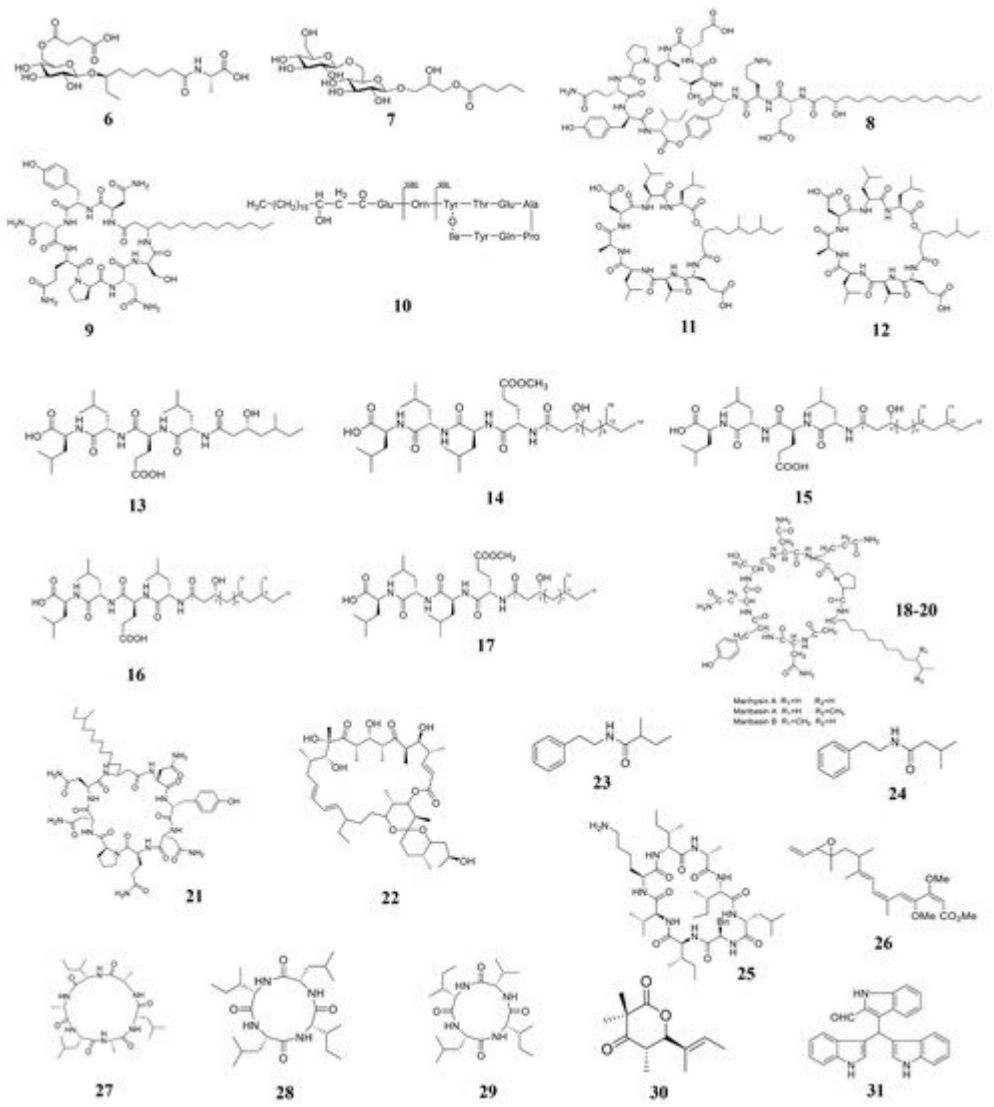

Figure 1. Chemical structures of the compounds identified from marine bacteria. **6** Ieodoglucomide C, **7** ieodoglycolipid, **8** plipastatin A1, **9** iturin A, **10** Fengycin BS155, **11**–**12** gageopeptins A and B, **13**–**16** gageopeptides A–D, **17** gageotetrin B, **18**–**20** Lipopeptides, **21** mojavensin A, **22** oligomycin A, **23** 2-methyl-N-(2′-phenylethyl)-butanamide, **24** 3-methyl-N-(2′-phenylethyl)-butanamide, **25** Champacyclin, **26** Haliangicin, **27**–**29** Halolitoralin, **30** helicascolide C, **31** Trisindolal.

5. Affect Cytoskeleton Formation

The cytoskeleton also plays important roles for fungal development and infection processes [21], whose components could be bound by the marine compounds and inhibit fungal growth and infection. For instance, the marine organisms derived compounds **46**–**48** (Figure 2) can inhibit the growth of *Colletotrichum* species and *B. cinerea* [22], the mechanism is that compounds **46**–**48** target the fungal β-tubulin proteins and subsequently suppress cell division [22].

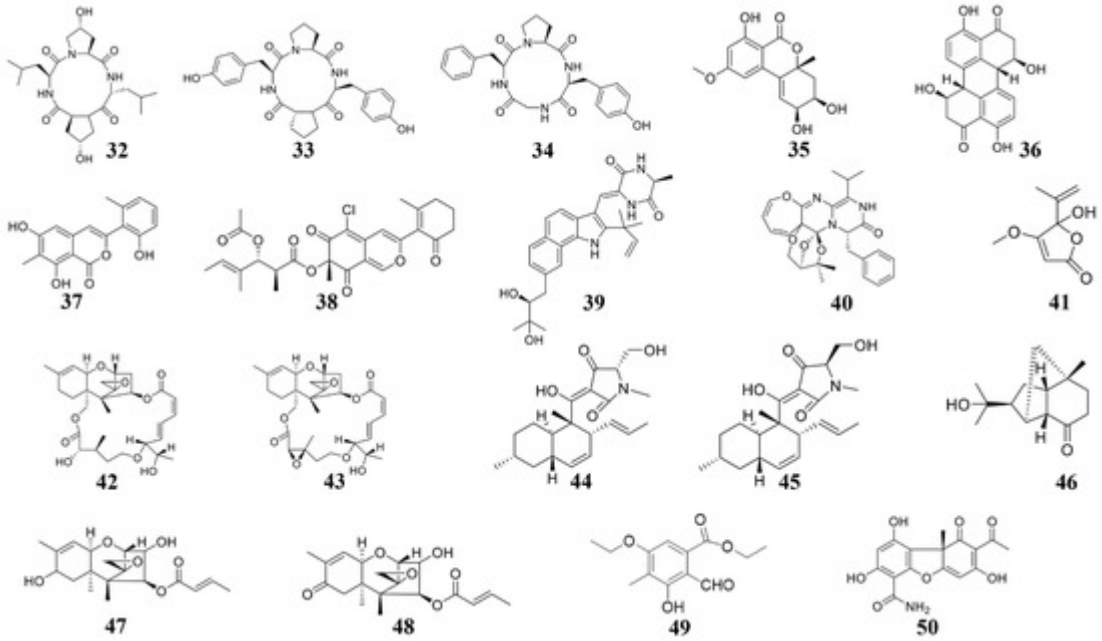

Figure 2. Chemical structures of the compounds identified from marine fungi. **32** Cyclo-(L-leucyl-*trans*-4-hydroxy-L-prolyl-D-leucyl-*trans*-4-hydroxy-L-proline), **33** cyclo (D-Pro-L-Tyr-L-Pro-L-Tyr), **34** cyclo (Gly-L-Phe-L-Pro-L-Tyr), **35** Benzopyranone, **36** Stemphyperylenol, **37** pleosporalone A, **38** pleosporalones B, **39** rubrumazine B, **40** Varioxepine A, **41** Penicillic acid, **42** roridin A, **43** roridin D, **44** equisetin, **45** epi-equisetin, **46**–**48** sesquiterpenes, **49** ethyl 5-ethoxy-2-formyl-3-hydroxy-4-methylbenzoate, **50** (-)-cercosporamide.

6. Affect Bacterial QS System

QS system can help bacteria to monitor the quantity change of itself or other bacteria in the surrounding environment, according to the concentration change of specific signal molecule autoinducer. When the signal molecule reaches a certain concentration threshold, it can start the expression of related genes in the bacteria to adapt to the environmental changes. When the QS system of bacteria is blocked, bacteria cannot communicate with the surrounding environment and failed to infect the host plant. Interestingly, some marine natural compounds can also target and interrupt the bacterial QS system to prevent infection of the bacterial pathogens [23][24]. For example, 2-methyl-n-(2'-phenylethyl)-butanamide and 3-methyl-n-(2'-phenylethyl)-butanamide, two marine-derived compounds, can destroy the QS system of rice pathogenic bacterium *B. glumae* (ATCC 333,617), therefore interrupt virulence feature production, including proteases, toxins, as well as some other immune-evasion factors [25]. In this situation, the QS signal is blocked by the marine compounds, and the bacteria fail to attack the host.

7. Induction of the Plant Immune System

Some marine natural products can not directly inhibit or kill bacteria against plant pathogens, but be used as elicitors to stimulate the plant immune system to inhibit or kill bacteria, which serve as an indirect antibacterial or bactericidal effect [26]. Ji et al. and Righini et al. isolated a series of compounds (**60**, **61**, polysaccharides) from marine organisms (Figure 3) [27][28]. The activity test of these compounds showed that they could not directly inhibit

the growth of plant pathogens, but stimulate the plants to resist to plant pathogens [27][28]. This elegant work clearly showed that the marine compounds could indirectly inhibit plant pathogens by inducing the host immune system.

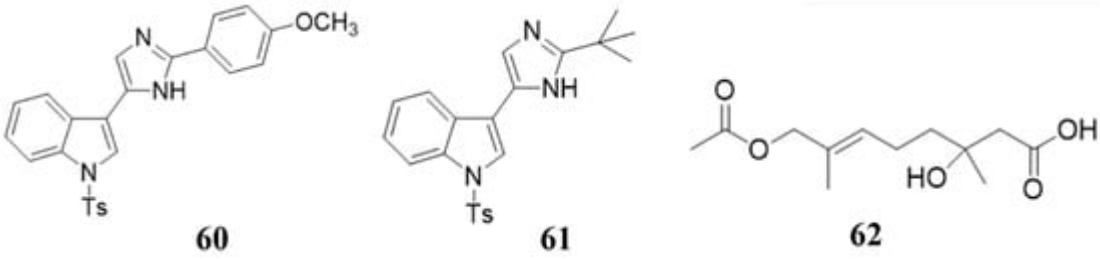

Figure 3. Chemical structures of the compounds **60** (nortopsentin alkaloid 2e), **61** (nortopsentin alkaloid 2k), and **62** penicimonoterpene (±).

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