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Review 综述

高盐环境微生物代谢产物的研究进展

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摘　要：高盐环境微生物(包括嗜盐菌和耐盐菌)广泛分布于盐湖、海洋及盐渍土等极端生境，因其独特的代谢适应机制而成为结构新颖天然产物的重要来源。本文概述了其分类地位与生态分布，重点总结了初级代谢产物中四氢嘧啶、甘氨酸甜菜碱等相容性溶质的化学结构，以及它们在渗透压调节和生物大分子保护中的核心作用；系统梳理了次级代谢产物中生物碱、萜类、甾体及聚酮类化合物的结构类型，归纳了这些化合物所展现的抗菌、抗肿瘤、抗氧化、酶抑制及光保护等生物活性，并探讨了构效关系。基于代谢产物的独特性质，分析了其在医药健康、生物材料、环境修复等领域的应用前景，为高盐环境微生物资源的深度开发及新型生物活性分子的研发提供理论参考。

关键词：高盐环境微生物；嗜盐菌；代谢产物；相容性溶质；生物活性；应用前景

Research progress in metabolites of microorganisms in high-salt environments

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Abstract: Microorganisms in high-salt environments (including halophilic and halotolerant

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bacteria) are widely distributed in extreme habitats such as salt lakes, oceans, and saline soils. Due to their unique metabolic adaptation mechanisms, they have become an important source of structurally novel natural products. This article outlines their taxonomic status and ecological distribution, with a focus on summarizing the chemical structures of compatible solutes such as ectoine and glycine betaine among primary metabolites, and their core roles in osmotic pressure regulation and biomacromolecule protection. The structural types of secondary metabolites, including alkaloids, terpenoids, steroids, and polyketides, are systematically reviewed. Furthermore, this article summarizes the biological activities such as antibacterial, antitumor, antioxidant, enzyme inhibitory, and photoprotective effects and discusses the structure-activity relationships of secondary metabolites. Considering the unique properties of these metabolites, this article analyzes their application prospects in fields such as medicine and health, biomaterials, and environmental remediation. This review aims to provide a theoretical reference for the in-depth development of microbial resources in high-salt environments and the discovery of novel bioactive molecules.

Keywords: microorganisms in high-salt environments; halophilic bacteria; metabolites; compatible solutes; biological activity; application prospects

极端环境微生物(extremophiles)是发现结构新颖、活性独特天然产物的重要资源[1-2]。其中，高盐环境微生物为适应高盐、强辐射及营养贫瘠等极端条件，进化出独特的遗传与代谢机制，如渗透压调节策略[“盐进(salt-in)”或“有机溶质外排(organic-solute-out)”]，进而驱动其合成多样化的次级代谢产物[3-4]。这些化合物是高盐环境微生物在极端生境中执行化学防御与竞争的关键，也为解决抗生素耐药性、开发抗肿瘤先导物等提供了宝贵的分子资源库[5]。然而，该领域研究仍面临两大瓶颈：(1) 绝大多数高盐环境微生物属于“微生物暗物质”，难以通过传统方法培养，限制了物种多样性及其代谢潜力的挖掘[6]；(2) 即便对于可培养菌株，其生物合成基因簇(biosynthetic gene clusters, BGCs)在常规条件下多呈“沉默”或低表达状态，导致产物产量低、难以检测[7-8]。因此，突破培养限制并激活沉默基因簇已成为核心科学问题。当前，多组学联用技术与合成生物学策略正推动该领域取得进展。基因组、转录组与代谢组学整合可高效鉴定潜在 BGCs 并揭示调控网络；合成生物学手段则可通过异源表达或途径重构实现沉默簇的激活与优化。目前已从高盐环境微生物中发掘出包括生物碱、聚酮、萜类在内的多种结构类型化合物，展现出抗菌、抗肿瘤、抗氧化等活性，在医药健康、绿色工业及环境修复中具有广阔应用前景。高盐环境微生物代谢产物的深度解析，需依托多学科技术融合以突破培养与表达瓶颈、释放其生物活性分子潜力，进而加速从基础研究到产业应用的转化进程。

1 高盐环境微生物的生物学分类、形态及分布

1.1 高盐环境微生物的生物学分类

高盐环境微生物的分类可从系统发育归属与盐浓度适应性 2 个维度进行系统梳理。在系统发育层面，高盐环境微生物主要分为真菌、古菌域(Archaea)和细菌域(Bacteria)[9]。根据现有研究，绝大多数已知的嗜盐真菌隶属于 2 大真菌门：子囊菌门(*Ascomycota*)和担子菌门(*Basidiomycota*)[10]。在子囊菌门中嗜盐种类分布广泛。其中，曲霉属(*Aspergillus*)和青霉属(*Penicillium*)是高盐环境中最为常见的丝状真菌代表[11]。这些菌属具有极强的环境适应能力，能在盐田、盐渍土等多种生境中被分离出来。

此外，座囊菌纲(*Dothideomycetes*)的枝孢属(*Cladosporium*)和链格孢属(*Alternaria*)也包含众多耐盐乃至嗜盐的物种。在担子菌门中节担菌纲(*Wallemiomycetes*)的节担菌属(*Wallemia*)是嗜盐真菌中最具代表性的类群[12]。古菌域中的嗜盐类群多属极端嗜盐菌，主要代表为盐古杆菌纲(*Halobacteria*)，包括需盐小杆菌属(*Halobacterium*)、盐球古菌属(*Halococcus*)等，其细胞结构及代谢机制显著区别于细菌[13]。细菌域中的嗜盐菌则广泛分布于多个门类，如γ-变形菌纲(*Gammaproteobacteria*)中的盐单胞菌属(*Halomonas*)和放线菌门(*Actinomycetota*)中的放线多孢菌属(*Actinopolyspora*)[14]。在盐浓度适应性层面，微生物分类采用 Kushner[15]提出的体系，依据最适生长 NaCl 浓度将嗜盐微生物划分为 7 类，反映了微生物对渗透压的进化适应策略，涵盖从非嗜盐到极端嗜盐的连续谱系，其中耐盐菌虽可在高盐环境中存活，但最适盐浓度较低[16]。表 1 总结了分类标准与代表性类群。

1.2　高盐环境微生物的形态特征

高盐环境微生物的形态特征与其对高盐环境的适应性密切相关，不同类群的细胞形态及结构呈现出显著的特化现象，这些特化结构是它们长期适应高盐胁迫的进化结果[17]。细菌域中的嗜盐菌主要以杆状和球状为主要形态，如盐杆菌属(*Salibacter*)细胞直径为 0.6−1.5 μm，长度可达 6 μm[14]；滨海沉积物盐单胞菌新种(*Halomonas marinisediminis* sp. nov.)呈球状或短杆状，通过侧生鞭毛实现运动，从而增强其对环境资源的获取能力[18]。为应对高盐环境的渗透压压力，嗜盐菌的细胞结构演化出了多重适应性特征。Yu 等[19]在对新分离的嗜盐菌株河口俊片菌(*Lampropedia aestuarii*) GYF-1 的研究中利用显微成像技术清晰地展示了其在固体培养基上形成的片状、扁平的菌落形态，以及细胞聚集形成的方形或矩形四联体结构，这种独特的排列方式有利于其在盐环境中生存。嗜盐菌的形态极为丰富，涵盖了从经典的球状、杆状到独特的方形、多形性等多种类型。

1.3　高盐环境微生物的分布规律

高盐环境微生物的分布规律受盐浓度梯度、离子组成及环境因子的严格调控，呈现出明显的生态位分异性。其栖息地主要包括自然高盐环境(如海洋、盐湖、盐渍土壤)和人工高盐系统(如发酵罐、高盐废水)[20]。在不同盐度梯度下，高盐环境微生物群落呈现出连续的演替格局[21]。在盐湖系统中盐度梯度直接驱动高盐环境微生物的空间分布：高盐核心区(盐浓度>20%)以极端嗜盐古菌为主，它们通过“盐进”策略(积累 K^+ 及相容性溶质)维持胞内渗透平衡；而过渡区(盐浓度 3%−15%)则以中度嗜盐菌为优势类群，依赖有机溶质合成来适应中盐环境[22-23]。盐渍土壤及海洋沉积物中的嗜盐菌分布则受盐分类型

表1　按盐浓度适应性分类[15-16]

Table 1　Classification by salt concentration adaptability[15-16]

Classification	Salt tolerance limit (mol/L)	Examples of microorganisms
Non-halophilic bacteria	<0.2	Most freshwater microorganisms, common eubacteria
Slightly halophilic bacteria	0.2−0.5	Most marine microorganisms
Moderately halophilic bacteria	0.5−2.5	*Vibrio costicola*, species of *Pseudomonas*, *Paracoccus denitrificans*
Extreme borderline halophilic bacteria	2.5−4.0	*Ectothiorhodospira halophila*, *Actinopolyspora halophila*
Extremely halophilic bacteria	4.0−5.9	*Halobacterium*, *Halococcus morrhuae*
Halotolerant bacteria	Tolerable to salt environment	*Staphylococcus epidermidis*, solute-tolerant yeast, fungi
Extremely halotolerant bacteria	Survive at 2.5 mol/L salt concentration	

($NaCl$、Mg^{2+}、SO_4^{2-})及有机质含量的双重影响。例如，Mg^{2+}富集区域多见嗜盐硫酸盐还原菌，而有机质丰富的根际土壤中 *Halomonas* 属丰度显著升高[24-25]。此外，高盐环境微生物的分布具有地理区域性，不同盐湖(如新疆艾丁湖、印度 Sambhar 盐湖)因离子组成及气候差异形成特有种群结构，如 Sambhar 湖中嗜盐菌多样性以中度嗜盐菌为主且富含色素合成类群[26]。全球范围内，高盐环境微生物的分布规律进一步受温度、pH 及营养可用性调控，高温碱性环境(如 Wadi El Natrun 盐湖)更利于高盐环境微生物的发掘。表 2 的分布规律不仅反映了其生理适应性，也为开发高盐环境微生物资源(如酶制剂、生物修复)提供了生态学依据。

2　高盐环境微生物代谢产物

2.1　初级代谢产物

高盐环境微生物为适应渗透胁迫，进化出合成相容性溶质、胞外多糖(exopolysaccharide, EPS)及聚羟基脂肪酸酯(polyhydroxyalkanoates, PHA)的独特策略。相容性溶质中四氢嘧啶(ectoine, ECT)以 1,4,5,6-四氢-2-甲基-4-嘧啶羧酸为核心骨架，通过优先排挤出蛋白质水合层稳定生物大分子构象[27-28]；其羟基化衍生物 5-羟基四氢嘧啶(5-hydroxyectoine, 5-HE)因 C-5 位羟基增强氢键网络，抗氧化及耐热干燥能力更优[29]，且 ectoine 可通过抑制环氧合酶-2 (cyclooxygenase-2, COX-2)、基质金属蛋白酶(matrix metalloproteinases, MMPs)以及肿瘤坏死因子-α (tumor necrosis factor-α, TNF-α)、白细胞介素-1β (interleukin-1β, IL-1β)等促炎因子发挥抗炎与软骨保护作用[30-31]。甘氨酸甜菜碱作为完全 N-甲基化两性离子化合物，其季铵阳离子头基可直接结合带负电大分子，跨膜转运能力强，是应对渗透压骤变的首选溶质，还可作为甲基供体参与甲硫氨酸循环[32-33]。菌株的盐胁迫适应性由溶质合成与转运能力决定，如缺乏渗透保护剂摄取系统的菌株对盐敏感[34]；需盐色盐杆菌(*Chromohalobacter salexigens*)则通过上调 *gbcA*、*gbcB* 等基因协同积累多种溶质[35]。EPS 的生物活性由单糖组成与糖苷键构型决定，伸长盐单胞菌(*Halomonas elongata*) S6 的 EPS 可抑制病原菌生物膜形成[36]；独岛枝芽孢杆菌(*Virgibacillus dokdonensis*)的 EPS 能激活免疫应答[37]；特基拉芽孢杆菌(*Bacillus tequilensis*)-GM 的 EPS 抗癌效果与分子量、乙酰化程度相关[38]；地中海富盐菌(*Haloferax mediterranei*)的硫酸化 EPS 具有类肝素抗凝血活性[39]；窄环境盐单胞菌(*Halomonas stenophila*) B-100 含 *N*-乙酰氨基葡

表2　高盐环境微生物分布规律

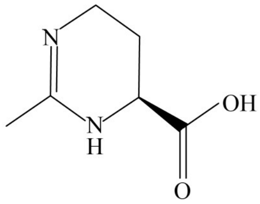
Table 2　Distribution patterns of microorganisms in high-salt environments

Habitat type	Environmental characteristics	Dominant halophilic bacterial groups	References
Salt lake	High-salt core area: salt concentration >20% Transition area: salt concentration 3%−15% Part in high-temperature and alkaline environment	High-salt core area: extremely halophilic archaea (e.g., *Haloarchaea*) Transition area: moderately halophilic bacteria (e.g., *Halomonas*, *Gracilibacillus*) High-temperature and alkaline environment: halophilic actinomycetes, *Bacillus*	[22-23]
Saline soil	Affected by salt types ($NaCl$, Mg^{2+}, SO_4^{2-}) and organic matter content Rhizosphere soil with abundant organic matter	Mg^{2+} enriched area: halophilic sulfate-reducing bacteria (e.g., *Desulfocella*) Rhizosphere soil: *Halomonas* sp.	[24-25]
Marine sediment	Regulated by salt types and organic matter content, with geographical regionality	Dominated by moderately halophilic bacteria, some with pigment-synthesizing groups	[24-26]
Artificial high-salt system	Artificial high-salt environment including fermenters, high-salt wastewater, etc.		[20]

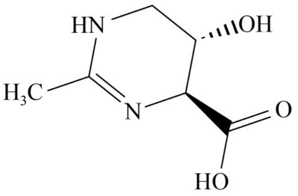
萄糖(*N*-acetylglucosamine, GlcNAc)的 EPS 可抑制致病菌生物膜[40]。PHA 由高盐环境微生物独特的聚羟基脂肪酸酯合酶(polyhydroxyalkanoate synthase, PhaC)合成，侧链基团调控材料热塑性[41]。PhaC 的保守催化三联体(Cys-Asp-His)通过 *N*-端螺旋域二聚化适应高盐环境[42]。沙漠盐单胞菌(*Halomonas desertis*) G11 的 PhaC1 在高盐下保持高活性[43]；盐单胞菌属(*Halomonas* sp.) MC140 的基因冗余赋予酶活性多样性[44]；海冰来源盐单胞菌属(*Halomonas* sp.) 363 的合酶可在低温高盐下实现短、中链 PHA 共聚，制备热性能可调的生物塑料[45-46]。上述构效关系为细胞保护剂、抗肿瘤药物及生物材料研发提供了关键分子模板。

2.2 次级代谢产物

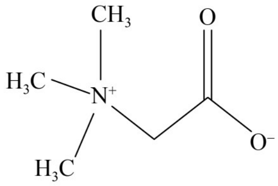
高盐环境微生物为适应极端生存压力，进化出独特的代谢途径，产生结构多样的次级代谢产物，成为药物研发的重要资源(图 1、表 3)。在生物碱方面，Borkunov 等[47]从海洋真菌中获得哌嗪衍生物 helvamides B–C (**4–6**)，其中 helvamide C 对白色念珠菌的抑制率达 31.54%。Siddharth 等[48]从嗜盐放线菌中分离出 1-乙酰-4-(4-羟苯基)哌嗪(**7**)，其对耐甲氧西林金黄色葡萄球菌(methicillin-resistant *Staphylococcus aureus*, MRSA)的最低抑菌浓度(minimum inhibitory concentration, MIC)为 7.81 μg/mL，且具有抗肿瘤活性。Li 等[49]发现吡喃并吡啶类生物碱(**8–11**)通过抑制一氧化氮(nitric oxide, NO)释放发挥抗炎作用。Teixeira 等[50]从南极真菌中获得喹啉类生物碱 viridicatin (**12**)和 viridicatol (**13**)，具有光保护活性。Zhang 等[51]分离出含萘醌哌嗪硫吗啉四环骨架的硫代生物碱 dassonmycins A–B (**14–15**)，具有抗菌和抗肿瘤活性。傅春青等[52]获得 7 种二酮哌嗪类生物碱(**16–22**)，部分抑制乙酰胆碱酯酶。在萜类和甾体方面，Kim 等[53]从嗜盐放线菌中获得含咔唑十氢萘稠合的吲哚倍半萜夏霉素 C–E (**23–25**)，其中夏霉素 D (**24**)对猪流行性腹泻病毒具有抑制作用[半数有效浓度(half maximal effective concentration, EC_{50}) = 0.93 μmol/L]。Chen 等[54]从深海真菌中获得罕见 6/5-5 三环降甾醇 Phosteoid A (**26**)。梁学诚等[55]鉴定出 9-羟基取代甾体(**27**)，对 K562 和 SGC7901 细胞具中等细胞毒性。傅春青等[52]获得多羟基甾体(**28**)，其抗氧化能力优于抗坏血酸，且强效抑制 α-葡萄糖苷酶[半数抑制浓度(median inhibition concentration, IC_{50})=2.662 μmol/L]。贾辉等[56]发现含氯吲哚二萜(**29–31**)具有抗植物病原菌活性。Cheng 等[57]报道 austalide Y (**32**)具细胞毒性，拉布丹型二萜(**33–34**)降糖活性优于阿卡波糖。在聚酮类化合物中，章宝丹等[58]从深海嗜盐青霉中获得 5 个聚酮(**35–39**)，疣孢菌素类(**35–38**)具有抗幽门螺杆菌活性，苯醌 peniquinone A (**39**)具有广谱抗菌活性。Jang 等[59]分离出含 6/6/8 三环的聚酮糖苷 jejuketomycins A–B (**40–41**)，可抑制癌细胞迁移。Van Anh 等[60]获得利福霉素类(**42–44**)，证实芳香环对细胞毒性起关键作用。梁莉芬等[61]鉴定的十四元内酯类(**45–48**)具有抗藤壶附着活性。Gavrilov 等[62]报道 rosamicin (**49**)具有选择性抗革兰氏阳性菌活性。在其他化合物方面，Athmika 等[63]从马尔佩盐单胞菌(*Halomonas malpeensis*)中获得玉米黄质(**50**)，其抗氧化活性显著。Arum 等[64]从克劳斯氏嗜碱盐芽孢杆菌(*Alkalihalobacillus clausii*) J1G 中提取的类胡萝卜素(**51**)具有抗氧化性，但在光照空气下易失活。Liu 等[65]报道环酯肽 miuraenamide A (**52**)具有强效抗真菌活性，并能稳定肌动蛋白。Han 等[66]分离的色酮衍生物(**53**)抑制 α-葡萄糖苷酶优于阿卡波糖。王聪等[67]获得的霉酚酸类(**54–56**)因 C-6′位取代基的差异对 AGS 细胞显示出显著细胞毒性。上述研究表明，高盐环境微生物来源的次级代谢产物凭借骨架变异与官能团修饰形成的结构多样性，在抗菌、抗炎、抗病毒、抗肿瘤、酶抑制及光保护等领域展现出重要应用潜力，为药物研发提供了优质天然模板。



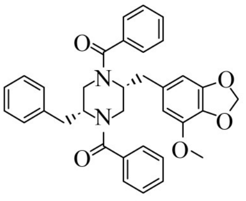
1 Ectoine



2 Hydroxyectoine



3 Glycine betaine



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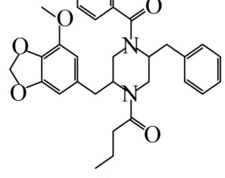

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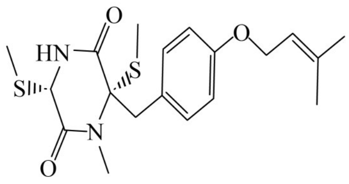

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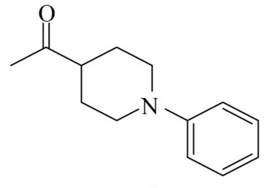

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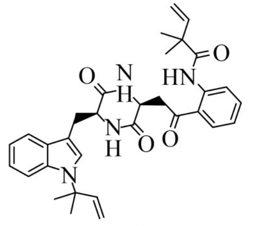

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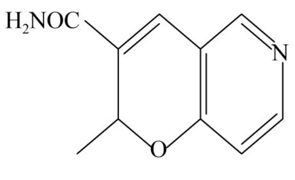

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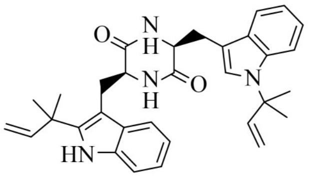

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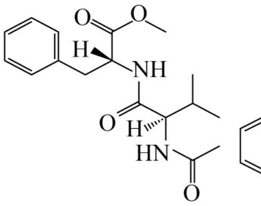

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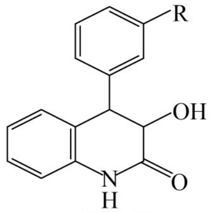
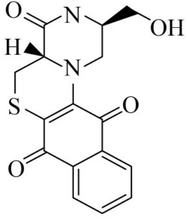


12 R=H
13 R=OH



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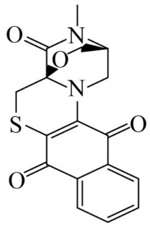

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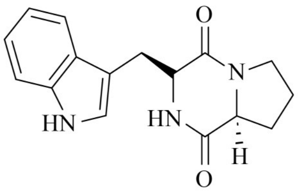

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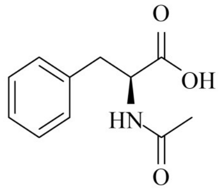

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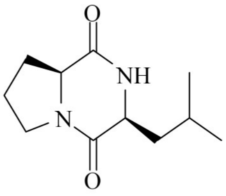

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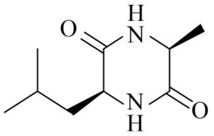

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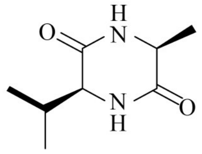

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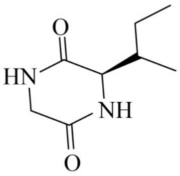

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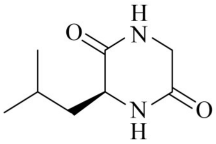

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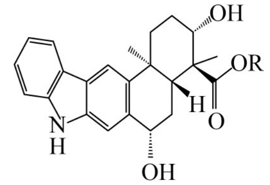
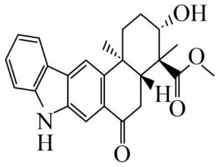


23 R=H
24 R=CH_3



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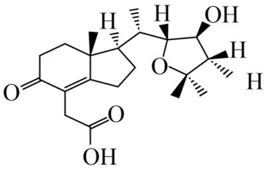

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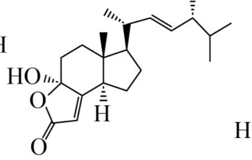

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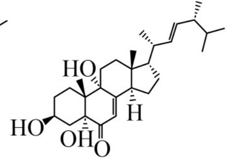

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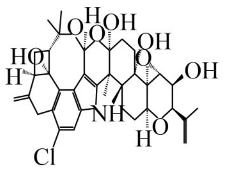
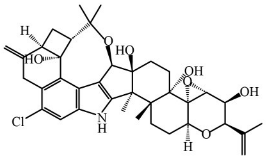


29 R=H
30 R=CH_3



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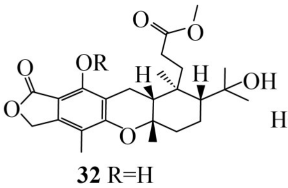
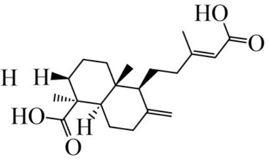


32 R=H
33 R=CH_3



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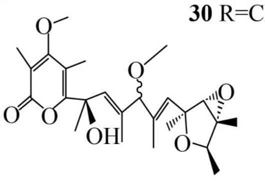

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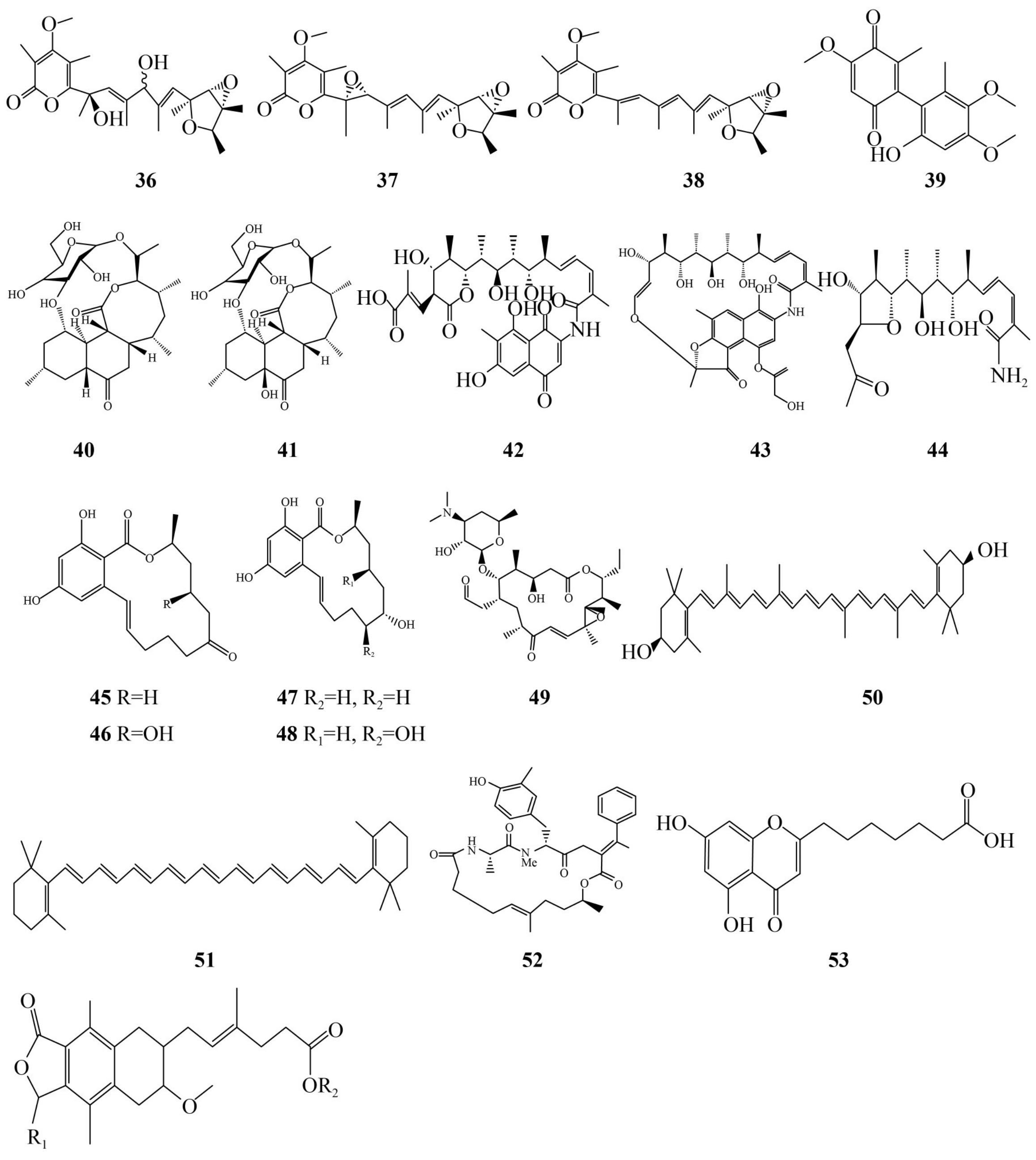

图1　化合物1–56结构式

Figure 1 Chemical structures of compounds **1–56**. Structural formulas of compounds **1–3** correspond to like-dissolves-like compounds; Structural formulas of compounds **4–22** correspond to alkaloid compounds; Structural formulas of compounds **23–34** correspond to terpenoid and steroid compounds; Structural formulas of compounds **35–49** correspond to polyketide compounds; Structural formulas of compounds **50–56** correspond to other substances.

表3　高盐环境微生物代谢产物特征

Table 3　Characteristics of metabolites from microorganisms in high-salt environments

Microbial strain	Salt tolerance characteristics	Metabolite	Structural features of the chemistry	Primary biological activity	References
Halomonas sp. XH26	Halophilic bacteria	Ectoine; 5-HE (Compounds **1**−**2**)	Ectoine: 1,4,5,6-tetrahydro-2-methyl-4-pyrimidinecarboxylic acid with a five-membered ring backbone; 5-HE: hydroxylation at the C-5 position, enhancing hydrogen bonding capacity	Reduces reactive oxygen species (ROS) and inflammatory factor expression; restores immune balance and mucin expression in a mouse model of dry eye, protecting the cornea	[27-31]
Chromohalobacter salexigens	Halophilic bacteria	Glycine betaine (Compound **3**)	A completely *N*-methylated glycine derivative, a zwitterion with a quaternary ammonium cationic head group	Involved in methyl metabolism, energy storage, and transmembrane transport systems	[32-35]
Halomonas elongata S6, *Virgibacillus dokdonensis*, *Chromohalobacter salexigen*, *Haloferax mediterranei*, *Halomonas stenophila* B-100	Halophilic bacteria	EPS	Rich in fucose and galactose, highly branched structure; molecular weight and degree of acetylation are key structural variables; contains *N*-acetylglucosamine	Anti-biofilm; immunomodulatory; exhibits heparin-like anticoagulant activity; significantly inhibits biofilm formation by pathogenic bacteria such as *Staphylococcus aureus*	[36-40]
Halomonas sp.	Halophilic bacteria	PHA	Diverse side chain groups (alkenyl, phenyl, alkyl); catalyzed by PHA synthase (PhaC)	Structural diversity dictates material properties (crystallinity, thermoplasticity)	[41-46]
Penicillium velutinum ZK-14	Marine-derived fungus	Compounds **4**−**6**	Helvamide B features a 2*R*,5*R* piperidine ring; helvamide C contains butyryl and benzoyl substitutions	Inhibits *Candida albicans*	[47]
Nocardiopsis sp. SCA30	Halophilic bacteria	Compound **7**	6/6 ring-fused structure with conjugation of a piperazine ring and a benzene ring	Antibacterial; antitumor	[48]
Penicillium sp. LSH-3-1	Marine-derived fungus	Compounds **8**−**11**	8: Diketopiperazine ring combined with an indole ring; 9: Pyranopyridine skeleton	Cytotoxicity; anti-inflammatory	[49]
Penicillium echinulatum	Marine-derived fungus	Compounds **12**−**13**	Quinoline alkaloids containing hydroxyl substitutions	Photoprotective activity	[50]
Nocardiopsis dassonvillei SCSIO 40065	Identified halophilic bacteria	Compounds **14**−**15**	Sulfur-containing tetracyclic skeleton; B possesses an additional ether bridge forming a cage-like structure	Antibacterial; cytotoxicity	[51]
Cladosporium cladosporioides GXIMD 00533	Halophilic fungi	Compounds **16**−**22**, Compound **28**	Diketopiperazine skeleton; polyhydroxylated steroid skeleton	Acetylcholinesterase inhibitory activity; antioxidant; hypoglycemic activity	[52]
Streptomyces sp. HK18	Halophilic actinomycetes	Compounds **23**−**25**	Indole sesquiterpenes featuring a unique structure with a carbazole skeleton fused to a decalin ring; chartreusin D possesses a methyl ester functional group at the C-24 position	Chartreusin D exhibits potent inhibitory activity against porcine epidemic diarrhea virus	[53]
Phomopsis tersa FS441	Marine-derived fungus	Compound **26**	Norsteroid with a rare 6/5-5 tricyclic skeleton		[54]

(待续)

(续表3)

Microbial strain	Salt tolerance characteristics	Metabolite	Structural features of the chemistry	Primary biological activity	References
Penicillium sp. G5A-11	Marine-derived fungus	Compound **27**	Based on an ergosterol nucleus, modified by hydroxyl substitution and lactone ring formation	Cytotoxicity: moderate activity against K562 and SGC7901 cells	[55]
Penicillium sp. HQ2-12	Marine-derived fungus	Compounds **29−31**	Indole diterpenes with a structure featuring a chlorine-substituted indole ring fused to a diterpene skeleton	Significant inhibitory activity against *Phomopsis citri*	[56]
Penicillium thomii YPGA3	Marine-derived fungus	Compounds **32−34**	Compound **32** is a new meroterpenoid; compound **33** is a diterpene	Compound **32** exhibits cytotoxicity; compounds **33** and **34** show superior α-glucosidase inhibitory activity compared to the positive control	[57]
Penicillium sp. LW23	Marine-derived fungus	Compounds **35−39**	**35−38**: Core structure is a polycyclic skeleton, with **37** containing a **6−7** epoxy ring and **38** featuring a double bond; **39**: Possesses a unique aromatic ring substitution structure	Compounds **37** and **38** show moderate antibacterial activity against *Helicobacter pylori*; Compound **39** exhibits inhibitory effects against various plant pathogens	[58]
Streptomyces sp. KCB15JA151	Soil-derived actinomycete	Compounds **40−41**	Polyketide glycoside with a rare 6/6/8 tricyclic ring system	Significantly inhibits the migration ability of cancer cells	[59]
Salinispora arenicola 225DD-027	Halophilic actinomycetes	Compounds **42−44**	**42**: Core structure features an aromatic ring linked to an ansa chain, with the hemiacetal at C-34a oxidized to a carbonyl group	Compound **42** exhibits moderate toxicity against various solid tumor and hematological cancer cells	[60]
Fusarium incarnatum GXIMD00527	Saltern-derived fungus	Compounds **45−48**	Core structure is a resorcinol aromatic ring connected to a macrolide	Compounds **45** and **48** effectively inhibit the attachment of barnacle larvae	[61]
Streptomyces sp. ACA25	Marine-derived *Streptomyces*	Compound **49**	Polyketide antibiotic	Exhibits antibacterial activity against Gram-positive bacteria	[62]
Halomonas malpeensis YU-PRIM-29T	Halophilic bacteria	Compound **50**	Zeaxanthin, possessing a conjugated double bond structure	Zeaxanthin exhibits 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging and antioxidant activities	[63]
Bacillus clausii J1G	Halophilic bacteria	Compound **51**	Carotenoid, containing carboxyl and alkane C−H groups	Crude extract shows DPPH scavenging activity	[64]
Paraliomyxa miuraensis SMH-27-4	Identified halophilic bacteria	Compound **52**	Cyclic depsipeptide	Extremely potent activity against plant pathogens; stabilizes actin filaments in tumor cells	[65]
Penicillium thomii YPGA3	Marine-derived fungus	Compound **53**	Chromone derivative, based on a 5,7-dioxochromone nucleus	Potent α-glucosidase inhibitory activity	[66]
Penicillium sp. HD-1-1	Marine-derived fungus	Compound **54−56**	Mycophenolic acid class, containing a benzofuranone chromophore	Compounds **55** and **56** exhibit strong cytotoxic activity against AGS gastric cancer cells	[67]

3 高盐环境微生物的应用领域

基于高盐环境微生物独特的生理代谢机制和多样化的活性产物，其在工业、医药开发、环境修复等领域展现出广阔的应用前景。

3.1 工业领域的应用

高盐环境微生物的工业应用聚焦于其独特的耐盐酶及生物聚合物等核心产物。耐盐酶，如淀粉酶、蛋白酶等，可在高盐、高离子强度条件下保持稳定与催化活性，无需低盐缓冲液，已广泛应用于食品发酵、洗涤剂、纺织及生物燃料生产领域，有效简化了工艺并降低了成本[68]。在生物聚合物方面，聚羟基烷酸酯(polyhydroxyalkanoates, PHAs)作为可生物降解的绿色塑料备受关注。Alsafadi 等[69]发现嗜盐古菌 *Haloferax mediterranei* 可直接利用海水合成 PHAs，显著减少了淡水资源消耗与生产成本；胞外多糖(EPS)因结构独特，可作为生物模板绿色合成纳米功能材料。Rasulov 等[70]利用盐碱土来源圆褐固氮菌(*Azotobacter chroococcum*) XU1 的 EPS，在温和水相条件下合成了尺寸均一的 Ag/AgCl 纳米颗粒，用作新型生物杀菌剂。此外，高盐环境微生物作为高效“细胞工厂”，在高附加值化合物生产中展现出巨大潜力。He 等[71]通过代谢工程改造蓝色产碱盐单胞菌(*Halomonas bluephagenesis*)，引入 4-羟基丁酸和 3-羟基戊酸合成途径并优化解毒系统，该菌株以葡萄糖为唯一碳源高效合成三元共聚物 3-羟丁酸-辅-4-羟丁酸-辅-3-羟基戊酸盐，在 100 L 发酵罐中细胞干重达 73 g/L，PHA 占比 78%。Liu 等[72]则为该菌建立了木糖酸与核酮糖-L-磷酸途径，通过基因调控实现了木糖向乙二醇(0.91 g/L)和乙醇酸(0.80 g/L)的转化，并同步积累了聚-β-羟基丁酸酯(poly-β-hydroxybutyrate, PHB)。这些突破拓展了底物利用范围与产物多样性，为高盐环境微生物规模化生产生物基材料及高值化学品奠定了坚实基础。

3.2 医药健康领域的应用

高盐环境微生物代谢产物在医药健康领域展现出显著应用潜力。嗜盐菌产生的四氢嘧啶(ectoine)、类胡萝卜素等次级代谢产物，凭借抗氧化、抗炎及保湿功能，已广泛应用于化妆品与药品开发[73]。朱德锐[74]对青海湖嗜盐菌的研究表明，其胞内积聚的四氢嘧啶具有显著细胞保护作用，为新型抗炎药物研发提供了潜在资源；田雪等[75]发现 5-羟基四氢嘧啶可维持蛋白质与 DNA 稳定性、保护细胞组织，且通过嗜盐菌混合培养、ECT “喂养”及培养条件优化能实现高效合成，为其医药应用提供了理论与技术支撑。此外，嗜盐真菌的次级代谢产物在抗肿瘤研究中表现突出，部分化合物对肿瘤细胞具有显著抑制作用[76]。Ectoine 已被开发为滴眼液、鼻喷雾剂和吸入剂，用于治疗眼部炎症、过敏性鼻炎及呼吸道疾病，其作用机制与稳定细胞膜、抗炎及保湿特性密切相关[77]；其产生的抗氧化、抗肿瘤活性物质及在纳米粒子合成中的应用，也为医疗保健领域开辟了新路径[78]。这些代谢产物因独特生物活性，成为新型抗肿瘤药物、抗炎药物及生物医用材料开发的重要资源，未来结合多组学技术与合成生物学策略，有望进一步挖掘其药用潜力，推动在生物医药领域的深度应用。

3.3 环境修复领域的应用

在环境修复领域，微生物及其代谢产物在污染治理中展现出显著潜力。在有机污染修复方面，丛枝菌根真菌通过与植物共生，可增强植物对重金属(如镉)的吸收与固定能力，提升土壤微生物多样性，从而有效降低污染物生物有效性，为矿区土壤修复提供有效方案[79]。针对石油污染的盐碱土壤与海洋环境，高盐环境微生物成为修复主力军。多数高盐环境微生物能够以石油烃(C10−C35)和多环芳烃为碳源生长，如 *Halomonas* sp. 在 5% NaCl 浓度下对石油烃降解率达 55%−85%[80]。此外，高盐环境微生物群

落可高效去除高盐废水中的化学需氧量(chemical oxygen demand, COD)、苯酚、氰化物等有毒物质[81]，采用高盐环境微生物的生物反应器处理汽车服务站废水，COD 去除率高达 93%[82]。汪恩旭等[83]分离的兼性好氧反硝化嗜盐菌海杆菌属(*Marinobacter* sp.) W-8 在好氧、厌氧及低氧环境中均能高效脱氮，且碳源需求低、污泥产量少，为高盐高硝态氮废水处理提供了理论与技术支撑。在重金属污染治理中，高盐环境微生物分泌的胞外多糖展现出优异的生物吸附潜力，其细胞表面丰富的官能团及带电荷的 EPS 可通过络合、离子交换等机制吸附固定水体中的 Pb^{2+}、Hg^{2+}、Ag^{+}等重金属离子，降低其生物毒性与迁移能力。Rasulov 等[84]证实，盐碱土来源的固氮菌圆褐固氮菌(*Azotobacter chroococcum*) XU1 的生物量及其 EPS 对多种重金属具有显著吸附能力，既实现了高盐环境下重金属废水的有效净化，也为资源回收创造了条件，提供了一种环境友好且可持续的复合污染治理方案。

4 总结与展望

高盐环境微生物作为一类适应极端生境的特殊生命形式，凭借其独特的代谢适应机制，已成为结构新颖、功能多样的天然产物重要来源。本文系统梳理了高盐环境微生物的分类地位与生态分布，重点总结了其初级代谢产物中相容性溶质(如四氢嘧啶、甘氨酸甜菜碱)的化学结构与生物学功能，以及次级代谢产物中生物碱、萜类、甾体、聚酮等结构类型及其抗菌、抗肿瘤、抗氧化、酶抑制等活性，并探讨了构效关系。同时，基于代谢产物的独特性质，分析了其在医药健康、生物材料、环境修复等领域的应用潜力。

尽管近年来该领域取得显著进展，但仍面临两大核心挑战：(1) 绝大多数高盐环境微生物属于“微生物暗物质”，难以通过传统方法培养，限制了物种多样性及其代谢潜力的挖掘；(2) 即便可培养菌株，其生物合成基因簇在常规条件下多呈沉默或低表达状态，导致产物产量低、难以检测。因此，突破培养限制、激活沉默基因簇成为当前研究的重点方向。未来研究应聚焦于以下几个方面：一是借助多组学技术(基因组、转录组、代谢组)系统揭示高盐环境微生物的代谢调控网络，挖掘新型生物合成基因簇；二是发展合成生物学策略，通过异源表达、途径重构等手段激活沉默基因簇，实现目标产物的高效合成与结构优化；三是推动从基础研究到应用转化的协同发展，结合代谢工程与发酵工程优化产物产量，拓展其在医药、农业、环保等领域的实际应用。跨学科技术的深度融合将为高盐环境微生物资源的深度开发与新型生物活性分子的发现提供强劲动力。

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